ANESTHESIA

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BY

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WITH TWO HUNDRED AND EIGHTY-THREE ILLUSTRATIONS IN THE TEXT

NEW YORK AND LONDON

D. APPLETON AND COMPANY

1914

Printed in the United States of America

"Even as a surgeon minding oft to cut
Some careless limb, before in use he puts
His violent engines in the victim's member,
Bringeth his patient in a senseless slumber;
And griefless then, guided by use and art,
To save the whole, saws off the infested part."

—Dubartas, 1592 A. D.

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PREFACE

The administration of anesthetics, along with practically every other phase of medicine and surgery, is undergoing a steady evolution. The development in the application of anesthetics has been most marked within recent years, so that any given anesthetic or method which is considered the best to-day may be entirely replaced by a safer and a better to-morrow. Even to-day there is not a little divergence of opinion as to which is the best method. No longer are the leaders in medicine and surgery satisfied with a form of anesthesia which simply renders the afflicted one insensible to pain during an operation, and which allows the surgeon to work with great freedom and confidence, but they insist further, and rightly, upon maintaining the patient's vitality, reducing the effect of shock as much as possible, and having the patient as comfortable as may be during recovery and convalescence.

"Every hospital, certainly every large hospital, should have as a regular member of its staff an attending anesthetist, as is the case in some, whose authority in his special department should be as complete as is that of the attending physician or surgeon in their fields. This arrangement will be particularly important during the next few years when the older methods of anesthesia—chloroform, ether, cocain, etc.,—will be competing with, and greatly modified by, newer procedures, e. g., nitrous oxid, intratracheal insufflation, spinal anesthesia, intravenous anesthesia, intra-arterial injection of novocain by the methods of Bier and Ramshoff, measures for the prevention and relief of acapnia, the prevention of pain associations, etc." *

The dignity of this special field in medicine can be greatly enhanced and its progress equally advanced by such organizations as the New York and American Societies of Anesthetists, wherein the theories and practice are fully presented and discussed with the liveliest interest and general profit.

* From the Report of the Committee on Anesthesia, American Medical Association, June, 1912.

The main purposes of this book are:

(1) To give in a practical and utilizable form the essentials of the subject of the administration of anesthetics;

(2) To save the busy medical practitioner or student the labor of weeding out from the voluminous literature upon the subject the facts which he must constantly bear in mind in the successful practice of this important branch of medicine;

(3) To emphasize, wherever possible, the thought that "to bring a living being to that borderland in which life in many respects so simulates death should at no time be a fool's occupation"; and

(4) While primarily intended as a work for the active practitioner and student, to suggest many lines for further research.

The authors will be grateful for suggestions, and especially for accounts of unusual experiences met with in practice.

Due consideration has been given to the historical development of anesthesia, but emphasis has been laid upon modern American practice without neglecting European procedures. This has been accomplished by happily securing the coöperation of successful investigators—to whom sincere thanks are here extended, and whose names appear at the heads of those chapters prepared by them—within the various fields of the subject. Ample space has, therefore, been given to methods of administration which are as yet in the experimental stage, although dominant prominence has gone to those methods whose utility has become established.

A list of anesthetics with valuable data and references (Chapter XX) is presented complete, as far as we are aware, for the first time. It is hoped that the contents of this chapter may prove of value not only to the profession of medicine, but to the professions of dentistry, pharmacy, and chemistry as well, for there the investigator may possibly find a drug more nearly ideal for his purposes than any now in general use for obtunding sensation or inducing unconsciousness.

As modern medicine now more generally recognizes the importance of a knowledge of chemistry in all its branches, that phase of the subject has been quite fully developed, not only along the lines of original purity of the drug used, the conditions favorable to its preservation in its highest purity, but its course within the body, resulting either in the destruction of the drug or its elimination from the body.

To some it might have been desirable to indicate from whom certain instruments could be obtained and to specify the quality of drugs supplied by the different manufacturers, but for obvious reasons that could not be. As for the latter, the absolute purity of the drug administered cannot be too strongly emphasized. The standards of purity given in the text are those determined after prolonged and most painstaking investigations. These standards of purity should be insisted upon by the physician. It is quite out of the question to have every sample to be used examined by an expert chemist—and only an expert chemist should pass upon the quality of an anesthetic—but occasional chemical examinations may be made, and, knowing the quality of the drug as supplied on the market, one must then place reliance upon the reputation of the firm supplying the drug. We have found the reputable houses anxious to provide drugs of the highest purity, but unfortunately close chemical supervision does not always obtain, and impure products do get upon the market through carelessness of workmen or failure to provide against deterioration of the drug, even though it leave the manufacturer of a proper grade.

James Tayloe Gwathmey.
Charles Baskerville.

New York City.

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ANESTHESIA

CHAPTER I

THE HISTORY OF ANESTHESIA

INTRODUCTORY REMARKS: Ancient History; Beginning of the Christian Era; Asiatic Sources; Middle Ages; Hypnotism; Real Beginnings of Surgical Anesthesia; Discovery of Ether Anesthesia; The Discovery of Nitrous Oxid for Surgical Anesthesia.

ETHER: Morton; First Public Demonstration; Letheon; Anesthesia in England.

CHLOROFORM: Theological Opposition to the Use of Anesthetics; The Early Use of Chloroform in Midwifery; Some Physicians Believe in Pain; Prejudice Developed against Chloroform; Scientific Administration of Ether and Chloroform; Efforts to Overcome Objections to Chloroform by Use of Substitutes and Improved Inhalers; A.C.E. Mixture; Substitutes; First Vapor Inhaler; Nitrous Oxid More Generally Appreciated; Nitrous Oxid and Oxygen; Discarding Chloroform for Ether; Improved Methods for Administering Ether; Warmed Ether Vapor; Chloroform Condemned; Medication before Anesthesia; The Use of Chloroform Accompanied with Danger; Chloroform and Oxygen; Combinations and Sequences in Anesthetics; Ethyl Chlorid; Importance of Trained Anesthetists.

BIBLIOGRAPHY.

INTRODUCTORY REMARKS

Sacred,[1] profane, and mythological literature abound in incident, fact and fancy, showing that from the earliest times man has sought to assuage grief and pain by some means of dulling consciousness. In these attempts many methods and diverse agents have been employed. The inhalation of fumes from various substances, weird incantations, the external and internal application of drugs and many strange con-

[1] The Bible and Talmud contain references to the ancient practice of inducing sleep by artificial means.

coctions, pressure upon important nerves and blood vessels, the "laying on of hands" or animal magnetism, mesmerism, hypnotism, and the many methods which come within the pale of modern science, as well as pseudo-science, have played their part in the evolution of anesthesia.

It is intended in this section to give a brief review of what is now known as *general,* or *inhalation, anesthesia.* The various other measures for the dulling of consciousness and for the induction of partial or complete insensibility to pain are fully discussed under their respective heads, and will be given only scant attention in this connection.

Ancient History.—During the classic era of Grecian literature, Homer in his "Odyssey"[1] caused Helen of Troy to put some drug into wine to "lull all pain and anger, and bring forgetfulness of every sorrow." It is not known what constituted Helen's *nepenthe,* some believing it to have been mandragora, while others maintain it was opium.

Five hundred years after Homer, Herodotus, the great historian of Greece, tells of a custom among Scythians of inhaling the fumes of a variety of hemp, which produced an exalted mental state, followed by sleep.

The chronicles of ancient Rome furnish similar evidence. For instance, these record the utterances of the renowned mythological oracle of Apollo at Delphi, which were probably nothing more nor less than the exaggerated ravings of the priestess Pythea. Her seemingly inspired sayings are attributed to the inhalation of carbon dioxid,[2] which is supposed to have been generated in the cavern. Having been removed to the altar before the convulsive stage set in, her mumblings were interpreted by the faithful as the voice of Apollo. The famous Grotta del Cane, near Naples, at the present time furnishes an example of conditions which may have been utilized for just such purposes.[3]

Beginning of the Christian Era.—That the use of mandragora was well known at the beginning of the Christian era is absolutely certain, for many references to it are made by the writers of that period. Dioscorides, a Greek physician, who lived about the middle of the first century, and who was for seventeen hundred years an authority on the science of healing, makes what is probably the earliest allusion to its use.[4] Galen,[5] another Greek and a contemporary of Dioscorides, makes mention of the power of mandragora to paralyze sensation and motion. Lucian, in speaking of Demosthenes, says he aroused his fellow citizens,

[1] Homer's "Odyssey"; 4, 220.

[2] Memphis marble and vinegar were used as a local anesthetic by the Romans!

[3] From the sides of the cavern, steam and carbon dioxid emanate in sufficient quantities to form a stratum in which dogs are first convulsed and then asphyxiated, while persons who are in a standing position above the stratum are unaffected.

[4] *De Med. Mat.,* Lib. 4, 76. The root of "atropa mandragora" was boiled in wine and administered prior to surgical operations.

[5] *Ibid.,* Lib. 7, 207.

who were as if put to sleep by mandragora. Roman historians, among them Pliny,[1] also described the use of mandragora from earliest times. The people of their country employed it extensively to relieve the suffering of victims of crucifixion.

Asiatic Sources.—Preparations of different drugs were made by the Jews and Chinese, and given to criminals to produce such a mental state that they would confess their crimes, or to make less agonizing the horrible tortures inflicted.

In view of the fact that it is indigenous to China, undoubtedly the Chinese were the first to use Indian hemp as a means of dulling the consciousness of pain. The Egyptians used this herb under the name of "*hashish*." The fumes of this, when inhaled, induced intoxication and mental exaltation.

A Chinese practitioner of the third century, Hoa-tho, gave to a patient a preparation of hemp, whereby he shortly became insensible "as if he had been drunk or deprived of life." We are told that after a certain number of days the patient found himself "reëstablished" without having experienced the slightest pain during the operation.

The ancients early noted that volatile substances acted more promptly and effectually when inhaled than other substances taken by the mouth, and inhalation was employed by the Greeks, Romans, Arabians and Chinese.

Middle Ages.—In the thirteenth century, an oil which put patients to sleep on occasions of painful operations was prepared and successfully used by Hugo de Lucca. It consisted "of opium, of the juice of the unripe mulberry, of hyoscyamus, of the juice of hemlock, of the juice of the leaves of mandragora, of the juice of the leaves of wood ivy, of lettuce seeds, of dock seeds, and water hemlock boiled with a sponge, which, for use, was soaked in hot water and applied to the nostril." To awaken the patient, another sponge, soaked in vinegar, was applied to the nose.

As late as 1534 this "spongia somnifera" was still in use. Shortly after this, Paré referred to it as a practice "used formerly by operators." The uncertain action of this concoction arising from necessary differences in preparation, from the method of application of the vapor, and from the ignorance of the strength of the various ingredients, led to its temporary abandonment. It is difficult to imagine why the preparation of anesthetics was neglected, when medicine was making the rapid progress which marked its development during the sixteenth century.

Hewitt[2] states: "In 1589 Giambattista Porta, a surgeon who practiced in Naples, used an essence made from hyoscyamus, solanum, poppy, and belladonna, enclosed in a leaden vessel, and, the lid being opened, the patient would draw in by breathing the most subtle strength of the

[1] *De Med. Mat.*, Lib. 35, 94.

[2] Hewitt, Frederick D.: "Anæsthetics," 4th ed., 3.

vapor, so that thereby he would be buried in a most profound sleep, nor be aware of what had been done to him."

Shakespeare makes several references to the soporific effects of various drugs, showing that a knowledge of this quality obtained in his day. Early in the seventeenth century, he makes Cornelius, the court physician, prescribe a drug which

> "Will stupefy and dull the sense awhile; but there is
> No danger in what show of death it makes,
> More than the locking up the spirits a time,
> To be more fresh, reviving."

It is thus seen that ancient, medieval and modern history furnish numerous examples of the use of drugs and other media which brought about partial or complete unconsciousness. Moreover, it is well established that the Assyrians accomplished the same end by the compression of blood vessels before circumcision; and in the early part of the seventeenth century this custom was revived by Valverdi, who compressed the nerves and blood vessels of the parts to be operated upon.

Hypnotism.—The foregoing résumé of historical references to methods employed in former times needs but the addition of a brief mention of the hypnotic effects induced by weird incantations, as practiced by the Egyptians, Persians, Indians, and others. This leads up to the time of Greatrakes, the noted "Irish stroker," who produced sleep as a result of his magnetic touch, or "the laying on of hands." He was probably the most noted advocate of this method prior to Mesmer, the Swiss physician, who, about the middle of the eighteenth century, investigated the phenomena of animal magnetism along scientific lines, applying his researches to curative ends and enunciating a doctrine which became known as "mesmerism," after the founder.

Real Beginnings of Surgical Anesthesia.—It was at the close of the eighteenth century that modern surgical anesthesia was foreshadowed, with the discovery of hydrogen in 1766, nitrogen in 1772, and oxygen and nitrous oxid in 1774. "Pneumatic chemistry," as it were, opened up a field of experimentation which made possible surgical operations under conditions which Humphrey Davy described as "uneasiness being swallowed for a few minutes by pleasure."

Soon after the discovery of these gases, attempts were made to put them to practical use. In 1785 Pierson, of Birmingham, England, used ether inhalation for asthma, and in 1789 the Medical Pneumatic Institute was organized under Dr. Beddoes, where huge reservoirs of gases were installed for the treatment of phthisis and other diseases by inhalation. This Institute, which was superintended by Humphrey Davy, while not successful in itself, was important in that it led to Davy's experiments with nitrous oxid. By 1799 and 1800 Davy had become sufficiently well acquainted with this gas to use it for the alleviation of headache and also for the extraction of one of his own wisdom teeth. This latter event led him to make the historic prediction, "Since nitrous oxid seems capable of destroying physical pain, it may be used in surgical operations, where there is no great effusion of blood." The value of this suggestion was not recognized for nearly half a century.

Warren, of Boston, used "sulphuric ether" in 1805 on a patient suffering with phthisis, and in 1806 it was used in attacks of asthma. Faraday seems to have been the first to recognize the value of "sulphuric ether" as an anesthetic. In 1818, there appeared a paragraph attributed to Faraday in the *Quarterly Journal of Science and Arts,* in which it was pointed out that "when the vapor of ether is mixed with common air and inhaled, it produces effects very similar to those occasioned by nitrous oxid."

An incident occurred on November 6, 1821, which, had it been correctly interpreted, might have led to an earlier discovery of general anesthesia. On that day, Stockman, of Utica, gave an exhibition in Rome, N. Y., of the effects of nitrous oxid. After the demonstration, the lecturer, on adjourning to a back room, found there a young man completely anesthetized with his mouth to the faucet of the gas tank. He had been stealing the gas for its exhilarating effect and had been overcome by it.

The first successful experiments upon lower animals, for the purpose of rendering them insensible to pain by means of the inhalation of gases, were made by Henry Hill Hickman [1] between the years of 1820 and 1828. Hickman was twenty years of age when he became a member of the Royal College of Surgeons and began his career as a country practitioner in the little town of Ludlow, Shropshire, England.

"Impressed by the agonizing sufferings of those on whom he was called to operate, he resolved to seek some method of alleviating their pain by rendering them unconscious before the operation. With this object, he commenced a series of experiments on animals, first, by producing semi-asphyxiation by the exclusion of atmospheric air; then by causing them to inhale small quantities of carbon dioxid, and later nitrous oxid gas. After rendering the animals unconscious, he excised the ears, amputated their legs, made incisions, then dressed the wounds, noted the time they took to heal, and the period of their complete recovery. He carried on these experiments for some time, and at last met with considerable success. This convinced him that, could he but carry out his experiments on the human subject, his methods would become of the greatest value to mankind in making painless the performance of major surgical operations."

[1] Henry Hill Hickman: "A Forgotten Pioneer of Anesthesia," *Brit. Med. J.*, April 13, 1912, 843.

His notes on some of these interesting experiments are still extant in his own handwriting, of which the following is an extract:

"*Experiment 1, March 20th.*—I took a puppy a month old and placed it on a piece of wood surrounded by water, over which I put a glass cover so as to prevent the access of atmospheric air; in ten minutes he showed great marks of uneasiness, in twelve minutes respiration became difficult, and in seventeen minutes ceased altogether; at eighteen minutes I took off one of the ears, which was not followed by hemorrhage; respiration soon returned, and the animal did not appear to be the least sensible of pain; in three days the ear was perfectly healed.

Fig. 1.—Henry Hill Hickman.

"*Experiment 2.*—Four days after, the same puppy was exposed to a decomposition of the carbonate of lime by sulphuric acid. In one minute respiration ceased; I cut off the other ear, which was followed by very trifling hemorrhage, and, as before, the puppy did not appear to suffer any pain; in four days the wound healed. The day after the operation he seemed to require an additional quantity of food, which induced me to weigh him, and I found he gained 9 oz., 1 drachm and 24 grains in nine days."

While Hickman was successful, he was unable to demonstrate "the results of his experiments before his professional brethren, and everywhere he was met with the greatest scepticism and his system was generally derided and condemned as dangerous and useless. . . . Disheartened by his failure to secure a hearing from the profession in his own country, he at length resolved to lay the matter before the Royal Academy of Medicine in Paris, and drew up a memorial to King Charles X. praying for permission to perform his experiments before the leading medical men of that city." The king sent the letter to the Royal Academy of Medicine and notified Hickman. The Academy appointed Gerardin [1] to investigate the matter and report to them. He reported as follows on October 21, 1828:

"Painless Operations.—M. Gerardin reported on a letter written to

[1] Gerardin: *Archives générales,* Paris, 18, 453.

His Majesty Charles X. by Mr. Hickman, a London surgeon, in which that gentleman asserted he had discovered a means of performing the most troublesome and dangerous operations without pain. The method consisted in producing temporary insensibility by the methodical introduction of certain vapors into the lungs. Mr. Hickman had made numerous experiments on animals, and was desirous of obtaining the coöperation of the leading physicians and surgeons of Paris, in order to make the same experiments on the human subject."

French surgeons proved to be no more liberal in their attitude than had been their British colleagues. When Gerardin's report was presented only one member (Larry) championed Hickman's cause, offering himself as a subject for experimentation. The other members sneered at the idea proposed by Hickman, and so the young surgeon, disappointed and hopeless, returned to England, where he died a few months later (1829) at the age of twenty-nine.

"In this tragic manner the curtain fell upon the life of Henry Hill Hickman, who practically sacrificed his career and gave his life in his attempts to gain recognition for his discovery of a method of producing anesthesia by inhalation and rendering patients unconscious to pain during severe surgical operations."

While the suggestion of painless surgery seemed to be in the air, no one laid definite hold upon it. In 1830, two deaths from nitrous oxid attracted much attention. Each was caused by the breaking of a jar containing the gas in the room where the victim was sleeping.

Discovery of Ether Anesthesia.—The efforts of the past culminated in the discovery of inhalation anesthesia, with ethyl ether as the agent, in 1842. The public had gradually become familiar with the inhaling of vapors. It is reported in the *American Journal of Science* for January, 1832, that Ives, of New Haven, used chloroform (see page 281) in medicine. Humphrey's book on "Medicated Vapors" appeared in 1831. At about this time scientific lecturers were in the habit of demonstrating the intoxicating properties of ether on young men; and many young people, especially medical students, held wild frolics under its influence, after inhaling it to the point of intoxication. It so happened that these lectures and ether parties were directly responsible for the discovery of surgical anesthesia.

In 1839, some young people held a quilting party near Athens, Ga., after which they finished the evening by inhaling ether. At the height of the frolic, a negro boy appeared at the door and was invited to partake of the ether, but he refused. Some of the boys dragged him in and forced a handkerchief, covered with ether, to his mouth and nose. After a long struggle he became quiet and the boys desisted. Instead of getting up, the negro lay as if asleep and, much to the terror of the culprits, did not awaken until medical attention was given an hour later.

The inhalation of ether and also nitrous oxid to the stage of excitement was a common occurrence in different parts of the country at this time.

It remained for Crawford W. Long,[1] of Georgia, to intelligently

[1] Crawford Williamson Long was born in Daniellsville, Madison County, Georgia, November 1, 1815. His family was prominent socially and in public affairs. Long graduated second in his class from Franklin College at the age of nineteen, and from the medical department of the University of Pennsylvania in 1839, after which time he spent one year ''walking'' the hospitals of New York City. As a student in the University of Pennsylvania he was under the immediate tutorship of George B. Wood. Da Costa (''Crawford W. Long,'' ''*Old Penn Weekly Review,* April 6, 1912) states: ''Wood's condemnation of the premature reporting of cases and drug actions may have decided Long a few years later to delay in publishing the report of the action of ether. He insisted that observers must never be content with a single experiment.'' Woods Hutchinson stated at the unveiling of the monument to Long at Jefferson, Georgia, that ''His discovery was no accident. His real genius and the proof of his greatness lay in his wisdom to see the possibilities. His courage to attempt experiments, the confidence in his own opinions, and the heartfelt love and sympathy for his suffering patients led him to employ the anesthetic he had discovered not once but many times. He was great in his courage, braving the possibility of the fearful consequences which would have followed failure in those early days of experiment. In many matters he was ahead of his day and generation. He was one of the first to hold that tuberculosis is curable, and that fresh air and diet will effect cures in this dread malady. He added to the sum of human immunity from horror and suffering long before Sir J. Y. Simpson used chloroform for the purpose.''

Jackson, in a letter to the *Bost. Med. and Surg. J.,* April 11, 1861, states, among other things, that, ''I then called on Profs. Joseph and John Le Conte, then of the University of Georgia, at Athens, and inquired if they knew Dr. Long, and what his character was for truth and veracity. They both assured me that they knew him well, and that no one who knew him in that town would doubt his word, and that he was an honorable man in all respects. . . . He is a very modest, retiring man and not disposed to bring his claims before any but a medical or scientific tribunal.''

The University of Pennsylvania, on March 30, 1912, unveiled a medallion to Long. The state of Georgia has sent his name to Washington, D. C., as one of her two most celebrated sons. Hewitt, Foy, and Buxton, of England, as well as Young, of Johns Hopkins Hospital, all give the credit to Long as the discoverer of surgical anesthesia.

J. F. Groves, in a letter to Hugh H. Young, of Johns Hopkins Hospital, under date of January 15, 1897, in giving an account of an operation, states the following: ''The patient was placed in a recumbent position on a bed, with the hand to be operated on in front for convenience of the surgeon. Dr. Long poured ether on a towel, and held it to the patient's nose and mouth, too, to get the benefit of inhalation from both sources. Dr. Long determined when the patient was sufficiently etherized to begin the operation by pinching or pricking him with a pin. Believing that no harm would come of its use for a considerable length of time, he profoundly anesthetized the patient, then gave me make use of facts which were common knowledge to all. Long and his pupils indulged frequently in "ether frolics," during which he was badly bruised, yet he noticed, upon recovery, that he had not been conscious of pain. Frequent observations of this fact, in connection with himself and his students, led Long to conceive the idea of using ether to prevent the pain of surgical operations.

When twenty-six years of age, and in the first year of his practice, Long determined to try the experiment with ether as soon as possible, and so, on March 30, 1842, he administered ether to Mr. James Venable and removed a small tumor from the neck. At the close of the operation the patient assured Long that he had not experienced even the slightest degree of pain.

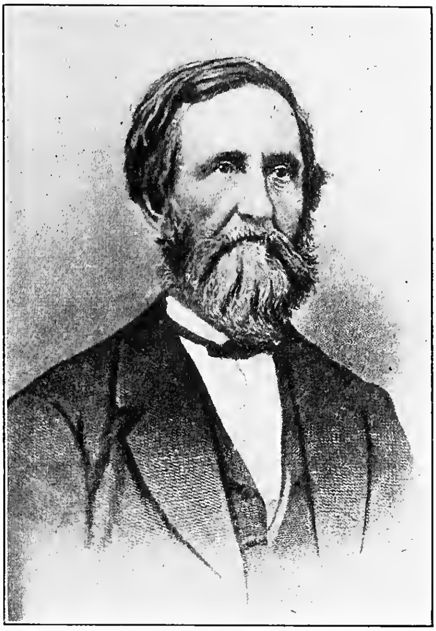


FIG. 2.—CRAWFORD W. LONG.

This experiment was so highly successful that Long continued to administer ether in surgical cases, recording about eight such cases between 1842 and 1845. But since his was the narrow sphere of a local country doctor, his surgical cases were few and his fame did not get beyond the restricted world in which he lived. He made no secret of his discovery, but did not advertise the fact until others had laid claim to the honor.[1]

the towel, and I kept up the influence by holding it still to the patient's nose. The patient was entirely unconscious—no struggling—patient passive in the hands of the operator."

[1] The original bill for services of Long to Mr. Venable is still in existence, and is as follows:

James Venable
to Dr. C. W. Long, Dr.

1842.

Jan. 28	Sulphuric Ether	$ .25
Mch. 30	Sulphuric Ether and Exsecting tumor	2.00
May 13	Sul. Ether	.25
June 6	Exsecting tumor	2.00
		$4.50

Long not only used ether upon patients, but behind closed doors he administered it to a medical student, and had the student administer the anesthetic to him, in order to discover the physiological action of the drug. Owing to the prejudice and ignorance of the populace, Long was prevented from using ether in as many cases as he might have. In a very scientific spirit he administered ether to a negro boy having two fingers to be amputated, removing one finger under the influence of ether and the second without ether. He did this to prove that insensibility to pain was due to the agent used.

"Dr. Long is necessarily deprived of the larger honor which would have been his due had he not delayed years after the universal acceptance of surgical anesthesia. It is also to be regretted that his published details of the mode of administering the ether and the depth of the anesthesia are so meager and unsatisfactory. While the accepted rule that scientific discovery dates from publication is a wise one, we need not in this instance withhold from Dr. Long the credit of independent and prior experiment and discovery, but we cannot assign to him any influence upon the historical development of our knowledge of surgical anesthesia, or any share in the introduction to the world at large of the blessings of this matchless discovery." [1]

In regard to this point, DaCosta [2] remarks: "Long has been criticised for not publishing his discovery at once. Jenner waited twenty years to publish his and after twenty years had only made twenty-three observations. Suppose someone had published about vaccination after Jenner had worked nineteen years, would Jenner any the less have been the discoverer?"

But being far removed from the turmoil and strife that environed the lives of the then three other claimants, Long was not embittered as were the others. He continued to practice medicine in Jackson County, Georgia, and died June 16, 1878, in the sixty-second year of his age.

The Discovery of Nitrous Oxid for Surgical Anesthesia.—In 1844, two years and eight months after Long anesthetized the first patient with ether, Horace Wells,[3] a dentist of Hartford, Conn., attended a lecture on "Laughing Gas" by G. Q. Colton, a chemist. He noticed (as had Long with ether) that a young man under the influence of nitrous oxid bruised himself very severely, yet was apparently unconscious of pain. Wells had long been studying the question of the painless extraction of teeth, and had previously reasoned that, if excitement from ordinary causes could make one indifferent to pain, the same would probably be true of artificial excitement.

[1] Welch, William H.: "A Consideration of the Introduction of Surgical Anesthesia," 9.

[2] *Loc. cit.*

[3] Horace Wells was born in Hartford, Windsor Co., Vt., Jan. 21, 1815.

This incident impressed upon him the belief that the administration of nitrous oxid would bring about the result for which he had been looking. He planned to test his conclusions on himself. The next day, December 11, 1844, Colton was called in to administer the gas, and, while Wells was under its influence, Riggs extracted one of his teeth. On recovering consciousness, Wells was so enthusiastic over the success of the operation that he made plans for its immediate use, and thereafter daily extracted teeth under its influence. Early in 1845, he went to Boston in order to lay the matter before the medical profession. He gave a public demonstration before the Harvard Medical College, but because he did not understand the proper administration of the gas—probably because he did not use a sufficient volume — the demonstration failed. Wells was a sensitive man, and this public failure overwhelmed him and he felt himself disgraced. He continued to administer gas in private practice for some time, but eventually gave up dentistry altogether. In 1847 his reason gave way and, early in 1848, he died by his own hand.

Fig. 3.—Horace Wells.

ETHER

On witnessing one of Wells' operations, H. O. Marcy remarked that as a student he had found that nitrous oxid and the vapor of "sulphuric ether," when inhaled, produced exactly the same effects. Wells had tried ether, but, owing to the choking sensations produced, resolved to adhere to nitrous oxid.

Morton.—It was left, however, to William T. G. Morton, a former pupil of Wells, to place the use of ether as an anesthetic upon a sound basis. His discovery was entirely independent of that of Long, who had preceded him four years.[1]

[1] "William Thomas Greene Morton (Patton, J. M.: "Anesthesia and Anesthetics," 17) was born in Massachusetts, studied dentistry in Baltimore, and

First Public Demonstration.—The first public demonstration of surgery without pain was given in the Massachusetts General Hospital,

was a successful practitioner in Boston. He experimented with drugs and with hypnotism in connection with the painless extraction of teeth, and, as we have seen, was associated with Wells in his investigations of nitrous oxid. After the public failure of the experiment of Wells, he abandoned gas and tried 'chloric ether' with unsatisfactory results. At the suggestion of his preceptor, Charles Jackson (Morton being at that time a student of medicine), a physician of Boston, but best known as a geologist and chemist, he experimented with sulphuric ether, beginning his experiments on animals.'' In connection with his experiments upon animals Morton's wife writes: ''Every spare hour he could get was spent in experiment. He used to make experiments nearly every day on 'Nig,' a black water spaniel, a good-sized dog that had belonged to his father. His clothes seemed always saturated with the smell of ether. One day he came running into the house in great distress (for he was always tender-hearted), leading the dog, which walked rather queerly, and said, 'Poor Nig, I have had him asleep a long time; I was afraid I had killed him.' '' Morton stated to his wife, ''The time will come, my dear, when I will banish pain from the world.'' ''At this time he used to bottle up all sorts of queer bugs and insects until the house was full of crawling things. He would administer ether to all of these little creatures and especially to the big green worms he found on grapevines.'' His friends laughed at these experiments, but Morton replied, ''I shall succeed. There must be some way of deadening pain.'' It was after this that he began experimenting upon himself.

Fig. 4.—William T. G. Morton.

''His success in this direction encouraged him to make a personal experiment, and, in September, 1846, he inhaled ether from a handkerchief while sitting in his operating chair. He was unconscious for several minutes, and, on regaining consciousness, he was so elated by his success that he decided to again inhale the drug and submit to an extraction while under its influence. At this moment the door bell rang and he admitted a man named Eben Frost, whose face was bandaged and who was in that state of mingled hope and consternation so familiar to all dental surgeons. He asked if it were not possible to mesmerize him, and readily consented to inhale ether when assured that it was superior to mesmerism. To the joy of the operator and the astonishment of the patient, the attempt was perfectly successful.'' Elizabeth Morton: ''The Discovery of Anesthesia,'' *McClure's Magazine,* Sept., 1896.

in the presence of the surgical and medical staff in the crowded amphitheater, on October 16, 1846. "Sulphuric ether" was used on this occasion, though Warren used "chloric ether"[1] thereafter, and preferred it.

"It was a trying moment to this medical student when he determined to exhibit his discovery of practical ether anesthesia before his classmates, professors, and the public. But so convinced was he, by reason of his experience gained in private practice, of success, that he was will-

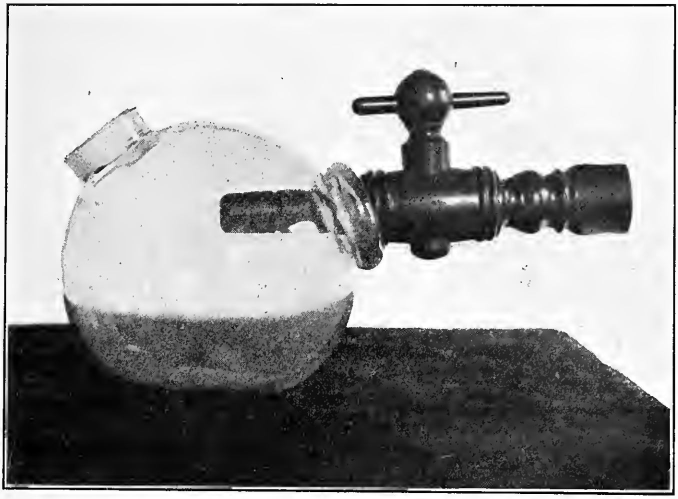


Fig. 5.—The Original Morton Inhaler.

ing to face this ordeal. Morton came into the amphitheater late, delayed by waiting for the completion of a new inhaler. Just a few minutes before, Dr. Warren had remarked, 'As Dr. Morton has not arrived, I presume he is otherwise engaged,' apparently conveying the idea that Dr. Morton was not likely to appear. As he was about to proceed with his operation Morton entered. Amidst that sea of faces he saw not one which was sympathizing. Blank incredulity, or, at the best, curiosity, alone was to be seen. Warren, turning to him, remarked: 'Well, sir, your patient is ready.' Adjusting his apparatus, Morton calmly administered the anesthetic and, turning to Dr. Warren, said: 'Dr. Warren, *your* patient is ready.' The silence of the tomb reigned in the large amphitheater while Dr. Warren made his first incision through the skin and dissected out a large tumor, while the patient made no sign nor moved a muscle of his body. When the operation was completed, Dr. Warren turned to the audience and said slowly and emphatically: 'Gen-

[1] See Baskerville and Hamor: *J. Ind. Eng. Chem.*, *4*, No. 3.

tlemen, *this* is no humbug,' and Bigelow remarked, 'I have seen something to-day that will go around the world.'"[1]

Operations under ether followed quickly, and from that time its use as an anesthetic spread rapidly throughout the world.

Fig. 6.—The Original Morton Inhaler.

It is almost inconceivable to those who now witness operations daily under anesthesia to appreciate what it really means to the patient and to those who are compelled to be present. No one has brought this out more forcibly than Hayden,[2] in an article in which he gives a description of an operation previous

[1] In July, 1868, Morton left his home for New York to reply to an article that had recently appeared in one of the monthlies advocating Jackson's claim to be the discoverer of ether anesthesia. His wife states that this article "agitated him to an extent she had never seen before." It was extremely hot, and after reaching New York he telegraphed his wife that he was ill and for her to come. Under the treatment of the distinguished Sayre, Morton rapidly improved and he attempted to drive his wife to a hotel on Washington Heights as a change from the hot city. On the way through Central Park he complained of feeling sleepy, but refused to give his wife the reins or to turn back. Suddenly he sprang from the carriage and stood on the ground, apparently in great distress. He quickly lost consciousness, and his wife called upon a policeman and Swann, a druggist, who assisted in placing Morton upon the grass, but he was past hope of recovery. He was taken at once to St. Luke's Hospital, but was dead by the time he reached there. At the time of his death he was forty-eight years of age. He was buried in Mount Auburn Cemetery in Boston in the presence of many noted physicians. Over his tomb an inscription written by Jacob Bigelow is placed, which states:

"William T. G. Morton, Inventor and Revealer of anesthetic inhalation, by whom pain in surgery was averted and annulled; before whom, in all times, surgery was agony; since whom, science has control of pain."

[2] Hayden, William R.: *Inter. J. Surg.*, 1896.

to the introduction of anesthesia, and of operations as they are conducted at this time.

Then

"With a meek, imploring look, and the startled air of a fawn, as her modest gaze meets the bold eyes fixed upon her, she is brought into the amphitheater crowded with men, anxious to see the shedding of her blood, and laid upon the table. With a knowledge and merciful regard

Fig. 7.—One of the Earliest Operations under Ether at the Massachusetts General Hospital.

as to the intensity of the agony which she is to suffer, opiates and stimulants have been freely given her, which, perhaps, at this last stage, are again repeated. She is cheered by kind words and the information that it will soon be over, and she freed forever from what now afflicts her; she is enjoined to be calm, and to keep quiet and still, and, with assistance at hand to hold her struggling form, the operation is commenced.

"But of what avail are all her attempts at fortitude? At the first clear, crisp cut of the scalpel, agonizing screams burst from her, and, with convulsive struggles, she endeavors to leap from the table. But force is nigh. Strong men throw themselves upon her and pinion her limbs. Shrieks upon shrieks make their horrible way into the stillness of the room, until the heart of the boldest sinks in his bosom, like a lump of lead.

"At length it is finished, and, prostrate with pain, weak from her exertions, and bruised by the violence used, she is borne from the amphitheater to her bed in the wards, to recover from the shock by slow degrees."

Now

"How would the same case be now? With a sweet, calm smile playing around her mouth,—an evidence of pleasant dreams,—her eyes fast closed as in a gentle sleep; her body extended languidly and listlessly as in the repose of childhood, surrounded by no ill-favored men whose powerful aid will be needed; with no crowd of medical men to guard against unforeseen accidents. The surgeon, and his two assistants to pass the necessary implements, or to assist in stanching the blood, are all who are required. At his leisure—not hurried by the demands of pain to complete as soon as possible—he can coolly prosecute his work, varying it to suit any exigency of the occasion, and ready to profit by any favorable contingency which its course may present.

"When finished, and all is in that proper condition which will demand no fresh interference for some time, the patient is awakened from her slumber, and receives the glad information that it is all over, and she is to be tortured no more. The one grateful look which answers this news can have no value placed upon it. Alone, it is worth a lifetime of exertion and trouble."

The formal announcement to the medical profession of this discovery was made by H. J. Bigelow [1] in a paper read before the Academy of Arts and Sciences, on November 3rd, and before the Boston Society of Medical Improvement, on November 9th, and published in the *Boston Medical and Surgical Journal,* November 18, 1846.[2]

Letheon.—On October 27, 1846, Morton and Jackson sought to patent their anesthetic under the name of "Letheon." From its odor it was soon recognized as "sulphuric ether." [3] Not long afterwards Jack-

[1] Bigelow (*Boston Med. and Surg. J.*, Nov. 18, 1846) called attention to the experiments which he conducted for the purpose of ascertaining the nature of "Letheon." His first experiment was with sulphuric ether, the odor of which was easily detected in Morton's preparation.

[2] Patton, Joseph M.: "Anesthesia and Anesthetics," 18.

[3] J. F. B. Flagg, M.D., D.D.S., one-time Professor of Anatomy and Physiology in the Philadelphia College of Dentistry, "was particularly prominent as having announced to the dental and medical world that the so-called 'Letheon' of Mr. Morton, of Boston, was simply washed sulphuric ether, thus securing to them an unpatentable material." *Med. and Surg. Reporter,* Phil., Dec. 7, 1872.

Flagg (Flagg, J. F. B.: "Ether and Chloroform," Phila., 1851), in reviewing briefly the history of the inhalation of ether, says: "The surgeons of Massachusetts General Hospital, together with a few initiated, become astonishingly fervent in their praises of an 'Invention,' which required the combined efforts of scientific attainments and mechanical skill to develop. Classon resigned his interest in the "invention" and attempted to show that he alone was the discoverer of anesthesia by ether. While he was writing his contentions to the French Institute, Horace Wells went in person to claim the honor of being the real discoverer of anesthesia, and thus a three-sided controversy was begun.

Fig. 8.—Charles T. Jackson.

"Partly with a view of keeping his discovery out of the hands of persons who might use it unwisely, and acting upon the advice of Rufus Choate and Caleb Cushing, lawyers of national reputation, Dr. Morton patented his application of sulphuric ether." [1]

While Morton probably had the right to patent his discovery, the fact that he did so was most regrettable, for the patent right caused much dissatisfaction and adverse comment. Many refused to accept it on the grounds of quackery. One year after its discovery, 1847, one of the largest hospitals in North America had not tried it at all. When Europe confirmed the efficacy of ether, the opposition subsided.

sical erudition came to their aid, and, for a season, good, old 'sulphuric ether' was made to succumb to the name of 'letheon.'

"A circular is broadly cast through the length and breadth of the country, announcing that a *compound* has been discovered, which, by breathing into the lungs, induces so deep a slumber as to enable us to perform the most painful surgical operations with entire unconsciousness on the part of the patient. In connection with this announcement are the names of Dr. Jackson and Dr. Morton, as its *combined* (?) discoverers.

"A patent is sought, and, under the protection of a caveat, agents are appointed to traverse the country, selling to all, *who will buy,* the right to use the *compound.* Thus qualifying everybody and anybody in the use of this powerful agent that would pay the sum of

"In cities over 150,000 inhabitants, $200 for seven years.

"In cities over 50,000 and less than 150,000, $150 for seven years.

"And so on, down to

"In cities under 5,000, $37 for seven years."

[1] Morton, Mrs. Elizabeth Whitman: "The Discovery of Anesthesia," *McClure's Magazine,* Sept., 1896.

In 1849 Morton petitioned Congress for a reward for his discovery. He was at once opposed by Jackson and the friends of Wells, who was then dead. The celebrated ether controversy thus begun occupied the attention of Congress for many years, and was characterized by the greatest animosity between these former bosom friends and companions.

Jackson's name is most closely associated with his claim to priority in the discovery of the anesthetic properties of ether, which was the subject of a long controversy, that was very painful to him. His claim was supported by the testimony of Francis Alger, J. B. S. Jackson, Martin Gray, and T. T. Bouve, to whose eulogy before the Boston Society of Natural History we are indebted for most of the facts given herewith. These gentlemen were his chosen friends, and were for a long time closely associated with him. J. B. S. Jackson was one of the signers of a remonstrance addressed to Congress against its making a grant of money to W. G. Morton, Jackson's rival in the claim of discovery, based upon the ground that the signers believed that the reward, so far as the question of discovery was concerned, ought to go to Jackson. Martin Gray published a pamphlet under his own name, maintaining that Jackson was the sole discoverer of anesthesia, and that Morton could only be considered to have performed a secondary part by proving that the administration of ether is safe in surgical operations. Bouve, who was for a considerable time a student in Jackson's laboratory, and afterward met him frequently in social intercourse, accorded to him the honor of having been the discoverer of the anesthetic properties of ether, but "never thought him entitled to the credit of its introduction into use, or even to that of having thoroughly verified what he claimed to be true respecting the safety of administering it. He had experimented upon himself, and had afterward demonstrated respecting it, even going so far as to recommend its use by others, and this constituted discovery; but he did not prove to others what he was himself convinced of, and allowed precious time to pass—yes, much time—without making any application of the discovery. Indeed, had it not been that Mr. Morton sought from him means to prevent pain when extracting teeth, it is doubtful if the world would have had the advantage of the discovery for years, if ever. The truth is, Dr. Jackson was a great genius and had remarkable intuitive perceptions of scientific truths, but, from some peculiarities hard to comprehend, he often contented himself with enunciating what he recognized as fact, without striving to substantiate it. He himself admitted his shortcomings in this respect. When Dr. Gray had written his essay upon the discovery of ether, claiming for Dr. Jackson all the merits of its introduction, I objected to his view of the matter, and took the ground that the world was indebted to both Jackson and Morton for the great boon; to one as the scientific discoverer and suggester of its use in surgical operations, to the other for his application of it and its practical introduction.

"Dr. Jackson, learning of this, upon meeting me remarked that I was thought not to be friendly to him in the matter. I then said: 'Doctor, you have known for a long period what Mr. Morton is now demonstrating to be true, but have allowed it to remain a dormant fact in your mind. If he had not sought information from you, might it not have remained so for some years longer?' He answered that possibly it might. I think it may fairly be said that without both Jackson and Morton the world might have been none the happier for what either would have done; one supplemented the other. To them together belongs the great honor of having served humanity beyond what language can express." [1]

"For five years Long refused to take part in the conflict, but finally, in 1854, persuaded by his friends that in that way alone could he obtain recognition of his claims, he wrote to Senator Dawson giving an account of his work. It seems that Dawson was a friend of Jackson, for he wrote to him of this new claimant and requested him to investigate his case. This Jackson did, calling upon Long at his home in Athens on March 8, 1854.

"Dr. Jackson finally acknowledged the justice of Dr. Long's claims and wrote to Senator Dawson to that effect.

"On April 15, 1854, the appropriation bill [2] was up before the Senate for its final reading. The friends of Wells and Morton, relying on the volumes of manuscript they had presented, were confidently awaiting the result, when Senator Dawson arose and said that he had a letter from Jackson which acknowledged that a Dr. Long in Georgia had undoubtedly used ether before any of the claimants for the appropriation.

"Coming as it did from so prominent a contestant, this announcement fell like a thunderbolt on the rival claimants, and from that time they seem to have lost all hope of gaining the reward, and passively allowed the bill to die.

"Desirous only of preventing another from being recognized by Congress as the discoverer, and not wishing any pecuniary reward himself, Long never pushed the matter farther, and his documents of proof were never even brought up before Congress." [3]

Anesthesia in England.—Bigelow took some ether with him to London and the first operation (extraction of a tooth) was performed on December 19, 1846, at the home of Bott, of Gower Street.[4] Two days

[1] *Pop. Sci. Mon.*, 1881, *19*, 405.

[2] The bill proposed to appropriate $100,000 as a recompense to the real discoverer.

[3] Young, Hugh H.: "Long, the Discoverer of Anesthesia," read before the Johns Hopkins Hospital Historical Society, Nov. 8, 1896.

[4] A very interesting account of the *first major operation* under ether in Europe is given by Dr. F. W. Cock in the *University College Hospital Magazine,*

later, ether was administered to patients at the University College Hospital by Squires, Liston operating. In 1847, J. Y. Simpson, a Scottish physician, first used ether in midwifery, and, finding that the pains of labor might be wholly abolished without interfering with uterine contractions, adopted it in his obstetric practice.

CHLOROFORM

On March 8, 1847, Flourens pointed out the anesthetic qualities of chloroform and ethyl chlorid, but his observations did not attract general attention. During the same year Simpson,[1] who had not been entirely satisfied with ether on account of its irritating qualities, inconvenience of administration and odor, consulted Waldie, a chemist of Liverpool. The latter suggested the use of chloroform, of which "chloric ether" was an alcoholic solution. The vapor of "chloric ether" had been previously used as an anesthetic with little success, but when Simpson had obtained the chloroform from Edinburgh and experimented with it, on November 4, 1847, he was more than satisfied with its anesthetic qualities. Thereafter he tried it in obstetric practice with success.[2]

as follows: "Dr. Bott, a general practitioner of Gower Street, W. C., informed Robert Liston, the surgeon of University College Hospital, or rather North London Hospital, as it was then called, that he had used ether successfully on a dental case in his own house. Liston sought the aid of Peter Squire, the well known chemist of Oxford Street, in order to fashion an apparatus for administering ether, and the inhaler was first tried on his nephew, William Squire. The latter, profiting by the experience on himself, gave the anesthetic to Liston's patient. The patient was a man of thirty-six years suffering from disorganized knee-joint, and it was decided to amputate. The mouthpiece was applied by Squire and the patient soon sank into insensibility. William Cadge, Liston's junior, compressed the femoral artery, and Ransome, the house surgeon, held the limb. Liston rapidly completed the operation in twenty-five seconds, according to Palmer, the dresser. The inhalation had been stopped as the operation was begun. On coming round, the patient tried to lift himself, and asked when the operation was going to begin. On being shown the stump he fell back and wept. Liston acknowledged the success of the new anesthetic by the remark, 'The Yankee dodge, gentlemen, beats mesmerism hollow.' This was a sarcastic hit at Dr. Elliotson, a physician of the same hospital, who practiced the occult art in connection with medicine. The notes of this case are still extant. The dresser, who wrote them, remarks that not the slightest groan was heard from the patient, nor was his countenance at all expressive of pain."

[1] J. Y. Simpson was born at Bathgate, Linlithgowshire, Scotland, June 7, 1811. In 1832 he received the degree of Doctor of Medicine. On Nov. 4, 1847, he discovered the anesthetic properties of chloroform, and made known the fact in a paper on Nov. 10, 1847. He received the highest honors from the British Government for this discovery. He died at Edinburgh, Scotland, May 6, 1870, in the fifty-ninth year of his life.

[2] Simpson, Sir James: "New Anæsthetic," 1847, 7; *Illustrated London News*, Dec. 4, 1847, 370-2. Simpson, E. B., *Century, 25*, 412; *Liv. Age, 66*, 720;

On November 10, 1847, the slow but steady progress of the use of ether received an effectual setback by the publication of Simpson's famous pamphlet on a "New Anæsthetic Agent as a Substitute for Sulphuric Ether in Surgery and Midwifery."

Because of Simpson's writing and his efforts in behalf of chloroform, the use of this new anesthetic spread with remarkable activity, and soon had almost entirely supplanted ether in general surgery. Its progress was hastened also by its ease of management and speedy action, and because its vapor was much pleasanter to take than that of ether.

Fig. 9.—Sir James Y. Simpson. "To whose genius and benevolence the world owes the blessings derived from the use of chloroform for the relief of suffering."

Theological Opposition to the Use of Anesthetics.—One of the most singular struggles of medical science during modern times occurred in our own days and in a Protestant country. Just as there resulted a theological and sectarian condemnation of and opposition to inoculation, vaccination, and the use of coca and quinin, so did the advocacy of the use of anesthetics in obstetrical cases by James Young Simpson meet with a vigorous storm of protest. The hostility of the Scotch ecclesiastical authorities to the alleviation of pain in childbirth had its source in an old belief in Scotland. In 1591, for example, a lady of rank, one Eufame Macalyane, was charged with seeking the assistance of Agnes Sampson for the relief of pain at the time of the birth of her two sons, and was accordingly burned alive on the Castle Hill of Edinburgh;[1] and this view, which stood for nothing kind, merciful, or humane, persisted even to the middle of the nineteenth century. Simpson's use of chloroform was denounced from the pulpit as impious and contrary to Holy Writ; and Biblical texts were numerously cited, the general declaration being that to use chloroform was "to avoid one part of the primeval curse on women." As in the time of witchcraft, so strong was the power of the church, so universal the belief in the guilt of all women, that, notwithstanding the fact that Simpson wrote pamphlet after pam-

Mon. J. Med. Sci., Sept., 1847; Ednb. Medico-Chir. Soc., Nov. 11, 1848. J. Y. Simpson's "Anæsthesia," 1849, 93, 145, 182, 193, 203. Chloroform of the density 1.48 was used by Simpson in 1847.

[1] Dalyell's "Darker Superstitions of Scotland," 130, 133.

phlet to defend the blessing he had introduced, he seemed about to be overcome, when he seized a new weapon, which was, according to White,[1] probably the most absurd by which a great cause was ever won: "My opponents forget," he said, "the twenty-first verse of the second chapter of Genesis; it is the record of the first surgical operation ever performed, and that text proves that the Maker of the universe, before He took the rib from Adam's side for the creation of Eve, caused a deep sleep to fall upon Adam." We are told that this was a stunning blow, but that it did not entirely kill the sectarian opposition, for the leaders of the resistance had strength left to maintain that the "deep sleep of Adam took place before the introduction of pain into the world—in a state of innocence." However, Thomas Chalmers, a new champion, now intervened, and, with a few pungent remarks, dispersed the enemy forever, and the greatest victory of science against suffering was gained.[2]

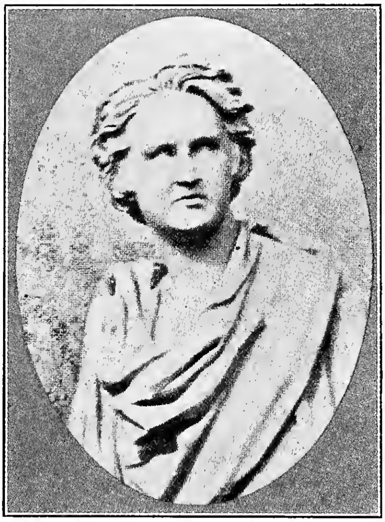


FIG. 10.—BUST OF SIR JAMES Y. SIMPSON. (In the National Gallery, Edinburgh, Scotland.)

When anesthetics were first used in obstetrics in the United States, prominent New England clergymen also assailed their administrators as having sacrilegiously thwarted "the curse," but such "impious frustration of the curse of the Almighty upon woman"[3] began to be regarded as the greatest boon ever conferred by science upon mankind, shortly after the vigorous support of Chalmers in Scotland.

The Early Use of Chloroform in Midwifery.—The records of the Dublin Lying-in Hospital show that the mortality with anesthesia was one in three hundred and twenty, and that the women were delivered within two hours from the commencement of labor. Without anesthesia, the average labor case was twenty hours with a mortality of one in eleven.

Some Physicians Believe in Pain.—In spite of these statistics, we find some doctors pleading earnestly against anesthesia in those days. "Pain during operations is in a majority of cases even desirable, and its prevention or annihilation is, for the most part, hazardous to the

[1] "A History of the Warfare of Science with Theology," 1908, *2*, 63.

[2] Duns' "Life of Sir J. Y. Simpson," 1873, 215-222; 256-260.

[3] For the views of an enlightened woman on this question, see Matilda Joslyn Gage's "Woman, Church and State," 241, 242, 244 and 433.

patient." A French physiologist stated that it was a trivial matter to suffer, and a discovery whose object was to prevent pain was of a slight interest only.

Prejudice Developed against Chloroform.—Until January 28, 1848, chloroform was believed to be a safe anesthetic, but the death of a young woman on that day, while under the influence of chloroform, and several other deaths not long after, gave good cause for the suspicion that the drug might be more dangerous than at first supposed.

Scientific Administration of Ether and Chloroform.—John Snow, believing that in a too concentrated vapor of chloroform lay the danger, invented an inhaler in 1847 which was designed to regulate the percentage of vapor. After several years of experience with anesthetics, he published, in 1858, as the result of his experiments, the first attempt to place the administration of ether and chloroform upon a scientific basis. He was the first to describe the effect of inhaling definite percentages of chloroform vapor and air, and experimented to discover the manner in which death occurred under chloroform, ether, and other anesthetics. He came to the conclusion that chloroform caused death by primary cardiac paralysis, due to the inhalation of a too concentrated vapor.

Efforts to Overcome Objections to Chloroform by Use of Substitutes and Improved Inhalers.—Because of his belief in the dangers of chloroform, Snow investigated amylene[1] as an anesthetic and was the first to administer it. His death checked considerably the advance in the scientific investigation of anesthetic agents.

J. T. Clover, a worthy successor of Snow, was the first to improve the principle of chloroform administration. He published, in 1862, an account of his chloroform inhaler, by means of which the percentages of chloroform and air could be more accurately regulated than hitherto.

"A.C.E. Mixture."—The agitation of the question of the physiological effects of anesthetics caused an investigation to be made by a Committee of the Royal Medical and Chirurgical Society of Great Britain. This Committee, appointed "to inquire into the uses and the physiological, therapeutical, and toxicological effects of chloroform," reported in 1864. They agreed with Snow that the concentrated vapor of chloroform was dangerous, and, because of the inconvenience of the administration of ether, recommended the "A.C.E. mixture" as a substitute. This was originally used by George Harley and was composed of alcohol, one part, chloroform, two parts, and ether, three parts. The committee also urged the free admixture of air as of first importance. A detailed account of this and other mixtures will be found in Chapter XX, p. 688.

Substitutes.—Two or three new anesthetics were introduced about this time, but while they may have been favorably received in certain

[1] See Chap. XX, p. 698.

circles, and for a limited period of time, they never gained general favor. In 1861, "Kerosolene" was introduced in Boston by Dickinson, Bowditch, and Merrill. In 1867, Benjamin Richardson introduced "bichlorid of methylene." For a time many surgeons were very enthusiastic over the drug, claiming that it had fewer drawbacks than any other. American surgeons were not so enthusiastic, believing that its dangers differed only in degree from those of chloroform.

First Vapor Inhaler.—On November 30, 1867, in an article in the *Medical Times and Gazette*, Junker described a very ingenious apparatus for the administration of chloroform, especially valuable in operations on the nose, throat, or mouth.

Nitrous Oxid More Generally Appreciated.—For nearly twenty years little was heard of nitrous oxid, but in 1863, because of the efforts of the same Colton from whom Wells had received his first inspiration, nitrous oxid began to regain the ground it had lost.

In that year, Colton formed an association of dentists to perform operations with the use of nitrous oxid, and by 1867 had recorded 20,000 administrations without an accident. These results strongly attracted the dental profession. Rymer, of London, administered the gas successfully there in 1864, and in 1867 Colton demonstrated in Paris before Evans, an American dentist. This led to its general introduction into England, for, during the following year, Colton had his own apparatus taken to that country by Evans, who administered the gas before the Dental Hospital of London. On Dec. 7, 1868, a joint committee of the Odontological Society and the Dental Hospital issued a report which favored nitrous oxid so highly that it has since held the highest position among the anesthetics of modern dentistry. The analgesic properties of nitrous oxid in dentistry are of recent development.

Nitrous Oxid and Oxygen.—In 1870, Colton published a pamphlet showing the result of the physiological action of the gas in its practical application to the original discoveries of Davy, Wells, and others. A long step toward making nitrous oxid more practicable was taken in 1868, when E. Andrews, of Chicago, reported for the first time the use of a mixture of nitrous oxid and oxygen with most satisfactory results. He published accounts of several cases, in which, by mixing oxygen with nitrous oxid, he had obtained a more satisfactory form of anesthesia than with nitrous oxid alone. But since the medical profession had always insisted on the exclusion of air, Andrews failed to get the notice he deserved. The late Paul Bert, ten years afterwards, again drew attention to the same procedure.

In order to overcome its too feeble action, the large amount of gas necessary, and the limited time during which anesthesia could be produced, Bert gave a mixture of nitrous oxid and oxygen (85 : 15) under increased atmospheric pressure. He argued that the pressure was necessary in order to have a uniform mixture of the gases, but Hewitt and others believed that pressure was not essential. Bert's apparatus for positive pressure was tried with only partial success, it being too cumbersome and expensive. Hewitt states that the most recent and best development in modern anesthetics is the combination of oxygen with nitrous oxid, producing a non-asphyxial and absolutely safe form of anesthesia.

Discarding Chloroform for Ether.—During the year 1870 Simpson wrote to Bigelow in Boston: "Chloroform is the greatest triumph of all, for it has, if not entirely, yet nearly entirely, superseded the use of 'sulphuric ether.'" In spite of this statement, the use of ether had, in the main, held its position against chloroform in the United States. In 1890, after twenty years filled with records of accidents from the use of chloroform, surgeons all over the world began to discard it for ether.

Improved Methods for Administering Ether.—Pollack, Warrington, and Hayward warned against the use of chloroform, and Clover's experiments did not lead him to the belief that chloroform could be made as safe as ether. He became less and less inclined to use it, substituting nitrous oxid in minor operations. He improved the methods for administering the latter gas and introduced its use as a preliminary to ether. Clover also discovered the proper principles of ether administration, and pointed out the advantages of air limitation during the etherization. In 1876, he published an account of his apparatus for the administration of nitrous oxid and ether, either separately or in succession.

Warmed Ether Vapor.—The introduction of Clover's portable regulating ether inhaler in 1877 went a long way toward solving the question of the rapid and safe administration of ether. This inhaler has gained a wider reputation than any other apparatus of its kind. Its use has shown the value of warmed ether vapor with regard to after-effects.

Chloroform Condemned.—During this year, 1877, Clover adopted "bichlorid of ethidene" (ethylidene chlorid), which Snow had used in 1851; but, since a death resulted from it, it did not gain favor. The report of the "Glasgow Committee" of the British Medical Association, issued in 1879, agreed with Snow and his followers in stating that blood pressure and heart action under chloroform were distinctly reduced; and while, where fatalities occurred, respiration usually ceased first, the heart might be primarily paralyzed. The report of the First Medical Association Committee, issued in 1880, stated that many deaths from chloroform were clearly proven to be the result of carelessness or ignorance. Chloroform was condemned and ether also, though in a less marked degree. The committee recommended "bichlorid of ethidene," but this drug is now practically unknown.

The dispute reached such proportions that, in order to settle it, the Hyderabad Chloroform Commission was appointed in 1889. This was financed by the Nizam of Hyderabad at the suggestion of Surgeon-Major Lawrie, whose views had long been with the Edinburgh School. After numerous experiments, the commission filed a report agreeing entirely with Syme and the supporters of chloroform. The conclusions thus stated were not accepted by the medical profession generally, and so a second Hyderabad Commission was appointed, the Nizam again supplying the funds. This time experiments were carried on upon a larger scale, and observations were made on many of the lower animals; but the report, issued in 1891, was a corroboration of the conclusions reached by the First Commission.

Medication before Anesthesia.—In 1881, Alexander Crombil, Surgeon at the Calcutta Medical College Hospital, strongly advocated a combination of the use of morphin and chloroform. He said that he had never seen a death from chloroform, and ascribed his success to the use of a hypodermic of morphin before the administration of the chloroform. This idea came from Claude Bernard, who reported experiments on dogs along similar lines in 1869. Another attempt to show the cause of death under chloroform was made by Lauder Brunton in 1887. He stated his theory to show that incomplete anesthesia with chloroform was the most frequent cause of fatal results. George Foy, in 1889, supported these views.

The Use of Chloroform Accompanied with Danger.—The Second Committee of the British Medical Association appointed to investigate the effects of anesthetics, their safety, and methods of administration, after studying reports of 26,000 cases in hospital and private practice, concluded that no method of using chloroform was free from danger. They found ether singularly safe in healthy individuals, though minor troubles more commonly resulted from its use. Their final conclusion was that the most important factor in the administration of anesthetics was the experience already acquired by the administrator.

The Third Committee of the British Medical Association was appointed in 1901, to put the determination of chloroform quantitatively upon a sound basis. They endeavored to discover the smallest possible dose, by volume in the atmosphere breathed, necessary to produce anesthesia; and also the smallest possible dose necessary to maintain anesthesia after loss of consciousness. They recommended an inhaler devised by Vernon Harcourt, which permitted a maximum of 2 per cent of chloroform vapor with gradations downward.

Chloroform and Oxygen.—In an attempt to make chloroform safer for anesthetic purposes, Neudorfer, of Vienna, introduced the use of chloroform and oxygen in 1886.[1] Bertel advocated it before the St.

[1] His method was described in the *Lon. Med. Record.*

Petersburg Medical Society, as also did von Idelson. It did not gain favor because of the lack of a device for regulating proportions. Kreutzmann, of San Francisco, in 1887, wrote a description of a simple arrangement for administering chloroform and oxygen. He used the Junker Inhaler and spoke very highly of the results. He commented on its greater rapidity, lack of marked excitement, quicker return to consciousness and fewer unpleasant after-effects. On January 25, 1896, the *British Medical Journal* stated that the number of cases of the use of chloroform and oxygen were then too few for any general conclusions to be drawn. Oxygen was used with chloroform by Schall, of Brooklyn, in 1895, and Northrop, of Philadelphia, and this combination has been the routine anesthetic in a hospital of Pittsburgh for nine years.

Combinations and Sequences in Anesthetics.—Among other recent advances, it may be noted that anesthetics are used more in combination and sequence than ever before. In pulmonary anesthetics, the placing of rebreathing upon a scientific basis by Gatch, and the combination of general and local anesthetics by Crile, are noteworthy advances. For spinal and regional anesthesia, electrical, rectal, intratracheal insufflation, morphin, and intravenous anesthesia, and hypnotism, the reader is referred to the chapters dealing especially with the different forms of anesthesia.

Ethyl Chlorid.—Ethyl chlorid is being used more and more where it is impossible to use nitrous oxid, on account of the difficulty of procuring the gas in tanks, etc., in certain localities.

Its general properties were discovered by Carlson in 1896; in 1902, it was introduced in England as a general anesthetic, and in the latter country it has recently almost displaced nitrous oxid.

Importance of Trained Anesthetists.—The tendency of the present day is toward absolute accuracy in the choice of anesthetics and in the amount administered. This, together with a competent anesthetist who has been thoroughly trained for that particular work,[1] insures to the patient of the twentieth century complete oblivion from pain during surgical operations, with a minimum of discomfort and risk.

BIBLIOGRAPHY

"Anæsthetics Ancient and Modern; an Historical Sketch of Anæsthesia." Burroughs, Wellcome & Co., London, 1907.

Bigelow, Henry J.: "Surgical Anæsthesia, Addresses and Other Papers." Boston, 1900.

Buxton, Dudley W.: "Crawford Williamson Long (1815-1879), the Pioneer of Anæsthesia, and the First to Suggest and Employ Ether

[1] See Chap. IX, p. 361.

Inhalation during Surgical Operations." Reprinted from the *Proceedings of the Royal Society of Medicine,* 1912, *5,* 19-45.

Colton, J. Q.: "Anæsthesia: Who Made and Developed This Great Discovery?" A. G. Sherwood & Co., New York, 1886.

——— "A True History of the Discovery of Anesthesia," A. G. Sherwood & Co., New York, 1896.

Emerson, E. W.: "A History of the Gift of Painless Surgery." Houghton, Mifflin & Co., Boston and New York, 1896.

Foster, Burnside: "The History of the Discovery of Anesthesia." St. Paul, Minn., 1896.

Foy, G.: "Anæsthetics, Ancient and Modern." London, 1889.

Hayden, William R.: "History of Anesthesia, or Painless Surgery." *Inter. J. Surg.,* New York, 1896.

Hodges, Richard Manning: "The Introduction of Sulphuric Ether," 1891.

Lyman, Henry M.: "The Discovery of Anesthesia." *Va. Med. Mon.,* Sept., 1886.

McManus, James: "Notes on the History of Anesthesia." Hartford, Clark & Smith, 1894.

Maduro: "The Status of General Anesthesia, in 1900." *Med. News,* Sept., 1900.

Morton, William James: "Memoranda Relating to the Discovery of Surgical Anesthesia," and Wm. T. G. Morton: "Relation to This Event." New York, 1905.

Nevius, Laird W.: "The Discovery of Modern Anesthesia. By Whom Was It Made? A Brief Statement of Facts." New York, 1894.

Old Penn, April 6, 1912, *10,* No. 19, 587.

Patton, J. M.: "Anesthesia and Anesthetics."

"Report to the House of Representatives of the United States of America, Vindicating the Rights of Charles T. Jackson to the Discovery of the Anæsthetic Effects of Ether Vapor, and Disproving the Claims of W. T. G. Morton, to That Discovery. Testimony in Relation to the Claims of Dr. Horace Wells, with Evidence Explanatory Thereto." Washington, 1853.

Rice, Nathan P.: "Trials of a Public Benefactor." New York, 1859.

Shaw, S. Parsons: "Who Discovered Anesthesia?" Palmer & Howe, Manchester, 1868.

Sims, James Marion: "The Discovery of Anesthesia." J. W. Ferguson & Son, Richmond, 1877.

Simpson, Sir James Young: "Anesthesia, etc." D. Appleton & Co., New York, 1872.

——— "Answer to Religious Objections Advanced Against the Employment of Anæsthetic Agents in Midwifery and Surgery." London, 1847.

Smith, Truman: "An Inquiry into the Origin of Modern Anesthesia." Hartford, Brown & Gross, 1867.

"Testimony Establishing the Claim of William T. G. Morton, M.D., on the Ether Discovery."

"The Semi-Centennial of Anesthesia, October 16, 1896," Mass. Gen. Hospital, Boston, 1897.

United States Congress. Senate Report from Select Committee, etc., 32nd Congress, 2nd Session, Rep. Com. No. 421, Feb. 19, 1853.

Warren, Edward: "Some Account of the Letheon, or Who Was the Discoverer?" Dutton & Wentworth, Boston, 1847.

Warren, J. Collins: "The Influence of Anesthesia on the Surgery of the Nineteenth Century," 1896.

Warren, J. M.: "The History of Anesthetics from an American Point of View."

Welch, William H.: "A Consideration of the Introduction of Surgical Anesthesia."

Young, Hugh H.: "Long, the Discoverer of Anesthesia." *Johns Hopkins Hist. Bull.,* Nos. 77-78, Aug.-Sept., 1897.

CHAPTER II

GENERAL PHYSIOLOGY OF INHALATION ANESTHESIA

Introductory Remarks: Definition of Terms; Chief Anesthetic Agents.

Theories of the Action of General Anesthetics: Spencer's Theory; Binz's Theory; Bernard's Theory; Dubois' Theory; Schleich's Theory; Müller's Theory; Meyer-Overton Theory; Wright's Theory; Traube's Theory; Mathews-Brown Theory; Moore-Roaf Theory; Gill's Theory; Höber's Theory; Baglioni's Theory; Reicher's Theory; Gros's Conclusions; Burker's Theory; Verworn's Theory; Conclusions of Lillie; Conclusions.

Effects of Inhalation Anesthetics upon Various Parts of the Organism: The Respiratory System; The Circulatory System; The Muscular System; The Glandular System; The Nervous System.

Factors Which May Be Said to Modify the Physiology of Anesthesia as Ordinarily Induced: Warming the Agent; Experiments on Warming Ether; Effects of Moisture; Combining Oxygen with the Agent; The Influence upon Anesthesia of Oxygen Intra-abdominally Administered; Preceding the Administration with Oil of Bitter Orange Peel; Utilizing Carbon Dioxid.

INTRODUCTORY REMARKS

All attempts to give a detailed account of the action of anesthetic agents in general upon the organism reveal the practical impossibility of proceeding very far without employing a modifying phrase, "this varies with the agent employed," "according to conditions," "with chloroform," "with ether," etc. Therefore relatively little space is given here to the general physiology, special attention being directed to the particular physiology of each agent in the individual chapters where the several drugs are discussed in detail. In fact, the special physiology of ether, chloroform, or other inhalation anesthetic agent, is of far more value to the practical anesthetist than is the physiology which is applicable alike to all, the former having been evolved largely from clinical observation, whereas the latter is the outcome chiefly of laboratory experimentation, many points concerning which have not been definitely determined.

Definition of Terms.—The term "general anesthetic" is employed in contradistinction to local or spinal analgesic. The state of general anesthesia, or unconsciousness concurrent with insensibility to pain, is usually brought about by inhalation, but may be induced by various agencies introduced into the organism by other channels than the respiratory system. It may perhaps also be induced by hypnotism and electrical influences.

The various narcotic and analgesic drugs which are administered by mouth or otherwise are excluded from discussion in this chapter.

The state induced by the administration of inhalation anesthetics is designated, by the usually accepted phraseology, general anesthesia, anesthesia, and narcosis, all signifying unconsciousness with general loss of sensation, including, of course, loss of pain sense.

Analgesia, loss of sensibility to pain, is not to be confounded with the above terms. The terms "light anesthesia" and "heavy anesthesia," whose use has been challenged by some writers[1] are not incorrect, if considered to apply merely to degrees or stages of anesthesia.

Certain factors are generally accepted as entering into the physicochemical relations of the anesthetic agent to the organism, giving rise to results which may be noted and controlled clinically. These factors are as follows:

(1) It should be of such nature or combination, or must be capable of such methods of administration, as will reduce the danger to life to a minimum.

(2) The anesthetic agent should possess such physical properties that it is easily taken into the system.

(3) It should produce the general, complete, or temporary inhibition of action of the nervous mechanism presiding over cerebration, sensation, and motion.

(4) It should be capable of administration with the least interference with respiration, circulation, or other vital processes.

(5) It should act in such manner that its immediate effects are at all times under the control of the administrator.

(6) It should reduce general shock to a minimum.

(7) It should not cause serious or lasting after-effects, the organism promptly resuming the physiological functions existent immediately before the administration of the anesthetic.

In the light of recent laboratory and clinical experiments, a further requirement may be added to those heretofore generally accepted as applying to the satisfactory inhalation anesthetic; this is:

(8) The agent should be of such a nature or combination as to render possible the practically complete elimination of the second stage of an-

[1] "Review of Blumfeld's Treatise," *Lancet,* Sept. 21, 1912.

esthesia—the stage of excitement—during which the dangerous phenomena of anesthesia are often noted.

Chief Anesthetic Agents.—The chief agents and combinations of agents which fulfil the above requirements are: (1) nitrous oxid; (2) ether; (3) ethyl chlorid; (4) chloroform; (5) combinations and sequences of the above with each other and with oxygen.

THEORIES OF THE ACTION OF GENERAL ANESTHETICS

Inasmuch as there are still "mysteries of anesthesia," many points of physiology upon which expert opinions differ, we present a brief review of the theories concerning the mode of action of anesthetics, as advanced by the earlier investigators as well as by more recent writers. No attempt has been made to catalogue all the theories proposed, or to follow strict chronological sequence.

Spencer's Theory.[1]—Narcotic and anesthetic agents are commonly supposed to have special relations to the nervous tissue, rather than to other tissues. *Because of the different effects produced, it is even supposed that some of them have elective affinities for the matter composing certain nervous centers rather than for that composing others.* As the same anesthetic does not act in the same way on all persons, but here affects one center more, and there another, it must be assumed that the chemical compositions of these centers are in such cases interchanged. Since, in the same individual, the same quantity of the same anesthetic will produce quite different effects in different states of the circulation, the hypothesis requires the supposition that these contrasts of chemical composition among the nervous centers interchange from hour to hour.

The various substances that affect the nervous system—the narcotic and anesthetic agents—are substances that produce changes in albuminous matters, their respective effects being modified by the various conditions under which they act. "Agents having powerful affinities for components of the tissues and fluids," according to Spencer, "given in small quantities to avoid destruction of the membranes, can scarcely reach the nervous system in uncombined states; and may be expected to work their respective effects through the instrumentalities of the compounds they have formed. The most conspicuous effects will be wrought by those agents which, while they can produce molecular changes in albuminous substances, have not such powerful affinities for them, or for their elements, as to be arrested on their way to the nervous system. The anesthetics and narcotics may fairly be regarded as fulfilling this requirement." It need not be supposed that the anesthetic or narcotic has more affinity for protein-substance of nerve corpuscle or nerve fiber

[1] Spencer, Herbert: "Synthetic Philosophy," Vol. I; "Principles of Psychology," Appendix; "On the Actions of Anæsthetics and Narcotics," 631.

than for the other forms of protein-substance with which it comes in contact. Its effect is comprehensible, however, as resulting from the structural relations of nerve corpuscle and nerve fiber.

In order to understand why excitement precedes narcosis, one must observe the different relations of nerve corpuscle and nerve fiber to the blood. The vesicular tissue of the nervous system is far more vascular than its fibrous tissue. While the matter of the nerve vesicles is so arranged as to offer the least possible obstacle to the reception of the fluid from the adjacent capillaries, the matter of nerve fibers is shielded by a medullary sheath. When any agent, therefore, which is capable of so changing the molecular state of nerve matter as to arrest its function is carried into the blood, the first action is upon the nerve corpuscles. "Each change produced in one of these," according to Spencer, "implies a disengagement of molecular motion that is immediately propagated along the connected nerve fibers, and excites the parts to which they run. Every nerve corpuscle being thus quickly acted upon, and emitting successive discharges as the successive molecular transformations are wrought in it, there results a general exaltation of state, physically in the invigorated pulse and contractions of the muscles, and as shown psychically in the rush of vivid ideas and intensified feelings." While this is going on, while some molecules of the anesthetic agent have thus quickly passed from the closely adjacent capillaries into the almost naked matter of the nerve corpuscles, other such molecules are elsewhere on their way through the outer coats of the nerve tubes and the medullary sheaths within these, reaching, in time, the bundles of fibrillæ forming the axis-cylinders. The isomeric changes which they immediately begin to produce in these at first add to the general excitement. As the anesthetic invades a nerve fiber more and more, a greater and greater number of its molecules are rendered unable to transfer a wave of the peculiar isomeric change which constitutes a nervous discharge, and finally the fiber becomes impermeable.

The impermeability, other things being equal, takes place sooner in the longer nerve fibers than in the shorter, the probability being that, after a given interval, a long fiber is more likely than a short fiber to be invaded at some parts of its course. This presumably explains why, in an animal, anesthesia occurs first in the hinder extremities, the parts of the surface nearer to the nervous centers losing their sensibility later.

Numerous factors (point of absorption; rapidity of absorption; quantity absorbed; relative molecular mobility of the agent; its chemical relation to the blood and other substances; general state of circulation and of circulation in each nervous center; and character of nerve fibers acted upon) coöperate to cause variation in the effects produced by the various agents, by different doses and by the same dose under different conditions. It is not necessary, therefore, to assign elective affinities for special centers as the only possible causes of the special effects.

Binz's Theory.[1]—*The ganglion cell,* according to Binz, *is the point of attack of the anesthetic agent.* In his experiments, fresh sections of the brain cortex of rabbits were placed in a one per cent solution of morphin hydrochlorid, or exposed to chlorin vapors. The effect of coagulation-necrosis was produced, as is seen when protoplasmic poisons of neutral reaction are allowed to act upon large transparent infusoria. The protoplasm is at first darkened, and the movements become sluggish; later on the protoplasm becomes granulated, and the movements cease. Recuperation may take place from the first stage, by washing away the poisons, but not from the last stage. The first stage is likened by Binz to the sleep of the cell; the last to death. The first trace of coagulation may redissolve but coagulation itself does not.

Bernard's Theory.[2]—Bernard regarded the *ganglion cell* as the point of attack of the narcotic agent. In his opinion, the mechanism of anesthesia is always the same, in spite of the difference of the narcotic agent; for they all produce one identical modification in the ganglion cell. This modification of the ganglion cell consists in a semi-coagulation of the protoplasm of the nerve-cell, this semi-coagulation being merely transitory, the protoplasm resuming its previous state after the removal of the narcotic agent from the cell. This view was derived from the rigidity of muscle fibers after their exposure to chlorin vapors.

Müller[3] points out that the same mechanism cannot be assumed to underlie all narcoses, the mechanism of indifferent narcotics differing from the mechanism of narcosis caused by many basic narcotics. He believes, however, that a *semi-coagulation of the protoplasm is produced by the majority of the basic narcotics.*

Dubois' Theory.[4]—Dubois proposed a modification of Bernard's theory, holding that *narcotics act by producing a dehydration of the protoplasm,* or by *decreasing the dissociation of the inhibition-water of the tissues.* Organisms which are exposed to the action of these dehydrating substances are transformed into a state of latent vitality.

Müller[5] points out that this theory is entirely erroneous, the water that is withdrawn being derived from the "cell juice," but not from the protoplasm. Richet states that a compound becomes a more efficient

[1] Binz, C.: "Ueber Anaesthetika," *Deutsche Klinik,* 1860, No. 29, 277; "Ozonisierte Luft, ein schlafmachendes Gas," *Berl. klin. Wochnschr.,* 1882, No. 1, 6; "Die Wirkung ozonisierter Luft auf das Gehirn," *Berl. klin. Wochnschr.,* 1884, No. 40, 633.

[2] Bernard, C.: "L'anésthésie," Union méd., Paris, 1869, *8,* 109.

[3] Müller, B.: "Narkologie," *I.*

[4] Dubois, R.: "Contribution à l'étude de la physiologie générale des anesthésiques," *Séances et Mem. Soc. de Biol.,* Oct. 24, 1885, 625.

[5] Müller: *Loc. cit.*

narcotic, or a stronger poison, the slighter its solubility in water. This assertion applies to a definite number of narcotics, up to a certain degree. All indifferent narcotics, of difficult solubility in water, have the property of penetrating quickly to the entire protoplasm and require only a few seconds to get into the cell juice. Overton's statement holds good, that the strongest narcotics are those compounds which at the same time combine a very slight solubility in water with a very great solubility in ether, olive oil, or the lecithin mixtures.

Schleich's Theory.[1]—According to Schleich, *the first influence of the anesthetic agent is manifested by the stimulation of peripheral organs, followed by local stimulation at the end apparatus of the sense-organs.* The effects upon the central apparatus are as follows:

The blood circulates in the neuroglia in very fine vessels, and the first effect of the narcotic is felt as a heavy, dull sensation over the entire head; the result of the neuroglia irritation would be sleep, if the ganglion cells were not themselves stimulated at about the same time. As a matter of fact, this sleep can be produced in the early stage in certain individuals, for example in children, by very gradual anesthetization. The small quantities of the anesthetic which at first circulate in the blood may cause a stimulation of the vasomotors, and thereby a narrowing of the vessels, on account of the close connection of the neuroglia protoplasm cells with the vessels. The function of the protoplasm cells is thereby diminished, due to limited fluid; the inhibition is lessened; ideas and thoughts travel about unchecked. It is not until the onset of vasomotor paralysis that the vessels become larger, so that the narcotic agent can stimulate the protoplasm cells directly. The roaming ideas are now restricted. The inhibitory function of the neuroglia advances and penetrates between the individual sensory associations. The situation becomes blurred; momentary consciousness is lost; only individual ideas reach consciousness; the condition takes on more and more similarity to sleep, at first restless and full of dreams, later on deep and quiet. The pupils are still sensitive to light stimuli, but no longer reach their full width on closure of the lids; the contraction increases as the narcosis advances. The pupils are contracted also in sleep. There probably exists a reflex arc between neuroglia irritation and oculomotor function, or sympathetic paralysis, respectively.

Poisons such as chloroform are relatively mild, because they are first accompanied by neuroglia irritation, whereas the true cell poisons penetrate at once into the ganglion cells, exerting their relative influence beyond the protective action of the neuroglia, and acting upon the ganglion cells by way of the lymph spaces and blood vessels. Narcoses with chloroform, ether, alcohol, etc., are increased physiological mechanisms, namely, changes in repletion with blood and irritations of the neuroglia.

[1] Schleich: "Zur Infiltrations Anaesthesie," *Therap. Monatsh.*, 1894, 429.

When these substances are administered in definite quantities which create a state of equilibrium between the action of the narcotic and the power of resistance of the neuroglia, their effect becomes narcotic, and this effect increases the more the scale of equilibrium tips toward the narcotic, until finally the neuroglia is overcome, and the effect is then the same as that of the cell poisons which directly attack the ganglion cell, omitting the neuroglia.

Schleich considers the narcotic agents as primary neuroglia poisons, and their antagonists (the cell poisons) as primary cell poisons. He also assumes a variable sensitiveness of the neuroglia in the different developmental stages. The effect of chloroform, and the majority of narcotics, upon the individual centers of the human brain, pursues a course in inverse ratio to the phylogenetic development of the centers. The extraordinarily poisonous effect of chloroform and of morphin upon certain individuals is explained by him as due to the fact that, in these cases, the neuroglia does not react to the ordinary toxic dose by a stimulation, but directly by paralysis.

Müller's Theory.[1]—After considering various theories of narcosis, Müller formulated his own view concerning the mechanism of anesthesia.

After the narcotic agent has reached the ganglion cells of the cerebral cortex, *it exerts its action upon the lecithin-cholesterin mixture of the ganglion cell, causing it to undergo a physical transformation.* According to Schleich's theory, the plasma cells of the neuroglia are also important and possess inhibitory properties; they surround each functionating ganglion cell and communicate directly with a vessel. As the plasma cells are directly connected with the perivascular lymph spaces of the vessels, and are themselves surrounded by lymph spaces, the narcotic agent which is contained in a definite concentration in the blood plasm must be taken up by the lymph of the lymph spaces, and an equilibrium in the concentration of the two fluids in the narcotic must become established. It depends upon the composition of the protoplasm of the plasma cells, how much narcotic they will take up before this reaches the ganglion cell. The paralysis of the plasma cell represents that instant at which the quantity of the narcotic in the plasma cell is such that no additional amount can be taken up. The narcotic, at this moment, gets also into the ganglion cell. The plasma cell is now passed without its protoplasm taking up anything of the narcotic, and the ganglion cell takes up the narcotic from the intercellular lymph. The function of the neuroglia explains the different effects of the narcotic upon the individual centers. By assuming the presence of lecithin-cholesterin mixtures also in the plasma cells, it becomes intelligible that they possess the capacity of dissolving the narcotic agents. Possibly,

[1] Müller, B.: *Loc. cit.*

these plasma cells contain still another similar substance, which does not exist in the ganglion cells, and thereby invests the plasma cells with the capacity of fixing still larger quantities of the narcotic. This other body may be contained in larger amounts in the phylogenetically older plasma cells than in the younger cells, thus accounting for the prolonged resistance in still another way. The significance of the solubility of the narcotic in the cells of the neuroglia is at once evident, when the function of the neuroglia is interpreted as something more than connective tissue function. The different effect upon the ganglion cells is explained by the different number of existing plasma cells. The action of the neuroglia consists in modifying the solubility of the narcotic agent and thereby controlling the rate of its penetration into the ganglion cells.

Meyer-Overton Theory.—In 1899 Hans Meyer announced his theory of narcosis;[1] the following year E. Overton described his theory of anesthesia;[2] and in 1905 Meyer restated his theory.[3] Since these two theories were formulated independently and without conference,[4] and in general agree, this explanation of anesthesia is usually referred to as the Meyer-Overton theory.

According to Meyer, *the narcotizing substance enters into a loose physico-chemical combination with the vitally important lipoids of the cell, perhaps with lecithin, and in so doing changes their normal relationship to the other cell constituents, through which an inhibition of the entire cell chemism results.* The narcosis disappears as soon as the loose, reversible combination, dependent upon the solution tension, breaks up.

In accordance with these views Meyer formulated the following statements:

"(1) All primarily indifferent chemical substances which are solvents for fat and substances resembling fat must exert a narcotic action upon living protoplasm, in so far as they can diffuse therein.

"(2) The effect must manifest itself first, and most strongly, in those cells in whose chemical structure these fatty or lipoid substances predominate and presumably are the essential carriers of the cell function, —namely, in the first place, in the nerve cells.

"(3) The relative efficiency of such narcotic agents must be dependent upon their mechanical affinity for lipoid substances, on the one hand, and for the remaining body constituents, i. e., principally

[1] *Archiv f. exper. Pathol. u. Pharmakol.*, May 16, 1899, 110, 119.

[2] "Studien über die Narkose, zugleich ein Beiträg zur allgemeinen Pharmakologie," Jena, 1901.

[3] "The Theory of Narcosis," Harvey Lectures, 1905, *1; J. Am. Med. Assn.*, Jan. 20, 1906, 167.

[4] *J. Am. Med. Assn.*, Jan. 29, 1906, 169.

water, on the other hand. It is dependent, therefore, upon the division coefficient which determines their distribution in a mixture of water and lipoid substances."

Overton carried out extensive observations and investigations concerning the osmotic properties of living plant cells and animal cells, followed by experimentation with general anesthesia. He was firmly convinced of the fact that the mode of action of anesthetic agents can in no way be explained on the basis of chemical reaction; for the reason that many of the strongest indifferent narcotics belong chemically to the most stable and sluggish compounds. The effect of narcotic agents is essentially a function of their lipoid solubility.

Overton showed that substances may be divided into different groups according to the rapidity with which they diffuse into protoplasm, the rate of diffusion, as a general rule, depending upon the solubility of the substances in fat, lecithin, and lipoid substances of that type. If S_f represents the solubility of the substance in fat, and S_w that of the same substance in water, then the ratio $\frac{S_f}{S_w}$ is termed the distribution coefficient of the substance. According to Overton, the value of this coefficient determines the velocity of diffusion into cell protoplasm.

It has been indicated by Meyer and Overton[1] that anesthetics and narcotics are usually substances which diffuse rapidly, and that, therefore, these substances should have a high distribution coefficient. Meyer accordingly compared the aliphatic narcotics, and found that the narcotic power of these was roughly proportional to the magnitude of the distribution coefficient. This finding has been expressed as follows: The strength of the narcotic action of a compound is dependent upon its solubility in lipoid substance.[2] But, as has been pointed out by May,[3] this is not exactly correct, since it depends not so much on its actual solubility in lipoid substances as upon the ratio of its solubility in lipoids to that of its solubility in water.

Meyer compared the narcotic power of the aliphatic narcotics by ascertaining the smallest concentration which would produce a definite physiological effect, and he expressed the values as fractions of a normal solution, calling these the "liminal values." He and Baum[4] discussed the work of Dubois[5] in reference to which they advanced the theory that the relative strengths of anesthetics are dependent upon their mechanical affinity for fatty substances, like lecithin in the protoplasm, on the one hand, and to the other constituents in the protoplasm, especially

[1] *Arch. f. exp. Path. u. Pharm.*, 1901, *42*, 109 and 119.
[2] See Höber's Theory, p. 46.
[3] *Loc. cit.*
[4] *Arch. f. exp. Path. u. Pharm. 42*, 109.
[5] See Dubois' Theory, p. 34.

water, on the other hand. In support of these views, they showed that the proportion between solubility in fat and solubility in water of a number of narcotics runs parallel with their anesthetizing activity.

The theory of Overton and Meyer is well supported by the parallelism of narcotic effect and distribution coefficient. Then, too, a number of subsidiary facts appear to lend it additional support; for example, the observation of Mansfield,[1] that some narcotics have a more powerful action when administered to starved animals, the explanation suggested being that in these there is less tissue fat to absorb some of the narcotic and that a greater portion of the latter is in consequence absorbed by the central nervous system; and the observation of Tunnicliffe and Rosenheim [2] that the addition of lecithin protracts the effect of chloroform on the heart.[3]

However, other facts seem to show that the theory is, to say the least, incomplete. For instance, the peripheral nerves contain a large amount of lipoid substance, yet they are much less affected by the aliphatic narcotics. It has also been pointed out by Cushny [4] that many aromatic compounds have a high distribution coefficient, but are nevertheless devoid of narcotic action. There is, however, a possible explanation of these facts in Traube's theory (see p. 42) of surface tension.

It appears reasonable to conclude from these facts:

(1) That the rapid penetration of the cells should be the most essential condition of enabling a substance to exert its effect on the interior of the cells.

(2) That, after the substance has gained entrance, its solubility in the cell lipoids may be the important factor in determining narcotic action.

The Meyer-Overton theory is more than merely interesting. It ostensibly gives a simple explanation of narcosis and seems to afford a means of elucidating other processes, as phagocytosis.[5] In support of the combination of, say, chloroform with lecithin, we have the analogous conduct of this compound with salicylid,[6] leprarin,[7] and even water;[8] and further support is given to the Meyer-Overton theory by the finding

[1] *Centr. Physiol.*, *20*, 664.

[2] *Proc. Physiol. Soc.*, 1903, 15.

[3] Tunnicliffe and Rosenheim studied the action of chloroform and ether on the heart by adding them to saline fluid perfused through the heart by Locke's method. The depressing action on the heart produced by chloroform was found to be very marked, but if lecithin was also added the effect was found to be delayed.

[4] Cushny: "Text-book of Pharmacology," 1904, 128.

[5] See Graham: *J. Am. Med. Assn.*, March 26, 1910, 1044.

[6] Anschütz: *Ann.*, *273*, 94.

[7] Kassner: *Arch. Pharm.*, *237*, 44.

[8] See *Z. anal. Chem.*, *25*, 118.

of Nerking,[1] that, in the case of animals to which a solution of lecithin has been administered, the anesthesia lasted for "a much shorter time" than in the case of the control animals, and the work of Graham,[2] who found that lecithin and olive oil added to etherized blood restored phagocytosis. Although the theory is well supported by certain evidence, it is too specific to be altogether satisfactory.

There is much uncertainty as to the mode of action of anesthetics and particularly as to their effect upon permeability. While some writers hold that anesthetics increase permeability, others take the opposite view.[3] As pointed out by Osterhout,[4] to clear up this confusion appears to be a necessary step toward a theory of anesthesia. He seems to have attained a definite solution of the problem in the cases he describes—a result due to the employment of quantitative methods.

The experiments of Osterhout were made by measuring the conductance of living tissues of a marine plant, *laminaria*. Under the conditions of the experiment, an increase or decrease of conductance signified a corresponding increase or decrease of permeability.[5] The anesthetics (ethyl ether, chloroform, chloral hydrate, and alcohol) were mixed with sea water and sufficient concentrated sea water was then added to make the conductivity equal to that of sea water. The material was then placed in the mixture and its conductance was measured at frequent intervals.

Two distinct effects were observable in the experiments conducted by Osterhout. One was a toxic effect evidenced by an increase in permeability, while the other involved a decrease in permeability. He was forced to the conclusion, from the results obtained, that it was the reversible change, involving a decrease of permeability, which was associated with the anesthetic action. This is indeed reasonable.[6] Osterhout pointed out that the fact that typical anesthetics decrease the permeability of the tissue to ions is significant in view of the fact that the transmission of nervous and other stimuli is believed to depend on the movement of ions within the tissues.

Wright's Theory.[7]—Wright undertook an investigation to determine

[1] *Münch. med. Woch.*, 1908, 1733.

[2] *J. Am. Med. Assn.*, March 20, 1910, 1043.

[3] Cf. Höber: "Physikalische Chemie der Zelle und der Gewebe," 1911, 219, 223, 489; Lillie: *Am. J. Physiol.*, 1912, *29*, 372; *30*, 1; and Lepeschkin: *Ber. d. bot. Ges.*, 1911, *29*, 349.

[4] *Science*, n. s., *37*, No. 942, 111.

[5] The method is described in *Science*, n. s., *35*, 112 (1912).

[6] The distinctive mark of an anesthetic is the reversibility of its action; hence it can hardly be concluded that this action is associated with an irreversible change in permeability. Such a change is not peculiar to anesthetics, although common to all toxic substances.

[7] Wright, Hamilton: "The Action of Ether and Chloroform on the Neurons of Rabbits and Dogs," *J. Physiol.*, 1900-1, *26*, 30, 362.

whether chloroform and ether produce any transient or permanent changes in the cortical or spinal neurons.

In rabbits he found that these agents produced changes in the nerve cells of both the brain and spinal cord. These changes were slight at first, but became more marked as the anesthesia continued. The principal change was described by him as "rarefaction." In the advanced cases he employed the term "skeleton cell," and, in the most marked cases, he found that a "pseudo-degenerative" change had set in.

In dogs there were practically no changes up to two hours, but, between that time and four hours, changes occurred in the nerve cells similar in kind to those observed in rabbits, although less in degree. These changes became more marked as the anesthetic was continued.

Wright regarded the changes observed in the cells and their processes as due directly to the influence of the anesthetic, and not due indirectly to the capillary anemia which is produced.

Inasmuch as it is generally conceded that ether and chloroform circulate in the blood as such, producing no biochemical changes in the blood, Wright concluded that the *neuronal changes are biochemical in nature, and are produced by the anesthetic that reaches them via the blood stream.*

There is nothing, he holds, to suggest that chloroform or ether could cause these changes mechanically; the supposition that they act chemically is extremely probable.

It is obviously impossible to say that these changes occur in human beings. Wright did not consider, however, that there is any analogy between the changes described and those biochemical anabolic and katabolic changes that occur in daily life, and mark sleeping and waking hours. He regarded the action of narcotics, such as ether and chloroform, as pathological, not very intensely so, yet as something which is remote from physiological processes. In sleep there is probably an opportunity, he says, for the constituents of the nerve cells to undergo anabolic changes, whereas in the unconsciousness produced by anesthetics the process appears to be associated with an exhaustion of them.

A subsequent series of experiments[1] was undertaken (1) to determine whether a still more prolonged period of anesthesia renders the changes more intense, and (2) to ascertain whether the pseudo-degenerative change is permanent: the answer to the first question was affirmative; to the second, negative.

In the cases in which the anesthesia was kept up longest it was found that even the nuclei and the nucleoli were affected, the latter being the last part of the cell to show the effect of the drugs. The slow return of the conjunctival reflex in these cases, he thought, indicated that after a certain period of anesthesia (six hours in the dog)

[1] Wright: *Ibid.*, page 363.

the depression of neuronal function becomes more rapidly profound, and that there is a limit to the time of safe anesthesia. The histological changes observed induced this view. A greater alteration occurred in the cells during the three hours between the sixth and the ninth hours of anesthesia than during the five hours between the first and the sixth hours.

The changes observed in the cells were transitory, disappearing with the disappearance of the drugs from the circulation and tissues, or soon thereafter. Forty-eight hours after nine hours of ether narcosis the cells were found to be practically normal.

The rarefaction of the cell substance and the formation of moniliform (necklace-like) swelling noted in the dendrons, according to Wright, may modify nervous function. "To such changes," he says, "may perhaps be attributed those losses of memory, slight manias and melancholias that are now and then reported to follow prolonged anesthesia in the human subject."

Traube's Theory.[1]—In his theory of the production of general anesthesia, Traube contradicts the lipoid solubility, claimed by Overton, as the primary cause of the penetration of the anesthetic agent into the cell. This cause, according to Traube, consists in the *surface tension.* When two fluids of different surface tension are separated through a membrane, the fluid having the lower tension can find its way to that with the higher tension; so that the difference between the surface tensions explains the entrance of the anesthetizing fluid into the cells.[2] He also claims the existence of a close conformity between the narcotic efficiency and the surface tension in the case of *pure* anesthetic agents which are free from toxic side-effects.

Mathews-Brown Theory.—Mathews[3] made Nef's bivalent carbon hypothesis[4] the basis of a hypothesis for protoplasmic respiration which

[1] Traube: "Theorie der Osmose und Narkose," *Arch. ges. Physiol.,* 1904, *105,* 451; *Phil. Mag.* (6), *8,* 704; *Z. physiol. Chem., 105,* 541.

[2] When the drug has thus gained entrance to the cell, it may exercise its narcotic power in proportion to its solubility in the cell lipoids.

[3] Mathews, A. P.: *Biol. Bull.,* 1905, *8,* 331.

[4] The bivalent carbon hypothesis of Nef (*J. Am. Chem. Soc., 26,* 1549) approaches the action of narcotic agents to the fundamental reactions of organic chemistry. According to his investigations of the chemistry of the element carbon, protoplasmic respiration can be explained as a vital reaction through the decomposition of water, on the basis of a change in valence of the carbon atom from four to two. The quadrivalence of carbon is not constant, the existence of carbon compounds containing bivalent carbon having been definitely established. The bivalent carbon compound of cells, or their respiratory elements, are the point of attack of the entering anesthetic agent. The action is assisted by a rise in temperature. Substances which are perfectly indifferent chemically, such as the volatile saturated hydrocarbons, may produce anesthesia by entering into a loose chemico-physical combination with certain cell constituents,

Brown[1] considers plausible. *The bivalent carbon compound of the protoplasm, which, according to Mathews, may be either simple or complex, decomposes the water of the tissues into its elements. The oxygen, combining with the compounds constituting protoplasm, oxidizes them. The hydrogen, uniting with free oxygen or other substance in the tissues, passes off as gas.*

Mathews holds that anesthetics inhibit the action of the bivalent carbon, thereby decreasing the respiration of the cell protoplasm, resulting in the stage known as anesthesia.

Brown, referring to this theory, thought it more likely that the substances producing a narcosis do so, "not by an action on any one of the essential processes of the protoplasm, but from the combined influence of all of them. The rôle that the lipoids of the cell play in narcosis may be only that of a solvent or gatherer for the narcotic, or more, depending upon whether or not the lipoid is concerned with the essential living processes of the cell."

Mathews had previously called Brown's attention to the fact that starfish eggs were greatly affected by chloroform, ether, etc. The effect appeared to be a partial liquefaction of the protoplasm. Mathews suggested that possibly the power of each member of this group of compounds to liquefy the starfish eggs might be proportional to its narcotic power. Mathews had made some experiments along this line, a report of which was published. This work was repeated and extended by Brown, who made a comparative study of a number of the compounds in common use as anesthetics, narcotics and hypnotics.

The change produced in the eggs was found to be a profound one. The eggs enlarged and became lighter in color; the protoplasm became less granular, and finally there was a rupture of the envelope at some spot, the contents flowing out.

Brown called attention, in this connection, to Hermann's[2] observation of a similar change in red blood corpuscles when treated with anesthetics. The process indicated that the contents of the cell had been increased, in amount and fluidity. The explanation, according to Brown, seems to be that the narcotics are taken up by the fat-like bodies of the egg.

From his comparative studies Brown concluded, in part, as follows:

"(1) That anesthetics and narcotics, at certain concentrations, cause a profound change in the eggs of starfish. This change appears to be a

the effect disappearing as soon as this loose reversible combination ceases. From this point of view, narcosis represents an inhibition of the entire chemism of the nerve cell, through changes in the normal mutual relations of the cell constituents.

[1] Brown, Orville Harry: "A Pharmacological Study of Anesthetics and Narcotics," *Am. J. Physiol.*, 1905-6, *15*, 85.

[2] Hermann: *Arch. Anat. Physiol., Wes. Med.*, 1866, 27.

partial liquefaction. The power of the compounds in bringing this about is indicative of their power as narcotics; i. e., the narcotic substance which produces liquefaction of the eggs in a dilute solution will also, in small amounts, produce narcosis.

"(2) That anesthetics and narcotics do not cause the liquefaction if they are sufficiently concentrated or sufficiently diluted. The concentrated solution causes a change which has the appearance of a coagulation.

"(3) The most important rôle of the lipoids in bringing about anesthesia probably is one of accumulation. If they are concerned with the essential process of the cell, then their part is most likely a broader one.

"(4) Anesthesia is very possibly the result of an inhibition, by the compounds, of the enzymotic processes of the cell, as suggested by Neilson and Terry.[1]

"(5) Mathews' idea that the anesthetics produce their results by their influence upon the respiratory elements—the bivalent carbon compound—of the cell is a tenable one.

"(6) Nef's bivalent carbon hypothesis may help to explain the more rapid narcosis when the temperature is slightly raised."

Moore-Roaf Theory.[2]—Moore and Roaf have found that the action of the numerous substances used as anesthetics probably depends on the general type of interaction between it and the cell protoplasm. In regard to chloroform, they pointed out that attention was not restricted to the action on nervous structures, since all cells (bacteria, amebæ, ciliated cells, etc.) are equally affected. It was therefore concluded that the action must take place with some chemical constituent present in all varieties of protoplasm, and that theories based on the high content of nerve cells in lecithin and fatty constituents may be disregarded. Proteid is the substance of all others universally present in all cells, and Moore and Roaf found that chloroform formed loose compounds with many proteids; in fact, that it would precipitate them if in excess.[3] This, they thought, explains the greater solubility of chloroform in the blood, or in serum and hemoglobin solutions, than in water or in saline solutions.

Their theory of narcosis may thus be expressed: *The loose compound of proteid-chloroform is similar to oxyhemoglobin. When anesthesia occurs, the proteid-chloroform compound of the blood has parted with its chloroform to the cell proteids; the compound here formed undergoes dissociation when the chloroform pressure is reduced on*

[1] Neilson and Terry: *Am. J. Physiol.*, 1905, *14*, 248.

[2] Moore and Roaf: *Proc. Roy. Soc.*, *73*, 382.

[3] Formanek (*Z. physiol, Chem.*, *29*, 416) has also found that both chloroform and chloral hydrate are good precipitants of the blood pigment, particularly at 56° C. He recognized that chloroform is a precipitant for proteids.

cessation of administering the anesthetic, and anesthesia thus ceases.

Later, Moore and Roaf[1] supplied confirmation to the theory that chloroform and other anesthetics form unstable compounds with proteids, and that they produce their effects by thus interfering with the chemical activities of protoplasm. They learned that the solubility of the anesthetic was greater in serum than in water, and that beyond a certain concentration, which was definite for each anesthetic, precipitation of the compound with proteid occurred. It was found that the vapor pressure was always higher in an aqueous solution than in solutions which contained proteid, and determinations of freezing points and electrical conductivity supported the main contention of the investigators.[2]

Edie[3] investigated the proteids of serum and hemoglobin in reference to the work of Moore and Roaf. It was found that the compound of chloroform and hemoglobin was less stable than carboxy-hemoglobin, and that when sufficient chloroform was added to produce precipitation the amount of chloroform found in the precipitate was constant. In the case of the serum proteids, also, the amount of chloroform was found to be fairly constant.

The action of chloroform and hemoglobin has also been studied by Krüger,[4] whose experiments showed that chloroform was not an indifferent reagent toward hemoglobin, but that it changed it into a more insoluble modification without apparently producing any profound chemical alteration.

The following determined facts seem to lend the theory of Moore and Roaf additional support:

(1) It has been shown by Carlson and Luckhardt[5] that during chloroform or ether anesthesia the osmotic concentration of the blood rises. This varies with the depth, and not with the duration, of the anesthesia. The main factor in this observation appears to be that the ether or chloroform itself is dissolved in the blood, although there are other factors which cannot be altogether excluded.

(2) Camus and Nicloux[6] have found that ethyl chlorid is taken up by the blood with great rapidity and is also eliminated with rapidity.

(3) Livon[7] found that during anesthesia produced in dogs by amy-

[1] Moore and Roaf: *Proc. Roy. Soc., B., 77,* 86.

[2] *Thompson, Yates, and Johnston, Lab. Report,* Liverpool, 1905-6, 151-94; and *cf.* the investigations of Buglia and Simon: *Arch. ital. biol., 48,* 1.

[3] *Thompson, Yates, and Johnston, Lab. Report,* Liverpool, 1905, 6, 195.

[4] *Beitr. chem. Physiol. Path., 3,* 67. *Cf.* Gianasso: *Riforma Medica, 22* No. 19, who is of the opinion that chloroform destroys the red corpuscles of the blood.

[5] *Compt. rend. Soc. biol., 55,* 143.

[6] *Ibid., 145,* 1437.

[7] *Ibid., 55,* 143.

lene there is no arrest of internal combustion; but, on extracting the blood gases, amylene was found as a constituent.

Gill's Theory.[1]—Gill's observations concerned chloroform, which, according to his theory, *abstracts oxygen from the blood, being itself destroyed in the process.* "The deoxygenation factor," according to Gill, "which is their proximate cause, thus intermediates between the indirect phenomena and their ultimate cause, which is chloroform." The relation between chloroform and the blood is held by him to be twofold. It causes deoxygenation by the diminishment of the normal supply of air to the alveoli of the lungs, and by its physiologico-chemical action it is indirectly the cause of the suspension of the functions of the cerebral centers.

Höber's Theory.[2]—In his studies on the physical chemistry of excitation (of muscle) and of narcosis, Höber found that isotonic solutions of normal salts of the alkali metals produce currents of rest of varying intensity and direction when applied locally to the non-injured sartorius muscle of the frog. When arranged according to their power of producing this current, the various anions and cations form two series, which coincide with those which have been deduced from their action on the solubility of egg-white and of lecithin.[3] This coincidence is one of the reasons for Höber's conclusion that excitation and the electrical reaction accompanying it are closely connected with the consistency of the muscle colloids.

According to Höber, narcotics inhibit the change in the colloids (of the axis cylinder), which change accompanies the normal current of action, and, in accordance with the current theory of narcosis, due to Meyer and Overton, this colloidal change is supposed to occur in the lecithin. *Narcosis would therefore consist, first, in the accumulation of the lipoid-soluble narcotic in the lipoid substance (lecithin), and, second, in the inhibition of the colloidal changes which excitation normally produces in this substance.*

Baglioni's Theory.[4]—Baglioni maintains that narcotic effect depends

[1] Gill, Richard: "The $CHCl_3$ Problems," 1906, *2*, Physiological Action.

[2] *Pflüger's Archiv*, 1907, *120*, 492; *J. Chem. Soc.*, *94*, ii, 121.

[3] An examination of the effect of normal salts on the precipitation of egg-albumen, serum-albumin, and lecithin, and on the catalysis of methyl and ethyl acetates by acid and by alkali, was made by Höber (*Beitr. chem. Physiol. Path.*, *11*, 35). The results obtained by catalysis were quite regular; for instance, the chlorids of the alkali metals accelerated the acid catalysis in the order of their atomic weights, lithium chlorid being most, and cæsium chlorid least, active. In neutral solutions, the order of efficiency as precipitants became irregular, and depended simultaneously on both ions.

On the efficiency of various salts of the alkali metals as lecithin precipitants, see also Porges and Neubauer: *Biochem, Z.*, *7*, 152.

[4] Francis and Fortescue-Brickdale: "The Chemical Basis of Pharmacology," 1908, 86.

on the deprivation of oxygen from the "inogen" compounds in the central nervous system; narcosis is a reducing process. This theory is based on the fact that, in the case of various groups of benzenephenol derivatives, the paralyzing action of the substance is inversely proportional to the amount of oxygen already in the side-chain, and that deprivation of oxygen by breathing inert gases, as carbon dioxid or hydrogen, produces symptoms similar to those of chloroform. Support to the view is had from the work of Herter,[1] who showed that chloroform, ether, and chloral hydrate diminish the oxidizing capacity of tissues. The theory of Baglioni indicates a possible mode of the action of narcotics after they have entered the cell. The other theories mainly pertain to the conditions which determine entrance into the cell substance.

Reicher's Theory.[2]—Reicher carried out a series of experimental studies on anesthetized dogs, in which he invariably found a considerable increase of the fat, or the lipoids, in the circulating blood. From this he drew the conclusion *that the narcotic effect is not due to the fixation of the anesthetic in the lipoids of the brain, but rather to the washing out of the lipoids from the brain.* The Meyer-Overton theory should accordingly be revised. Through the lipemia there occurs a profound impairment of the fat metabolism, which, in its turn, leads to acetone intoxication.[3] Again, the acetone intoxication explains a part of the fundamental disturbances of the nervous system produced by the general anesthesia.

The modification of the Meyer-Overton theory, as proposed by Reicher on the basis of his findings, is as follows: The decisive factor for the efficiency of an anesthetic consists in its relative solubility in the lipoids. There takes place not simply a change of the normal physical condition, not merely a fixation in a sort of rigid solution, without the extrusion of lipoids from the cell; there occurs also an expulsion of vital lipoids and fats, in an as yet unknown mutual action between the anesthetic agent and the cell lipoids, this interaction perhaps playing a part in the occurrence of the general anesthesia; the lipoid remains for a long time chemically and microscopically demonstrable in the blood, as well as histologically demonstrable in the organs.

Kramer's[4] experiments do not bear out Reicher's assumption as to the cause of the lipemia. The explanation of this phenomenon,

[1] Herter and Richards: *Am. J. Physiol., 12,* 207. See also Wright: *J. Physiol., 26,* 362.

[2] Reicher, K.: "Chemisch-experimentelle Studien zur Kenntniss der Narkose," *Zeitschr. klin. Med.,* 1908, *65,* 235.

[3] These results refer to aliphatic derivatives.

[4] "The Rôle of the Lipoids and Particularly Lecithin in Narcosis," *J. Exper. Med.,* 1913, *17,* No. 2.

according to Kramer, is still an open question, for from his observations he concluded:

"1. The intravenous injection of five to thirty cubic centimeters of a 5 or 10 per cent emulsion of lecithin, depending upon the size of the animal used, does not interfere with the induction of anesthesia, and this can be accomplished as readily in animals thus injected as in controls.

"2. In six out of nine experiments lecithin had no effect upon the rapidity with which the various phenomena which indicate the animal's recovery from the effects of the anesthetic appeared."

Gros's Conclusions.[1]—Gros's experimental investigations of *the relationship of general and local anesthetics,* on the basis of physical chemistry, *show that the latter have, in many respects, the same properties and effects as the former.* General anesthetics possess the following three properties:[2]

(1) A general action on protoplasm.

(2) An elective action upon the nervous system, especially the central nervous system.

(3) The possibility of restitution of the functions which have been disturbed by the anesthetic agent.

Bürker's Theory.[3]—According to Bürker, anesthesia is produced in such a way that, in the first place, *the anesthetic agent accumulates especially in the nervous system,* on account of its marked lipoid solubility. This accumulation, as such, does not suffice, but *a chemical reaction results, the anesthetic agent appropriating the active oxygen.* In consequence, this substance is withdrawn from the nervous tissue which is so arid of oxygen, and *this oxygen deprivation leads to temporary asphyxiation, with paralysis of the physiological function.* The products which originate in the oxidation of the anesthetic agent may be considered as partially responsible for the untoward after-effects of general anesthesia.

This theory is based upon the following observation, as well as upon

[1] Gros, O.: "Ueber Narkotika und Lokalanesthetika," *Arch. exp. Path. u. Pharm.,* 1910, *63,* 80.

[2] These three properties are likewise found in the local anesthetics, cocain, eucain, stovain, alypin and novocain, which are protoplasmic poisons. The more strongly a general anesthetic acts upon the central nervous system, the stronger is its action also as a local anesthetic.

The theory of Meyer and Overton is also applicable to local anesthetics. As compared to general anesthetics, the local agents show the important difference that the sensory nervous system is more sensitive toward them, in a general way, than the motor nervous system.

The anesthetic potential of the local anesthetic salt depends on that of the base and the degree of hydrolytic dissociation.

[3] Bürker: "Eine neue Theorie der Narkose," *Centralbl. Physiol.,* 1911, *24,* 103; *Münch. med. Woch.,* 1910, *27,* 1445.

certain other well-known facts: When an electric current is passed through acidulated water, saturated with ether or some other anesthetic agent, only a very small amount of oxygen is liberated at the anode, the remaining oxygen being utilized for the oxidation of the ether, with the production of carbon monoxid, carbonic acid, acetaldehyd, etc. Bürker's experiments, in his opinion, are promising in regard to the rational selection of the anesthetic agents by means of electrolysis; and, at the same time, they elucidate the character of the oxidation processes in the living substance. It is also noteworthy, in this connection, that a $\frac{M}{10}$ solution of grape-sugar (1.8 per cent) has practically no influence upon the course of the electrolysis, in acid and neutral solutions, showing that the active oxygen alone is evidently insufficient for its complete combustion.

The chemical indifference of the anesthetic agents, or a purely mechanical change in the condition of the plasma colloids, in the sense of Meyer and Overton, can hardly be admitted, according to Bürker, whose experiments indicate a temporary asphyxiation of the nervous system, in general anesthesia in the sense of Verworn and his school. The mechanism of this asphyxiation is suggested by the results of the electrolytic experiments. The bad after-effects of general anesthesia are accounted for by the changed metabolism in general, which would be entirely inexplicable in the case of a chemical indifference of the anesthetic agent. The metabolism is altered in a similar way as in diabetes, a disturbance of the normal oxidation processes being probably responsible.

Verworn's Theory.[1]—Verworn, in his recent monograph, contributes the result of his investigations, after ten years' work on the elucidation of the mechanism of anesthetics by means of experiments. On the basis of his findings, he groups anesthesia under the headings of the *manifold paralyses which originate through a disturbance of the oxygen metabolism. General anesthesia is equivalent to asphyxiation of the tissues.* This asphyctic state does not occur in consequence of the deficiency in oxygen as such, but it arises through the inhibition of the oxidation processes by the anesthetic agents. Accordingly, asphyxiation may also occur in the presence of abundant oxygen contents of the medium in the surroundings of the tissue or of the tissues themselves. In asphyxiation through the anesthetic the paralysis is acute; in asphyxiation in a medium free from oxygen the paralysis is more gradual in onset.

In discussing the potential fashions in which the anesthetic, by penetrating into the cell, suppresses its capacity for the production of oxidations, Verworn inclines to the explanation that the anesthetic agent prevents the transmission of oxygen from the medium and the reserve stores

[1] Verworn, M.: "Narkose" (Monograph), Jena, 1912.

in the cell to the oxidizing materials. This explanation is most readily compatible with the laws of lipoid solubility and anesthetic action, formulated by Meyer and Overton; in this connection, Verworn assumes that the lipoids are in some way closely related to the oxygen carriers.

In conclusion, the author explains the difference between sleep and general anesthesia: In sleep, a reaction takes place, with the assistance of the oxygen; whereas, in general anesthesia, the restitution is inhibited through the prevention of the oxygen of the oxidation processes. Hence, these processes are radically different.

Commenting on the view of Verworn, Lillie [1] points out that "cell-division—*e. g.*, in developing egg-cells—usually ceases if the oxygen supply is insufficient. Contractile activities are decreased or abolished. Many organisms, however, show only slight immediate effects; this is true of many Protozoa; Vorticellæ, for instance, remain contractile for some time after simple removal of oxygen from the medium, although they are at once paralyzed by anesthetics. "Such facts oppose the view held by Verworn and others, that the anesthetic acts primarily on the oxidative mechanism of the cell. It is true that the rate of oxidation in active tissues is lowered during anesthesia, but this effect is rather a consequence than a cause of the lessened activity. Obviously wherever free oxygen is necessary to the normal activities of a tissue its withdrawal will arrest those activities. But the effects produced by lack of oxygen are not to be identified with anesthesia because of such incidental resemblances."

The Conclusions of Lillie.[2]—Lillie has indicated that under certain well-defined artificial conditions, as well as under some that are normal, "the living system—organism, tissue or cell—becomes temporarily inactive and irresponsive to stimuli. When such an artificially induced state of inhibition is well marked and lasting it is called anesthesia, or, in a somewhat more restricted sense, narcosis. This condition may last for hours or even days, but apparently not indefinitely; and, when it passes off, the normal vital activities and properties return unimpaired. This apparently complete *reversibility* is one of the most remarkable features of anesthesia, and distinguishes it from death—a perhaps related but characteristically irreversible change. The terms 'anesthesia' and 'narcosis' are somewhat differently applied, although they have the same essential significance; the former relates to any temporarily insensitive condition, however produced, while 'narcosis' usually means an anesthesia produced by chemical substances."

Lillie used the term *anesthesia* to designate *"any temporary or reversible lowering or loss of the normal vital responsiveness, or of the normal automatic vital activity, under the influence of certain artificial sub-*

[1] *Science*, n. s., *37*, 959.
[2] *Ibid.*, Nos. 965, 959-972.

stances or conditions. Anesthesia, as thus defined, may be exhibited by the most various organisms and cells, if not by all. It is fully as characteristic of plant cells as of animal cells, although its manifestations may be less obvious and striking in the former group of organisms. In its most familiar aspect the complete organism, *e. g.*, a man, or an isolated living tissue, as a nerve or muscle, fails during anesthesia to show any response to a stimulus which normally excites it strongly. In other words, the capability of responding to stimuli—what we call 'irritability'—is in anesthesia diminished or lost. When the condition passes off the normal responsiveness returns unimpaired." [1]

However, such decrease of the vital activity or responsiveness is not a solely artificial phenomenon. Conditions physiologically resembling anesthesia occur normally in the life of many organisms; sleep is, for example, a variety of physiological, regularly recurring narcosis, and all irritable tissues lose their responsiveness for a brief period following excitation. The last-mentioned state, the so-called "refractory period," has been compared with narcosis by some physiologists. There are also noteworthy resemblances between narcosis and fatigue. Thus the degree of irritability of a tissue may vary within a wide range under normal as well as artificial conditions.

Lillie calls attention to a number of physical conditions which may deprive a cell temporarily of irritability; for example, mechanical shock and electrical currents may have this effect.[2]

[1] "Thus a muscle exposed to ether vapor soon ceases to contract on stimulation; under the same conditions a nerve ceases to conduct; in motile plants like sensitive plants the characteristic osmotic motor mechanisms cease to act. Automatic activities like ameboid movement, ciliary movement, protoplasmic flowing, cell division, and growth may also be brought temporarily to a rest by anesthetics. Claude Bernard showed that seedlings ceased growth in an ether-impregnated atmosphere, and resumed it when the ether was removed. Fertilized egg-cells cease to divide in the presence of an anesthetic in appropriate concentration, although they remain living and proceed with cell-division and development when the anesthetic is removed. Other less evident cell-processes, including metabolism, are similarly affected; *the rate of oxidation is usually diminished during anesthesia* though there are exceptions to this rule."

[2] "Under certain conditions the electric current may produce effects closely resembling typical anesthesia. (See Chapter XVI, p. 628.) This occurs when a weak constant current is passed through an irritable tissue like muscle or nerve; during the flow of the current the irritability of the tissue is modified in the neighborhood of the two electrodes, being heightened at the cathode and lowered at the anode; and in this latter region the nerve may become completely insensitive to stimuli that ordinarily cause strong excitation. The inexcitable state thus produced is called "anelectrotonus"; it is in reality a form of local anesthesia, and as such has been employed for the alleviation of pain in sciatica and similar conditions. Muscle is affected in a similar manner; the frog's heart may thus be rendered locally incapable of contraction, as in the simple class experiment familiar to all physiologists. This action of the current probably depends on its altering the electrical polarization normal to the

"Irritability may, however, be more readily modified by the use of chemical substances than by any other means, and, as is well known, many such substances are in daily use in medical and surgical practice for procuring local or general insensibility to pain—*hence the application of the name 'anesthetic' to the large class of substances possessing this property.*"

Before considering the mechanism of stimulation and of its modification by anesthetics, Lillie reviewed the most recent conceptions of the nature of the physico-chemical constitution of the living cell. He regards it as clear that the living protoplasm is a "polyphasic system," that is, a mixture consisting of various substances and solutions which are only partly miscible with one another, and are thus interrelated like the different phases of an emulsion or similar system. "These several phases, which are partly solid, partly liquid, appear in each living cell to have a constant and definite arrangement, whose exact nature varies characteristically from cell to cell. There appears typically to be a solid or semi-solid structural substratum consisting of colloidal material, most of which is in a water-swollen or hydrated state; in addition to this more fixed and permanent part of the cell organization, numerous simpler substances are present—sugars, salts, amino-acids and others—largely in a state of simple aqueous solution, but probably partly absorbed at the surfaces of the colloidal phases. There is evidence that it is by the oxidation of certain of these substances, especially sugar, rather than of the colloidal material, that most of the energy manifested in the cell-processes is set free. The colloidal substratum furnishes the conditions under which the energy-yielding oxidations and other metabolic changes take place, and apparently determines their course, character, and velocity. The solid colloidal material of the cell may in one sense be considered as a by-product of the metabolic activities of the protoplasm; it appears, once formed, to undergo itself relatively slight change, but to influence profoundly, by its presence and arrangement, the character of cell-metabolism. The colloids are of varied chemical nature; they are chiefly proteins and lipoids, and it is to be noted that they are built up by various forms of molecular union and polymerization from relatively simple substances furnished by the environment. This is true not only of plants, but also of the individual cells of higher animals, where the material which goes to form proteins reaches the cell in the form of amino-acids, or of simple polypeptides."

membranes of the irritable elements—only in a direction the inverse of that causing stimulation. There is much evidence that the state of polarization of the semipermeable membranes bounding the irritable elements is an important factor in determining the degree of responsiveness to stimulation; the facts of electrotonus indicate that by altering the polarization by an external current the irritability of the tissue may be changed in the direction either of increase or of decrease.''

"However simply organized a cell may seem, there are certain elements of structure which appear always to be present, and to play a fundamentally important rôle in stimulation and in other life-processes. These are the *membranes*. Most, if not all, living cells are delimited from the medium in which they live by thin, semi-permeable colloidal surface-films, the so-called plasma-membranes. Similar semi-permeable partitions are often found in the cell-interior, *e. g.*, about nuclei, vacuoles, chromatophores, and other structures. They appear to be formed of the same colloids as the other protoplasmic structures, namely, proteins and lipoids. These colloids, like many other organic substances, have, when dissolved in water, a marked influence in lowering the surface-tension of the solvent. Any substance thus acting tends, by the operation of Gibbs' principle, to collect or condense on the free surfaces; if the substance is colloidal in nature it may there pass out of solution and form a solid surface-film or membrane; and it is probably under conditions essentially like these that the cell-membranes are formed. Artificial membranes similar in many of their properties to the plasma or nuclear membranes of cells may be formed in protein solutions about droplets of chloroform, mercury or other water-immiscible substances. Now the plasma-membranes of irritable cells undoubtedly play a fundamentally important part in stimulation, as will be seen below, so that it will be necessary to consider first some of the essential properties of these membranes before passing to the consideration of the stimulation-process itself and its modification by anesthetics.

"The plasma-membranes are typically *semi-permeable* structures—so much so that living cells form in many cases the most convenient and rapidly acting osmometers that we possess. Two provisos are necessary in making use of living cells as osmometers: first, the dissolved substance must not by its own action impair the semi-permeability of the membrane, and, second, it must not appreciably penetrate the membrane during the time occupied by the experiment. The plasma-membranes are, in fact, semi-permeable only in relation to certain classes of substances; toward others they show themselves freely permeable, and the character of these substances is important, because indication is thus afforded of the chemical nature of the materials composing the membranes." *This,* in Lillie's opinion, *is a matter of fundamental importance in the theory of anesthesia.*

"The plasma-membrane is characteristically and intimately concerned in the stimulation process. During stimulation it appears to undergo a sudden and quickly reversible increase of permeability. The electrical variation is one expression of this change, but there are others as well. Thus the movements of sensitive plants, which occur under the same conditions of stimulation as those of irritable animal tissues, are due to a collapse of turgid cells, consequent upon a sudden loss of the semi-permeable properties of the plasma-membranes enclosing the osmotically active solution or cell-sap. Here at least is one irritable tissue where the connection between permeability increase and stimulation seems unmistakable."

With regard to why anesthetics interfere with the stimulation-process, Lillie pointed out that in the first place they can be shown experimentally to interfere with both of the characteristic manifestations of stimulation, (1) the action-current and (2) the change of permeability. If these are the critical or primary events on which the other effects following stimulation depend, it is evident that suppression of these must involve a suppression of the entire series of processes resulting from stimulation, including the oxidations, the contraction-changes and the other special features of the response.

That the action-current as well as the mechanical response of a muscle is suppressed by anesthetization has long been known. In nerves also, anesthesia abolishes the action-current. On the foregoing hypothesis, the electrical variation is the expression of some alteration in the plasma-membrane, involving a temporary increase of permeability. Höber [1] has found that potassium salts, which deprive nerves of irritability and render them locally negative, cause at the same time a visible alteration in the axis-cylinders; these structures swell and stain more diffusely; he found further that these effects are checked or prevented if the nerves are first anesthetized with ethyl urethan. Experiments on voluntary muscle gave analogous results. If a frog's muscle is partly dipped into an isotonic solution of a potassium or rubidium salt the tissue contracts somewhat and becomes locally negative; this effect is also inhibited or retarded in the presence of an anesthetic. If the local negativity is the expression of a change produced by the salt in the colloids of the plasma-membrane, rendering the latter more permeable than before, Höber's results indicate that the anesthetic decreases the susceptibility to such changes of permeability. If this is the case we can partly understand why the anesthetized tissue becomes less susceptible to stimulation, since stimulation involves an increase of permeability.

Lillie concluded that, if an anesthetic acts by so modifying the plasma-membrane of the irritable cell as to render difficult or impossible the rapid variations of permeability which are essential to stimulation, "it ought to act similarly on other cells, *i. e.*, it should protect these cells also against the action of permeability-increasing substances or agencies. If an organism can be found whose cells undergo immediate and obvious increase of permeability under conditions which at the same time cause stimulation, it should become possible to determine whether suppressing the stimulating action of a given agency is equivalent to a suppression

[1] See page 46.

of its permeability-increasing action. The two effects ought to show a definite parallelism if the above hypothesis is well based."

Lillie investigated the antagonism between salts and anesthetics,[1] and his results may be summarized as follows:

1. In the action of pure isotonic sodium chlorid solutions on *Arenicola* larvæ the most evident effects are: (1) strong stimulation of the musculature, causing intense and prolonged contraction; (2) increase in the permeability of the pigment-cell membranes sufficient to allow visible exit of pigment; (3) immediate arrest of ciliary movement, followed by disintegration of the cilia; and (4) a general toxic action.

2. In the presence of a large number of anesthetics, in concentrations corresponding to those producing typical neuromuscular anesthesia in sea water, all of these characteristic immediate effects of the pure salt solution are diminished or prevented.

3. In general, the permeability-increasing action and the stimulating action of the salt solution undergo closely parallel decrease or prevention in the presence of the anesthetic. Prevention of sudden permeability increase thus seems equivalent to prevention of stimulation; it is also equivalent to prevention of the immediate toxic action of the solution. The anti-stimulating and the anti-cytolytic effects of the anesthetic thus show a definite parallelism.

4. *In anesthesia the essential effect is a temporary alteration in the condition of the surface films or plasma membranes of the irritable elements, of such a kind that these membranes no longer undergo, under the usual conditions of stimulation, the rapid increase of permeability essential to this process.*

5. *The membranes thus become during anesthesia increasingly resistant to permeability-increasing agencies:* this involves increased resistance to those forms of toxic action which depend on destruction of the normal semi-permeability of the membranes. Hence the association of an anti-cytolytic or antitoxic action with the anti-stimulating action of the anesthetic. The observations made by Lillie also indicate that the degree of resistance of the membranes, and of other colloidal structures like cilia, is intimately dependent on the state of their component lipoids.

Conclusions.—It appears to be established beyond doubt that the anesthetic is in solution in the blood during narcosis,[2] and the thorough

[1] *Am. J. Physiol.*, 1913, *31*, No. 5, 255. See also *Science*, n. s. *37*, Nos. 959, 764.

[2] The investigations of Tissot (*Compt. rend.*, *142*, 234) show that in animals rapidly anesthetized by chloroform the amount present in the blood may exceed 50 mg., more than 70 mg. per 100 c.c., and may even reach 70 to 80 mg. If, however, the anesthesia is slowly induced, it sinks to 45 or even 35 mg. More than 70 mg. per 100 c.c. of arterial blood often causes death. Tissot found that the amount in venous blood is always less than in arterial blood. His

investigations of Moore and Roaf strongly point to the fact that an unstable compound is formed with hemoglobin, just as occurs in the case of proteid. It is probable that, in every case, anesthesia occurs when the unstable compound parts with the anesthetic to the cell proteids, and that penetration of the cells by virtue of the anesthetic to the cell lipoid occurs simultaneously. In this way, the relative power of the various anesthetics may be explained, for narcotic action is here dependent upon solubility in blood, stability of the compound, if any, formed with hemoglobin, rapidity of penetration of the cells, and nature of the solution in the cell lipoids.

EFFECTS OF INHALATION ANESTHETICS UPON VARIOUS PARTS OF THE ORGANISM

When a volatile agent such as chloroform, ether, ethyl chlorid or nitrous oxid is inhaled, the first action, naturally, is upon the respiratory system. Passing from the air vesicles of the lungs into the pulmonary blood stream, the general anesthetic now acts upon the nervous mechanism, and, through this, upon the muscular and glandular structures, the entire organism thus becoming more or less profoundly influenced. It is readily conceivable that the effects upon these interdependent vital functions cannot be considered as isolated phenomena, but must be dealt with as correlated features of the complete mechanism of anesthesia.

It is easily understood that it is impossible to trace the effects of the agent in successive steps and in a manner that is applicable to all cases. The phenomena may vary more or less with the agent employed, with the subject anesthetized, with the method of administration, and with various conditions. For these reasons, the discussion of the physiological action of general anesthesia upon the human subject must of necessity be general. The more specific action of the individual agents is given further consideration under the respective subjects. It is to be understood, furthermore, that the phenomena observed are those of a clinical character, rather than those noted by the experimental physiologist.

Effects upon the Respiratory System.—The effect of anesthetic agents upon the respiratory system may be considered under two heads:

(1) The primary or local action of the agent upon the upper respiratory passages.

(2) The secondary or general action upon the respiratory system, resulting from the stimulation of the respiratory center, and from the effect upon the muscular system, produced by the circulating anesthetic.

Local Effect.—The direct action of the inhaled anesthetic upon the

work seems to explain satisfactorily the cause of chloroform poisoning, especially when considered in conjunction with the work of Moore and Roaf.

respiratory passages may cause coughing, a sense of suffocation, and temporary suspension of respiration ("holding the breath").

General Effect.—This varies with the agent employed, the method used, the subject anesthetized, and other factors; it also varies with the stage of anesthesia.

Ordinarily, particularly where the local effects are inconsequent, normal respiration becomes deeper as the respiratory center is more and more profoundly influenced by the circulating anesthetic, and more rapid if an asphyxial element enters. During the earlier stages of anesthesia breathing may be interfered with by psychic impulses. This is particularly apt to be the case with nervous, excitable subjects, and those who, through fear, resist the action of the anesthetic. With nitrous oxid or other agents so administered as to cause a pronounced exclusion of oxygen from the respiratory apparatus, there is apt to be exaggerated or stertorous breathing, and the muscles of respiration are prone to assume a condition of tonic or clonic spasm. (See Effects upon the Muscular System.) There may be temporary suspension of respiration (apnea), due, according to recent researches,[1] to a fall of carbon dioxid pressure in the respiratory center, while the oxygen pressure is still sufficiently high not to give rise to excitement of the respiratory center. This condition, sometimes called "physiological apnea," may merge into true asphyxia in the event of "pushing" the anesthetic or of allowing undue physical constriction in any part of the respiratory tract.

It is to be borne in mind by the anesthetist that the rate, rhythm, and amplitude of respiration are subject to various modifications by traumatic, thermal, and electrical stimuli.

The interpretation by the administrator of the various respiratory sounds is discussed under administration.

Effects upon the Circulatory System.—The effects of the anesthetic agent upon the *blood* itself, upon the *heart,* and upon *blood pressure* vary with the drug employed. The circulatory changes which are more or less characteristic in the different anesthetics will be considered more in detail under the special physiology of each agent.

Experimental physiologists are not agreed concerning the various factors which influence the circulatory mechanism during inhalation anesthesia, nor are they agreed with reference to the effects of the anesthetic agent upon the blood itself. Certain data are sufficiently well established, however, to be of practical value, and to these attention will be confined.

The only changes produced in the chemical composition of the blood by the circulating anesthetic, according to many physiologists, are those arising from a diminished supply of oxygen. It has been claimed, however, by other investigators, that the hemoglobin content of the red

[1] *J. Physiol., 32,* 225.

corpuscles is markedly decreased; that there is destruction of the red corpuscles (DaCosta), and that the urobilinuria which may occur two or three days after anesthesia is probably the result of this destruction. It is also claimed that lecithin and cholesterin are increased, fat, according to Reicher, being increased up to two or three times the normal amount. Disintegration of the fat and albuminoid bodies is sufficient to lead to the increased secretion of acetone. The specific gravity of the blood commences to rise shortly after the beginning of the operation, the increase continuing for several days thereafter, according to observations made by Sherrington and Copeman [1] on healthy animals.

Poggiolini [2] investigated the morphological changes of the blood, in ether and chloroform narcosis, in a series of experiments on healthy rabbits. The different results which have so far been obtained in the examination of the influence of ether or chloroform narcosis upon the blood are referred by him to the fact that the influence of existing diseases, of the operation itself, and of the binding of the animal have not been sufficiently considered. His experimental findings led him to the following conclusions:

The changes of the blood constituents, noted after ether or chloroform narcosis, are independent of the duration of the narcosis, of the quantity of the narcotic, of the frequency of the narcosis, and of the time-interval between the individual narcoses. Deep narcosis, with ether or chloroform, induces leukocytosis, of variable duration and degree. At the same time, the relative composition of the leukocytes is changed, either the lymphocytes or the neutrophile polynuclear cells undergoing an increase. The change of the leukocyte picture persists for a longer time in chloroform narcosis than after ether narcosis. The red blood corpuscles and the hemoglobin present rather variable changes, independent of each other, after the two narcoses. However, after chloroform narcosis there are regular destructive and retrogressive changes of the red blood corpuscles, which are absent after ether narcosis. Accordingly, inhaled chloroform appears to be more toxic, and of a more prolonged action, than ether, in the opinion of Poggiolini.

The psychic state influences the circulation in the initial stage of anesthesia, as manifested by pallor, lividity, syncope, and even death. The cardiac and vasomotor centers are more or less frequently influenced in such cases, these exigencies being more apt to occur in nervous and excitable patients, particularly those who are frightened before beginning the inhalation.

Just as the efficient function of the respiratory system during anes-

[1] Sherrington and Copeman: "Variations Experimentally Produced in the Specific Gravity of the Blood," *J. Physiol.*, 1893, *14*, 52. See section on "Shock."

[2] Poggiolini: "Le modificationi morphologiche del sangue nella narcosi eterea e nella cloro-narcosi," *Il Policlinico*, 1911, Sez. Chir. *18*, 3-5.

thesia is dependent, in part, upon the circulatory system, so is the proper condition of the circulation dependent upon respiration. Obstruction of the respiratory passages, however slight, has its concomitant circulatory disturbance. A slight degree of obstruction gives rise to a corresponding degree of venous congestion, manifested by freer bleeding at the site of operation, and perhaps by the swelling of the tongue and adjacent parts, these changes being greater in some subjects than in others.

The action of the anesthetic upon the heart may be primary, but, as a rule, it is secondary. The muscles of the heart, as well as those of the arterioles, are directly affected by the anesthetic, the effect varying according to the particular agent, the method of administration, and the extent to which it is carried. The effect may be that of direct stimulation (as with ether) or of direct sedation (as with chloroform).

Changes in the blood pressure are dependent upon the anesthetic employed and the body position. With nitrous oxid there is a marked rise in blood pressure; with ethyl chlorid there is, according to some observers, a slight rise, according to others none; with ether there is first a rise and then, with deep narcosis, a slight fall; with chloroform there is, according to universal agreement, a fall in blood pressure. The mechanism of the rise or fall is a disputed point. Some physiologists have maintained that the fall is the result of direct vascular dilatation; others hold that it is due to dilatation of nervous origin. Recent experiments tend to establish the correctness of the former view.

Various other factors influence the circulation during anesthesia, such as hemorrhage resulting from the operative procedure, the position of the patient, deep breathing, and positive pressure. According to Eppinger and Hofbauer,[1] "the pulse in patients whose diaphragm was unusually high or low showed that the circulation in the legs was better when the diaphragm was high, as the quadrate foramen was thus left open. When the diaphragm is low, this foramen is more squeezed together and the flow of blood up from the lower part of the body is thus impeded. At the same time, deep breathing pushes the diaphragm low down and it thus presses on the liver and liver veins and thus promotes the circulation in the region."

Effects upon the Muscular System.—The effects of inhalation anesthetics upon the muscular system may be considered under two headings:

(1) *Direct*, which are of interest to the experimental physiologist rather than to the practical anesthetist, inasmuch as they involve the direct contact of the muscle with the anesthetic agent, a contingency which does not normally arise in clinical work.

(2) *Indirect*, which are of nervous origin.

The indirect muscular phenomena of general anesthesia are almost

[1] "Kreislauf und Zwerchfell," *Zeitsch. f. klin. Med., 72,* No. 1.

entirely controllable by certain methods of administration, to which reference will be made in detail later. Under these circumstances, namely, the administration of oil of bitter orange peel as a preliminary to the anesthetic agent, the conscious voluntary movements of the preliminary stages of narcosis are practically held in abeyance. The uncontrollable muscular movements in the stage of excitement are absent because there is no such stage. Subconscious purposive movements and simple tonic spasm, local or general, are not noted. The coördinated movements sometimes noted in deep anesthesia as ordinarily induced are absent, as are likewise the tremors of moderate narcosis.

The usual conscious, subconscious, and unconscious movements, the tremors and clonic spasms noted during the administration of any of the inhalation anesthetic agents, or the ordinary combination of these, are more or less completely held in abeyance by the action of oil of orange, administered as a preliminary to these agents. (See Preceding the Administration with Oil of Bitter-Orange Peel, p. 91.) For further details concerning effects upon muscular system, see Special Physiology of each agent.

Effects upon the Glandular System.—The effects of general anesthetics upon the glandular system may be considered under two heads:

(1) The immediate effects, or those noted during the administration.

(2) The secondary, or after-effects, or those observed after the subsidence of anesthesia, when the anesthetic agent is no longer circulating in the blood.

Both the immediate and the after-effects vary with the anesthetic agent, with the method of administration, with the degree to which narcosis is carried, and with various other factors to be discussed more in detail under the special physiology of each anesthetic.

The immediate effects involve particularly the mucous, salivary, sweat, and lachrymal glands. The secretion of mucus and saliva is greater during light and moderate narcosis, whereas it is decreased during the deeper stages. The same holds true with lachrymation with all the general anesthetic agents. The sweat glands are more or less affected in the various stages of narcosis by the different anesthetics. In the presence of cyanosis or severe shock with any agent, the sweat glands become hyperactive, as evidenced by the "cold perspiration" which subsides with the restoration of proper respiration and circulation.

Renal function is interfered with during the administration, according to some observers, being increased up to the point at which the corneal reflex disappears and completely arrested during profound anesthesia. This decreased secretion of urine during the administration may continue to the point of complete suppression, resulting in death. Various intermediate degrees of suppression and concentration, with increased chlorids, phosphates, urea, casts, and albumin in greater or less quantity, have been noted, the urine gradually returning to normal within a week after the anesthesia.

These observations apply to chloroform and ether. The occurrence of albuminuria during the administration of inhalation anesthetics is said to occur with some of the agents and not with others.

Fatty degeneration of the liver, kidneys, heart, and other organs may occur, particularly after repeated administrations of chloroform, unless safeguarded by heat, moisture, oxygen, and rebreathing, together with enemas of normal saline, olive oil, and glucose.[1]

Effects upon the Nervous System.—The sequence in which the parts of the nervous system are involved in the production of general anesthesia is still the subject of discussion among experimental physiologists as well as practical anesthetists. English and American investigators hold that the cerebral cortex is first involved; the basic ganglia and cerebellum,[2] second; the sensory centers of the cord which connect the brain with the periphery, third; the cerebro-spinal motor tracts and centers, fourth; and the respiratory, vasomotor, and cardiac centers of the medulla, fifth. Inhibition of all functions, and death, follow. According to Dastre and other French observers, the sensory nuclei of the cord or the cerebral ganglia are affected before the cortical centers are involved.

The order in which the special senses are affected by the general anesthetic cannot be definitely stated. The majority of observers seem to be agreed that sight is lost before hearing, and that taste persists longer than either of these. With nitrous oxid, hearing is the last sense to disappear and the first to reappear. The sense of smell is very easily lost, as is witnessed in the effect of oil of bitter orange peel, to which reference has been made.

The reflex phenomena of general anesthesia may occur during any stage of narcosis, from the beginning of the induction period to the period immediately preceding inhibition of respiration. They vary considerably with different patients.

The reflex circulatory phenomena are of special importance from a practical point of view. They may arise during all stages of anesthesia, and they may vary in intensity from slight reflex vasomotor stimulation

[1] See Chapter on Treatment, Preliminary, During, and After Anesthesia.

[2] Francis and Fortescue-Brickdale ("The Chemical Basis of Pharmacology," 1908, 81) state that the physiological action of the entire group of aliphatic narcotics is first on the higher centers of the cerebrum, then on the lower centers of the medulla and cord. Eventually, continue these authors, the reflexes are completely abolished, and this constitutes an important distinction between this group and the alkaloidal narcotics, of which the principal representative is morphin. In large doses morphin increases reflex irritability, and in small doses does not depress it.

or inhibition, with consequent rise or fall of blood pressure during the earlier stages, to profound circulatory shock during the stage of deep narcosis. They vary with the anesthetic employed, being more commonly manifested with chloroform than with ether; with the method of administration, being largely eliminated by the modern methods (see Chapter VIII); with the degree to which the anesthesia is carried; and with the state of the nerve centers (vasomotor, cardio-inhibitory, cardio-accelerator) acted upon by the anesthetic agent.

Reflex circulatory disturbances of a serious nature, occurring during the earlier stages of anesthesia, before consciousness is entirely lost, are often of psychic origin. It is important, for this reason, that the surgical procedure be not commenced until anesthesia is complete.

The occurrence of circulatory shock after the induction of general anesthesia has been the subject of much serious investigation, the work of Crile [1] being particularly noteworthy.[2]

Reflex respiratory phenomena are more frequently present during the lighter than during deeper degrees of narcosis. It is to be borne in mind, however, that the psychic stimuli of the conscious stages of anesthesia may give place to the traumatic stimuli of the stage of surgical anesthesia. These stimuli, applied in any part of the body, may cause reflex spasmodic movement of the tongue, whereby this organ is drawn over the laryngeal orifice, giving rise to laryngeal spasm, respiratory and expiratory spasm, coughing, retching, and stertorous breathing.

When these phenomena assume a serious and menacing character, the condition is described as "respiratory shock." This is most apt to supervene during moderate anesthesia.

FACTORS WHICH MAY BE SAID TO MODIFY THE PHYSIOLOGY OF ANESTHESIA AS ORDINARILY INDUCED

It has been suggested [3] that the phenomena resulting from the administration of inhalation anesthetic agents more properly come under the head of pathology than of physiology. However this may be, certain it is, as elsewhere stated, that practically every phenomenon varies with the particular anesthetic agent administered, with the general condition of the patient, with the condition of the blood, and with various other factors.

For these reasons, it has been deemed advisable to consider here certain factors which, introduced into the administration of inhalation anesthetics, may be said to modify, to a more or less pronounced degree,

[1] Crile, G. W.: "Surgical Shock." Also, *Boston Med. and Surg. J.*, March, 1903.

[2] Chapter on Treatment, p. 41.

[3] Wright, Hamilton: *Loc. cit.*

some of the phenomena ordinarily observed, and commonly considered under the head of physiology. These factors are:

1, Warming the agent; 2, utilizing moisture; 3, combining oxygen with the agent; 4, preceding the administration with oil of bitter orange peel; 5, utilizing carbon dioxid; 6, rebreathing.[1]

The consideration of these factors, particularly the first, necessarily involves the introduction of a certain amount of technique, which, of itself, would no doubt more properly come within the chapter on Administration, or perhaps Special Physiology. The following discussion may be considered, therefore, as an addendum to General Physiology.

Warming the Agent.—The value of warmed anesthetics has been recognized by many anesthetists since Clover [2] devised his double-current apparatus, by means of which the expired air warmed the anesthetic agent. Since that time various attempts have been made to deliver to the patient warmed ether or other agent,[3] but in each instance the apparatus was found to be inadequate, too complicated for practical use, or otherwise unsatisfactory.

It was not until 1905, however, that systematic laboratory experiments and clinical observations were begun,[4] with a view to determining the relative value of the various inhalation anesthetics when these are administered cold and when they are warmed to the temperature of the blood (98.6° F.). These observations were made by Gwathmey particularly with reference to: (1) safety as regards life; (2) the maintenance of body temperature, and the consequent lessening of the danger of shock; (3) recovery from the anesthetic; and (4) after-effects. Other phenomena were also noted.

Safety to Life.—First, with chloroform: In order to determine the value of chloroform as regards life when heated to 100° F. and at room temperature, Gwathmey [5] made a number of experiments, using compressed air and passing this air through chloroform at room temperature and then to a special animal mask, using a Junker inhaler for the chloroform. He found that it took 6.57 minutes on the average to kill sixteen animals. Employing the same technique with the addition of another Junker inhaler, filled with warm water and placed in a warm receptacle between the chloroform and animal mask, he found that the average time required to kill seventeen animals was 20.35 minutes,[6] thus

[1] Chapter on Rebreathing.

[2] Clover: *Brit. Med. J.*, March 15, 1873, 282; July 15, 1876, 74; Jan. 20, 1877.

[3] (1) Hawksley: *Brit. Med. J.*, Aug. 2, 1873, 177. (2) Foy: "Anesthetics, Ancient and Modern," 141.

[4] Gwathmey: *Med. Rec.*, Oct. 14, 1905; *N. Y. Med. J.*, Feb., 1908; *J. Am. Med. Assn.*, Oct. 27, 1906; *Am. J. Surg.*, July, 1908. See also Coburn: *Med. Rec.*, March 1, 1913.

[5] For technique, see p. 317.

[6] See table, p. 64.

showing that chloroform at blood temperature is three times as safe as chloroform at room temperature.

TIME REQUIRED TO KILL ANIMALS WITH CHLOROFORM AND AIR

No. of experiment	No. of minutes required to kill at 100° F.	No. of minutes required to kill at normal temperature
1	18	4.5
2	57	3
3	26.5	7.5
4	24.5	7
5	15	4
6	16	4
7	15	3.5
8	8	7.5
9	13	9
10	22	5.5
11	12	7
12	17	10
13	21	6
14	25	9
15	27	10
16	17	7.5
17	12	....
	17)346	16)105
	20.35	6.57

Second, with nitrous oxid and oxygen instead of chloroform, and passing the mixed gases through a tube, first at room temperature, and then surrounding the tube with hot water, and, last, surrounding the tube with ice, and in all instances measuring the temperature accurately by a thermometer placed in a bent tube, using the same animal mask and giving all animals first six per cent of oxygen with nitrous oxid for five minutes, and then reducing the amount of oxygen to three per cent, the following results were obtained: Twelve animals were anesthetized and killed by nitrous oxid and oxygen at room temperature. The average time for the eye and extremity reflexes to be abolished was 4 minutes. The average time required to kill was 9 minutes and 20 seconds. The shortest time was 4 minutes and the longest 12 minutes. Nine of these animals struggled violently until anesthetized; two were quickly asphyxiated; one weakling remained quiet after two minutes. In all cases, heart action, rapid at the start, ran from 150 up to 200 during the frightened struggles; as anesthesia progressed, it again became irregular, with marked second sound accentuation, and very rapid and weak just before death. The respiration in all cases was irregular, and gasping to variable degrees. In all cases tonic convulsions occurred just before death. In 25 per cent of the cases convulsions occurred during the first three to five minutes (probably anoxemic);

continuation of heart action after respiration ceased: average time, 2 minutes; longest, 3 minutes; shortest, 1 minute.

Twelve animals were anesthetized with warm nitrous oxid and oxygen by having the tube containing the mixture of gases passed through a hot water bath kept at a temperature of 98° C. The same proportions were used as in the administration of the cold gases. In all other respects the technique was the same as far as the experimenter could possibly make it.

Abolition of Reflexes.—Two animals (weaklings), anesthetized with 6 per cent oxygen mixture, lost their reflexes at the end of 5 minutes; 6 animals had reflexes abolished with the 3 per cent oxygen mixture in 12 to 25 minutes, the average time being 18 minutes. Four were not anesthetized at the end of 30 minutes. After the removal of the inhaler, 2 were able to walk in from one to two minutes. The other 2 were killed. Eight animals were killed by the anesthetic; the average time was 18 minutes. Four were in good condition at the end of 30 minutes; two were disposed of as noted above; and two were put away for future work. The shortest time was 12 minutes; the longest time, 28 minutes. Eight struggled from 1 to 3 minutes because held, and the remainder did not struggle after the first few breaths.

Heart Action.—After preliminary excitement, action was regular in force and frequency until death approached, when it became rapid and weak.

Respiration.—In all cases respiration was quiet and regular after the first few minutes, becoming gasping just before death.

Convulsions.—No early convulsions occurred. Mild tonic convulsions occurred just before death. Continuation of heart action after cessation of respiration: average, 3½ minutes; shortest, 2 minutes; longest, 5 minutes.

The third series of experiments was conducted in precisely the same manner as the first two, as regards technique, percentage of oxygen, etc., with this difference: the tube containing the mixture of gases passed through a vessel packed in ice. The U-shaped tube containing the thermometer was also packed in ice. The thermometer did not vary from 33° to 34° F. during the administration. Ten animals were killed. The results were as follows: After eight to ten breaths of this cold mixture, violent struggling ensued and breathing ceased almost immediately. Fibrillary twitchings greatly resembling a chill occurred in all animals after the first minute of inhaling the mixture. The average time required to kill was 5 minutes and 34 seconds, or about 4 minutes less than at the normal temperature, and 13 minutes less than the 8 animals killed by the warmed gases. The shortest time was 3 minutes and 55 seconds; the longest time, 7 minutes.

From the above, it will be seen that warmed nitrous oxid and oxygen is much safer than using this mixture of gases at the room temperature, and very much safer than the cold gases.

The following case history illustrates very clearly the difference between cold and warm nitrous oxid and oxygen as observed in the human subject. A large number of similar histories could be cited.

Female. Age, about 45 years. April 19, 1907. Patient was given 1/4 grain of morphin and 1/150 grain of atropin thirty minutes before the operation. Operation (laparotomy) lasted two hours, during the whole of which time the patient was kept under the influence of nitrous oxid and oxygen, without the aid of any other anesthetic. A fibroid tumor weighing thirty-five pounds was removed. At the end of one hour the anesthetist's (J. T. G.) gas tanks became exhausted, and he was compelled to use the hospital tanks, which unfortunately were of such size and condition that he could not use his hot-water attachments. As soon as he began using the cold gases, the respirations showed a marked decrease in number and were slightly labored, but, with this exception, the narcosis was entirely satisfactory, the patient making an uneventful recovery and without nausea or vomiting.

Third, with ether: Only a few experiments were conducted with ether, but the number was sufficient to fully convince one that warm ether acts similarly to warm chloroform and warm nitrous oxid; that is, it is twice as safe, as shown by the fact that it took over twice as long to kill the animals with warm ether vapor as with cold.

Fourth, with ethyl chlorid: We have made no experiments with warm ethyl chlorid, but by analogy we may conclude that, as chloroform, ether, and nitrous oxid are increased in value by heat, the value of ethyl chlorid would likewise increase.

From the animal experiments with the different anesthetics, i. e., chloroform, ether, and nitrous oxid and oxygen, first at the room temperature, and then heated to the temperature of the blood, and finally with nitrous oxid and oxygen at + 33° to + 34° F., we conclude that all anesthetics heated to the temperature of the blood are increased in value as regards life, without decreasing their anesthetic effect. From these experiments it is also evident that to these highly sensitive creatures the warm gases were much pleasanter to inhale. From clinical experience it can be stated positively that the facts learned in the laboratory are beyond all question true also in practice.

The Maintenance of Body Temperature.—A large number of observations have been made with reference to the effect of narcosis upon the body temperature.[1] The loss of body temperature observed in all

[1] Kapeler: "Anæsthetica," *Deut. Chir.*, 1880, 33, 168; Hare: "Experiments to Determine the Influence of Etherization on the Normal Bodily Temperature, etc.," *Therap. Gaz.*, 1888, *12*, 317; Dastre: "Les anesthétiques: physiologie et applications chirurgicales," Paris, 1890; Allen: "Effect of

instances, both in the experiments upon animals and in clinical observations upon the human subject, has been variously explained as being due to diminution of oxidation, to radiation of heat from uncovered portions of the body, to the effect of the anesthetic agent upon the regulatory centers, to the increased output of heat in consequence of dilatation of the cutaneous vessels, etc.

Whatever the cause of this loss of body temperature, it is interesting to note that even a fraction of a degree of elevation of temperature of the anesthetic agent above that of the room will have a marked effect in maintaining the body temperature of the patient. The author's observations in this regard have been amply verified by those of Davis,[1] both upon animals and upon human subjects.

In twenty-six patients anesthetized with warm ether vapor, there was a loss of body temperature averaging .29° F. as against the loss of 1.02° F. in one hundred and forty cases anesthetized under similar conditions with the open drop method. The shortest period of anesthesia in which the temperature was noted was forty minutes, the longest four and three-quarter hours. The temperature was taken by rectum immediately before starting and immediately after the removal of the anesthetic.

These experiments of Davis upon human beings undergoing surgical operations are most conclusive. The practical application of this lies in the fact that in the majority of instances the patient's temperature is necessarily lowered by the surgical operation, and also by the anesthetic as usually administered.

In this connection it may be well to emphasize the fact, mentioned by Davis,[2] that an undue elevation of the body temperature, as a consequence of employing a warmed anesthetic agent or as a result of other measures, may prove injurious. In one of his animal experiments the body temperature of the subject was elevated by means of an electrothermal pad and blankets. There was a rise of 4.14° F. in one and three-quarter hours, at which point death suddenly occurred. An overdose of ether was a presumptive factor, but the chief factor was thought to be this great increase in temperature.

The following are the charts of two human subjects, in which death was supposed by Davis to have been caused by giving a warmed anesthetic for too long a time. In the second case, that of a child five months old, it would seem that the shock from too long an anesthetic

Anesthesia upon the Body Temperature and Blood Pressure,'' *Trans. Am. Surg. Assn.*, 1896, *14*, 367; Morley: ''The Effect of Anesthesia upon the Body Temperature,'' *Am. Gynecology*, 1903, No. 3, 300.

[1] Davis: ''On the Effect of Narcosis upon the Body Temperature,'' *Johns Hopkins Hosp. Bull.*, April, 1909, 118.

[2] *Loc. cit.*

and not the warmed ether vapor was the immediate cause of death. The following are the records:[1]

CASE 1

Date—October 7, 1908.

Name—H. G.
Address—Johns Hopkins Hospital.
Age—35. *Sex*—M.
Surgeon—Cushing.
Operation—Cerebellar Exploration.
Anesthetic—Ether Vapor Warmed. *Method*—Open.
Amount—225 gm. *Duration*—3 hours.
Temp. before anesth.—38. *Narcotics*—None.
Temp. after anesth.—40.44. *Stimulants*—None.
Temp. operating room—31.1 *Complications.*

Temperature two hours after the anesthetic, 41.3°. Patient died one hour later.

CASE 2

Date—May 29, 1908.

Name—C. C.
Address—Johns Hopkins Hospital.
Age—5 M. *Sex*—M. *Weight*—
Surgeon—Cushing.
Operation—Spina Bifida.
Anesthetic—Ether Vapor Warmed. *Method*—Open.
Amount—50 gm. *Duration*—$2\frac{1}{4}$ hours.
Temp. before anesth.—38. *Narcotics*—None.
Temp. after anesth.—39.8 *Stimulants*—None.
Temperature operation room—29.5.

Complications

Anesthesia ended 5.00 p. m., Temperature, 39.8.
5.30 p. m., Temperature, 40.5.
6.00 p. m., Temperature, 40.1.
6.30 p. m., Temperature, 40.2.
7.00 p. m., Temperature, 40.5.
7.30 p. m., Temperature, 40.8.
8.00 p. m., Temperature, 41.4.
Died, 8.25 p. m.

It may be interesting in this connection, before considering the question further, to note some observations concerning the temperature stimulus as applied to certain agents.

[1] Private communication from Dr. Davis.

Hoffmann,[1] in his discussion of the cooling-off of the inspired air and its causative connection with post-operative pulmonary affections, says that, in the ether-drop-anesthesia according to Witzel, there occurs an automatic regulation of the ether contents of the inspired air. This self-regulation is brought about through a considerable refrigeration of the temperature of the inspired air. This cooling can be avoided without disturbance of the automatic regulation, by the utilization of a suitable mask.

Stursberg[2] discussed the behavior of blood pressure under the action of temperature-stimuli in ether and chloroform anesthesia, as well as its bearing upon the occurrence of subsequent complications. In ether narcosis it will be found that a cold stimulus is followed by vascular contraction, possibly without a later reactive dilatation, thus supplying the conditions for "catching cold."

The action of chloroform, Stursberg found, is not generally followed by extensive vascular contraction on the refrigeration of the skin; consequently, the distribution of the blood is not altered in the sense of an induced hyperemia of the internal organs, which does away with a condition favoring the origin of "colds."

Recovery from the Anesthetic.—With the idea of testing the influence of heat upon the *recovery* of the subject from the anesthetic, Gwathmey anesthetized three animals at the same time, under glass receptacles, for ten minutes, afterward placing them in receptacles, one at 0° F., another at 100° F., the third being allowed, as a control, to come out in the room temperature. The animals were changed in position on three successive days. In each instance, the animal in the warm chamber made a slightly more rapid recovery than the others. The animal in the cold box came out in chills, while the one in the room temperature came out a close second to the one in the warm box.

With reference to human beings, it may be stated that, by applying hot towels to the patient's face, or by aerating the lungs with hot air toward the close of any anesthesia, the patient recovers quickly from the anesthetic.

It will thus be seen that recovery from the anesthetic is facilitated by the natural inhalation of warmed atmospheric air, or by the artificial introduction into the lungs of a current of warmed air. Experimental and clinical observations have abundantly verified these findings with reference to the use of warmed anesthetics.

[1] Hoffmann, M.: "Ueber die Abkühlung der Inspirationsluft bei der Aethertropfnarkose, ihre Bedeutung und ihre Verhütung," *Mittlg. a. d. Grenzgeb. d. Med. u. Chir.*, 1910, *21*, 869.

[2] Stursberg, H.: "Ueber das Verhalten des Blutdruckes unter des Einwirkung von Temperaturreizen in Aether und Chloroform Narkose," *Mittlg. a. d. Grenzgeb. d. Med. u. Chir.*, 1911, *22*, 1.

After-Effects.—A great deal has been written, by many investigators, concerning the immediate and delayed after-effects associated with inhalation anesthesia. Observations made by Clover and others of the earliest workers in this field tended to prove that the after-effects are lessened when a warmed vapor is used. Subsequent laboratory experiments and clinical observations have amply verified these findings.

A warmed vapor (provided it is not too warm) gives rise to less irritation to the air passages, and thus decreases the danger of post-anesthetic bronchitis and pneumonia.

The warmed vapor, being less irritating to the buccal mucous membranes, causes less stimulation of the salivary and mucous glands, and consequently there is a less profuse secretion of saliva and mucus than is apt to occur when cold vapor is administered. The anesthesia, therefore, is accompanied and followed by less nausea and vomiting than occur as a consequence of the hypersecretion of these nauseating fluids when a cold vapor is employed. This observation is particularly striking with ether.

The late after-effects, such as acid intoxication and its consequences, have received voluminous attention from many observers, among whom there is no unanimity regarding the cause of these manifestations. Doubt has been expressed by some concerning the existence of such sequels. Idiosyncrasy, gastro-intestinal disturbances, preëxisting metabolic fault, nervous influence, and failure of complete elimination of the agent from the blood, with consequent degenerative changes in the vascular elements and other tissues, are some of the explanations offered.

Whatever the cause, it seems to be fairly well agreed that acidosis, and other late after-effects, occur in a certain proportion of cases.

With the administration of warmed anesthetics, according to the method described in the section on Administration (p. 63), both the immediate and the delayed after-effects are reduced to a minimum.[1]

Experiments on Warming Ether.—It is maintained by some investi-

[1] It has been known for a long time that during chloroform and ether anesthesia the temperature of the body is lowered, and the opinion has been advanced that the great fall of temperature may be partially responsible for the development of pneumonia.

A. Läwen (*Münch. med. Woch.*, 1911, 2097) has studied the question as to whether post-operative pneumonia can be avoided by warming the anesthetic prior to its inhalation. He therefore experimented with an apparatus by means of which the chloroform and ether vapors could be warmed. His results show that pneumonia cannot be thus avoided, though he does not doubt that a small proportion of cases of post-operative pneumonia may be prevented by the proposed modification of the method of inhalation anesthesia. He considers that the warmed anesthetics are only suitable for prolonged abdominal operations, and for operations in which the wounds are extensive, such as in amputation of the breast. He also considers the warmed anesthetic to be indicated for patients who have lost much blood or who are suffering from shock.

gators that ether vapor cannot be heated. Seelig[1] conducted a series of experiments for the purpose of establishing the correctness of this view.

The authors of this book, wishing to settle the disputed point with reference to the possibility of heating anesthetic vapors, undertook a series of experiments to determine whether the vapor is really warmed by being passed through a coil ten feet long placed in a heater, according to a method in actual practice.

A rubber tube, of the same length as that used in actual practice, with a thermometer placed at one end and also a thermometer for room

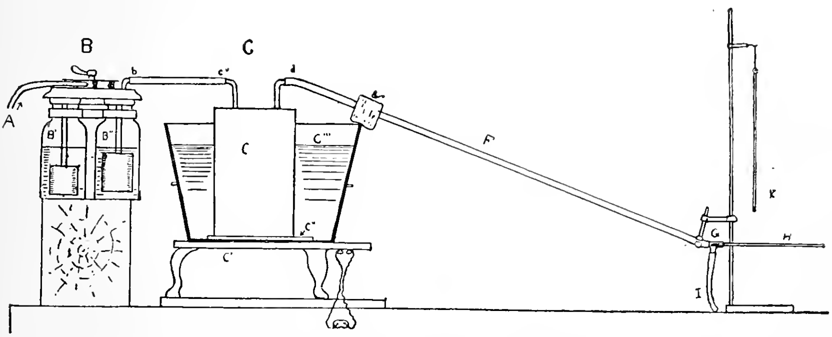


Fig. 11.—Gwathmey's Vapor Apparatus with the Tube Leading from the Heater as in Actual Practice. a. Compressed air; b. Gwathmey anesthetic apparatus; b^I. ether container; b^{II}. water; b. ether vapor exit; c. vapor heating apparatus; c^I. electric hot plate; c^{II}. asbestos mat insulator; c^{III}. water bath; c^{IV}. thermolite heater; c^V. inlet to heater; d. exit for heated vapor; e. asbestos insulator; f. 60 cm. rubber tube; g. glass T-tube; h. 200° C. thermometer; i. drain; k. thermometer for room temperature. (From S. G. Davis.)

temperature, was employed (see Fig. 11). Compressed air was passed through for one hour.

(Joss[2] has found that ether cools the air inhaled 33° to 44° F. below the temperature of the room. The cooled air undoubtedly lowers the resisting powers of the cilia of the ciliated epithelium lining the upper air passages when these passages become chilled. Infection is more likely to find its way into the finer air passages as salivation increases under the chilled anesthetic.)

These experiments gave the following data:

From Table 1 it will be seen that the temperature of the ether vapor can be raised to any degree desired and maintained at that point. The vapor may be heated by different methods, but this is probably one of the easiest, as with this simple apparatus one is not dependent upon electricity as the heat source.

[1] Seelig, M. G.: "The Fallacy of Warmed Ether Vapor," *Inter. Med. J.*, Sept., 1911; see also, Cotton and Boothby: "The Uselessness of Warming Anæsthetic Vapor," *Surg., Gyn. and Obst.*, Dec., 1912.

[2] *Mitteil. a. d. Grenzgeb. d. Med. u. Chir.*, *22*, No. 40.

TABLE 1—*Using Rubber Tube with Continuous Flow*

Amount of ether taken, 4 ounces.
Amount of ether used, 3.5 ounces in one hour.
Compressed air flow, continuously through ether.
Room temperature, 24° C., Nov. 4, 1911.

Temperature, 65 cm. from heater (usual distance)	After 5 minutes....	29.25° C.	Ether container warmed as is *necessary.* Heated ether container.
	After 10 minutes....	29°	
	After 15 minutes....	31°	
	After 20 minutes....	31°	
	After 25 minutes....	30°	
	After 30 minutes....	30.25°	
	After 35 minutes....	32.25°	
	After 40 minutes....	32°	
	After 45 minutes....	32°	
	After 50 minutes....	30°	
	After 55 minutes....	30°	

In order to determine the temperature of ether at different distances from Davis' heater, which was attached to the Gwathmey three-bottle vapor inhaler, a series of experiments were conducted in the chemical

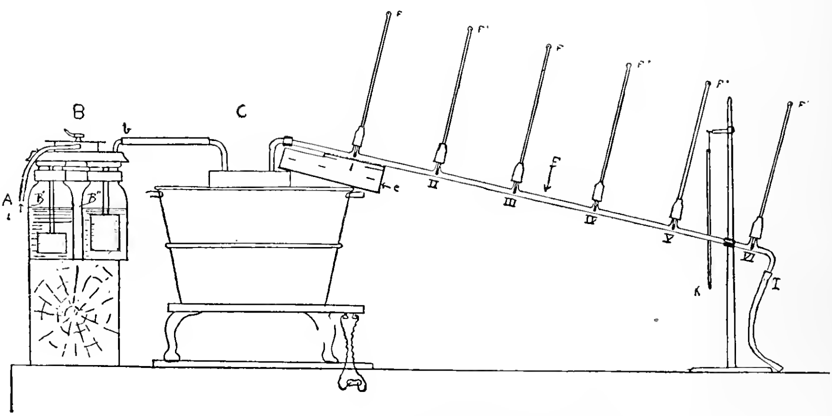


FIG. 12.—GWATHMEY'S VAPOR INHALER WITH HEATING APPARATUS. F. Glass tube divided into six parts of 10 cm. each; F.′ thermometers; I. drain; K. thermometer for room temperature; E. asbestos insulator.

laboratories of the College of the City of New York by the authors. The experiments were carried out by Mr. W. A. Hamor.

A special glass tube was constructed with uniform side tube openings 10 cm. apart, into which thermometers were inserted (see Fig. 12). At the side-tube exits and over the thermometers, a tightly fitting rubber collar was placed to prevent leakage. The glass tube was attached to a thermolite coil-heater, immersed in a water bath, which was kept at the boiling point by an electric hot-plate. The Gwathmey vapor apparatus was attached to this heater; compressed air was passed through the ether bottle, the resulting ether-vapor-air stream then passing through the water-bottle of the vapor-apparatus, and finally through the heater and the tube into which were inserted thermometers. Readings were made every five minutes for one hour and the room temperature was noted at the same time. The following table shows the results:

TABLE 2—*Using Glass Air Condenser Attached to Heater*

Amount of ether taken, 4 ounces.
Amount of ether used, 3 ounces.
Compressed air flow, continuously through ether.
Room temperature, 23.5° C.

Temperature in Degrees Centigrade at Various Distances

November 4, 1911

Time in minutes	5	10	15	20	25[1]	30	35	40	45	50	55	60
From heater:												
At 10 cm....	36	40.5	42	38.5	40	41	40	44	44.5	45	16	47
At 20 cm....	27	33.5	34	32	33.5	33.5	33	35	35	34.5	34.5	35
At 30 cm....	25	30.5	30	29	30.5	30	29	31	30.5	30.5	30	30
At 40 cm....	24	28	28	28	28	28	27	29	29	29	29	29
At 50 cm....	24	26.5	26	26	26.5	26	26	28	28	28	27.5	27.5
At 60 cm. ..	24	26	25.5	25	26	25.5	25.5	26.5	26.5	26.5	26.5	26.5

[1] Rearrangement of flow.

Boothby[1] has maintained that "warmed ether *per se*" possesses no merits over "cold ether," that is, not warmed. According to him, the concentration of the ether vapor in the air passing over or through the ether varies with the temperature of the liquid ether itself, that is, as the ether evaporates more or less rapidly the temperature of the liquid is lowered with a decrease in concentration of ether vapor in the effluent mixture from the vaporizer, hence the patient does not get enough ether. The specific heat of ether vapor is very small, consequently the mixture quickly acquires room temperature. Air, the volume of which per minute was determined by a Bohr meter, was passed over the surface of ether placed in a Wolff bottle, wherein the ether presented a surface area of about 50 sq. cm. The temperature of the liquid ether was noted with a thermometer immersed about 1.5 cm. in the ether. The tempera-

[1] Discussion before the New York Society of Anesthetists, 1913. Copies of the curves were courteously provided by Dr. Boothby.

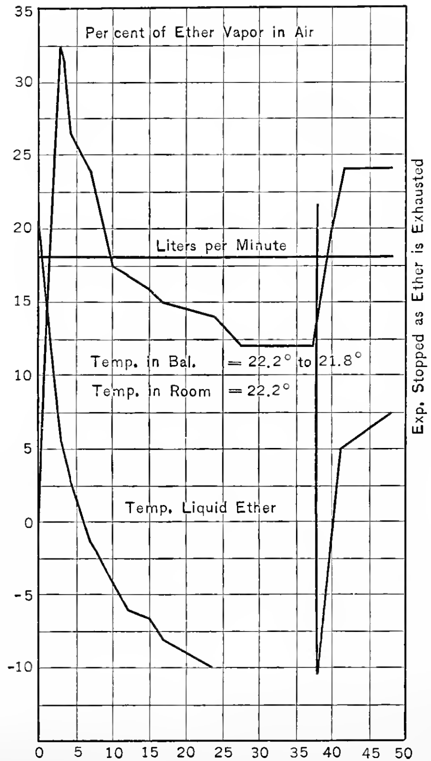


Fig. 13a.—Boothby Curve.

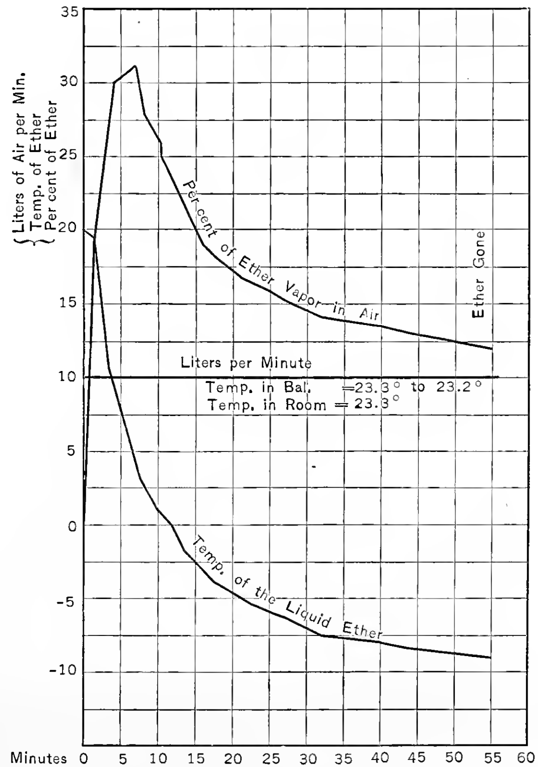


Fig. 13b.—Boothby Curve.

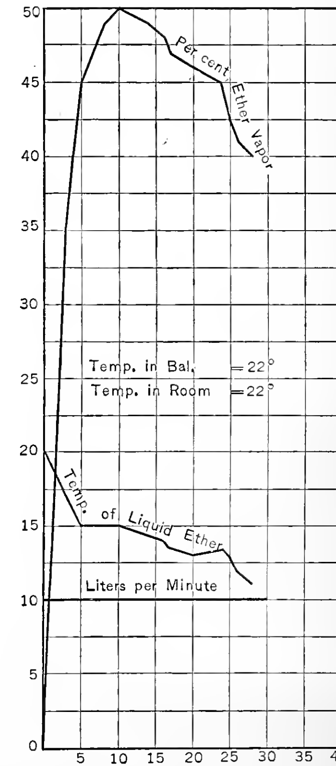


Fig. 13c.—Boothby Curve.

ture of the air-ether mixture coming from the apparatus was noted in a Waller gas balance, which served to indicate the composition of the mix-

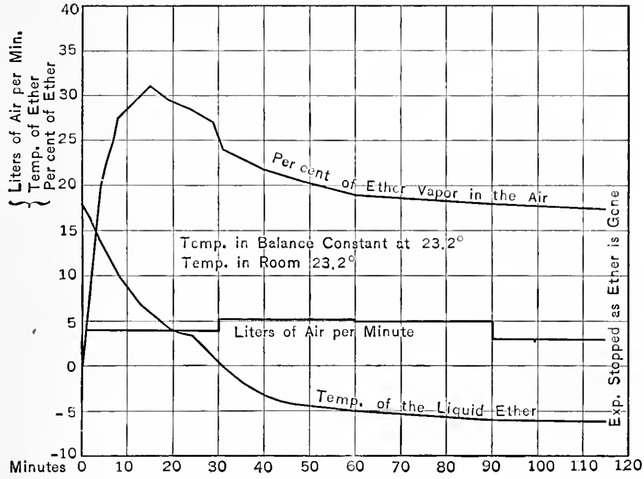


FIG. 13D.—BOOTHBY CURVE.

ture. The curves obtained by Boothby are given herewith, sufficiently labeled to be self-explanatory. In connection with Boothby's conclusions the following facts demand consideration:

(1) Ether given by the "vapor method" does not go, mixed with air or oxygen, first into a ballon or reservoir subsequently to be breathed by the patient, but directly to the patient, hence it enters the air passages before it has had time to acquire room temperature. (See Authors' Experiments, p. 63.)

(2) Ether administered in any way by inhalation eventually reaches body temperature in the lungs. The total shortage of heat is not taken from the entire surface of the lungs, but is localized in the bronchial passages, that is, there is local chilling or heating if the vapor be too hot.

(3) Davis has shown clinically that very beneficial results are had even if the vapor be produced from cold ether, provided it is subsequently warmed. (See Chapter on Administration, p. 67.)

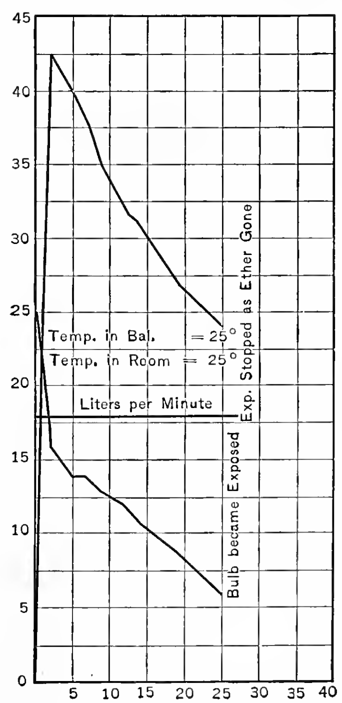


FIG. 13E.—BOOTHBY CURVE.

From the preceding table it will be seen that ether vapor may be heated, and the heating maintained for any length of time and delivered to a patient as predetermined by the anesthetist. For instance, we see that at 60 cm. from the heater at the end of sixty minutes the temperature was three degrees C. higher than the room temperature. About the same amounts of ether and air were used in this experiment as are usual in practice.

Air was passed through the ether and water-bottle of the vapor-apparatus *without* the heater and readings kept up for forty-five minutes. The following table gives the result:

TABLE 3—*Non-Warmed—Room Temperature*

		Room temperature
After 5 minutes	27.5° C.	28° C.
After 10 minutes	27°	28°
After 15 minutes	27.5°	28°
After 20 minutes	27.5°	28°
After 25 minutes	27.5°	28°
After 30 minutes	27.5°	28°
After 35 minutes	27°	27°
After 40 minutes	27°	27°
After 45 minutes	27°	27°

From this table it will be seen that at the end of forty-five minutes the vapor was approximately *sixteen degrees* F. below blood temperature.

The results show that ether vapor can be heated easily and inexpensively, and that it can be delivered to the patient at any desired temperature, within limits, by placing the heater or warming device at different distances from the patient's face.

Effects of Moisture.—Since 1909, Gwathmey has employed warmed *moist* vapors for pulmonary anesthetics. Baskerville [1] has called attention to the importance of moisture, among other factors which influence the course of anesthesia. "It has been shown," he says, "that the administration of moist ether, free from aldehyd, at body temperature, is rarely followed by nausea (less than ten per cent), and the usual strain upon the kidneys is not observed."

"Nitrous oxid, ether, and chloroform," he continues, "each exerts its specific physiological effect in producing anesthesia without asphyxiation, provided the respiratory and cardiac functions are approximately normal. This may be and is being accomplished by administering these gasified drugs with sufficient oxygen not to interfere seriously with the

[1] Baskerville: "The Chemistry of Anesthetics," *Science*, n. s., Aug. 11, 1911.

normal function of the hemoglobin of carrying oxygen to the capillaries, and sustaining cardiac stimulation, and by maintaining the usual concentration of carbon dioxid in, and providing its regular elimination from, the blood; for it is the respiratory stimulant (Yandall Henderson). Other factors involved are temperature and moisture. The anesthetics are carried into the system at body temperature. This may be and is being accomplished by warming, and, in the case of ether and anesthetic chloroform, by passing the vapor through heated water, which, at body temperature, not only removes the oxidation products, but saturates the gas with moisture (Gwathmey method). The osmotic action of the alveolar cells is thus affected only to the extent of the density of the gases introduced into the lungs, and not, as normally is the case, by temperature (always lower) and desiccation as well."

Brüning,[1] finding compressed air relatively much more harmful to the lungs than pure oxygen, or air in the Geppert apparatus, instituted experiments to determine the factors which cause the difference in effect. Differences in the temperature could not, in his opinion, be responsible, as repeated measurements always showed 25° to 30° in all the gases, uniformly. For the same reason, the strength of the air current could not be responsible. The remaining factor was the content in moisture of the different gases.

The oxygen and the air from the steel cylinders had only a relative humidity of 10-15 per cent. These values are so low that the sojourn in such dry air would normally be harmful for man and might lead to pneumonia. We feel most comfortable in air which contains between 40-60 per cent moisture.

Inspiration of Compressed Air With Water Vapor.—In a series of experiments upon mice, different degrees of moisture were obtained by allowing water to drip into the air stream. The desired humidity was produced in such a way that water was poured into the ether-flask of the Roth-Dräger apparatus, with a regulated outflow of the water, so that, after some practice, the gas-mixture would be maintained fairly constant at the desired humidity. (See Table 4, page 78.)

The table shows that the lungs presented nothing pathological, with moisture contents of the air from 50-70 per cent. Even after three breathing periods no changes were found. But when the moisture contents were diminished below 40 per cent, or increased to 100 per cent, hemorrhages at once made their appearance. As the air in Geppert's apparatus contains approximately 95 per cent relative moisture, the occurrence of slight pulmonary lesions is readily understood. The entire

[1] Brüning, A.: "Studien zur Narkosenfrage, ins besondere über die Anwendung von Sauerstoff und komprimierter Luft," *Deut. Z. Chir.*, 1911-12, *113*, 532.

TABLE 4—*Inspiration of Compressed Air With Water Vapor*
Mouse

No.	Duration of exp.	Time to sacrifice or second exp.	Second exp.	Time to sacrifice	Macroscopical lung findings	Moisture contents of air
36	1¼ hours	at once			Nothing pathological	70%
45	1¾ hours	at once			Some hyperemia, otherwise normal	35%
41	2 hours	at once			Normal appearance	55%
42	2 hours	7 hours			Some hyperemia, otherwise normal	55%
37	1¼ hours	19½ hours	2 hours	at once	Nothing pathological	70.65%
38	1¼ hours	19½ hours	2 hours	22 hours free	3d experiment, ¾ hour, killed at once. Lungs normal	70.65+%
46	1¼ hours	at once			Marked hyperemia, some hemorrhages	100%

experimental series justifies the conclusion that too much dryness and too much moisture are injurious for the lungs; but when these extremes are avoided, oxygen, compressed air, and the Geppert apparatus can be equally recommended.

A later series of experiments showed similar pulmonary changes from artificially dried air, as after the breathing of air that had been compressed; therefore, the cause of the hemorrhages cannot be referable to any abnormal composition of the air in the steel cylinders.

It still remains to be shown why the lungs are less injured by oxygen, although it has only a relative moisture content of 10-15 per cent, than by the equally dry air; and also why the dryness as such can act harmfully. Injuries through very dry air are explained by Brüning as follows:

The alveolar epithelia are lined with a thin layer of water, which is derived from the blood, and by its constant evaporation invests the expired air with its high content of moisture. In this thin layer, oxygen is dissolved and is carried from here by diffusion to the blood corpuscles. When the moisture contents of the inspired air are abnormally low, the water evaporates very rapidly, the capillaries—which are exposed for a large part of their circumference—dry out, and permit the blood corpuscles to pass between them. In addition, the secretion-pressure for oxygen drops, through the lesion of the endothelia, and the organism reacts by an increased blood supply—hyperemia—in order to take up the same quantity of oxygen through an increased surface. In the further course, inflammatory manifestations on the bronchi make their appearance. The slight bloody extravasates, on breathing of pure oxygen, are interpreted by Brüning as a chemical injury. The passage through a dried-out cell being necessarily hindered, the oxygen remains for a longer time in contact with the protoplasm; or the cell must exert an increased activity, in order to accomplish the same functional results. Consequently, there are over-stimulation and over-taxation of the cell.

On breathing an air saturated with water-vapor, the evaporation of the alveolar moisture proceeds more slowly, the water-layer at the walls is likely to be thicker and to stimulate the cells by its constant oxygen-contents. The secretion-pressure of the endothelia is normally subject to constant fluctuations, in the opinion of Brüning, corresponding to inspiration and expiration, so that the cellular protoplasm regularly enjoys a brief rest.

The slightness of the pulmonary changes, on the breathing of pure oxygen, is attributed by Brüning to the increased oxygen partial pressure, which facilitates diffusion and secretion.

Brüning concluded, from his experiments, that, in the brief time of a general anesthesia, injury to the lungs is to be feared only under employment of compressed air from the steel cylinders, and that this can be avoided by moistening the air to about 50 per cent.

The examination of the lungs, after the inhalation of the different gases, showed very considerable difference. After the inspiration of compressed air, the lungs of mice invariably showed extensive hemorrhages and bronchitic symptoms, which were especially evident after long duration of the experiment, or several repetitions. The air in Geppert's apparatus and oxygen have a similar effect, but to a much less degree. The lesions are dependent upon the relative moisture of the air, and can be avoided by moistening the inspiration air with water vapor, up to 50-80 per cent. Too high a vapor-saturation acts in the same sense as too much dryness. The absence of grave lesions in oxygen-breathing, in spite of low moisture, is referable to specific properties of the oxygen.

Brüning's experiments led to the following practical conclusions:

(1) General anesthesia by means of the Roth-Dräger apparatus,

under utilization of oxygen, is preferable to general anesthesia under employment of compressed air, unless the moisture of the air is artificially increased to 50 per cent.

(2) General anesthesia with oxygen is equivalent to general anesthesia by means of the Geppert apparatus.

(3) In the accidents of general anesthesia, artificial respiration alone is always efficient for the introduction of enough oxygen into the body; the breathing of pure oxygen offers no advantages.

(4) The majority of the advantages, claimed for oxygen, are only due to the more accurate dosage by means of the modern anesthetic apparatus.

Combining Oxygen with the Agent.—In 1904, experiments were conducted (J. T. G.)[1] to determine the value of oxygen, as compared with atmospheric air, in combination with different anesthetic agents, attention having been particularly directed to the subject by certain statements made by Hewitt.

With reference to nitrous oxid Hewitt says: "It is now established beyond all doubt that, by employing certain percentages of atmospheric air with nitrous oxid, a better form of anesthesia can be obtained than with the undiluted gas, and that, by using oxygen instead of atmospheric air, a still better form of anesthesia is obtainable."

Concerning chloroform, however, Hewitt's views are not so favorable: "It is doubtful whether there is any great advantage in the addition of oxygen to atmospheric air during the administration of chloroform, save perhaps in cases in which much respiratory difficulty is present, and in these cases the use of any tightly fitting inhaling apparatus would almost certainly neutralize the theoretical advantages of using oxygen."

Reasons for Using Oxygen.—The advocacy of the combination of oxygen with inhalation anesthetics is based largely upon the experiments of Priestley, Demarquay, Richet, Paul Bert, and others, and upon the clinical observations of Andrews, of Chicago, with nitrous oxid, and of Neudorfer, of Vienna, with chloroform.

The reason for giving oxygen with nitrous oxid is explained by Hewitt[2] in the following manner: "A mixture of 40 per cent of air and 60 per cent of nitrous oxid would contain about 8 per cent of oxygen and 32 per cent of nitrogen; and although the 8 per cent of oxygen would be sufficient to nearly or completely preserve the natural color of the patient's face, and to suppress clonic muscular spasm, the 60 per cent of nitrous oxid would be insufficient to produce tranquil anesthesia. If, however, instead of using air for oxygenating purposes, we employ oxygen, we shall be able to replace the 32 per cent of useless

[1] Gwathmey, J. T.: "Experiments to Determine the Value of Oxygen in Combination with the Different General Anesthetics," *Med. Rec.*, Nov. 19, 1904.

[2] Hewitt: "Anæsthetics," 4th ed., 311.

nitrogen by a corresponding quantity of useful nitrous oxid, and the proportion of the latter will now rise to 92 per cent."

From this it will be seen that there is a physiological basis for the combination of oxygen with nitrous oxid. Clinical experience bears out the theoretical calculations.

The ground for using oxygen with chloroform or the "C.E. mixture," ether, or ethyl chlorid, is as well founded, theoretically and clinically, as is that of its combination with nitrous oxid.

Normally for every volume of inspired air, 4.8 per cent of oxygen is abstracted, 4.3 per cent of carbon dioxid being substituted. During anesthesia the blood becomes more and more venous from an obstruction to the entrance of air into the lungs, and from the blood failing to take from the air its usual supply of oxygen. Asphyxia is produced more by the diminution of oxygen than by the increased amount of carbon dioxid. According to Patton,[1] Rumph found a decrease of 40 per cent of carbon dioxid eliminated in the respiratory exchanges, and Richet found a decrease of 50 per cent in the elimination of carbon dioxid in chloralized dogs.

Bert's experiments with chloroform show a progressive diminution in oxygen absorbed, and of carbon dioxid given off. Lorrain Smith has shown that dyspnea from changes in the gaseous composition of the blood may be due to a deficiency of oxygen.

Richet states that blood which contains an anesthetic in solution preserves, when shaken with ether, its full ability for fixing oxygen. Irregular forms of breathing may also occur from too little oxygen, as in the closed administration of volatile agents; or, from carbon dioxid dyspnea, as in rebreathing during the administration.

The experiments of Priestley and others, of placing small animals under two different receivers, one filled with oxygen and the other with air, showed that those under the oxygen receiver survived twice as long as the others; also, that the death of birds in the oxygen was not accompanied by convulsions as was that of birds that died in the air; furthermore, that the heart retained its irritability for several hours when death took place in oxygen.

Demarquay[2] immersed two kittens in water and kept them there until they had lost consciousness. One had previously been confined for twenty minutes in a glass case, containing two parts of oxygen and one of air, and the other had breathed only atmospheric air. On removing them from the water there was only a slight movement of the lower jaw. At the end of five minutes and a half, the superoxygenated kitten

[1] Patton, Joseph M.: "Anesthesia and Anesthetics," 1903.

[2] Demarquay, J. N.: "Essay on Medical Pneumatology: Physiological, Clinical, and Therapeutic Investigation of the Gases," Translated by Samuel S. Wallian, A.M., M.D., 1889.

arose, totteringly walked around, and made an uneventful recovery. The other partially recovered at the end of fifteen minutes, but died the next day. These experiments were repeated a number of times, and always with the same result.

The above experiments, illustrating the value of oxygen as compared to air, have been practically paralleled by Gwathmey. Regardless of the anesthetic used, animals have lived twice as long with oxygen as with air. With oxygen the heart continued to beat long after respiration ceased.

It may be added here that the heart always continued to beat a variable length of time after respiration ceased, whether air or oxygen was used, and with all anesthetics. Greater success in reviving them after cessation of respiratory and cardiac activity has come with the use of oxygen than with air.

The after-effects produced upon animals have been carefully studied. Inasmuch as oxygen is constantly employed clinically, with both chloroform and ether, it may be stated positively that the after-effects are reduced to a minimum.

Experiments with Animals.—In the experiments conducted by Gwathmey a closed mask with an expiratory valve, with the light rubber bag just behind the mask, was used. This animal mask was a cone-shaped brass cylinder 3½ inches in diameter at the base and 1½ inches at the apex. Over the base, or open end, were stretched two thicknesses of thin rubber, fastened around the margin of the cone by a rubber band. A small opening 1¼ inches in diameter was cut in the center, into which the animal's nose was placed. The technique in each instance was as nearly as possible the same, the same amount of anesthetic being used in each experiment, and the flow of air and oxygen being regulated.

To make these experiments as accurate as possible, over one hundred animals were killed, and the average time recorded. It has not been deemed necessary to enter into details of the exact weight, age, size, and physical condition of each animal. It may be said, however, that animals as nearly alike as possible in all essential respects were selected for each comparison. The results, in detail, as will be seen from the tables on pages 84 and 85, varied in accordance with the individual characteristics and conditions; as a whole, they confirmed the claim that the use of oxygen in connection with any form of anesthetic practically eliminates the percentage of danger which has hitherto been recognized as inseparable from the practice of anesthesia.

In order to determine the difference in toxicity of the drugs used, the time was taken from the application of the mask to the stoppage of the heart. As the toxic effects came on so rapidly, observations on the pulse, respiration, and blood pressure were of little value.

Twenty-six animals were killed with chloroform and air, the average time being nine minutes; the shortest time, three minutes; the longest, seventeen minutes. Thirty-eight animals were killed with chloroform and oxygen, the average time being twenty-one minutes; the shortest time, five minutes; and the longest, one hour and a half. (See p. 84.)

With ether and air twelve were killed, the average time being nineteen minutes, the shortest fifteen, and the longest thirty-three minutes. Seven were killed with the same anesthetic and oxygen, the average time being thirty-five minutes, the shortest twenty-five minutes, and the longest one hour. (See p. 85.)

With one part of chloroform and two parts of ether, thirteen animals were killed, six with air and seven with oxygen. The average time with air was nineteen minutes; with oxygen, thirty-five minutes. The shortest time with this mixture and air was fifteen minutes; the longest time, thirty minutes. The shortest time with oxygen was sixteen minutes; the longest, one hour and ten minutes. (See p. 85.)

From the above it will be seen that chloroform with oxygen is safer than chloroform with air, and is also safer than any of the other general anesthetics with air. This means that, instead of giving a very high mortality, chloroform with oxygen is as safe as ether with air.

From the above experiments and clinical observations it may be deduced that *oxygen increases the value of all anesthetics in rendering their administration safer to the patient without decreasing the anesthetic quality.*

In a recent paper Brüning[1] discusses the value of oxygen employed in connection with narcotics. He states that oxygen alone will not account for the improved narcosis witnessed in the administration of anesthetics with perfected apparatus. He attributes this to the exact and equal dosage, and maintains that compressed air is equally useful if the moisture of the lungs is artificially increased to 50 per cent. (See p. 86.)

In accidents in narcosis, according to Brüning, artificial respiration alone is always sufficient to introduce oxygen into the body. Pure oxygen inhalation offers no advantage. The smaller proportion of anesthetic needed when oxygen is employed he attributes solely to the improved dosage facilities with the Roth-Dräger apparatus. The minimizing of the after-effects, such as headache, vomiting, etc., he attributes to the diminished amount of chloroform employed. The employment of oxygen inhalation after narcosis is of no special value, as deep breathing and a thorough ventilation of the lungs promote the more rapid elimination of the anesthetic.

Brüning states that a patient with rosy lips and a pink appearance might suddenly become asphyxiated, as saturation with chloroform

[1] Brüning: *Loc. cit.*

TABLE 5.

The figures in the first column indicate the number of the experiment; the second column, the number of minutes required to kill.

	With Air			With Oxygen
1	4½	Chloroform	1	26
2	3	"	2	5
3	7½	"	3	10
4	7	"	4	5½
5	4	"	5	30
6	4	"	6	40
7	3½	"	7	28
8	7½	"	8	13
9	9	"	9	5
10	5½	"	10	8
11	7	"	11	15
12	10	"	12	17
13	6	"	13	30
14	9	"	14	30
15	10	"	15	13
16	7½	"	16	18
17	10½	"	17	14
18	10	"	18	30
19	10	"	19	16½
20	17	"	20	37
21	16	"	21	28½
22	13	"	22	33
23	16	"	23	8
24	11	"	24	10½
25	12	"	25	10
26	12	"	26	10½
		"	27	18
		"	28	7
		"	29	18½
		"	30	41½
		"	31	13
		"	32	26
		"	33	7½
		"	34	90
		"	35	14
		"	36	26
		"	37	23
		"	38	33½
	232½ total; 8.94 average.			809½ total; 21.3 average

	With Air			With Oxygen
1	15	Ether	1	25
2	18	"	2	29½
3	27	"	3	33½
4	15	"	4	34
5	33	"	5	27
6	16	"	6	40
7	18	"	7	61½
8	21	"		
9	16	"		
10	9	"		
11	18½	"		
12	28½	"		
	235 total; 19 average.			250½ total; 35 average.

	With Air	Mixed Chloroform and Ether (1:2)		With Oxygen
1	15	" " " "	1	40
2	30	" " " "	2	16
3	10½	" " " "	3	70
4	15	" " " "	4	37
5	17	" " " "	5	42
6	30	" " " "	6	22
		" " " "	7	28½
	117½ total; 19 average.			255½ total; 36 average.

	With Air			With Oxygen
1	21	Anesthol	1	38
2	26	"	2	14½
3	10	"	3	74
	57 total; 19 average.			126 total; 42 average.

	With Air	Summary		With Oxygen
1	9	Chloroform	1	21
2	19	Chloroform and Ether	2	35
3	12	Ether	3	35
4	19	Anesthol	4	42

would not change the color of the blood. He claims that more oxygen is set free in the plasma of the blood, and that the color depends only upon its richness in oxygen and not upon its carbon dioxid. Zuntz[1] holds that animals die as soon under oxygen-chloroform as under air-chloroform. In chloroform poisoning, according to Brüning, the first thing to do is to reduce the concentration of poison in the blood and to eliminate it from the body. To do this, the circulation must be maintained so that the hypersaturated blood may go through the lungs and be purified. This is best accomplished by radical, artificial breathing, thus securing a thorough expansion of the lungs. In this way, so much oxygen is introduced into the lungs that the inhalation of concentrated oxygen is unnecessary. Vidal[2] asserts that in primary disturbances of the respiration only artificial breathing is necessary, as, owing to the blood becoming rich in oxygen, eupnea, which delays the excretion of chloroform, occurs.

In treating accidents in narcosis a suggestion is made that oxygen might exercise a directly injurious chemical action on the body cells. Brüning quotes Paul Bert as stating that animals die when exposed to a hyper-pressure of 3-4 atmospheres of pure oxygen. As animals, on inhalation of ordinary air, died only on a hyper-pressure of 15 to 20 atmospheres, he thought the danger lay not in the pressure, but in the oxygen.

Brüning makes the peculiar statement that, from his experimentation, the administration of oxygen after the narcosis only delays the awakening, inasmuch as it never hastens the elimination of chloroform. Furthermore, in his opinion, it is no antidote to chloroform in narcosis accidents. Deep, free breathing is always sufficient to eliminate the chloroform from the system.

The difference in the results of Brüning's experiments and those of Gwathmey can be explained only by the employment of an entirely different technique and different apparatus under different conditions of climate. In Gwathmey's experiments, results were obtained by eliminating as far as possible every factor that might tend to confuse. Rebreathing, as advocated by Gatch, was used constantly, both with oxygen and compressed air. There is not the slightest question but that, under proper conditions, oxygen, in a very great measure, prevents poisoning, especially in chloroform or ether narcosis.

Müller's[3] experimental findings are divided into three groups, namely chloroform-oxygen narcosis; ether-oxygen narcosis; and combined narcosis, the latter being subdivided according to sequence,

[1] Zuntz: *Berl. klin. Woch.*, 1901, No. 20.

[2] Vidal: *Zentr. Chir.*, 1911, No. 11.

[3] Müller, B.: "Ueber den Einfluss der Gange mischnarkosen auf die inneren Organe," *Arch. f. klin. Chir.*, 1905, *71*, 420.

namely, chloroform-ether-oxygen narcosis and ether-chloroform-oxygen narcosis.

Chloroform-oxygen narcosis diminishes the blood pressure, which drops constantly from the beginning of tolerance to the end, rising again when the patient awakens. The diminution of the blood pressure is considerably less in chloroform-oxygen narcosis than in simple chloroform narcosis. The height of the blood pressure never drops so low below the normal blood pressure as in simple chloroform narcosis, and the course of the oxygen-mixture narcosis is of uniform appearance. But remissions are not altogether absent, and the chloroform effect can therefore not be entirely overcome. The number of respirations undergoes a greater diminution with chloroform alone than with the oxygen-mixture narcosis, in which it approximates the normal standard.

Concerning the effect of the oxygen narcosis upon the internal organs, the advantage of the addition of oxygen to chloroform consists in the removal of the carbon dioxid and in its substitution by oxygen, which induces a greater power of resistance on the part of the individual cells. The fatty changes of the cells, as well as the effect upon the heart, are not so severe in mixed as in simple chloroform narcosis. The mixed narcosis also involves a considerable saving of chloroform.

In the oxygen-ether narcosis no depressive effect upon the blood pressure was demonstrable. The level of the blood pressure was always above normal, so that the blood pressure was invariably increased, exactly the opposite to chloroform-oxygen narcosis. Ether-oxygen acts upon the internal organs in an analogous fashion to ether, but the changes are less considerable, especially the salivation and fatty metamorphosis. The difference is due to similar factors to those in chloroform-oxygen inhalation, namely, the lessened consumption of ether, the supply of oxygen, and the prevention of carbon dioxid intoxication. Ether-oxygen narcosis possesses less narcotic power as compared to simple ether narcosis, especially in resistant individuals, habitual users of alcohol, etc.

Combined oxygen inhalation, with ether and chloroform, is utilized for the avoidance of the disadvantages of these two methods of narcosis; it diminishes the toxic effects of ether as well as of chloroform, but requires accurate dosage, careful observation of the patient, and a knowledge of the indications and contraindications for the individual anesthetic agents. The effects of *ether,* for example, are merely diminished, but still present, so that certain dangers are involved in the narcosis if the patient is predisposed. Therefore, definite indications must always be present for this narcosis, for there are patients who are predisposed to a toxic effect of ether and unable to tolerate this narcosis. Ether-oxygen narcosis furthermore possesses less narcotic power than simple ether narcosis, and this is especially important in resistant individuals, such as neurasthenics and habitual users of alcohol, who in many cases cannot be brought under the influence of ether-oxygen narcosis. A reduced narcotic power is also frequently noted in chloroform-oxygen narcosis, so that it is difficult or impossible to narcotize alcoholic individuals. In order to avoid the disadvantages of chloroform-oxygen narcosis as well as of ether-oxygen narcosis, a combination of the two narcoses has been created in the form of combined oxygen narcosis, which is subdivided into chloroform-ether-oxygen narcosis and ether-chloroform-oxygen narcosis. By means of these combined narcoses the dangers and disadvantages of inhalation narcosis are much reduced. The favorable effects of these narcoses are due to diminution of the toxic action of ether as well as chloroform.

Müller[1] investigated the fatty changes of the vital parenchymatous internal organs in animals after simple and mixed narcoses. It was found that any narcosis gives rise to a more or less well-marked incipient fatty metamorphosis in the internal organs. The change in the kidney is frequently not marked enough for albuminuria to appear, but some alteration of the epithelia is present after all narcoses. This incipient fatty metamorphosis, which does not attack all cells at once, promptly subsides again. An existing fatty metamorphosis, such as is caused, for example, by a preceding narcosis, becomes seriously aggravated by a repeated inhalation of narcotic agents. It makes no difference what anesthetic is used; chloroform, chloral hydrate, and ethyl bromid have the most energetic action in this respect; the last named agent being altogether useless for prolonged narcosis. Ether acts in a general way less strongly upon the heart and brain, but, after several narcoses with ether, fatty changes are likewise found in these organs. Each prolonged ether narcosis is followed by small pneumonic foci in the lungs, with mucus in the alveoli, collection of blood corpuscles in the alveoli, and round cell infiltration in the surrounding tissue. These lung changes are of slight degree with chloroform. On the other hand, the liver and the kidney are affected less by ether than by chloroform. In a general way, there is a certain uniformity about the injurious effects of the various narcotics, except graded differences in the intensity of the action. Mixtures of chloroform and ether were found to be by no means better anesthetics, but rather possessed worse properties. The experiments showed that any mixture which contained chloroform did not act very differently from a pure chloroform narcosis. Mixed ether narcoses were followed, like the pure ether narcoses, by pneumonias of the above-described type.

The practical application of these findings consists in the best possible abbreviation of the narcosis; the avoidance of repeated narcosis

[1] Müller, B.: "Ueber Fettmetamorphose in den inneren parenchymatösen lebenswichtigen Organen nach einfachen und Misch-Narkosen." *Arch. f. klin. Chir.*, 1905, *75*, 896.

Fig. 14.—Oxygen Passing through Rubber Coil Immersed in Hot Water (Service of Dr. Bainbridge).

Fig. 15.—Intra-abdominal Administration of Oxygen in Case of Intestinal Adhesions.

within three to six days; and the examination of the organs before each narcosis, as to a preëxisting fatty metamorphosis. Certain affections are a strict contra-indication against any narcosis, especially fatty metamorphosis in the heart, kidneys, and liver.

The Influence upon Anesthesia of Oxygen Intra-abdominally Administered.—It is not proposed in the present volume to consider surgical subjects such as may relate to or modify the administration of anesthetics. However, it is of importance to note the effect upon anesthesia of oxygen administered intra-abdominally, according to the method of Bainbridge,[1] who instituted, for purposes not connected with anesthesia, a series of animal experiments with oxygen and air, which verified, in a remarkable manner, our experiments with oxygen and the different anesthetics.

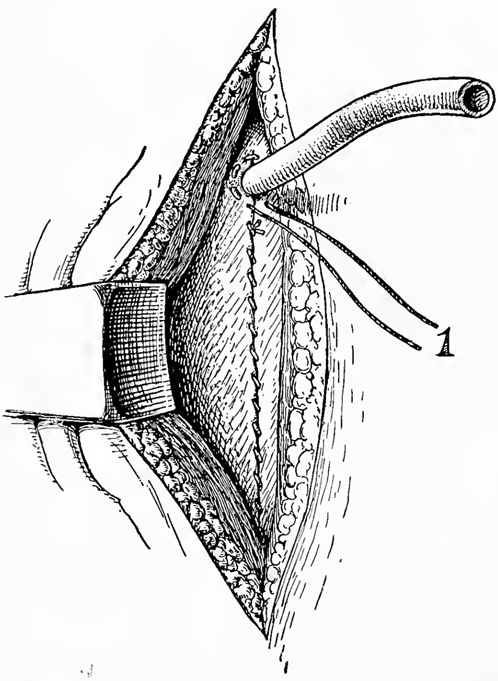


FIG. 16.—SUTURING OF THE PERITONEUM. Continuous stitch to inserted tube; purse-string stitch (1) encircling tube.

In a series of experiments to determine the difference between oxygen and air, oxygen was introduced into the abdomen following the technique as described upon human beings. It was found that oxygen was completely absorbed in all cases left undisturbed for seventy-two hours. There was a slight increase in pulse rate and respiration, also a slight rise in blood pressure. The effect upon the degree of anesthesia was marked, the animal showing a tendency to recover almost immediately from the influence of the anesthetic. In cases where the anesthesia was profound, reflexes quickly became active. Animals into which the oxygen had been introduced were able to stand up from two to ten minutes after the discontinuance of the anesthetic. All reactions were more prompt when warmed oxygen was used instead of oxygen at normal temperature. The dark blood was changed to scarlet. In no

[1] Bainbridge, W. S.: *Annals of Surgery,* March, 1909; *N. Y. J. Med.,* June, 1908; *N. Y. Med. J.,* Apr., 1909.

case was there macroscopic evidence that oxygen was an irritant to the peritoneum or any of the abdominal viscera. It was also found that oxygen stimulated intestinal peristalsis.

When air was introduced instead of oxygen, the pulse, respiration, and blood pressure were particularly influenced, and the degree of anes-

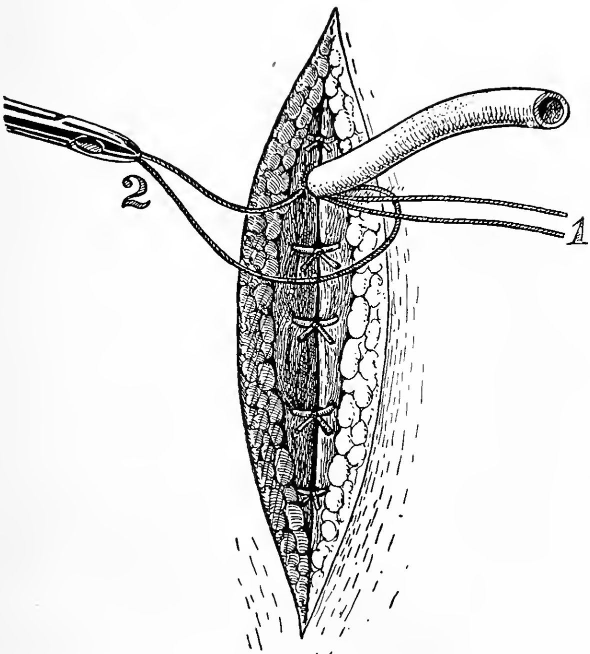


Fig. 17.—Aponeurosis United with Interrupted Sutures, the Muscle Having Been Previously Sutured. (1) Untied ends of peritoneal purse-string; (2) Untied suture through aponeurosis, passing halfway around tube.

thesia was not affected. The time required for recovery after the anesthetic agent had been discontinued was from fifteen to twenty-five minutes.

In the abdominal administration of oxygen Bainbridge employs a gas containing 94-97 per cent oxygen. The gas is warmed to a temperature of 90°-100° F., by passing it through a rubber tube from the tank in which it is compressed into a wash bottle filled with hot water. From this bottle the partially warmed gas passes through the exit tube. This long exit tube is again connected to a piece of glass tubing, and to this, in turn, is attached a piece of sterile rubber tube, through which the gas is introduced into the abdominal cavity. (Figs 14 and 15.)

Animal experiments and clinical experience in a large number of cases have proven that oxygen can be safely administered intra-abdominally, that it lessens shock, controls hemorrhage from small vessels, lessens the degree of cyanosis, nausea, and vomiting, prevents the formation of adhesions, and stimulates to such a degree that more anesthetic is necessary in order to keep the patient anesthetized until the completion of the operation. The technique of closing the wound and withdrawing the rubber tube, so as to prevent the leakage of oxygen, either into the tissues or into the surrounding atmosphere, is shown in Figures 16, 17, 18, and 19.

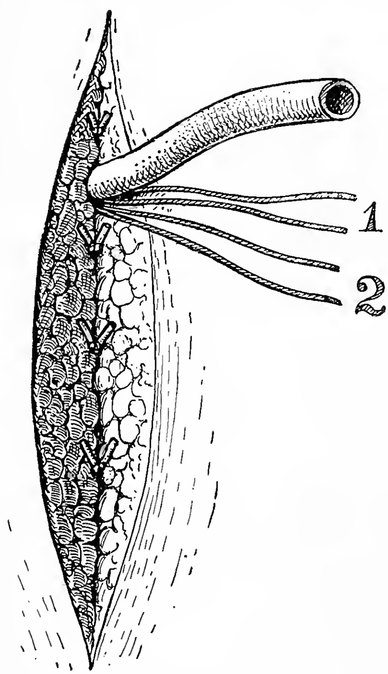


Fig. 18.—Superficial Fascia United. (1) Untied peritoneal purse-string; (2) Untied aponeurosis suture.

Preceding the Administration with Oil of Bitter Orange Peel.—A procedure which exerts a striking influence upon the course of anesthesia is the preliminary administration by inhalation of oil of orange (25 per cent oil of bitter orange peel, U. S. P., with 75 per cent of alcohol, U. S. P.).

Gwathmey,[1] who first employed this method, had long been in the habit of preceding the anesthesia by the administration of a one per cent vapor of cologne or whiskey, the agent being placed in one of the bottles of his three-bottle vapor apparatus (see illustration, p. 225). Later he adopted oil of bergamot or terpineol [2] for the purpose of masking the odor of ether vapor. (See Chapter VIII.)

Finding the induction period of anesthesia thus deprived of its terrors for many patients, particularly for nervous women and frightened children, the subject lapsing quietly into unconsciousness when the anesthetic vapor was turned on, a search was instituted for a substance with a more penetrating yet none the less agreeable odor, which could be vaporized and utilized as a preliminary to ether or other inhalation anesthetic agent.

With this object in view, the authors experimented with a number of

[1] Gwathmey: "The Vapor Method of Anesthesia," *Med. Rec.*, Oct. 14, 1905.

[2] Gwathmey: Terpineol ("lilacine") serves to mask the odor of ether vapor, and is a respiratory antiseptic, but, like oil of sweet orange, is less satisfactory than oil of bitter orange peel, because of its very sweet odor.

odoriferous substances.[1] From the table (page 94), by Passy,[2] quoted by Tigerstedt,[3] and rearranged here in the sequence of penetrating power, it will be seen that other odoriferous substances exceed oil of orange in penetrative power. To these, however, some patients might find objection, whereas to the delightful odor of oil of bitter orange peel it is hardly likely that anyone would object.[4]

The table shows how many milligrams of odorous substances, respectively, must be contained in one liter of air in order to produce a barely perceptible olfactory sensation. The list illustrates the functional capacity of the human olfactory organ in regard to quantity.

Zwaademaker,[5] using the olfactometer, noticed that in the case of certain odoriferous substances the threshold, or very first beginning, of perception takes on a high value, under increasing concentration, after a certain optimum has been reached.

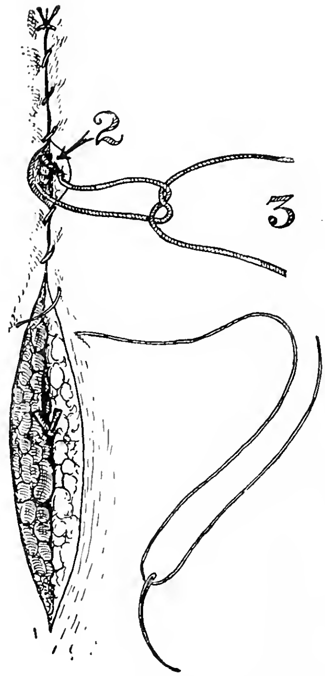


FIG. 19.—TUBE WITHDRAWN; PERITONEAL PURSE-STRING TIED; KNOT BENEATH APONEUROSIS. (3) Aponeurosis suture. Figure illustrates practicability of placing skin-stitches while tube remains in the abdomen.

With the above facts in mind, Gwathmey employed oil of bitter orange peel in alcoholic solution, first using it by the drop method with ether. He found that in this way the odor of ether was completely masked, not only for the patient but for the occupants of the operating room as well. The patient passed into the stage of surgical anesthesia as one dropping into a profound sleep. There was no stage of excitement, the nausea and vomiting being materially reduced. The

[1] Nussbaum (*Rundschau,* 1888, 759) found that the odor of chloroform vapor might be masked by means of oil of cloves. In the experiments of the authors, the masking agents tried (terpineol, oil of bergamot, oil of patchouli, oil of lemon, orange, etc.) were superimposed upon water at 37° C., and the anesthetic vapor was then passed through.

[2] Passy: "Forme périodique du pouvoir odorant dans la série grasse," *Compt. rend. Acad. d. Sciences,* 1893, *116,* 1007.

[3] Tigerstedt: "Lehrbuch der Physiologie des Menschen," 1902, *2,* 132.

[4] Eulimen, a pure limonene (density, 0.850 at 15° C.; boiling point, 175° C.), prepared according to a patented process (D. R.-P. 204, 163), has been proposed as an addition to narcotic mixtures ("Riedel's Mentor," 1911, 152).

[5] Zwaademaker, H.: "Die Physiologie des Geruches," Leipsic, 1895.

TABLE 6.

	Milligrams per liter of air	
Mint leaves (*Folia Menthæ*)	0.0000005	— 0.00001
Essence of Wintergreen	0.000005	— 0.0004
Orange essence	0.00005	— 0.001
Ether	0.0005	— 0.004
Camphor	0.005	—
Natural musk	0.01	— 0.1

entire administration progressed smoothly, and the patient recovered from the anesthetic with none of the after-effects so frequently noted with ether.[1]

Woolsey, of Brooklyn, developed and perfected the method of employing the oil of orange-ether sequence by the closed method with the three-bottle vapor inhaler. He has a record of over 200 cases. He uses it wherever the nitrous oxid-ether sequence is indicated and prefers it to the latter method. It is unquestionably of inestimable value, especially where the transportation back and forth of the nitrous oxid cylinders is a matter of consideration. The technique is as follows:[2]

The water bottle is filled with the usual amount of water, namely, 2½ to 3 ounces. A solution of oil of orange, of the composition described, in one- to two-dram quantity, is placed in the water. Ether (four to six drams) is placed in the chloroform bottle, which receptacle is surrounded by lukewarm water. The usual quantity of ether (4 ounces)

[1] French has used the drop method of oil of orange-ether in over 50 cases; he states: "One of the most important and valuable recent contributions to anesthesia methods is the ability to omit, or bridge, the second stage, or stage of excitement, and, judging by the results obtained, we are deeply impressed with the desirability of attaining narcosis without struggle. This can, without doubt, be accomplished, in the period of induction, with nitrous oxid; but, in our judgment, it can be done with greater ease and certainty with the essence of orange. It unquestionably requires a large experience with the administration of nitrous oxid to enable one to dovetail it so accurately with the ether which follows that the stage of excitement will be eliminated. It can, however, be done, and when done successfully, if all other things are equal, we can safely predict the best prospect for the operation and the best condition during recovery. The remarkable effects of the oil of orange as a preliminary to ether have been demonstrated in our clinic, and have proved to our satisfaction that, with it, the administration of ether is made far less disagreeable and that it greatly assists in the reduction of shock by bridging the stage of excitement. We have used it repeatedly with perfect success, the patients sinking into complete anesthesia as a child falls to sleep. Our observations thus far have brought the belief that an anesthesia conducted in this way is a contributive factor in reducing hemorrhage, also in reducing the quantity of the anesthetic and in shortening and modifying the anesthetic after-effects." French, Thomas R.: "Nitrous Oxid, Essence of Orange, Ether, and Sequestration in General Anesthesia," *N. Y. Med. J.*, May 24, 1913.

[2] See also "Vapor Method of Anesthesia."

is placed in the ether bottle. The index is turned to "Air," and the bag is filled with the air pumped through the water bottle, which contains the oil of orange. The mask is placed upon the patient's face, and the patient breathes back and forth in the bag. The air is pumped vigorously so as to keep the bag two-thirds full at all times. The index is turned gradually toward "Chloroform," the receptacle in which the four to six drams of ether are placed. The patient is now getting a very small amount of ether, which is apparently imperceptible. The index is gradually turned to full "Chloroform," the patient getting more and more of the mild attenuated ether vapor. If, at this time, the patient coughs, sneezes, or swallows, or shows in any way that he perceives the ether, the index is immediately turned back to "Air." The same procedure is repeated until the index reaches full "Chloroform." When this is accomplished the index is turned back to air again and gradually turned toward "Ether." The expiratory valve is, at all times, only slightly open. The bag remains moderately distended, a slight positive pressure being a decided advantage in some cases, the expiratory valve permitting a continuous but small escape of air. The patient will now be found to be in a state of full surgical anesthesia, the average time required to reach this stage being four and one-half minutes. Anesthesia is maintained with the index turned for one-eighth to one-quarter of an inch from air, but between "air" and "ether," constant pumping being continued at all times. The breathing, as a rule, is quiet and regular, approximating the breathing in chloroform anesthesia more nearly than that usually seen with ether. The lid reflex is absent, the eyeballs are rolling, but the patient is sufficiently relaxed for all surgical operations. The usual amount of ether used with this method is two or three ounces for the first hour and one ounce for the second. The after-effects are usually conspicuous by their absence. The patient goes under in practically the same way as with a good nitrous oxid-ether sequence. *There is no struggling or other indication of the second stage.* The pulse is normal, the color reflex good, and there is no disturbing mucous râle.

The physiological basis for the beneficial effect of oil of orange in the administration of inhalation anesthetics may be found in the prevention of reflex stimulation, by the anesthetic agent, of certain sensory nerves. Dastre[1] attributed early syncope to reflex stimulation of the pneumogastric and trigeminal nerves, particularly the sensory branches supplying the nasal mucous membrane and the larynx. Embley[2] has also emphasized the part played by the increased excitability of the vagus mechanism, particularly during the early part of the administration. In his inhalation experiments Embley found that failure of respiration is mainly due to fall in blood pressure. With good blood

[1] "Les anesthétiques," Paris, 1901, 104-109.

[2] Embley: *Brit. Med. J.*, April 5, 12, 19, 1902.

pressure, failure of respiration (his experiments concerned chloroform) is practically impossible. Restoration of respiration is dependent upon restoration of blood pressure. The chances of dangerous vagus inhibition are greatly increased by imperfect respiration.

From these findings it would seem fair to assume that any factor which prevents undue reflex inhibition of the nervous mechanism of respiration and which, by its stimulation of the respiratory center, prevents fall in blood pressure, will have a beneficial influence upon the course of the anesthesia. The oil of orange seems to exert this beneficial influence by dulling the sense of smell to such an extent that the odor of the anesthetic agent is not noticeable during the administration. It has been determined by our laboratory experiments upon guinea-pigs that the oil of orange exhibits no pronounced anesthetic effect upon these animals. The exact nature of its physiological action is, therefore, yet to be determined.

The smoothness of the anesthesia seems to the authors to be dependent upon the power of oil of orange to obtund the olfactory nerve to such an extent that the odor of the ether vapor is not noticeable. This view has not been verified by laboratory experimentation, however.

Concerning this "Mystery of Ether Anesthesia,"[1] as this action of oil of orange has been called, the following comment is made:

"We are confronted here with a problem that has so far eluded solution. The problem of noci and anoci associations finds instant solution, at least as far as its practical aspect is concerned. With a few drops of oil of orange (in alcoholic solution) we accomplish all that formerly demanded much preliminary psychic care, gas-oxygen inhalations, and injections of novocain, and quinin and urea hydrochlorid before and after anesthesia. Are pleasant odors narcotic to the olfactory nerve? Is that some explanation of their widespread and age-long use? Certain unpleasant odors are undoubtedly terrifying to animals, those of their enemies, for example. If pleasant odors are indeed sedative to the olfactory nerve, does that suffice to explain their extraordinary influence, at least when followed by ether, over the entire nervous system? Is there merely an association of ideas? The smell of ether is associated with the surgical knife in the minds of adults, and is terrifying to children from its irritating qualities. Perhaps the very familiarity and the harmlessness associated with the odors of flowers and fruit are sufficient to suggest powerfully to the subject that what he is about to undergo cannot be dangerous, or even unfamiliar."

Utilizing Carbon Dioxid.—The physiological importance of the carbon dioxid content of the blood has only recently come to be fully recognized. Of still more recent origin is the demonstration of its relation to the administration of inhalation anesthetics.

[1] "A Mystery of Ether Anesthesia," Editorial, *N. Y. Med. J.*, Sept. 14, 1912.

Extensive investigations by physiologists in America and Europe have established the fact that carbon dioxid is not merely a waste-product, but performs a distinct rôle as a "harmone," or chemical-regulator of various functions. The carbon dioxid content of the blood, according to Henderson,[1] exercises regulative influences upon the heart-rate, upon the vascular tonus, upon the peristalsis of the alimentary canal, upon the mental condition, and upon a number of other functions of the body. From the data presented by him it appears that even a slight reduction in the carbon dioxid content of the arterial blood causes a marked quickening of the heart-rate. "Further reduction," he says, "induces an extreme tachycardia, complete cessation of peristalsis, failure of many reflexes, and coma. If an extreme reduction of the CO_2 content of the blood is effected very rapidly, the heart comes into a state bordering on tetanus. This cardiac tetanus practically abolishes the pumping action of the heart. Arterial pressure falls and death results.

"If the reduction in the arterial CO_2 is less extreme, but is maintained for a considerable time (an hour or more, according to the extent of the reduction), so that the tension of CO_2 in the venous blood and in the tissues is reduced, symptoms and conditions result which are similar, in many respects, to those occurring in mountain sickness and are apparently identical with those of surgical shock. Arterial pressure falls to a very low level, and, if the condition is continued, the circulation fails. The fall is not due merely to tachycardia, for the heart-rate in the later stages is not always extremely rapid, but is caused by a loss of tonus in the peripheral veins and capillaries, and by the consequent stagnation of the blood in these vessels. The mental condition of the subject is comatose. The reflexes are greatly reduced in responsiveness. Vigorous stimulation of afferent nerves causes no rise of arterial pressure. The condition of the nervous system and the stage of excitement through which it develops are not due primarily to the fall of arterial pressure. They precede the fall. Although the coma is, of course, intensified by a low pressure, it may occur to a considerable extent coincidently with the high pressure of the earlier stages.

"The respiration, when the subject is left to breathe naturally, becomes very shallow. It is liable to pass into apnea. This condition is the direct effect of the reduced CO_2 tension in the respiratory center."

The reduction of carbon dioxid leading to the conditions described can be effected by various means detailed by Henderson, among which may be mentioned as having a practical bearing upon anesthesia: (1) artificial respiration; (2) the hyperpnea incident to the stage of excitement of incomplete anesthesia; (3) the hyperpnea produced by vigor-

[1] Henderson, Yandell: "Acapnia and Shock," *Am. J. Physiol.*, Feb. 1, 1908; Feb. 1, 1909; April 1, 1909; Feb. 1, 1910; June 1, 1910; Nov. 1, 1910; Aug. 1, 1911.

ous and prolonged stimulation of the afferent nerves; (4) exposure of the abdominal viscera to the air so as to allow a free exhalation of carbon dioxid from the surface of these organs. Variations in the oxygen content of the blood, according to Henderson, play little part, if any, in the production of these conditions. The regulation of the carbon dioxid tension of the air in the pulmonary alveoli, and the extent to which carbon dioxid is eliminated from the blood in its passage through the lungs, appeared to him to be the most important factors in the prevention of shock. In experiments in which he had induced shock, Henderson found that restoration of carbon dioxid to the tissues and blood (or rather the maintenance of a condition which permits the tissues rapidly to restore their CO_2) proved effective in inducing rapid recovery. "Under all conditions, except during hyperpnea, in which condition the cardiac activity is increased sympathetically with the respiratory excitement, and, to a certain extent, even in this condition, the heart-rate can be kept down and the development of shock prevented." [1]

It is important to note that in the absence of respiratory excitement the heart-rate is an index which varies inversely as the carbon dioxid content of the arterial blood. The investigations which led Henderson to make his extensive experiments and observations, and his own work, are briefly reviewed in the section on Shock (see p. 383).

The experiments of Henderson and the observations of Mosso [2] led Levi,[3] in 1910, to consider the practicability of utilizing mixtures of carbon dioxid with oxygen for the purpose of stimulating the bulbar centers in surgical cases in which the automatic activity of these centers is temporarily paralyzed in consequence of the effects of chloroform or ether, or operative trauma, or of a combination of these causes. He first experimented on animals. Failure of respiration was induced by means of the single or combined action of nitrites, chloroform, and morphin. The animals were then made to inhale a mixture of oxygen with carbon dioxid in percentages from 10 to 30. In every case he noted an almost immediate return of the breathing and the effects of the inhalation were

[1] Henderson's method for regulating the heart rate in his early experiments "depended upon the manipulation of the hand bellows with which artificial respiration was administered, and on the adjustment of the escape vent in the side of the cannula tied into the trachea. As the pulmonary ventilation was increased or diminished, the heart rate was correspondingly accelerated or retarded."

[2] Mosso: *Arch. exp. Path. u. Pharm.*, 1906, *54*, 285.

[3] Levi, Ettore: "The Clinical Use of Carbon Dioxid with Oxygen," *J. Am. Med. Assn.*, March 16, 1912.

Also: "Nota preventia sulle applicazioni terapeutiche, nella pratica chirurgica e medica di mischele li ossigeno e di anidriole carbonica," *Acad. med. fis.*, Frienze, March 16, 1910; "Studi sull'azione fisiopatologica dell'anidriole carbonica, e sulle applicazioni terapeutiche, nella pratica chirurgica e medica, di mescele di ossigeno ed'anidriole carbonica," *Rev. Crit. di Clin. Med.*, 1910, Nos. 30 and 31.

found to last for some time after the mixture had been discontinued.

He then administered these gas mixtures to patients who were in a state of partial or complete coma as a consequence of trauma or extensive and prolonged operation. With mixtures of from 5 to 20 per cent of carbon dioxid in oxygen, the depth of breathing and the regularity of the rhythm were notably improved. His most satisfactory results were obtained with a mixture containing 15 per cent of carbon dioxid. In cases which exhibited Cheyne-Stokes respiration, normal breathing was restored, continuing so for some time after the inhalation of the gas mixture ceased. Marked improvement in circulation was also noted, the disappearance of cyanosis being one of the most striking features.

In routine practice Levi employs the mixture of carbon dioxid and oxygen as soon as the slightest tendency to failure of respiratory or cardiac function appears. The almost invariable result, during nearly two years of experience with the method in hundreds of cases, has been a rapid return of normal heart action and breathing. The best results were noted where the condition of shock had not progressed too far, although striking beneficial results were obtained even in the latter cases.

It is interesting to note that Levi's observations with this method seemed to him to afford an explanation, to some extent, of the good effects obtained with the method employed in connection with artificially reduced circulation (see Sequestration Method, p. 467). "It seems probable," he says, "that the remarkable rapidity with which patients subjected to narcosis under this condition recover consciousness, as observed by many authors, is due to the sudden return to the general circulation of a large amount of blood rich in carbon dioxid, when the lower limbs are unbandaged. Following up this suggestion, we have found that the use of a gas mixture containing from 10 per cent to 15 per cent of carbon dioxid after the completion of an operation is very effective in causing a prompt awakening of the patient. It seems also to tend to decrease the post-chloroformal vomiting. This is doubtless referable to the rapid elimination of chloroform from the blood and tissues under the influence of the increased respiration induced by the carbon dioxid."

Levi does not give the technique by which he obtains the definite percentages of carbon dioxid. Henderson has perfected an apparatus for definitely controlling the percentages of carbon dioxid. The requisite carbon dioxid percentage may be maintained by means of rebreathing as follows: When too much carbon dioxid is lost, as judged by the symptoms detailed (p. 97), the amount may be increased by allowing the subject to rebreathe for from three to six minutes, according to requirements, the anesthetic agent being discontinued meanwhile. When the breathing becomes forced and other signs of distress appear, suggesting too much carbon dioxid, rebreathing is discontinued and the administration of the anesthetic is resumed. Four per cent has been found to be the limit of safety.

CHAPTER III

THE USE OF REBREATHING IN THE ADMINISTRATION OF ANESTHETICS [1]

W. D. Gatch, M.D.

Ether: Effect of Ether Vapor on Respiratory Passages; Comparison of Toxic Effects Following Use of Open and Closed Methods; Effect of Over-Concentration of Ether Vapor.

Nitrous Oxid Alone and Combined with Ether: Method of Administration; Basis of Technique; Practical Advice; Maintenance of Ether Balance; Elimination of Ether from the System; Effect of Morphin on Ether Elimination; Clinical Results; Long Operations; Fatalities; Cardiac Cases; Hypercapnia; Acapnia; Ether and Acapnia; Other Advantages of Rebreathing; Post-Anesthetic Nausea; Post-Anesthetic Abdominal Distention; Post-Anesthetic Lung Complications; Method Demands Experience.

Chloroform and Ethyl Chlorid: Suggested Investigations; Dangers; Advantages.

Rebreathing in the administration of ether and chloroform has been under discussion ever since the introduction of these agents as anesthetics. With the introduction of etherization by the open method, rebreathing has fallen into disfavor, and many writers condemn it.[2] When properly regulated, and when the oxygen supply is ample, rebreathing can be put to a valuable use. The evidence in favor of this is derived partly from a series of 2,500 nitrous oxid-oxygen and nitrous oxid-oxygen-ether anesthesias given by a closed method at Halsted's clinic, and partly from the recent and very important work of the

[1] Taken from a paper read before the Section on Pathology and Physiology of the American Medical Association, at the Sixty-second Annual Session, Los Angeles, June, 1911. Reprinted, with modifications, by courtesy of *J. Am. Med. Assn.*

[2] Cunningham and Anderson: "Methods of Administering Ether," *J. Am. Med. Assn.*, Nov. 7, 1908, 1574.

physiologists, Henderson,[1] Hill,[2] Haldane,[3] and others, on the carbon dioxid metabolism of the body.

ETHER

The subject can be approached most simply by considering the harmful results supposed to follow the administration of ether by the use of closed masks. Ether only will be considered for the present, because most of the investigations bearing on the subject of rebreathing have dealt with this anesthetic. The ill effects in question may be grouped under two heads:

(1) Injury to the lungs; (2) general toxic effects.

Effect of Ether Vapor on Respiratory Passages.—Dreser,[4] Offergeld,[5] Poppert,[6] and Hölscher,[7] have studied very carefully the effects of ether vapor on the respiratory passages. Dreser regards any concentration of vapor which cannot be inhaled by the patient while in the conscious state without discomfort and coughing as harmful to the lungs. Applying this test he fixed on 6 to 7 per cent as the highest concentration which should be used. Offergeld, experimenting on animals, found that the lungs, after etherization by a closed method, showed much graver injuries than after etherization by an open method. With the closed method he found extensive fatty degeneration and desquamation of the epithelium of the air-passages, also many minute hemorrhages into the alveoli; many of the animals died of bronchopneumonia. With the open method the pulmonary lesions were of a comparatively unimportant character, unless the administration was frequently repeated at short intervals. Poppert, whose experiments were similar to Offergeld's, concluded that ether vapor was more irritating to the lungs the greater its

[1] Henderson: "Acapnia and Shock" (a series of papers), *Am. J. Physiol.*, 1908, *21*, 126; 1909, *23*, 345; 1909, *24*, 66; 1910, *25*, 310; 1910, *26*, 385; 1910, *26*, 260; 1910, *27*, 152.

[2] Hill and Flack: "The Effect of Excess of Carbon Dioxide and of Want of Oxygen on the Respiration and the Circulation," *J. Physiol.*, June 30, 1908; "The Influence of Oxygen Inhalations on Muscular Work," *J. Physiol.*, July 1, 1910.

[3] Haldane and Poulton: "The Effects of Want of Oxygen on Respiration," *J. Physiol.*, 1908, 390.

[4] Dreser: "A Contribution to the Study of Anesthesia by Ether," *Johns Hopkins Hosp. Bull.*, Jan., 1895.

[5] Offergeld: "Lungenkomplicationen nach Aethernarkosen," *Arch. f. klin. Chir.*, 1907, *83*, 505.

[6] Poppert: "Experimentelle und klinische Beiträge zur Aethernarkose und zur Aether-Chloroform-Mischnarkose," *Deutsch. Z. Chir.*, *67*, 505.

[7] Hölscher: "Experimentelle Untersuchungen über die Entstehung der Erkrankungen der Luftwege nach Aethernarkose," *Arch. f. klin. Chir.*, 1898, *55*, 175.

concentration. Hölscher studied the distribution of secretion in the air-passages during ether narcosis. He found that there was only a very slight secretion from the epithelium situated below the level of the larynx. By putting coloring materials into the mouths of anesthetized animals he proved that mucus and saliva might be aspirated into the deepest air-passages. His conclusion was that "affections of the air-passages occurring after ether are, for the most part, due to the aspiration of infectious mouth contents."

The experimental results dealing with the effects of ether vapor on the lungs may be summarized as follows:

(1) The irritant action of the vapor varies according to its concentration.

(2) Post-operative lung complications are frequently caused by the aspiration of mouth contents.

(3) The greater severity of the pulmonary lesions found after experimental etherizations by the closed method can be satisfactorily accounted for by the great concentration of ether vapor in the closed masks and by the greater liability to aspirate mouth contents when these are used.

Comparison of Toxic Effects Following the Use of Open and Closed Methods.—We now have to consider why the general toxic effects which follow ether anesthesia are more severe after the closed method than after the open method. Writers are almost unanimous in asserting that this is the case. The work of Ladd and Osgood [1] is very important in this connection. These authors studied the frequency of post-anesthetic vomiting in patients after etherization with the Blake cone, and in those etherized by the "gauze ether" method. Vomiting was much more frequent and severe among the former patients than among the latter. With the Blake cone cases they found acetone in the urine after operation in 88 per cent of the cases, while with the "gauze ether" cases they found it in only 26 per cent. The technique and advantages of the open method are discussed by Miss Magaw,[2] who reports 14,000 cases with most satisfactory results. In short, there is no doubt that this method of etherization is better than the rather crude closed methods that it has replaced. Its disadvantages and dangers will be referred to later.

The causes commonly held responsible for the ill effects which follow the closed method are the following: (1) anoxemia; (2) overconcentration of ether vapor; (3) toxic organic substances in the expired air; and (4) excess of carbon dioxid in the expired air.

There is reason to believe that the first and second of these possible causes are the real ones. From our present knowledge, the third is not

[1] Ladd and Osgood: "Gauze Ether," *Ann. Surg.*, Sept., 1907.

[2] Magaw, Alice: "A Review of Over 14,000 Cases of Surgical Anesthesia," *Surg., Gynec. and Obstet.*, 1906, *3*, 795.

important, since physiologists have demonstrated that there are no organic poisons in the expired air, or at least for practical purposes of anesthesia our clinical results indicate that such substances, even if they exist, need not be seriously considered.[1] The excess of carbon dioxid is harmless and can be utilized to good advantage.

Effect of Overconcentration of Ether Vapor.—It is evident that anoxemia and overdosage of ether—evils almost unavoidable when this anesthetic is given in a tightly closed mask—must do harm. It is known that a deficiency of oxygen quickly causes the gravest injuries to the tissues. Dreser found that the gas within a closed etherizing mask would, at times, put out a burning candle. He also found that the ether vapor within the closed mask sometimes reached a concentration as high as 34 per cent, while 6 to 7 per cent is the greatest concentration which can be inhaled without irritation to the air-passages. With such an overdosage of ether as this, it is true that the excess of carbon dioxid within the closed mask is injurious, for it stimulates the respiration powerfully, and leads quickly to an overabsorption of ether by the blood.

If the truth of what has just been stated be admitted, it follows that, if we can prevent anoxemia, overconcentration of vapor, and too great a depth of anesthesia, we can obviate most of the serious objections to the closed method of giving ether.

NITROUS OXID, ALONE AND COMBINED WITH ETHER

The principles laid down in the foregoing paragraphs have been used in developing a method of anesthesia, the technique and advantages of which will now be described. Nitrous oxid and, if necessary, ether are the anesthetics used. The apparatus employed[1] consists essentially of a mask connected by a piece of flexible tubing to a rubber bag. This forms a closed space into which the patient breathes. On the mask is a valve-box by means of which the patient can be made to breathe to and

[1] Crowder, Thomas R.: "A Study of the Ventilation of Sleeping-Cars," *Arch. Int. Med.*, Jan. 15, 1911, *85*; Haldane and Smith: "The Physiologic Effects of Air Vitiated by Respiration," *J. Path. and Bact.*, 1892 and 1893, *1*, 168, 318; Erclents Flügge: "Report of Experiments at the Institute of Hygiene at Breslau," *Z. f. Hyg.*, 1905, 363, 388, 405 and 433; Hill and Walker: "The Relative Influence of the Heat and Chemical Impurity of Close Air," *J. Physiol.*, Nov. 9, 1910.

Rosenau and Amos (*J. Med. Res.*, 1911, 25, 35) claim to have found in the expired air minute quantities of organic matter. They expressly state, however, that their work does not necessarily indicate that this material is poisonous. Their results await confirmation.

[1] The apparatus is described elsewhere in detail. It will be noted that the arrangement for giving ether has been changed so as to permit of a more accurate dosage. The method of administration is practically unchanged, except that Gatch now allows rebreathing for somewhat longer intervals.

fro into the bag, or to inspire from the bag and expire into the air, thus emptying the bag. The bag is attached to a small box, through which the current of gas must pass back and forth from the bag to mask. Into this box nitrous oxid and oxygen are admitted, and ether, drop by drop, from a receptacle above. The ether is vaporized in the box from a series

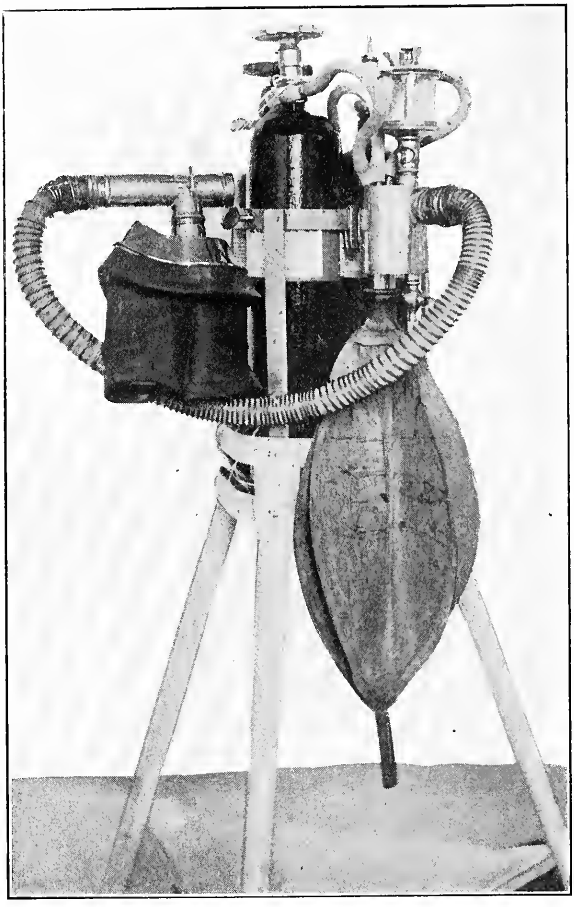


FIG. 20.—GATCH NITROUS OXID-OXYGEN APPARATUS.

of drip-plates and any excess of liquid ether can be drained off at once by a stopcock.

Method of Administration.—The mask is adjusted carefully to the patient's face and the bag filled with nitrous oxid containing a very small amount of oxygen. The patient is made to breathe this mixture in and out through valves, thus replacing all the air in his lungs with nitrous oxid and oxygen. The bag is next refilled with the same mixture of gases, which the patient is made to rebreathe for from five to eight minutes. At the end of this time he is allowed to empty the bag, breath by breath, into the air, after which it is refilled, and the same procedure is repeated. Oxygen is given, without any attempt to estimate its exact percentage to the nitrous oxid, in quantities just sufficient to prevent cyanosis. If desired, nitrous oxid can easily be given under positive pressure, by keeping the bag slightly overdistended. This is sometimes a useful procedure in managing difficult cases. Anesthesia is usually established in less than two minutes. If the anesthesia is unsatisfactory with nitrous oxid alone, ether is added. This com-

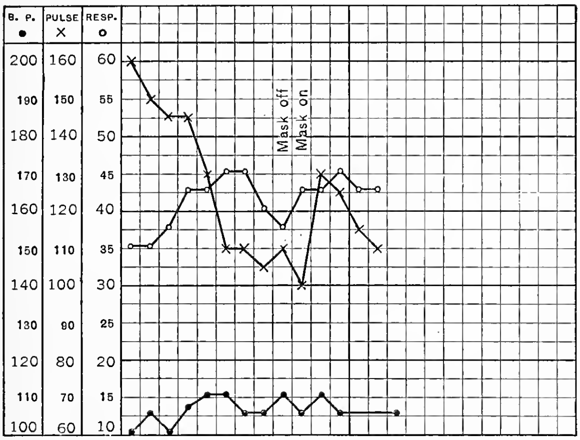


FIG. 21.—CHART SHOWING PULSE AND RESPIRATION WITH REBREATHING.

bined nitrous oxid-ether anesthesia has many points of practical and scientific interest.

Ether is not given till the patient's respiration has been stimulated by the accumulation of carbon dioxid which results from the rebreathing. It is then added drop by drop. The heated gases quickly evaporate it from the drip plates, and it is rapidly absorbed by the blood because of the increased pulmonary ventilation. The most difficult subjects can thus be deeply anesthetized.

Basis of the Technique.—Reference has already been made to Dreser's experiments, in which he proved that from 6 to 7 per cent of ether vapor is the greatest concentration which can be inhaled by a patient in the conscious state without irritation and coughing. Precautions must be taken to keep the concentration of ether vapor in the mixture of gases below this level in order to eliminate the possibility of injuring the lungs. This is quite easily accomplished, as the following simple calculation will show. The gas-bag, moderately distended, holds about 10 liters of gas, the mask and tubing hold about 1 liter, and the entire respiratory system of the patient holds about 3 liters. When the patient is rebreathing these all form one closed space, with a total capacity of about 15 liters. The problem therefore is simply to determine how much ether must be added to 15 liters of gas in order to make the concentration of ether vapor 7 per cent. Abel has calculated the amount of ether to be 4.2 c.c. However, the conditions of the problem are so variable that the amount of ether required cannot be determined with absolute accuracy. The varying temperature in the apparatus, the loss of ether through leaks and by absorption in the lungs, are factors for which no accurate data can be furnished, as they are variable. But absolute accuracy is not necessary, because the constant loss of ether

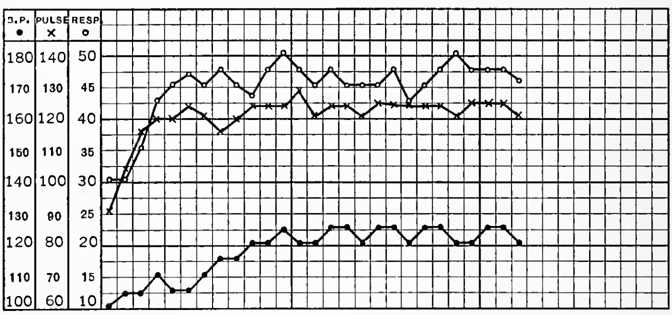


FIG. 22.—CHART OF THE PULSE, RESPIRATION AND BLOOD-PRESSURE DURING ANESTHESIA OF TWO HOURS AND FIFTEEN MINUTES' DURATION. Pulse: line with crosses. Respiration: line with circles. Blood-pressure: line with heavy dots. The patient was a woman of 65 with carcinoma of the sigmoid. The operation was closure of a fecal fistula by double lateral anastomosis, repair of an old wound in the abdominal wall, and colostomy. Note the constant level of the pulse and the maintained rise of blood-pressure. The temperature rose from 98.6° to 99.9.° The recovery was excellent.

gives us a wide margin of safety, so that ether can probably be added much faster than the calculation allows, without exceeding the danger limit.

Practical Advice.—With the drops of ether falling at the rate of 120 to the minute, it has been found that it takes two and one-quarter minutes to add the 4.2 c.c. Therefore, if we give ether at this rate and take precautions not to keep it dropping for more than two minutes at any one time, and to keep the bag constantly full of gas, we can be sure that the ether vapor will not reach a concentration greater than 7 per cent.

The anesthetist can estimate the approximate strength of ether vapor by its odor as it escapes from the valve-box.

Maintenance of Ether Balance.—It has been found unnecessary to give ether constantly during the administration. When enough has been given to produce satisfactory anesthesia, even in cases requiring a deep narcosis, the anesthesia can be maintained with nitrous oxid alone. This is to be explained by the fact that the rebreathing prevents the ether, once dissolved by the blood, from being thrown off as rapidly as it would otherwise be by the lungs, which are the organs by which it is practically all eliminated.[1] Suppose, for example, that a patient having a certain amount of ether dissolved in his blood is given some fresh nitrous oxid and oxygen to rebreathe. The ether will be thrown off from his lungs till the tension of its vapor in the gases being breathed will equal that in the blood. When this occurs no more ether will be eliminated until a new supply of gas is furnished.

Elimination of Ether from the System.—Not only can we prevent the elimination of ether by rebreathing, but we can also hasten the elimination by a rapid ventilation of the lungs with fresh gas. During the process of rebreathing, carbon dioxid accumulates in the body and stimulates the respiratory center so that the breathing becomes deep and rapid—often fifty or sixty respirations to the minute. When a patient, anesthetized in the manner described, and breathing at such a rate, is given a fresh supply of gas and allowed to discharge each breath into the air, he apparently rapidly rids himself of the small dose of ether he has been given. Thus it is possible to anesthetize a patient so deeply that he will not stir during a Whitehead or other operation requiring deep narcosis, and yet have him conscious before leaving the operating room. By careful administration we can, in most cases, keep the patient from knowing that he has been given any ether at all, so complete and rapid is its elimination.

It is recommended that this method of removing a volatile anesthetic by rapid ventilation of the lungs be used at the close of every administration of chloroform or ether. The increased pulmonary ventilation can be easily

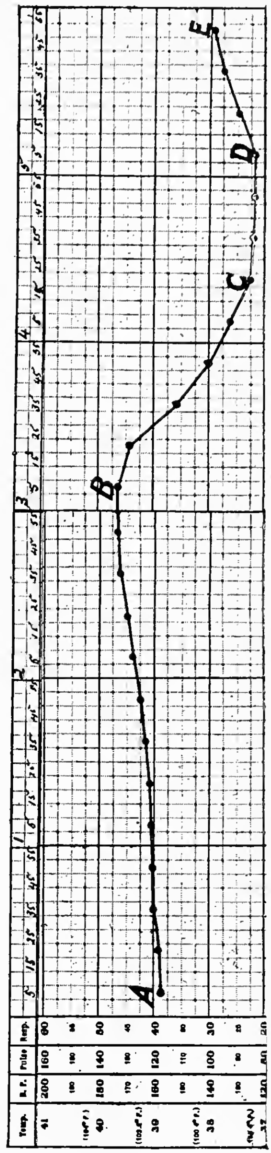


Fig. 23.—Chart Showing Value of Rebreathing During Operation.

[1] Hewitt: "Anæsthetics and Their Administration," 3rd ed., 50; Cushny: "Pharmacology and Therapeutics," 4th ed., 166; Cushny: "The Exhalation of Drugs by the Lungs," *J. Physiol.*, *40*, 17; Nicloux: "Elimination de l'éther contenu dans le sang aprés l'anesthésie pendant la periode de retour," *Compt. rend. Soc. biol.*, 1907, *1*, 8.

brought about by making the patient breathe in and out, through valves, air or oxygen containing a small percentage of carbon dioxid.

Effect of Morphin on Ether Elimination.—In this connection, it is interesting to consider the effect which morphin has on the elimination of ether or chloroform from the body. Morphin decreases markedly the rate of pulmonary ventilation.[1] Large doses of this drug must therefore retard the elimination of the anesthetic and thus increase its toxic action. It is often possible to detect the odor of ether or chloroform on the patient's breath for several hours after operation. This slow excretion may be due, in part at least, to the morphin, a hypodermic of which is desirable before or after almost every anesthesia. Perhaps this effect of morphin can be alleviated by means of the method just described for the quick elimination of the anesthetic.

During the stay of ether in the system its toxic action cannot be prevented. It has been found that the dose of ether, and its consequent ill effects, may be reduced to the minimum by employing a combination of this agent with nitrous oxid and morphin, the major part of the anesthesia in this case being produced by the nitrous oxid and morphin. The effect of ether, when thus administered, is relatively much greater than when given alone, for, as is well known, narcotic drugs, given in combination, reinforce the action of one another.[2] Thus the powerful joint effect of morphin and scopalamin has been explained.

Clinical Results.—The form of anesthesia herein described has been in use in the surgical clinic of the Johns Hopkins Hospital for two years, over 2,500 patients having been anesthetized by this method. It is there the routine form of anesthesia for all operations, except those on the face, upper air-passages, or cranium. In these it has been found inconvenient on account of the difficulty of keeping the mask in place.

Before the operation, the patient is given an enema and deprived of food for several hours, but is allowed to take small quantities of water. About thirty minutes before the anesthesia is begun a hypodermic of morphin and atropin is given, the dose for an adult being morphin 1/6 grain, atropin 1/100 grain. The anesthesia is started after the patient has been placed on the table and while the field of operation is being surrounded by sterile towels. It is established so quickly that the incision can usually be made in two minutes after the mask has been put on. Any depth of anesthesia which the condition of the patient and the nature of the operation may require can be easily obtained, because of the control of the patient's respiration which is given by the rebreath-

[1] Cushny: "Pharmacology and Therapeutics," 4th ed., 211.

[2] Führer: "Pharmakologische Untersuchungen über die Mischnarkose," *Münch. med. Woch.*, 1911, No. 4; Bürge: "Die Wirkung von Narkotikakombinationen," *Deutsch. med. Woch.*, 1910, No. 1, 20; No. 2, 62.

ing. In abdominal operations, if the increased activity of the respiration is inconvenient, it can be prevented by giving a fresh supply of gas at frequent intervals. The bleeding during nitrous oxid-oxygen or nitrous oxid-ether anesthesia is about the same as during open ether anesthesia. The patient's temperature, provided he is kept dry and covered, will be found elevated from 0.5° to 2° after an hour's operation. Thus any special device for heating the gases is unnecessary, since the patient himself attends to this.[1] With light narcosis, under nitrous oxid and oxygen alone, the pulse may be rapid (from 140 to 160 to the minute), but this is of no significance, provided it is regular and of good quality, and there is no hemorrhage. The rapid heart-rate decreases when ether is given.

Long Operations.—This form of anesthesia is especially well suited for long operations. In fact, the anesthesia does the patient so little harm that, within reasonable limits, the duration of the narcosis need not be considered. This is often advantageous to the surgeon, when deliberation and minute attention to detail are necessary. The following typical cases illustrate the method:

Case 1.—The patient was a negro man, aged 27, in good physical condition. Operation: Excision of a sarcoma from the right popliteal space, and blood-vessel transplantation. Duration of anesthesia, five hours. The pulse-rate per minute varied from 72 to 100. The blood-pressure at the end of four hours of anesthesia was 130 mm. of mercury. The patient regained consciousness before leaving the table. He had no headache, nausea, or vomiting though he was given water at once. His urine after operation contained no albumin or acetone. He was allowed to rebreathe at two and one-half and three-minute intervals. The narcosis was deep and quiet. Ether was given with the gas for the first half hour.

Case 2.—The patient was a white woman, aged 30, in rather poor condition. Operation: Resection of the ascending and transverse colon. Duration of anesthesia, two hours and five minutes. No ether was used. The narcosis was light, the patient at times moving her limbs. Recovery was immediate and unattended with headache or vomiting.

Case 3.—The patient was a colored woman, aged 30, in good condition. Operation: Excision of the right breast, pectoral muscles and axillary glands for advanced cancer of the breast, Thiersch skin grafting of the raw surface of the breast. Duration of anesthesia, three hours and fifty-five minutes; 2½ ounces of ether, 130 gallons of gas and 30 of oxygen were used. The anesthesia was quiet and satisfactory, the recovery immediate and without headache, nausea, or vomiting.

[1] On the subject of "Warmed Anesthetic Vapor," see Gwathmey, *N. Y. J. of Med.*, Feb., 1905.

Cautions.—A word of caution is, however, necessary. During any administration, and especially during a long administration, the patient's breathing must be kept free and unobstructed, and his color good. If a patient has to work hard for every breath he soon wears himself out. The color of the blood in the wound, the hue of the patient's face, and the character of his breathing, as shown by the movements of the rubber bag, are the best indicators of his condition. The surgeon himself can hardly fail to notice these. If the patient's breathing cannot be kept unobstructed, the use of the apparatus should be abandoned at once and some other method for the production of anesthesia employed.

Fatalities.—Three fatalities, during or immediately after operation, in the series of 2,500 cases have been recorded. How much the anesthesia was to blame for these may be judged from the following reports:

Fatality 1.—The patient was a colored woman, aged 44, with exophthalmic goiter of four years' standing. She had an irregular intermittent pulse, the rate of which had been between 120 and 140. Her heart was enlarged, and she had ascites and edema of the ankles. During the last week of her life she had several severe attacks of dyspnea, associated with extreme rapidity and irregularity of the pulse. For these she was given a course of digitalis, which improved her condition so much that it was thought she could withstand a partial thyroidectomy. When the mask was placed over her face, she made a very slight struggle and took several shallow breaths. The operator then saw the superficial veins of her neck suddenly dilate. This apparently marked the time of death, and occurred within half a minute of the time the anesthetic was started.

Fatality 2.—The patient was a man with aortic and mitral insufficiency, on whom it was proposed to do a perineal prostatectomy. He was given ether with the gas and oxygen. The anesthesia went very well till the patient was placed on the perineal table with his buttocks elevated; then he became cyanotic and died. An immediate autopsy revealed the presence of a large pericardial effusion, the presence of which had not been recognized before the operation.

Fatality 3.—The patient was a girl of 16, with multiple infectious arthritis; general condition poor. Operation: Injection of both knees with oil and manipulation of knees, ankles, and elbows. Duration of anesthesia, fifteen minutes. The anesthesia was uneventful, except for a marked increase in pulse-rate while each joint was being manipulated. At no time was the breathing obstructed. At the close the pulse-rate went up very rapidly; the color became cyanotic and could not be cleared up with oxygen. The breathing became weaker and weaker, and finally ceased. An autopsy showed a very large thymus and hypertrophy of all the lymphatic tissues. The pathologists gave *status lymphaticus* as the cause of death.

The first and second of these patients had circulatory disease of such gravity that the anesthesia is not to be seriously blamed for the deaths. How the third fatality was brought about it is hard to understand. The toxicity of nitrous oxid is certainly too low to have caused it.

Cardiac Cases.—Notwithstanding these fatalities, it is believed that this form of anesthesia, properly employed, is well suited for cardiac cases. Two cases of Cesarean section performed by J. W. Williams on women with serious valvular lesions will show the grounds for this belief. Both women were in about the seventh month of pregnancy, and in both delivery was necessary in order to save the life of the patient. One patient was *in extremis* and her death on the table was regarded by the operator as probable. Both women had such urgent dyspnea that the anesthetic had to be started with the patient sitting upright. The same method of administration was employed in each case. Each patient was given a hypodermic of morphin large enough to quiet her. In inducing anesthesia great care was exercised to avoid the least excitement or struggling on the part of the patient. Both were allowed to rebreathe oxygen till the respiration was stimulated before any nitrous oxid was given. Enough ether was used to give a quiet anesthesia. The operations were performed with the patients' bodies elevated at an angle of 20° to 30°. The pulse of both patients was much better during anesthesia than before, and the operator was able to proceed without undue haste. Both patients made an excellent recovery.

Hypercapnia.—Clinical experience has certainly shown that an excess of carbon dioxid in the blood—a hypercapnia during anesthesia to the degree allowed—is harmless. Hill and Flack state that "the effects of carbon dioxid on the heart can always be quickly recovered from, even if the blood-pressure has sunk to zero." These authors found that carbon dioxid up to a percentage of 35 in the air breathed stimulates the respiration, while above 35 it depresses it; also that percentages up to 22 produce a rise in blood pressure, while higher percentages cause a fall. Of course it is impracticable to determine exactly what percentage of carbon dioxid a patient is breathing. The anesthetist must regulate the time of rebreathing so that the patient's respiration is moderately stimulated. The periods of rebreathing for 10 liters of gas range from three to five minutes, any leakage from the apparatus being meanwhile made up by the addition of fresh gas.[1]

[1] After rebreathing 10 liters of oxygen for three minutes, it was found to contain 8.9 per cent CO_2. Allowing for the decreased CO_2 formation during anesthesia, it is probable that the percentage breathed by the patient is seldom above this.

Acapnia.—Does a deficiency of carbon dioxid in the blood—acapnia—do serious harm? Henderson has been able to reduce animals to a state of extreme shock by overventilation of their lungs. He asserts that acapnia causes complex osmotic changes in the tissues, which result in a passage of water from the blood into the lymph and into the tissue-cells, and a dilatation of the finer veins. Interference with the normal filling of the right side of the heart by this process is the essential phenomenon in surgical shock. In extreme cases of acapnia the blood-stream is so scant and the respiration so feeble that the tissues do not receive the necessary amount of oxygen. An asphyxial acidosis results which does the body-cells irreparable injury. Whether Henderson's theory be accepted or not it must be admitted that the accumulation of carbon dioxid by the process of rebreathing is an efficient stimulus to the respiration and circulation. In fact, it is used as a purely therapeutic measure in cases of morphin poisoning, in cases of so-called traumatic or toxemic shock, and wherever the respiration is feeble.[1] Oxygen can be given much more effectually and cheaply by the use of rebreathing than in the ordinary way. Thus, with anesthetics of low toxicity and the use of rebreathing, a very ill patient may be benefited by an anesthetic.

Ether and Acapnia.—On the other hand, when ether is given by the open method, we take a very efficient means of producing acapnia, because ether diminishes the formation of carbon dioxid by the tissues, and, by stimulating the respiration, hastens its elimination. Symptoms of a mild grade of acapnia under open ether anesthesia are common. Thus a patient who has perhaps been difficult to anesthetize, or who has been lightly under ether for some time and is breathing at a rapid rate, will gradually stop breathing. After an interval of perhaps two or three minutes, his respiration will start again but will not be normal for a long time. This occurrence, though alarming, is seldom followed by harmful results.

Hundreds of patients are etherized daily by the open method without developing symptoms of shock. What prevents a serious grade of acapnia in the great majority of cases? Several factors are concerned.[2]

(1) Many anesthesias are of too brief duration for acapnia to develop.

(2) There is frequently more or less obstruction to the breathing during narcosis, and this prevents acapnia.

[1] Patients with feeble pulse and respiration—so-called shock cases—should be made to rebreathe air in oxygen till their respiration is normal, before breathing the anesthetic.

[2] Levi, Ettore: "Studies on the Patho-physiologic Action of CO_2 and on the Therapeutic Applications in Surgery and Medicine of Mixture of O_2 and CO_2," *Estr. d. rev. crit. di clin. med.*, 1910, *11*, 30, 31.

(3) The slowing of the respiration which results from a preliminary hypodermic of morphin may protect from the same danger.[1]

(4) The so-called "open" method is usually not "open" at all, for the mask is so covered with towels or gauze that the patient does considerable rebreathing.

Other Advantages of Rebreathing.—Apart from the prevention of acapnia, rebreathing presents several other advantages over open ether anesthesia. The chief of these are:

(1) Lessened post-anesthetic vomiting.

(2) Decrease in number of cases of abdominal distention after operation.

(3) Practical abolition of post-anesthetic lung complications.[2]

Post-Anesthetic Nausea.—Vomiting after operation depends on many things besides the anesthetic. About 35 per cent of our patients vomit, but the vomiting is usually very slight. Of 200 patients only four had more than very transient vomiting. Of these cases one was a case of exophthalmic goiter, one a case of stone in the common bile-duct, one a case of spreading peritonitis from an appendix abscess, and one a case of intestinal reaction. The nausea alone seldom prevents a patient from taking water and nourishment at once after operation.

Post-Anesthetic Abdominal Distention.—Very little experimental work has been done regarding the question of abdominal distention following ether anesthesia. Cannon and Murphy[3] observed a great delay in the emptying of the stomach contents into the duodenum, and a slowing of the passage of food along the intestines after etherization. Figure 24, which is a tracing obtained from D. R. Hooker,[4] demonstrates

[1] Crile: "The Blood-pressure in Surgery," 281.

[2] Homans: "Post-Anesthetic Pulmonary Complications," *Bull. Johns Hopkins Hosp.*, April, 1909.

[3] Cannon and Murphy: "The Movements of the Stomach and Intestines in Some Surgical Conditions," *Ann. Surg.*, 1906, *13*, 513.

[4] Thanks are due Dr. Hooker for permission to publish this tracing and for the following note:

"Dr. Gatch has asked to have added a note covering some unpublished experiments done in the physiologic laboratory of the Johns Hopkins University, which appear to have a direct bearing on his own work.

"Cross-sections of blood vessels or intestine, to which a recording lever was attached, were hung in a moist chamber. In the use of tissue from warm-blooded animals the temperature of the chamber was maintained constant at 35° C. Through the chamber were passed alternately streams of oxygen and carbon dioxid gas. By this method the tissue studied was exposed to practically pure atmospheres of the gases. The experimental conditions, therefore, did not fall within physiologic limits, so far as the percentage of gas is concerned. Work is now in progress to investigate the effect of different percentages of oxygen and carbon dioxid. Aside from the result of this future work, however, the interesting fact has been demonstrated that the musculature of the blood vessels responds in atmospheres of the gases studied in an exactly opposite manner the paralyzing effect of a weak ether vapor on the pyloric ring of the frog. It also shows that carbon dioxid acts as a powerful stimulant to the muscle of the ring. Of course the conditions to which the bowel was subjected when this tracing was obtained were abnormal, yet the paralysis by ether is exactly what any clinician would expect. It is well recognized that an excess of carbon dioxid in the blood promotes peristalsis,

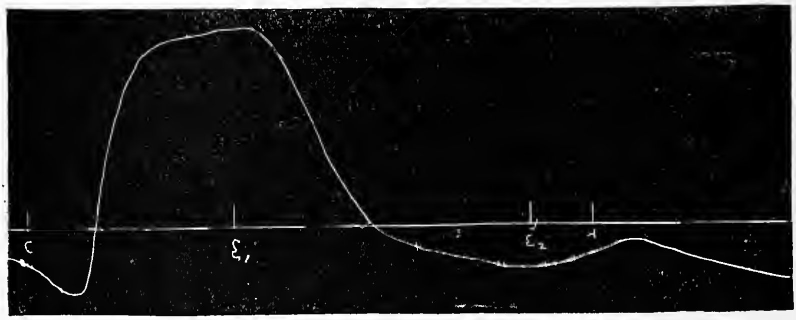


Fig. 24.—Tracing Obtained from the Pyloric Ring of a Frog Suspended in a Moist Chamber into Which Ether Vapor and Carbon Dioxid Could Be Passed. At c, carbon dioxid was passed over the muscle, causing a sharp contraction; at e_1 very dilute ether vapor was turned on with the carbon dioxid, causing immediate relaxation; at e_2 the ether was turned off.

to the musculature of the intestines. Carbon dioxid causes a marked improvement in the tone of the intestines and a marked relaxation of tone in the veins and arteries. On the other hand, oxygen causes a relaxation of tone in the intestines and an improvement of tone in the veins and arteries. These results were obtained in the case of both warm-blooded and cold-blooded animals and demonstrated with graphic records.

"If it be true that Henderson reasoned by analogy from the behavior of the smooth muscle in the intestine to that in the blood vessel (especially the veins) in developing the acapnia theory of surgical shock, it is obvious from these results that his reasoning was not entirely justifiable.

"The correlation of the difference in action of these gases in physiologic economy tempts speculation. The body seeks to rid itself of any excess of carbon dioxid. Jerusalem and Starling (*J. Physiol.*, 1910, *40*, 279) have shown that carbon dioxid (0.625 of an atmosphere) increases the efficiency of the isolated mammalian heart chiefly by improving its diastolic relaxation. Bayliss (*J. Physiol.*, 1901, *26*, 32) has shown that this gas relaxes vascular tone. It has long been known that in the intestine the same gas increases peristalsis, and Mall (*Johns Hopkins Hosp. Rep.*, 1896, *1*, 37) has suggested that rhythmic movements of the intestines may help to empty the venous plexuses in the walls and thus aid in driving the blood into the portal system. We have, therefore, a coördination of activity which greatly facilitates the circulation of blood and the consequent rapid elimination of the carbon dioxid. Oxygen in excess, on the contrary, would tend to bring about opposite effects with a resultant retardation of the circulation.

"In conclusion, it should be clear to the reader that this is a chemical regulation of the circulation entirely peripheral in its action. The action of the gases on the medullary centers is a wholly different question."

and Henderson[1] has shown that the normal intestinal movements which cease after a laparotomy can be restored by passing a stream of carbon dioxid over the exposed bowel. These experimental results are confirmed by clinical experience. It will be recalled that we use the smallest possible amount of ether, and produce a hypercapnia by making a patient rebreathe. In the 200 cases referred to above there was not a case of abdominal distention except after laparotomy, and among the laparotomies, seventy-five in number, it occurred in but three cases, these being the same patients who had considerable vomiting.

Post-Anesthetic Lung Complications.—In 2,500 cases of nitrous oxid-oxygen or nitrous oxid-oxygen-ether anesthesia there was but one case of post-anesthetic pneumonia; this was in a girl with general peritonitis, who recovered. This absence of pneumonia may have been partly accidental, since pneumonia after operation may be due to causes other than the anesthetic. The record is striking, however, and all the more so because patients with pulmonary tuberculosis, bronchitis, and empyema were anesthetized without hesitation. It contrasts markedly with the record after open ether. Here in a series of 400 cases there was one death from ether pneumonia, and two deaths, one with autopsy, from acute pulmonary tuberculosis.[2] The latter patients were both operated on for tuberculous glands of the neck. Both patients died rather late—in from two to three weeks—after operation, but they ran a high temperature from the first. It was the opinion of L. V. Hammond, who had charge of the work on tuberculosis at the Johns Hopkins Hospital, that the etherization had lighted up small apical foci of disease undetected before operation.

Method Demands Experience.—The impression must not be gained that this form of anesthesia is free from danger. It is without danger so far as post-operative effects are concerned. During the administration, however, there are dangers. These arise from causes which can generally be foreseen and which can always be prevented by careful and skillful administration. The method should not be used except by those who have made a special study of its problems.

CHLOROFORM AND ETHYL CHLORID

Suggested Investigations.—The foregoing discussion of the use of rebreathing in the administration of ether and nitrous oxid will apply, in part at least, to the administration of all anesthetics given by inhalation. It would seem that rebreathing in the administration of chloro-

[1] Henderson: "Shock after Laparotomy: Its Prevention, Production, and Relief," *Am. J. Physiol.*, 1909, *21*, 60.

[2] Walsh: "Chloroform Rather Than Ether Anesthesia in Tuberculosis," *J. Am. Med. Assn.*, Aug. 28, 1909.

form and ethyl chlorid would be attended by the same advantages that exist in the giving of ether and nitrous oxid. The general principles which govern the administration of these agents by a closed method are:

First: The problem of dosage, which must be taken into account because of the high toxicity of chloroform and ethyl chlorid. A definite measured quantity of the anesthetic should be added to each measured volume of the gas which serves as a vehicle for administering it. The narcosis should be begun with a very dilute anesthetic vapor.

Second: When once anesthesia is established, it should be maintained in the same way as with an ether anesthesia, namely, by preventing the elimination of the drug from the patient's blood by making him rebreathe oxygen or air. The elimination of the anesthetic at the close of the narcosis could be hastened by overventilation of the patient's lungs.

Dangers.—The chief dangers of this method are:

(1) Anoxemia due to a failure to give sufficient oxygen or to an obstructed airway.

(2) Impediments to the respiration, which, in a long anesthesia, may exhaust the patient.

(3) With cardiac cases, excitement during the period of induction.

Advantages.—The chief advantages of this method are:

(1) The rapidity and pleasantness with which anesthesia is established.

(2) The ease with which any depth of anesthesia can be secured.

(3) The prevention, to a very large extent, of post-anesthetic vomiting, pulmonary complications, and abdominal distention.

CHAPTER IV

NITROUS OXID

History: Early Use in Dentistry; Nitrous Oxid Administered with Oxygen; Physical Properties; Chemical Properties; Impurities of Nitrous Oxid; Standard of Purity.

Special Physiology: The Hyperoxygenation Theory; The Deoxygenation or Asphyxiation Theory; The Theory of the Specific Action of Nitrous Oxid upon the Brain Cells; Effects upon the Respiratory System; Effects upon the Circulatory System; Effects upon the Nervous System; Effects upon the Muscular System; Effects upon the Glandular System and Other Structures; Causes of Death; Stages of Anesthesia; Elimination; After-effects.

Comparison with Other Agents.

Indications and Contraindications.

Administration: Heating the Gas; Essential Features of Any Satisfactory Apparatus; Apparatus for Administering Nitrous Oxid Alone or With Air; Dangers of Administration of Nitrous Oxid Alone; Recognition of Asphyxial Symptoms; Administration of Nitrous Oxid Alone; Administration to Asphyxiation With and Without Valves; Use of Expiratory Valve Alone; Administration Without Valves; Precautions When Administered Alone; Administration of Nitrous Oxid With Air in Unknown Quantities; Administration of Nitrous Oxid With Definite Amounts of Air; Nitrous Oxid as a Sequence to Ether; Nitrous Oxid With Air; Technique of Ether-Nitrous Oxid (Air) Sequences; Technique With A.C.E.; Advantages of Ether (or Chloroform-Ether)-Nitrous Oxid Sequence; The Advantages of Administration of Nitrous Oxid With Oxygen; Superiority of Oxygen Over Air; The Administration of Nitrous Oxid With Indefinite Quantities of Oxygen; Gatch's Method of Administration; Davis' Method; Methods of Administration With Definite Quantities of Nitrous Oxid and Oxygen; Gwathmey's Method; Teter's Method; Technique to be Followed in Administering Nitrous Oxid and Oxygen With the Teter Apparatus and the Teter Nasal Inhaler; Nitrous Oxid Oxygen Endopharyngeally; Boothby and Cotton Apparatus; The Gwathmey-Woolsey Nitrous Oxid-Oxygen Apparatus.

HISTORY

In 1772, Priestley[1] discovered nitrous oxid, called by him "dephlogisticated nitrous air," by reducing nitrogen dioxid (NO_2), "gaseous oxide of azot," with moist iron filings. In 1793, Deimann and others prepared the gas by heating ammonium nitrate (NH_4NO_3), essentially the commercial process for its manufacture to-day.

In 1798, the "Pneumatic Institute" was founded for the purpose of investigating the "medical powers of factitious airs or gases" and was set up at Clifton by Dr. Beddoes. The immediate idea to be followed out was the treatment of phthisis and other lung troubles by inhalation of various gases. Humphrey Davy was assigned the office of superintending the experiments. One of the first outcomes of his researches, the result of his experimentation with nitrous oxid upon animals, is given in the following historical and often quoted sentence:[2] "As nitrous oxid in its extensive operation appears capable of destroying physical pain, it may probably be used to advantage during surgical operations in which no great effusion of blood takes place." Then Davy actually inhaled the gas and recorded his own sensations and the behavior of others after they had inhaled it.

Early Use in Dentistry.—In December, 1844, Colton delivered a lecture on nitrous oxid and other gases in Hartford, Connecticut. Horace Wells, a dentist of that place, was present. He noticed that a person under the influence of the gas was capable of sustaining a severe injury without apparently feeling any pain. This fact so impressed him that he requested Colton to administer the gas to him, and, while under its influence, had a tooth extracted without feeling the least pain. Upon regaining consciousness, he exclaimed, "A new era in tooth-pulling." From that time on he administered the gas to his patients with more or less success.[3] With the death of Wells, which occurred in 1848, and the introduction of ether, nitrous oxid was not thought of again as an anesthetic until Colton revived its use in 1863. Rymer in England and Hermann in Germany also undertook (1864-1866) some experiments with nitrous oxid.

[1] "Experiments and Observations on Different Kinds of Air," *1*, 3; "Memoirs of Joseph Priestley to the Year 1795," 1803, 1.

[2] Davy: "Researches, Chemical and Philosophical, Chiefly Concerning Nitrous Oxide," London, 1800.

[3] Upon attempting to make a public exhibition at the Massachusetts General Hospital the inhaler was removed, possibly too soon, and the patient gave a piercing cry. Wells was immediately looked upon as an imposter. He, a modest, retiring man, felt the imputation deeply, and, while continuing to administer the gas in private, never summoned sufficient courage to attempt another public exhibition. Later he gave up the practice of dentistry, became more or less unsettled in his mind, and died by his own hand.

In 1867, Colton was able to give a record of twenty thousand successful cases; and in 1868 an auspicious demonstration took place at the Dental Hospital in London, mainly through the financial assistance and patronage of the well-known American dentist, Evans, of Paris. At this period it was considered safe for short operations. Some surgeons, however, declaimed against nitrous oxid as unsatisfactory and dangerous. Nevertheless, a Joint Committee of the Odontological Society and of the Dental Hospital reported so favorably upon the value of the gas that it has since occupied the foremost place as an anesthetic in modern dentistry

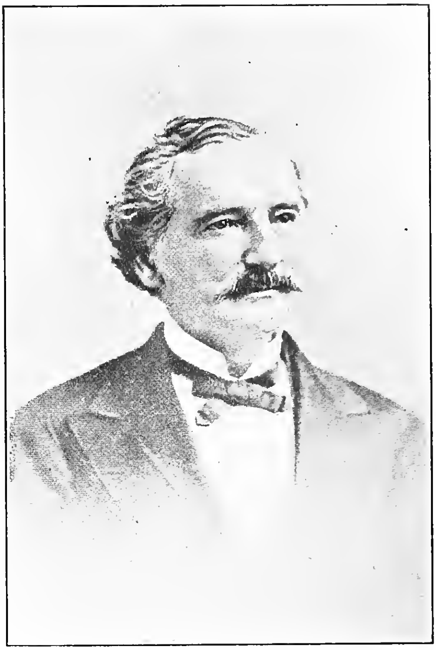


FIG. 25.—GARDNER Q. COLTON.

Nitrous Oxid Administered with Oxygen.—In 1868, Andrews published accounts of a number of cases in which he had obtained a non-asphyxial form of anesthesia by using oxygen with nitrous oxid.

It is now well established that an efficient anesthesia can be maintained by administering definite percentages of air with the gas. Also, by combining nitrous oxid with oxygen we may obtain a deeper, more satisfactory and safer anesthesia. Furthermore, by warming a mixture of the gas and oxygen, and by the addition of small amounts of ether and chloroform, a satisfactory form of anesthesia can be maintained for over 80 per cent of all surgical cases. Brown, of Cleveland, Ohio, was the first to use a warmed mixture of nitrous oxid and oxygen.[1] Clover and Coleman first attempted the continuous administration of nitrous oxid through the nose. Patterson, in 1899, improved upon this, and Kilpatrick,[2] in 1902, still further improved this method by placing a regulation expiratory valve upon the nosepiece. Teter improved the technique of nasal anesthesia by using oxygen and warm nitrous oxid with a perfected nosepiece. Karl Connell, of Roosevelt Hospital, has only recently improved the technique of administering nitrous oxid and oxygen by using nasal catheters and a pharyn-

[1] The first recorded experimentation with these gases at different temperatures on lower animals was by Gwathmey in 1906.

[2] *Medical Press*, July 18, 1902.

geal breathing tube to maintain a clear airway and also by rebreathing to decrease the amount of gases used.

Physical Properties.—Nitrous oxid, "laughing gas," nitrogen protoxid, nitrogen monoxid, N_2O, is a colorless gas at ordinary temperatures; it possesses a specific gravity of 1.527. One liter of the gas weighs 1.97 gm.; 100 cubic inches weigh 47.29 gm. Under a pressure of 50 atmospheres at + 7° C. (+ 44.6° F.) or 30 atmospheres at 0° C., it is converted into a colorless mobile liquid having a density of 0.937 (at 0° C.);[1] the liquid has the lowest refractive index of all liquids. The ease with which it may be liquefied is taken advantage of and liquid nitrous oxid is supplied on the market in steel cylinders of various capacities. A convenient size for short operations, or for preliminary administration to produce unconsciousness before the use of ether or chloroform, is a small tube weighing about 39 ounces gross, which holds 6 ounces of the gas. For hospital work vanadium-steel cylinders holding 200 to 250 gallons of the gas are serviceable.[2] Fifteen ounces of the liquid on evaporation yield about fifty gallons of the gas. The cylinders usually, and should always, have a statement upon an attached label indicating the weight of liquid within. By remembering that an ounce of the liquid yields about three and one-third gallons of the gas, at ordinary room temperature and pressure, the operator can readily know the amount of gas at his disposal. By weighing before and after use each time, and entering the difference upon the label, the anesthetist always knows what his supply is. This information is of vital importance in some cases.

Nitrous oxid, like other gases, expands when heated. The gas and liquid within the cylinder are under a theoretical pressure of at least 750 pounds per square inch even below room temperature. Often the pressure is over 1,000 pounds per square inch. If the cylinders are subjected to undue heat, the pressure may become so great as to burst the cylinder, producing serious consequences; therefore, any unnecessary heating of the cylinder should be avoided. Such accidental explosions have occurred.

The boiling point of nitrous oxid at 760 mm. pressure is —90° C.; the freezing point is —102° C. If the liquid is allowed to escape under atmospheric pressure through a small orifice, part of it is converted into a compact snow,[3] which has a temperature of —100° C. This snow, along with some ice produced from the moisture of the air by the low

[1] Faraday, 1823.

[2] According to the best modern practice, vanadium-steel cylinders are the safest, for, even if they burst, they are not shattered, but simply split along the seam.

[3] Wills: "A Modification of Thilorier's Method for Preparing Solid Carbon Dioxide," *J. Chem. Soc.*, *12*, ii, 21.

temperature, may sometimes choke the outlet and interfere with the regular flow of the gas. This difficulty will never be encountered when small amounts of the gas are used, if the simple precaution be taken to keep the outlet well above the level of the liquid within—in short, if the gas is drawn off with the cylinder in a vertical position, outlet upward.[1] When, however, the gas is to be used in prolonged cases it is desirable to heat the outlet.

Liquid nitrous oxid may be preserved with perfect safety for an indefinite time in steel cylinders provided with good valves. Some administrators [2] have noted differences between nitrous oxid which had and had not been liquefied. These differences undoubtedly were due to the admission of undetermined and variable amounts of air in preparation for or during administration, or to temperature conditions brought about by administering the gas from the liquid without the warming referred to above.[3]

Nitrous oxid is soluble in water, volume for volume, at 0° C.; the solubility diminishes greatly on elevation of the temperature of the water. The solution seems to be mainly physical, as we have no evidence of chemical union between the nitrous oxid and water as in the case of carbon dioxid and water, beyond the formation of an unstable hydroxid, N_2O6H_2O, at 0° C. The gas may be collected over warm water. It is quite soluble in absolute alcohol at zero.

Chemical Properties.—Nitrous oxid is quite stable, not being decomposed into its elementary constituents by heat, unless the temperature is very high. It supports combustion, if the combustion has been actively started; that is, a strongly burning taper is not extinguished when plunged into the gas, but continues to burn, utilizing the oxygen and liberating the nitrogen. Nitrous oxid has a pleasant odor and a slightly sweet taste. It may be respired without discomfort, with suitable apparatus. When pure it exhibits no irritant properties.

Impurities of Nitrous Oxid.—The manufacture of nitrous oxid depends upon heating ammonium nitrate,

$$NH_4NO_3 = N_2O + 2H_2O; \text{ or}$$

some combination of salts which produces ammonium nitrate, as, for example, $KNO_3 + NH_4Cl$; $3NaNO_3 + (NH_4)_3PO_4$; or $2NaNO_3 +$

[1] In connection with the devices for using cylinders in the horizontal position, see Sheppard: *Lancet*, 1891, 424; Hewitt, "Anæsthetics," 3rd ed., 268.

[2] Roberts: *Brit. J. Dent. Sci.*, Dec. 15, 1884.

[3] Smith and Leman: *J. Am. Chem. Soc.*, 1911, *33*, 1116, give analytical results indicating a difference in the gas when drawn from cylinders with the outlet upward or reversed. They state that there is less nitrous oxid and more air (than that originally in the cylinder) in the gas when first drawn from the upright cylinders. Cylinders should have all the air removed before filling. If this has not been the case and the cylinder is thoroughly shaken just before the use, the gas is of uniform composition, as has been shown by Baskerville.

$(NH_4)_2SO_4$.[1] The impurities liable to be present depend upon the materials used, proportions present, heat treatment, and conditions of the pumps and containers.[2]

Compressed nitrous oxid obtained in the American market from different manufacturers gave on analysis the following values:

ANALYSIS*

Sample No.	N_2O	H_2O	CO_2	NH_3	O_2	N_2, etc. by diff.	N_2O by explosion	N_2O by Cu + CO_2+H_2	N_2O by Cu + H_2
1	99.7	0.13	0	0.006	Present	0.16	97.5	99.4	99.7
2	96.6	0.15	0	0.001	Present	3.25	95.0	96.2	96.6
3	99.5	0.15	0	0	Present	0.35	97.3	99.3	99.5
4	95.9	0.16	Present	0	Present	3.94	94.1	95.6	95.9

* Baskerville and Stevenson, *loc cit.* The last column gives the figures contained by the new method devised by them.

Smith and Leman analyzed four cylinders of liquid nitrous oxid from different manufacturers, with the results shown on page 123.[3]

Standard of Purity.—Nitrous oxid which is to be used for anesthetic purposes should contain at least 95 per cent of N_2O and no solids,

[1] One of the authors (C. B.), in conjunction with Stevenson, has made an investigation of this subject and devised methods of analysis, for the details of which see *J. Ind. and Eng. Chem.*, Aug., 1911. Erdman and Stolzenberg, Berlin, *43*, 1708, Willard, *Compt. rend.* (1894) *118*, 646, found that a hydrate of nitrous oxid ($N_2O.6H_2O$) may be obtained by keeping at 0°, in a sealed tube, a mixture of liquid nitrous oxid and water. Ice does not appear to react with nitrous oxid. Willard (*ibid.*, *118*, 1096) found that nitrous oxid may be freed from air and nitrogen, the commonest contaminants, according to him, by the preparation of this hydrate, which, although scarcely decomposed below 0° under ordinary pressure, furnishes about 200 times its volume of gas when warmed above this temperature. He devised an apparatus for the purification of nitrous oxid by this means. [*Ann. Chim. Phys.* (7), *11*, 289.]

[2] Commercial nitrous oxid is apt to contain these impurities: Cl_2, No, NO_2, HNO_3, NH_3, HCl, CO_2, O_2, N_2, rare gases of the air, and organic matter (from lubricants). Of these the first six only produce any irritation of the respiratory mucous membrane, and they are usually removed in its manufacture, if present, by washing the gas in turn with solutions of sodium hydroxid, ferrous sulphate, and sulphuric acid. Further purification may be accomplished by the formation of a hydrate below 0° C., by fractional condensation and subsequent fractional distillation.

[3] *J. Am. Med. Assn.*, *57*, No. 7.

Percentage of	No. 1	No. 2	No. 3	No. 4
Nitrous oxid	95.4	93.4	95.8	96.1
Oxygen	0.0	1.4	1.1	0.1
Nitrogen	4.6	5.2	3.1	3.5
Carbon dioxid	0.0	0.0	0.0	0.3

liquids, combustible organic matter, chlorin, or other oxids of nitrogen.[1] The last two impurities may be tested for by slowly passing 10 liters through silver nitrate and ferrous sulphate solutions. No precipitate should be produced in the former, and no brown or black coloration in the latter.

SPECIAL PHYSIOLOGY

The evolution of knowledge concerning the physiological action of nitrous oxid administered by inhalation is striking and the changes of opinion are radical. The conceptions of the physiological action of this agent have, in a large measure, been controlled by the clinical methods of administration employed at various times. Three distinct steps in this process of elimination and up-building, based upon experimental and clinical data, may be traced.

The Hyperoxygenation Theory.—Sir Humphrey Davy believed that nitrous oxid was decomposed into its constituents, nitrogen and oxygen, during its passage through the circulation. It was thought that this produced superoxygenation of the blood, and that this overproduction of oxygen led to the formation of unusual amounts of carbon dioxid, which, in turn, produced a form of "internal asphyxia."

Oliver and Garrett[2] examined the gases of the blood of a dog while under nitrous oxid, with the results shown on page 124.

From these figures it will be seen that there is undoubtedly a large increase in nitrogen in the blood after nitrous oxid inhalation. There seems, however, to be no conclusive evidence that nitrous oxid splits up in the organism, the gas being too stable to be decomposed at the temperature of the blood. The increase in nitrogen, as shown by the fore-

[1] Lack of knowledge of the content of real N_2O may seriously interfere with the satisfactory use of this, the safest, anesthetic, especially when it is administered by the proper method, namely, mixed with oxygen. If the preparation contains more than 95 per cent N_2O, the variation in the proportion of the two gases will depend then, in fact, upon the amount of oxygen actually mixed, and the percentage is not seriously altered.

[2] *Lancet*, 1893, 683. (The analytical methods and technique employed in these determinations are not known.)

Normal Dog	Before Inhalation	After Inhalation
CO_2	34.3	15.66
O_2	22.0	3.49
N_2	1.8	11.23
N_2O	....	22.49

going figures, remains unexplained. Frankland[1] analyzed the expiratory products of several administrations and failed to find any distinct evidence of decomposition. The theory, therefore, that the brain cells are overpowered, so to speak, by an excess of oxygen, with the resulting phenomenon of anesthesia, was abandoned as being untenable.

The Deoxygenation or Asphyxiation Theory.—When it became fairly well established that nitrous oxid is too stable a gas to be decomposed upon its entrance into the circulation, as formerly supposed, opinion swayed in the opposite direction, and the theory proposed was that, the hemoglobin of the blood having a greater affinity for nitrous oxid than for oxygen the oxygen becomes displaced from the lungs and other tissues by the nitrous oxid, the brain cells and nervous centers being thus starved, so far as oxygen is concerned, are smothered, as it were, by nitrous oxid. To this condition the term asphyxiation is applied, and unconsciousness, or anesthesia, is the inevitable result. This mechanical displacement of oxygen by nitrous oxid, leading to "tissue asphyxia," has been characterized as a more dangerous view, from a practical standpoint, than the hyperoxygenation theory.

Hermann[2] concluded that nitrous oxid was simply absorbed by the blood plasma, and that its action was only that of asphyxiation, the conditions being accounted for by the exclusion of the oxygen normally breathed. He found that one hundred volumes of blood at body temperature would absorb sixty volumes of nitrous oxid. This ratio was later fixed by Bert as one hundred to forty-five.

This theory of so-called deoxygenation has been supported by Jolyet, Blance, Duret, Johnson, Reid, Amory, Wood, Cerna, and many others, and lately by Crile.

This theory held sway, as did the short-lived preceding hyperoxygenation theory, during the period when nitrous oxid was used almost exclusively for dental and very short surgical operations. During this time nitrous oxid was rarely inhaled pure. It was not only difficult to obtain a pure gas, but, when obtained, it was administered in such a way that it was variably diluted with air, the effects produced being, as a

[1] *St. Bartholomew's Hospital Record V.*
[2] *Brit. Med. J.*, 1868, 378.

rule, those of intoxication rather than anesthesia. Inasmuch as air exclusion, or oxygen exclusion, was considered the prime factor, the apparatus devised during that period aimed at this object. The apparatus devised by Colton was fitted with inspiratory and expiratory valves for the purpose of accomplishing the rigid exclusion of air.

The Theory of the Specific Action of Nitrous Oxid upon the Brain Cells.—Despite the fact that air-exclusion was aimed at, it was soon found that the alternate inhalation of nitrous oxid and air served to maintain a more or less complete anesthesia for protracted surgical operations. The asphyxiation theory was generally accepted until Andrews,[1] in 1868 (see History, p. 24), showed that anesthesia could be maintained over a longer or shorter time at will, by mixing oxygen with nitrous oxid. This, quite naturally, upset the deoxygenation theory, and led to the conclusion that the nitrous oxid must exercise some *specific action upon the brain cells.* The observations of Bert[2] and the early experiments of Buxton[3] verified the hypothesis that nitrous oxid produced narcosis by virtue of other than asphyxiating qualities.

This theory has held its own up to the present time, the variation of opinion bearing reference to *what constitutes the specific action of nitrous oxid upon the nervous centers.*

Kemp,[4] following a series of experiments begun in 1890, for the purpose of determining the validity or invalidity of the deoxygenation theory of nitrous oxid anesthesia, as the result of fourteen experiments, took a position intermediate between those who hold that the action of nitrous oxid and of nitrogen is the same, and those who hold that nitrous oxid is simply an indifferent gas, acting like nitrogen. He found that the difference in the action of the two gases, when given pure, was so masked by the rapid onset of asphyxia that any wide-reaching generalizations were unsatisfactory. Two points, however, he considered worthy of especial notice: (1) That anesthesia was induced more quickly with nitrous oxid than with nitrogen; (2) that the muscular movements which always supervene upon deprivation of oxygen were milder with nitrous oxid than with nitrogen.

A second set of experiments was conducted by Kemp, in which enough oxygen was given to sustain the life of the animal while the action of nitrous oxid and of nitrogen was being studied.

These experiments lead up to the present-day methods of administering nitrous oxid, and to the modification of the physiological action of

[1] Andrews: *J. Brit. Dent. Sci.*, 1869, 22.

[2] Bert: "Pression barométrique."

[3] Buxton, Dudley W.: (1) "On the Physiological Action of Nitrous Oxide," *Trans, Odontological Soc. of Great Brit.*, 1886, n. s., *18*, 133; (2) *Ibid.*, 1887, n. s., *19*, 90.

[4] Kemp, G. T.: "Nitrous Oxide Anæsthesia," *Brit Med. J.*, Nov. 20, 1897, 1480.

this and other inhalation anesthetic agents by oxygen, as detailed in the chapter on General Physiology, p. 30.

In the following discussion of the action of nitrous oxid upon the organism it is to be borne in mind that the gas, given alone, is under consideration. It is especially to be remembered, however, that the administration of nitrous oxid alone belongs to the past and not to the *present period of the science* of the administration of anesthetics.

Brunn,[1] who discusses the *mode of action of nitrous oxid,* recalls the demonstration by Bert of a specific narcotic efficiency on the part of nitrous oxid. Bert successfully avoided the onset of asphyxia by means of the inhalation of the nitrous oxid-oxygen mixture under pressure, proving at the same time that the narcosis could be arbitrarily lengthened. In this way he demonstrated the accuracy of his theoretical reflection, that it is the over-low partial pressure of the nitrous oxid—in the nitrous oxid and oxygen mixture as inhaled under ordinary atmospheric pressure—which prevents a sufficient absorption of nitrous oxid in the blood for the onset of narcosis. This deficit was successfully remedied by Bert through raising this partial pressure to the level of the atmospheric pressure.

Brunn emphasizes the fact that in order to understand the mode of action of nitrous oxid it is necessary to keep carefully apart the experiments with the inhalation of *pure nitrous oxid*—which always involves two factors, namely, the nitrous oxid action and the asphyxiation—and the experiments with the inhalation of nitrous oxid under a simultaneous supply of a sufficient quantity of oxygen.

Brunn refers to a series of fundamental experiments which were made by Goldstein,[2] who showed the narcotic effect of nitrous oxid on frogs. In comparative experiments, a frog ceased to react after five and a half minutes to strong external stimuli, in a nitrous oxid atmosphere, whereas the same frog had not yet lost its power of reaction after an hour and a quarter in a pure hydrogen atmosphere. However, the nitrous oxid narcosis was made to disappear again by the admixture of a small quantity of air.

For the explanation of this phenomenon, Goldstein regarded the assumption of diminished partial pressure as insufficient, and he believed, in contradistinction to Bert's views, that a rapid and complete narcosis was produced and maintained only when the effect of the nitrous oxid was combined with that of a deficiency in oxygen. This statement certainly holds good for "ordinary" nitrous oxid anesthesia, but he admitted himself that in a greater density of the nitrous oxid this was alone sufficient for the production of a complete narcosis.

[1] Brunn, M. v.: "Die Stickoxydulnarkose," "Die allgemein Narkose," 1913, 325.

[2] Brunn: Die allgemein Narkose," 1913, 325 *et seq.*

The study of the *respiration* of warm-blooded animals, under the effect of nitrous oxid, first led Goldstein to recognize the fact that in rabbits the respiration gradually becomes slower and more superficial, in an inclosed space with air as well as in a mixture of nitrous oxid and oxygen, until the respiration finally ceases, at 3-4 per cent oxygen contents of the gas mixture, without preceding signs of dyspnea. In sudden asphyxiation Goldstein distinguished three stages. The first is characterized by inspiratory efforts, to which are added, in the second stage, violent expiratory muscular efforts, combined with clonic convulsions; in the third stage there are infrequent inspiratory movements, the expiratory muscles remaining entirely inactive. Comparative experiments, with inhalation of nitrogen on the one hand and nitrous oxid on the other, yielded considerable differences. In the case of nitrous oxid, narcotic effects are almost instantaneously manifested, so that the dyspneic efforts do not reach nearly the same degree as in breathing nitrogen. The clonic convulsions are altogether absent. The second stage of the asphyxiation is more rapidly terminated. The most important difference, however, as compared to ordinary asphyxiation, according to Goldstein, is the appearance of loss of reflexes only just before the respiratory paralysis, namely, in the second half of the third stage of asphyxiation in ordinary asphyxiation; whereas, in nitrous oxid inhalation, the loss of reflexes is already present in the second stage, namely, long before the respiratory center is endangered.

In Goldstein's experience the inhalation of a mixture of 73 per cent nitrous oxid and 27 per cent oxygen, in dogs, was followed by a diminution in the number of respirations, while the depth was increased. The anesthesia, according to Goldstein, appears the more rapidly, and with a proportionately less degree of asphyxia, the higher the organization of the brain—namely, earlier in man than in the laboratory animals.

Effects upon the Respiratory System.—Experimental observations have established the fact that nitrous oxid, given pure, or alone, rapidly induces asphyxia by gradual paralysis of the respiratory center in consequence of the prolonged action of the increasingly deoxygenated, or venous, blood. The respirations, which at first become more rapid and deep, become convulsive as the deoxygenation process is continued, then slow and shallow, finally ceasing altogether. When the asphyxial element is absent, the convulsive character of the respirations is not noted.

Numerous experiments with animals have established the fact that when death is caused by pure nitrous oxid the usual post mortem signs of asphyxia are present. It has been emphasized by Hewitt [1] that the character of the pulse is greatly dependent upon the fullness and efficiency of the respiration. Whatever differences there may be between the phenomena produced by nitrous oxid, by nitrogen, and by mechan-

[1] Hewitt: "Anæsthetics," 1912, 90.

ical closure of the trachea, one and all, according to Hewitt, lead to fatal asphyxia.

Because of the lessened amount of tissue change which takes place in nitrous oxid anesthesia, the quantity of carbon dioxid given off by the lungs is decreased. The significance of this, with reference to the practical question of shock, is considered in the Chapter on Treatment Before, During, and After Anesthesia.

Nitrous oxid is not injurious to the *lungs,* being a non-irritating gas. The bronchial irritation of which some have complained is partially eliminated by warming the agent (see Chapter on General Physiology, p. 64). It is still further eliminated by passing the gases through water, as described on page 323.

For *men,* Goldstein[1] emphasizes the point that anesthesia sufficing for the performance of brief operations is already present prior to the extinction of the reflexes, at a time when the respiration is regular, deep, and of almost normal frequency. The pulse at this time is also approximately normal and of increased volume.

Effects upon the Circulatory System.—There is a divergence of opinion concerning the actual rôle played by nitrous oxid in the *blood.* According to Buxton's[2] view, nitrous oxid, when administered pure, enters the blood by diffusing through the thin walls of the air-cells in the lungs. A small quantity is dissolved in the blood, but the bulk of the gas is connected in some loose way with the constituents of the blood. Buxton's view is that it is probably associated more or less closely with the albumins and albuminoids of the *liquor sanguinis* and corpuscles. He does not think that there is any destruction of red blood corpuscles. He reports having carefully watched the corpuscles in the web of a frog's foot while the frog was in a bell-jar of nitrous oxid, and was able to observe not only the phenomena of the circulation under these conditions, but also to satisfy himself that no breaking up of corpuscles was evident. The loose association which nitrous oxid is assumed to form with hemoglobin, as proved by the darkened color taken on by arterial blood when it is shaken with the gas, seems to indicate that nitrous oxid is able to displace oxygen in its chemical union in the blood. This combination of nitrous oxid with the constituents of the blood, if such actually occurs, is very unstable and very different from that produced by carbon monoxid, which is cumulative. Blood which has been saturated with nitrous oxid gives it up at once when left in free contact with oxygen or the air, and this has been used as a strong argument against the acceptance of the formation of a compound, however loose it might be. This does not necessarily follow, for such conduct may readily be due to mass action, that is to say, both oxygen and

[1] Brunn: *Loc. cit.*

[2] Buxton: "Anæsthetics," 1907, 60.

nitrous oxid may form weak compounds with hemoglobin, the former being the stronger. Fresh hemoglobin will form compounds with the respective gases in proportion, not only in accord with the stability of the compounds, but in proportion to the relative quantities brought in contact with the hemoglobin. When the percentage of nitrogen monoxid in inspired air is very small it forms practically no appreciable amount of its loose compound, at least not a sufficient quantity to circulate in the system to produce its physiological effects beyond those of exhilaration, i. e., intoxication. When the inspired gas contains only nitrous oxid the percentage will be rapidly diminished; in fact, almost as fast as the oxyhemoglobin in the blood is brought in contact with it. By regulating the proportions of the two gases brought into contact with the blood, it is theoretically possible to keep the oxygenation of the tissues going on as in normal life and at the same time secure the true physiological effect of the nitrous oxid. In maintaining these conditions another important factor enters in, namely, carbon dioxid. Yandell Henderson [1] has demonstrated that the carbon dioxid in the blood is a respiratory stimulant. Therefore, overventilation with oxygen is to be avoided. In advocating rebreathing of nitrous oxid-oxygen mixture, Gatch [2] claims that the beneficial effects are due to the carbon dioxid which comes from the expired air. His practice is to allow rebreathing until the percentage of carbon dioxid in the gas in the bag reaches four per cent; that is to say, the composition of ordinary expired air as far as carbon dioxid is concerned. For a more detailed treatment of this the reader is referred to the Chapter on Rebreathing.

If the absorption is a phenomenon of simple solution—and that nitrous oxid displaces a certain amount of oxygen in the blood is generally accepted by all observers—then the amount actually absorbed by the blood will depend upon the percentage composition of the mixed gases inhaled; that is, the partial pressure exerted by the gas in question. When nitrous oxid containing practically no free oxygen is inhaled the normal oxygen content of the blood is quickly diminished. If the percentage of nitrous oxid in the inspired gases is reduced to the minimum by discontinuing its administration, that which was absorbed is quickly thrown out of the circulation by virtue of its vapor tension and oxygen takes its place, reproducing the normal conditions of the gaseous contents of the blood, as far as oxygen is concerned.

In the *blood,* according to the investigations of Klikowisch,[3] nitrous oxid causes no chemical or morphological changes of any kind, but it is

[1] "Acapnia and Shock," "Carbon Dioxide as a Factor in the Regulation of the Heart Rate," *Am. J. Physiol.*, Feb. 1, 1908, *21*, No. 1.

[2] "Nitrous Oxide-Oxygen Anesthesia by the Method of Rebreathing," *J. Am. Med. Assn.*, March 5, 1910.

[3] Brunn: *Loc. cit.*

in the blood merely in the form of a physical solution. It is proportionately rapidly reëxcreted on diminution of the partial pressure. Decomposition of the nitrous oxid in the blood into oxygen and nitrogen does not seem to occur. In the spectral analysis the behavior of blood that has been saturated with nitrous oxid is the same as that of blood containing oxyhemoglobin (Klikowisch, Rothmann). This also goes to show that nitrous oxid does not enter into any stable chemical combination with oxyhemoglobin. Besides the short duration of the narcosis, the absence of after-effects likewise points in the same direction. The opposite view of Ulbrich is declined by Rothmann, who explains the divergent findings of Ulbrich as due to the employment of too highly concentrated blood solutions, causing the absorption bands to become wider and less distinct.

Recently (1908) Hamburger and Ewing have expressed themselves in favor of the harmlessness of nitrous oxid for the blood. They found it to produce no permanent diminution of the hemoglobin, and no anemia, as well as no increased hemolysis. Although differences in the quantity of the hemoglobin and the red blood corpuscles may occur, they are of transitory character and devoid of surgical importance. The formation of reduced hemoglobin is not referable to the anesthetic, but to the associated asphyxia. An increase of the time of coagulation is common, but not invariably present.

The experiments of Buxton [1] and later of Wood and Cerna [2] indicate that nitrous oxid exerts a direct action upon the heart itself, having little or no direct influence upon the vasomotor centers of the brain cortex. Kemp,[3] on the other hand, holds that nitrous oxid can hardly be said to exert a direct action upon the heart, the cardiac effects being much more apt to depend upon the amount of oxygen admitted than upon the nitrous oxid. For further data concerning the modification of the anesthetic by oxygen or by atmospheric air, see Chapter II, General Physiology.

Blood pressure is always increased with nitrous oxid given alone. With a judicious use of air or oxygen nitrous oxid anesthesia may be continued for a sufficient time to permit of any ordinary surgical intervention with very little variation in blood pressure.

Concerning the *blood pressure,* Goldstein's [4] findings showed a marked increase to be exceptional, in contradistinction to the usual belief that blood pressure rapidly undergoes an enormous increase in the first stages of the asphyxiation. His first experiments concerned asphyxiations with nitrogen and hydrogen, but a considerable rise of the blood

[1] "Anæsthetics," 1907, 57 *et seq.*

[2] *Therap. Gaz.*, Aug., 1890.

[3] *Brit. Med. J.*, Nov. 20, 1897, 1482.

[4] Brunn: *Loc. cit.*

pressure was likewise absent with nitrous oxid, although some increase was present. The blood pressure underwent no essential changes when dogs and rabbits were given, in addition to the nitrous oxid, a quantity of air sufficient for the avoidance of dyspnea.

Effects Upon the Nervous System.—It has already been noted that the third distinct step in the evolution of knowledge concerning the physiological action of nitrous oxid had for its foundation the specific action of the agent upon the nervous system. The earlier experiments of Buxton, Wood and Cerna, and others, to which reference has already been made, confirmed the theory of the direct action of the gas upon the nervous system. Buxton,[1] in observations upon this subject, found that, while asphyxia caused diminution of the bulk of the brain and cord, nitrous oxid produced so great an enlargement as to force out the cerebrospinal fluid. He referred these changes to a vasomotor origin, and held that they explained many of the nervous phenomena elicited in persons narcotized with nitrous oxid. The most natural inference, from the study of the reflexes and other effects upon the nervous system, is, according to Kemp,[2] that nitrous oxid acts most powerfully upon the central nervous system, especially upon the brain cortex.

The effect of nitrous oxid, when first inhaled, is a pleasurable exhilaration, which varies with the individual, with the degree of dilution of the gas with oxygen or air, and with the method of administration employed. During this time the senses of the individual are rendered more acute; this is followed by analgesia; and then by anesthesia, during which last the patient is profoundly unconscious and insensitive to pain.

Hallucinations, frequently of an erotic nature, often mark the hyperesthetic stage which precedes anesthesia. These not infrequently persist after the complete return of consciousness. The practical and medicolegal significance of this phase of nitrous oxid anesthesia is easily apparent.

Effects Upon the Muscular System.—It is a well-established fact that nitrous oxid does not usually induce muscular relaxation when administered alone. When oxygen deprivation is complete, and the administration of nitrous oxid is continued, the limbs become rigid, the body sometimes assuming the position of opisthotonos. Sometimes rhythmic tremors of the upper extremities are noted. The muscular manifestations, other than general rigidity, are now seldom seen in nitrous oxid anesthesia, for the reason that it is practically never given alone, even for very short operations. For a further discussion of the muscular phenomena see Stages of Anesthesia, p. 59.

Effects Upon the Glandular System and Other Structures.—Nitrous

[1] Buxton: "Anæsthetics," 1907, 62.
[2] Kemp: *Loc. cit.*

oxid causes, according to Kemp,[1] a contraction of the renal vessels, so that urinary secretion is rapidly diminished. Inasmuch as nitrous oxid is not eliminated through the kidneys (see Chapter on Physiology, page 60), it would seem fair to assume that the gas exerts no unfavorable effect upon these organs, and that the albuminuria sometimes reported is due to other causes. Involuntary micturition may occur during nitrous oxid anesthesia.

The alimentary tract is not unfavorably affected by nitrous oxid unless its administration is pushed to an unnecessary degree. In such case there may be some nausea, vomiting, and even involuntary defecation.

The untoward symptoms which accompany nitrous oxid anesthesia are generally ascribed to unnecessary deoxygenation rather than to any irritant or other quality of the gas itself.

Causes of Death.—When nitrous oxid is given pure, or alone, death is always due to oxygen deprivation or asphyxia. The heart continues to beat after respiration has ceased, which proves that death is not due to failure of circulation. (For further data concerning the effects of overdose, which may lead to shock or to death, see Stages of Anesthesia, p. 59, and General Physiology, Chapter II.)

Stages of Anesthesia.—The stages of anesthesia when nitrous oxid is used alone are rarely seen. Attempts have been made to separate the phenomena and to classify them under distinct stages, but this is impossible for the reason that it takes only from thirty seconds to one minute to reach full surgical anesthesia, the time elapsing between consciousness and surgical anesthesia being so short that these different degrees cannot be noted.

Inasmuch as nitrous oxid is now so seldom given alone, but rather with air, with oxygen, or with the utilization of rebreathing, so that the duration of the anesthetic period can be prolonged at will, it is possible to note definite stages just as is the case with other inhalation anesthetics. The course of the anesthesia is smooth and practically featureless, as is the case with the other agents, unless there is faulty technique somewhere. A leak in the apparatus, a mask that does not fit snugly, too much oxygen, not enough nitrous oxid, neglect of preliminary medication—any one or a combination of these errors of technique may convert a featureless narcosis into one marked by more or less disagreeable complications. From experiments upon lower animals it is known that too much oxygen or too little nitrous oxid may act as an overdose, with the same phenomena noted with an overdose of ether or chloroform.

The *first stage* is marked by a subjective feeling of warmth in the lips, and a sort of numbness in the limbs and other parts of the body, quickly followed by a feeling of exhilaration, sometimes described as a

[1] Kemp: *N. Y. Med. J.*, Nov., 1899.

"thrilling." This may be, and generally is, accompanied by the impulse to breathe more rapidly and more deeply. Tinnitus, a feeling of fullness in the head, and a "smothering" sensation, if the nitrous oxid is "pushed" too rapidly, precede the loss of consciousness. Objectively, it is noted that the respirations are quickened and deepened, the pulse grows fuller, and blood pressure is raised. Twenty to thirty seconds is the average duration of this stage, which may be said to end with the disappearance of coördination and consciousness.

The *second stage,* or *stage of excitement,* is initiated with the loss of consciousness. Incoherent thoughts and words and purposeless muscular movements, particularly of the arms and legs, are now apt to occur. The laughing, crying, muttering, and incoördinate movements vary with the patient. As may be imagined from the name, "laughing gas," exhilaration rather than depression is apt to mark the psychic phenomena of this stage. It is during this period that fanciful, sometimes erotic, dreams, which may persist after the return of consciousness, occur. The pulse is still full, and somewhat more rapid than during the first stage. The respirations are more rapid and deeper than normal, or than during the first stage in cases where the right proportion of air or oxygen is not given. Swallowing movements, and sometimes stertor, are noted. The pupils become dilated, and a twitching of the eyelids is often followed by their separation. The skin now assumes the duskiness or lividity which is generally a feature of nitrous oxid anesthesia, and which is more or less marked according to the normal complexion of the individual and according to the care with which the administration is conducted. Hearing continues during this stage. While the patient is unconscious, any undue roughness or careless treatment may markedly increase the excitement, aggravating all the phenomena noted. No surgical intervention should be attempted during this stage.

The *third stage,* or the *stage of surgical anesthesia,* with perfect technique, is induced in about sixty seconds to four minutes, the time varying, of course, with the patient, with the purity of the nitrous oxid, and with the technique as regards the regulation of oxygen and other details. The stertorous, snoring breathing, with loss of rhythm, mentioned by many writers as marking the onset of the surgical stage of anesthesia, depends upon the method of administration, and especially upon the preliminary medication. Breathing should be automatic, regular, and without noise. The pulse is full and regular, and slightly increased in rapidity, from 80 to 90, though it may be normal. The lividity previously noted should not be increased in degree as anesthesia advances. The lid and other reflexes are abolished, and muscular relaxation is more or less complete, according to the purpose of the anesthesia and the technique employed.

In order to maintain this stage of surgical anesthesia, it is important not to give too much oxygen or too much nitrous oxid, with a corresponding increase or decrease of the other gas. The time required to reach this stage is so short that an inexperienced administrator may allow the patient to "come out" or to go on to the stage of overdose. In this connection it is to be borne in mind that nitrous oxid is stimulating, and that the patient must not be allowed to return to the second stage, or the stage of hypersensitiveness.

The automatic breathing, with or without stertor, the widely dilated or contracted pupils (varying with the preliminary medication), full and regular pulse, with a slight degree of cyanosis, indicate the third stage. Two or three stertorous respirations indicate complete anesthesia.

The *fourth stage*, or *stage of overdose*, supervenes through some error of technique by which asphyxia becomes the predominant feature of the narcosis. Breathing becomes embarrassed, usually through convulsive muscular spasm. The interference with respiration is first marked by hyperpnea (excessive breathing), then by dyspnea (difficult breathing). Violent or convulsive expiratory efforts, sometimes accompanied by general muscular spasms, mark the second stage of asphyxia. Following this there is a stage of exhaustion in which muscular spasm is superseded by muscular flaccidity. The pupils become more widely dilated, the lids are widely open, the conjunctivæ are insensitive, the pulse becomes imperceptible, respiration is marked by prolonged sighing inspirations, which gradually cease. Paralysis of the respiratory center is complete, and death supervenes. Marked cyanosis accompanies this condition of affairs. Interference with the passage of the blood through the pulmonary and systemic vessels, and accumulation, in consequence, of blood in the right side of the heart and in the systemic veins, with the circulation, in all parts of the body, of deoxygenated blood, explain the eventuation of the stage of overdose in nitrous oxid anesthesia.

This stage of anesthesia may be rendered more liable by certain prëexisting conditions, which are discussed under Contraindications. The length of time before it eventuates in death varies with the subject.

It may be noted that the time required to reach full surgical narcosis is from thirty seconds to four minutes, varying with the patient; that the available period for operation depends entirely upon the technique employed, ranging from thirty seconds to hours; and that the recovery period, when asphyxial symptoms do not occur, is completed in five minutes or less from the time the mask is removed.

Elimination.—The rapidity with which the blood will rid itself of nitrous oxid has been made the subject of study by Kemp,[1] who found, in animal experiments, that in less than two minutes the quantity of nitrous oxid in the blood fell from over twenty per cent to six and nine-

[1] Kemp: *Brit. Med. J.*, Nov. 20, 1897, 1480.

tenths per cent. The normal rapid recovery of patients, he holds, is quite in accord with these findings.

It has already been noted that nitrous oxid is not eliminated by the kidneys. The *lungs* furnish the channel of elimination of nitrous oxid.

After-Effects.—As already stated, there are less after-effects with this anesthetic than with any other. The only possibility of after-effects is when the subject is unsuited for this particular form of anesthesia; or when an irregular narcosis has been given; or when the nervous system is so upset for any reason that the least excitement is cause for anxiety. The *Lancet* of March, 1902, mentions a case in which, after a few minutes' inhalation, the patient remained practically asleep for four days. The undesirable patients so often referred to, that is, men with powerful build, are sometimes temporarily unbalanced after a short administration. Again, those with weak hearts may have slight pallor, feebleness of pulse, and faintness; as a general rule, however, all of these things are conspicuous by their absence.

COMPARISON WITH OTHER AGENTS

In the earlier period of nitrous oxid history this agent was hardly comparable with other inhalation anesthetics, inasmuch as it was not considered a true anesthetic. With modern methods, however, this no longer holds. Nitrous oxid is considered as truly an anesthetic as is ether or chloroform. Given with oxygen it ranks above either so far as safety to life is concerned. In point of after-effects it takes precedence over all other agents, since it is practically free from sequelæ if administered with a fair degree of care. Nitrous oxid and ether, with enough oxygen to prevent cyanosis, is the safest inhalation anesthetic, both as to life and after-effects.

INDICATIONS AND CONTRAINDICATIONS

Nitrous oxid alone is very limited in its indications. In fact, at this stage of development of methods of administration it is never indicated. It is distinctly contraindicated, even for very short operations, in young children (under four years), because of their immature musculature, which makes breathing in the bag difficult for them. It is also distinctly contraindicated with old persons, or persons with a generally weakened musculature, and in adults of whatever age whose arteries are sclerosed. Advanced phthisis, valvular disease, and women during any of the physiological epochs, when nervous and mental phenomena are apt to be easily exaggerated, present contraindications to the use of nitrous oxid alone.

When this gas is judiciously employed, with the careful admission of oxygen, the contraindications are modified. It is still contraindicated for children, because these patients take any anesthetic poorly with a closed method. (See Chapter VIII, Selection of Anesthetic.)

For strong, muscular, athletic, alcoholic and obese subjects, or persons with any obstruction to the air passages, such as enlarged tonsils, adenoids, etc., and for ophthalmic surgery, nitrous oxid is contraindicated, unless employed with the utmost skill.

ADMINISTRATION

Before discussing the different methods of administration it might be well to pause and consider a few necessary details.

Heating the Gas.—This is accomplished in several ways: (1) by an alcohol lamp, with a coil for the gas going through the upper portion of the heater, as in the Teter apparatus (see p. 152); (2) by a coil from the tank being placed in a hot water cup, as in the Gwathmey anesthetizer (p. 150); (3) by passing the gas through a coil contained in a metal cylinder filled with thermal salts, as used by Griffith Davis (see p. 148); (4) by passing the gas over water electrically heated (see p. 424).

The gas should be heated to the temperature of the body. Heating the gas admits of its uniform diffusion through the alveolar walls and usually enables the administrator to secure surgical anesthesia before the asphyxial signs occur.

Essential Features of Any Satisfactory Method or Apparatus.—All apparatus should embody the four fundamental principles underlying the successful administration of nitrous oxid and oxygen, that is to say, valvular and rebreathing, warmed vapors, moisture regulation of the pressure, and addition of other anesthetics when needed.

Apparatus for Administering Nitrous Oxid Alone or with Air.—All that is necessary for the administration of the gas alone is a tightly fitting mask, with valves which may be thrown out of use when rebreathing is to be utilized. To this mask a rubber bag is attached. Rubber tubing connects the bag with the gas cylinder. When air is added to the nitrous oxid an extra valve may be used to allow definite proportions of air.

Dangers of Administration of Nitrous Oxid Alone.—The majority of fatalities have occurred with the administration of nitrous oxid alone, and given through valves. Of these fatalities the greater number were men in robust health or alcoholics. Nitrous oxid has no *toxic* effect as have chloroform and ether. Death occurs as a result of asphyxiation.

The only possibility of a death by asphyxiation is the inability of the administrator to differentiate between asphyxial and anesthetic signs. Whether it is administered alone, with air or with oxygen, the anesthetist should be careful to keep a clear airway and see that no asphyxial symptoms occur at any time.

Recognition of Asphyxial Symptoms.—Embarrassed respiration, irregular, shallow, and jerky, is an asphyxial symptom. This may or may not be accompanied by stertor. The fingers and muscles of the arms and legs are thrown into clonic spasms, which quickly develop into tonic spasms with rigidity and muscular contraction of the muscles of the neck and chest. There is marked cyanosis. Eyelids may or may not be closed, but are usually open with lid reflex present. The respiration ceases. If at this point the mask is removed, in the vast majority of cases the patient comes out of this state apparently none the worse for the experience. The heart will always be found beating slowly and regularly, even after cessation of respiration. If, however, the mask is held rigidly in place at this point, so that the next long, deep breath is gas instead of air, a cessation of all the vital functions is apt to cease immediately. No administration of nitrous oxid should be attempted unless the anesthetist is prepared for a tracheotomy.

Administration of Nitrous Oxid Alone.—If given in this way, without mixture of air or oxygen, and without heating, it must necessarily be for short operations, and it must be given to the point of asphyxiation, then discontinued and administered again. This is the most dangerous way in which to administer the gas, and should never be attempted except in emergency cases or as a sequence. It is true that patients have been anesthetized in this way for short operations with a resulting fatality that is almost negligible; nevertheless, 90 per cent of all fatalities have occurred when the gas was thus administered.

Administration to Asphyxiation with and without Valves.—A crude method, practiced by many dentists, is to administer the gas to the point of asphyxiation, remove the mask, and make the extraction.

Use of Expiratory Valve Alone.—Another method is to use the expiratory valve alone, thus allowing to-and-fro breathing from the first, and increasing the pressure until full anesthesia ensues. This requires more gas and a little longer time, but it is almost as valuable as washing out the lungs by the valvular method, and then switching to to-and-fro breathing. It is preferable to using valves alone.

Administration without Valves.—The third method of giving the gas is without any valves, by allowing the gas to flow in the mask and simply increasing the pressure in the bag and allowing the surplus to escape under the margin of the mask, and continuing to increase the pressure until ingress of air between the face and the mask is impossible, and full anesthesia is secured. This is a makeshift, and a wasteful method, but it may be well to know that anesthesia can be satisfactorily induced in an emergency in this way.

Precautions When Administered Alone.—Whenever the gas is administered alone, as for the extraction of a tooth or the opening of an abscess, it is always best to have some method of switching from the valves to to-and-fro breathing. With some patients the asphyxial point

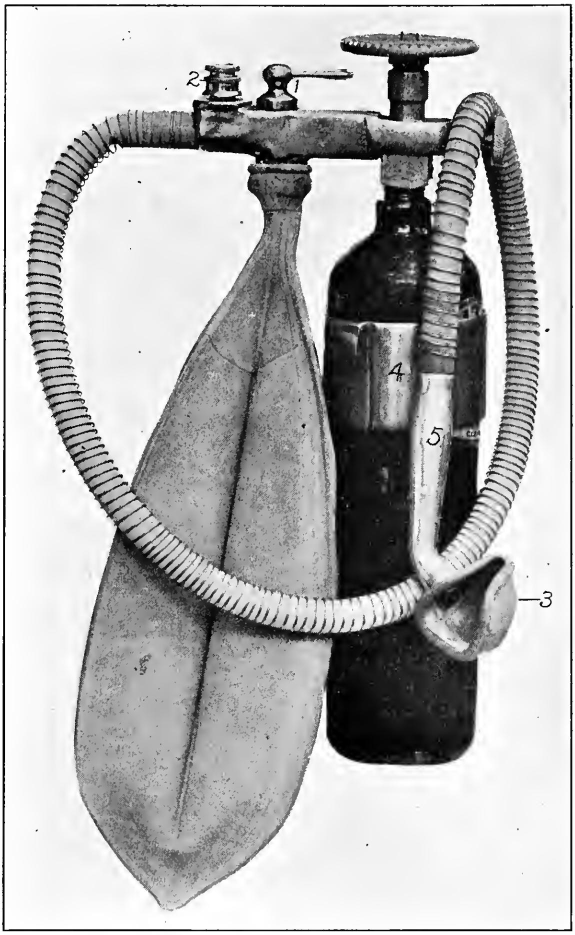


Fig. 26.—Guedel's Apparatus for the Self-administration of Nitrous Oxid and Air. Apparatus attached to cylinder. (1) Stopcock controlling flow of gas from supply bag. (2) Respiratory valve. (For detail *see* Fig. 27.) (3) Flexible rubber nose mask without valves. Valves are removed to body of apparatus so that mixture of gas and air can be regulated without disturbing the patient. (4) Metal band with hook for hanging apparatus to operating chair or table. In obstetrical work the apparatus is placed on its side on the bed. (5) Hollow metal handle for nose mask. Patient holds mask.

will be reached before true anesthesia occurs. This is the principal objection to the administration of nitrous oxid alone. When administered only part of the time through valves, the anesthetist should make the change before the asphyxial signs occur, and deepen the anesthesia by simply holding the mask in position and allowing the patient to breathe back and forth in the bag. The advantages gained by this method are that it is safer and also gives a deeper and longer period of available anesthesia with a smaller amount of gas; the after-effect will also be less. In fact, by closing either the mouth or nares, thus compelling the patient to breathe through the one open airway, and using this airway for the administration, a satisfactory anesthesia has been induced by inserting the rubber tube from the gas tank and grad-

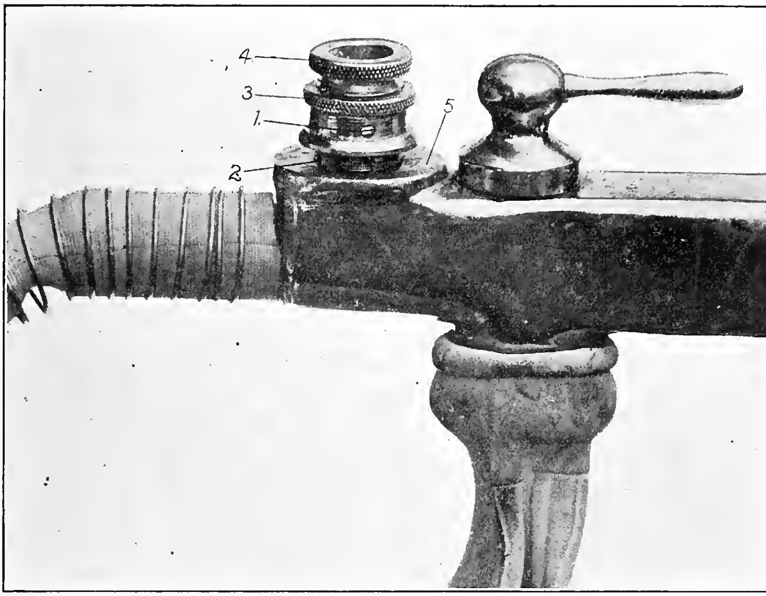


Fig. 27.—Guedel's Apparatus, Showing Detail Construction of Respiratory Valve. (1) Expiratory openings. A disc prevents the entrance of air during inspiration and permits the escape of part of the expired gases during expiration. (2) Inspiratory openings for admitting air which is mixed with the inspired gas. (3) Screw for regulating percentages of inspired air. (4) Screw limiting movements of disc for regulating amount of gas rebreathed. (5) Graduated dial showing percentages of air inspired.

ually increasing the pressure. This is a wasteful method and is not advocated. In all cases there should be some means of heating the gas before it reaches the patient.

Guedel has perfected an apparatus for the administration of nitrous oxid alone, and especially for the use of the analgesic stage of nitrous oxid. He recommends it specially for confinement cases. His cylinder of nitrous oxid is placed within convenient reach of the patient. The patient takes the apparatus and places it over the nose or mouth and inhales until the anesthetic stage is reached, when the hands drop to the side. It is also used by dentists for the analgesic stage of anesthesia.

The apparatus is commendable in that it is very simple and inexpensive. (See Figs. 26 and 27.)

Administration of Nitrous Oxid with Air in Unknown Quantities.—The continuous administration of nitrous oxid with enough air to prevent asphyxial symptoms places a severe tax upon the anesthetist's resources. With selected subjects and under proper conditions a safe and even plane of anesthesia can be maintained.

Directions.—(a) With valves alone: Place the mask in position and induce anesthesia as stated above. When stertor, irregular breathing, or automatic breathing announces surgical anesthesia, raise the mask for one respiration, then reapply and hold in position for from three to ten respirations, according to the patient, when another breath of air is given, and so continued.

(b) With valves and to-and-fro breathing: This method is better for the patient, keeping the pulse nearly normal, respirations deep and full, with better muscular relaxation, and is an easier anesthetic to maintain. In getting the patient under, the following procedure is usual:

(1) If the apparatus will allow, have the patient breathe air through the valves before turning on the gas.

(2) Turn on the nitrous oxid and allow the patient to breathe through valves from three to seven times.

(3) Now have to-and-fro breathing for as many times.

(4) Return to valves for three to seven breaths.

(5) Now have to-and-fro breathing as before.

This alternating from valves to to-and-fro breathing will occupy from forty seconds to a minute and a half, when the patient will be found to be deeply under the anesthetic.

If, now, the operation is to last for one hour or more, either the above or the following method can be used after surgical anesthesia has been established.

Use the expiratory valve alone, allowing a small but regular flow of the gas at all times, thus keeping the bag fairly distended by having rebreathing constantly and removing the mask whenever the stertor or other asphyxial signs become too marked. This method is especially useful for alcoholics and athletes, and all other patients in which a positive pressure is indicated. The above method has also been successfully employed in nose and throat work, using the nosepiece with expiratory valve and having a stopcock between the nosepiece and bag for an occasional breath of air. By regulating the expiratory valve any amount of pressure can be maintained in the lungs. This method of anesthesia can be kept up indefinitely, and is especially useful in adenoid and tonsil cases.

This rebreathing, together with the expiratory valves, can be more readily maintained when used as a sequence to the drop method of ether (p. 204), when the patient has been under the influence of the ether for ten to fifteen minutes, or toward the close of any operation lasting one hour or more.

The Administration of Nitrous Oxid with Definite Amounts of Air.—Hewitt has made a number of experiments to determine the exact percentage of nitrous oxid suitable to be administered with air. The following are the net results of these experiments: The best definite mixture for men is from 14 to 18 per cent of air; for women and children, 18 to 22 per cent of air.

If, during an administration of nitrous oxid with air, the supply of oxygen gives out, anesthesia can be continued by pushing back the bag containing the oxygen so that air can be admitted through the valve and allowing a continuous flow of from 14 to 22 per cent of air with the nitrous oxid. The best method of administration is for the anesthetist to be able to use the valves, and also switch to to-and-fro breathing at any time during the administration. Whenever, for any reason, no oxygen is at hand, it is necessary, if a continuous flow of air through the valves is to be allowed, that the apparatus is so arranged that the air supply is independent of the nitrous oxid.

Directions.—Anesthesia is instituted as follows: Place the index to the air valve so as to allow an intake of 25 per cent of air. Allow the full intake of nitrous oxid through that valve. After two or three inspirations, cut down the air intake to between 14 and 22 per cent. Turn the nitrous oxid valve so as to allow rebreathing continuously. From this time on the index to the air valve must be changed to suit the requirements of the case. If positive pressure is indicated, this can be accomplished by tightening the screw on the expiratory valve so that very little air escapes, at the same time increasing slightly the flow of nitrous oxid. In order to determine approximately the percentage of air being used, the flow of nitrous oxid must be an even one. Occasionally it will be necessary to cut off the air entirely and have to-and-fro breathing until the anesthesia is satisfactory; then return to the valve and continue. This form of anesthesia is especially useful as a sequence after surgical anesthesia has been maintained for thirty minutes or more, when, for any reason, the chloroform and ether should be reduced to a minimum.

Nitrous Oxid as a Sequence to Ether.—When nitrous oxid is used as a sequence to ether the reflexes should be allowed to become active before instituting the change. With the chloroform-ether-nitrous oxid sequence the reflexes should be very active and the change be made gradually; that is to say, allow rebreathing in the bag before turning on the nitrous oxid. Even in laparotomies, where absolute relaxation is required, after anesthesia has been maintained for thirty minutes or more, this method can be successfully substituted. This reduces the amount of ether or chloroform to a minimum, and, there being less strain upon the kidneys and lungs, the after-effects are reduced to a minimum.

Nitrous Oxid with Air.—As previously stated, when nitrous oxid and air are used as a sequence, the maintenance of an even plane of anesthesia is so easy and, at the same time, satisfactory that the description of the technique of this sequence is worthy of a place by itself.

Technique of Ether-Nitrous Oxid (Air) Sequence.—If ether by the drop method has been used and a change to nitrous oxid is desired, allow the reflexes to become slightly active; place the mask upon the face and turn to to-and-fro breathing, the bag being two-thirds full of the nitrous oxid. Note the results, and increase the pressure in the bag to intensify the anesthesia, or, if the anesthesia is satisfactory, maintain it by either of the methods already outlined. When the reflexes are abolished slight cyanosis sets in, and the anesthesia is now changed to one of nitrous oxid and air. When this occurs remove the mask whenever necessary for one inhalation or more, and then repeat, allowing the gas to flow in the bag slowly but regularly. If, however, the patient is very lightly under, allow breathing through valves for three to eight respirations, turn to to-and-fro breathing, then allow one to two breaths of air, and then return to the gas. Allow air whenever the reflexes are entirely abolished and cyanosis is marked and breathing stertorous.

Technique with A.C.E.—The technique with chloroform-ether, or the A.C.E. mixture is as follows:

Allow the eyelids and other reflexes to become somewhat active; place the mask upon the face as the patient exhales, the mask being arranged for to-and-fro breathing, but the bag empty. Remove the mask from face, allow patient one breath of pure air, and replace mask so that the exhalation enters the bag. Continue thus, alternately raising and replacing the mask until the bag is filled. When this occurs hold the mask in place. If reflexes are now abolished raise the mask and allow one breath of air and thus continue until reflexes begin to get quite active again. When this occurs turn on gas slowly, allowing rebreathing until they are lulled or abolished.

Advantages of Ether- (or Chloroform-Ether) Nitrous Oxid Sequence.—By instituting nitrous oxid anesthesia after any operation that has lasted at least one hour, the following results are accomplished:

A non-poisonous [1] anesthesia replaces a poisonous one at a time when a stronger anesthetic is capable of doing the greatest damage. The resisting powers of any individual at this time being reduced to a mini-

[1] The term non-poisonous is here used in a restricted sense as compared with chloroform and ether, which are active poisons to both the nerve and muscle fibers.

mum, the kidneys, lungs, and other parenchyma are thus possibly saved the *coup de grâce.* Nitrous oxid and air fulfil all demands at this time, the relaxation required being easily maintained.

The Advantages of Administration of Oxygen with Nitrous Oxid.—When oxygen is used with nitrous oxid, a safer, deeper, and more satisfactory anesthesia is obtained than is possible with air. When the nitrous oxid is heated and supplemented by warmed moist ether, when necessary, we have the best form of anesthesia, considered from every standpoint, available to-day. Those who have never used oxygen with nitrous oxid, and who have acquired the technique of administering it alone, will be surprised by the ease and latitude given by this combination. One of us (J. T. G.) has given several anesthesias lasting for two hours and more with nitrous oxid and oxygen without the aid of ether, chloroform, or ethyl chlorid, and in one instance the anesthetic was not preceded by any preliminary medication. With adults the preliminary medication gives a wider latitude to the anesthetist than if this were not used. When the subject is well selected, and the administration properly conducted, a slight increase in the percentage of oxygen being allowed from time to time as the operation proceeds, the mechanical breathing, color, and reflexes, together with the relaxation required, are sufficient guides for our use. The pulse and respiration will usually be normal, except when stimulated by the operation. If loud stertor commences or increases it is a sign for more oxygen. If muscular twitches are observed at any time this also is an indication for more oxygen.

In anesthetizing children under ten years of age, after surgical anesthesia is reached, it is best to raise the mask slightly from the face, about one-eighth of an inch, and allow the little patient to breathe the combined gases by having a plus pressure in the bag at all times, or by keeping the expiratory valve open and allowing rebreathing constantly. Weak, anemic men and middle-aged women can be successfully anesthetized with nitrous oxid and oxygen alone, provided the valves and rebreathing are used discriminately. With a vast majority of patients it is safer to supplement the nitrous oxid and oxygen with small amounts of ether.

Superiority of Oxygen Over Air.—The objection to using air is that it contains a large percentage of nitrogen which is useless for anesthetic purposes. Hewitt has illustrated this in the following manner: When air is given the equation could read like this:

$$\text{Air (by volume), 40 per cent} = \begin{cases} \text{8 per cent oxygen} \\ \text{32 per cent nitrogen} \end{cases}$$
$$\text{Nitrous oxid} \quad \text{60 per cent} = \text{60 per cent nitrous oxid}$$

This mixture, containing eight per cent of oxygen by volume, would be the proper amount as far as the oxygen is concerned. Sixty per cent of nitrous oxid would be insufficient to produce tranquil anesthesia. By using oxygen instead of air in the above equation we are able to replace the thirty-two parts of useless nitrogen by a corresponding quantity of useful nitrous oxid, the percentage of oxygen remaining the same. The equation would now read like this:

Oxygen = 8 per cent (by volume)
Nitrous oxid = 92 per cent (by volume)

This is about the average used with adult patients, and is perfectly satisfactory.

Administration of Nitrous Oxid with Indefinite Quantities of Oxygen.—Willis D. Gatch, formerly of Johns Hopkins Hospital, Baltimore, deserves the credit of emphasizing and placing upon a scientific basis the value of rebreathing. His apparatus consists—besides the cylinders

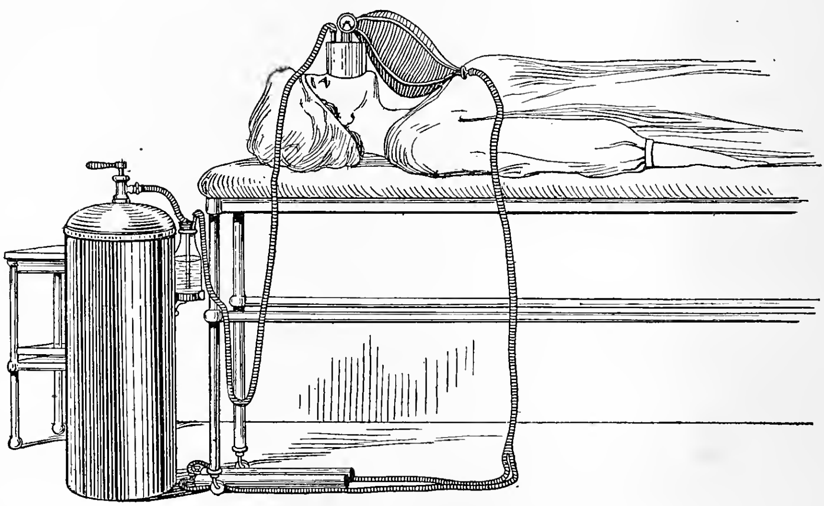


Fig. 28.—Diagrammatic Sketch Showing Simple Method of Administering Nitrous Oxid and Oxygen with Indefinite Quantities of the Agents Used.

of gas and oxygen, and connections—of one rubber bag, face-piece, and a two and a half-inch pipe connecting face-piece and bag. His mask consists principally of a rubber cuff, which is turned down over the ordinary mask so as to grasp the chin, cheeks, and nose of the patient. The patient may be made to breathe air or gas through valves or to-and-fro breathing into the bag. The main features of his apparatus are as follows:

(1) It is simple, light, and easily portable.
(2) It may be quickly sterilized by boiling.
(3) There is economy in the use of gas.

Gatch's Method of Administration.—"With the air-vent open, the cuff of the mask is fitted to the patient's face, care being taken to prevent the admission of air at the sides of the nose. In some cases it may be necessary to lay a piece of gauze across the bridge of the nose and draw the cuff over it, or to hold the cuff there with the finger. The inner tube of the valve-box is pushed to its mid-position and nitrous oxid admitted to the bag. The patient now inhales this gas and expires into the outer air, thus washing out, as it were, all the air from his lungs. This process is continued until he becomes very slightly cyanotic. Then the inner tube is pushed to its final position and the patient breathes to-and-fro into the bag. At this moment a small puff of oxygen is admitted to the bag, just enough to restore the natural color of the face. The patient now rebreathes a mixture of nitrous oxid and oxygen until the inner tube of the valve box is moved back to its mid-position. He then exhales each breath into the air until the bag is empty. The anesthetizer then fills it with a fresh mixture of gases, which the patient again rebreathes. No attempt is made to measure the exact percentage of oxygen given. This we regard as unnecessary. It is perfectly easy to add directly from the oxygen cylinder exactly the right amount of this gas to each bag of nitrous oxid. The patient's color is an extremely delicate indicator of the amount of oxygen he is getting. Our rule is to give just enough oxygen to keep the patient's color free of the least tint of cyanosis. The most elaborate device for regulating the percentages of the two gases can do nothing more than this."

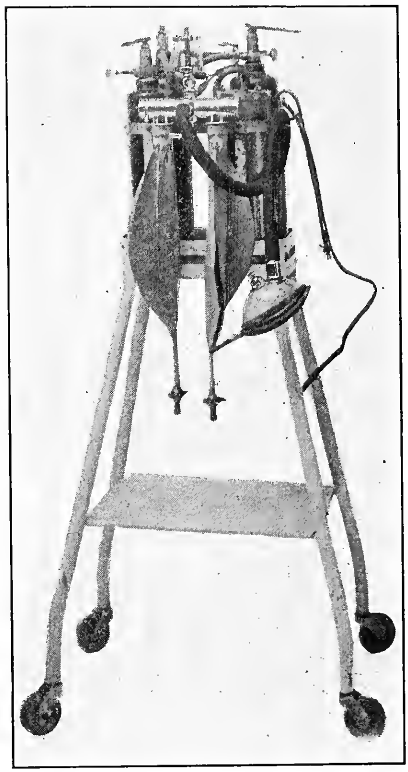


Fig. 29.—Davis Nitrous Oxid-Oxygen Apparatus.

All that is needed to successfully maintain surgical anesthesia with nitrous oxid and oxygen by the above method is any ordinary accurately fitting face-piece, and a mask with valves that will also allow rebreathing when indicated, and a rubber bag. Any inhaler used for the gas-ether sequence can be utilized to give gas and oxygen by the Gatch method. The stopcock at the end of the bag may be replaced by a Y-shaped connection having tubes leading respectively to the nitrous oxid and oxygen tanks. The bag is to

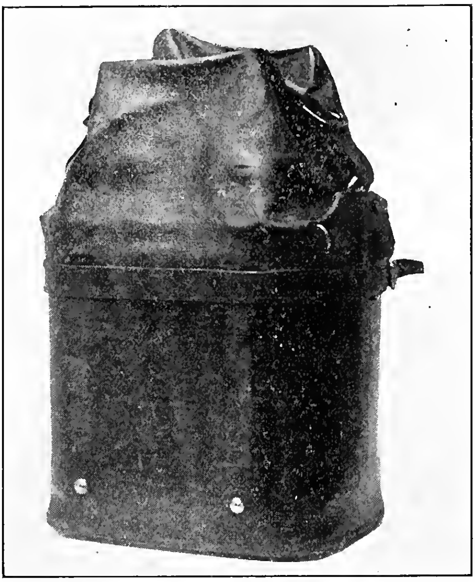


FIG. 30.—DAVIS APPARATUS CASE.—Contents: two 100 gal. cylinders of nitrous oxid, one 40 gal. cylinder of oxygen, thermic apparatus, and one two-bag gas-ether-oxygen inhaler.

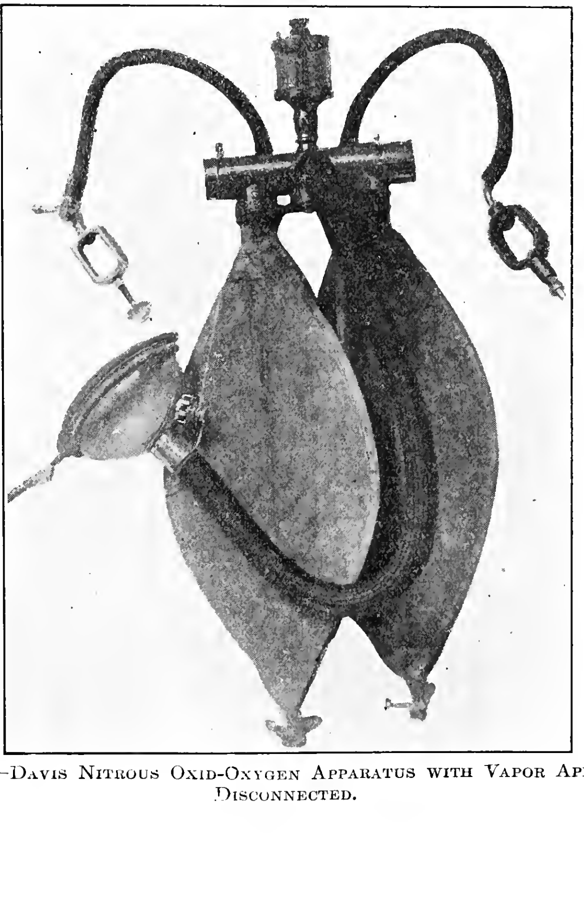


FIG. 31.—DAVIS NITROUS OXID-OXYGEN APPARATUS WITH VAPOR APPARATUS DISCONNECTED.

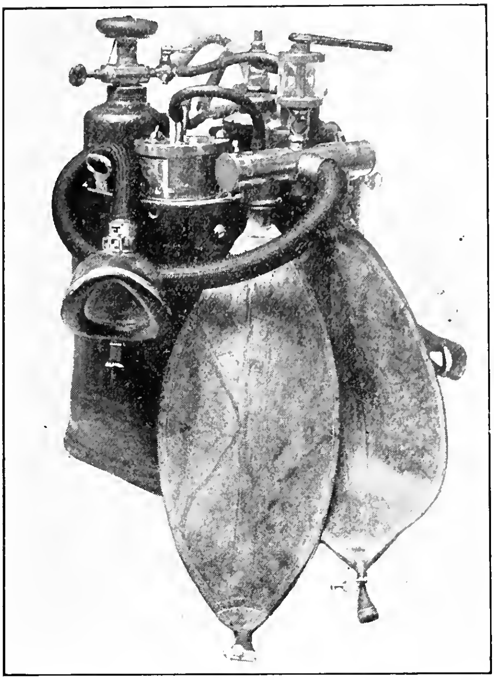


Fig. 32.—Davis Nitrous Oxid-Oxygen Apparatus Showing Heater.

Fig. 33.—Davis Nitrous Oxid-Oxygen Apparatus with Gwathmey Vapor Inhaler.

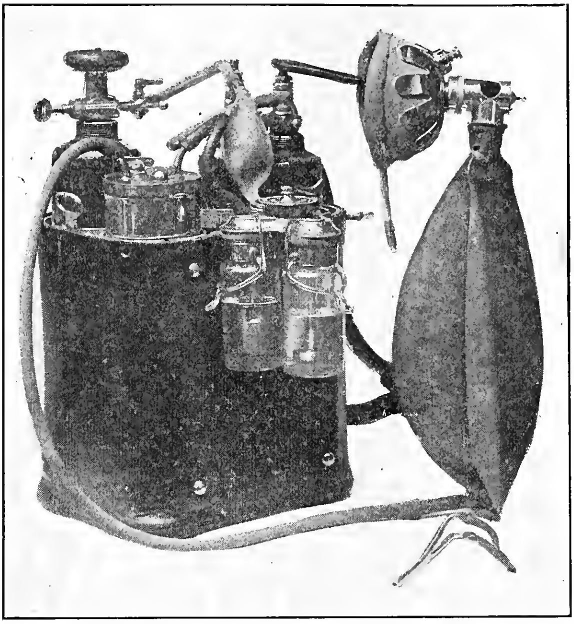


Fig. 34.—Davis Nitrous Oxid-Oxygen Apparatus with Gwathmey Vapor Inhaler. Same as Fig. 33 with cover.

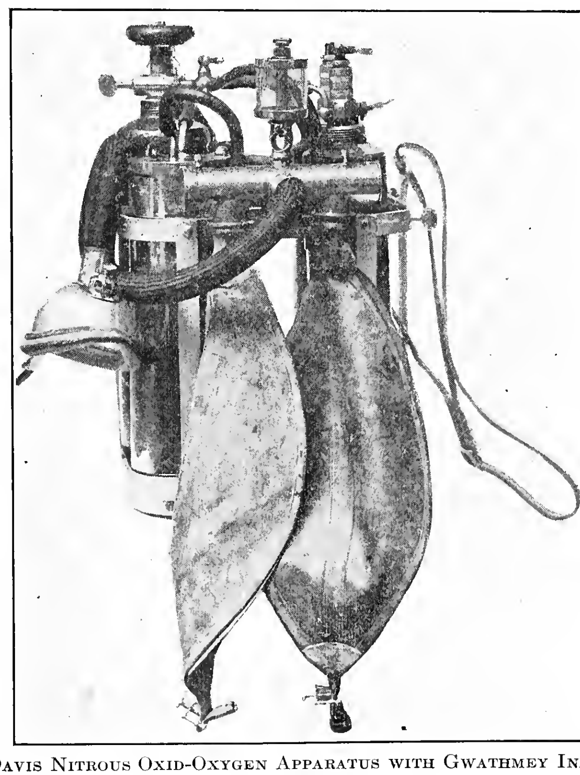


Fig. 35.—Davis Nitrous Oxid-Oxygen Apparatus with Gwathmey Inhaler. Same as Fig. 31 without cover.

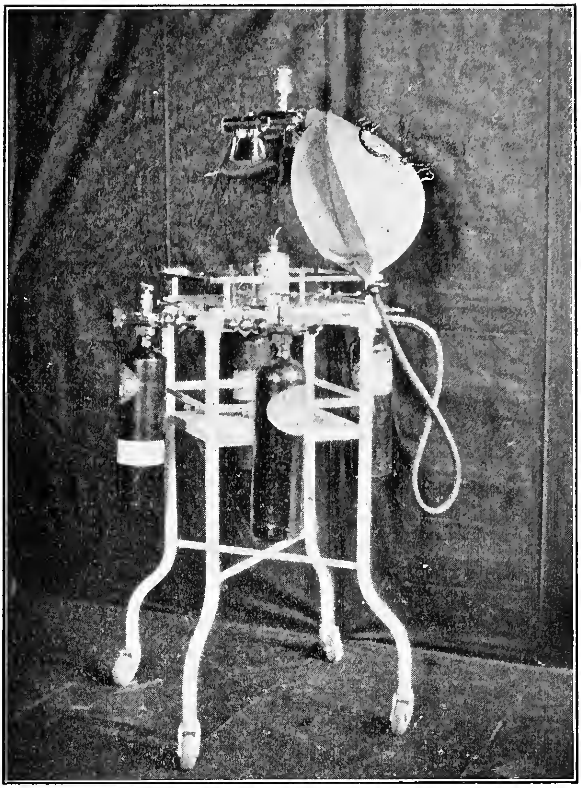


Fig. 36.—Coburn's Apparatus with Anesthetic Table and Cylinders Attached.

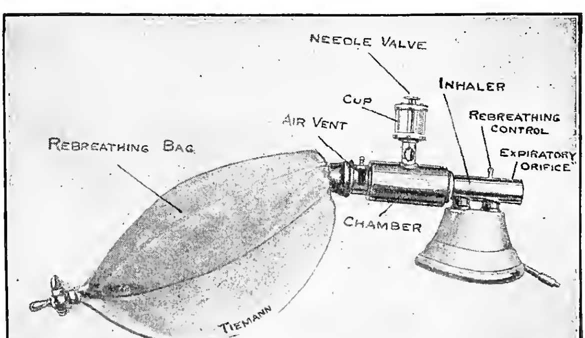


Fig. 37.—Coburn's Apparatus: Face-Piece and Bag.

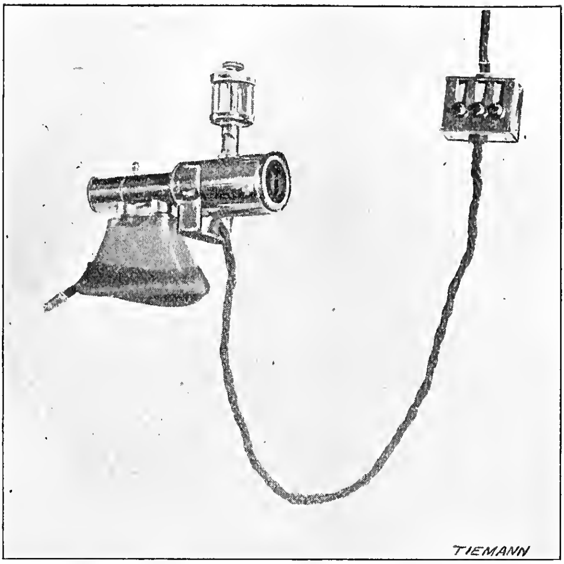


Fig. 38.—Coburn's Apparatus: Face-Piece and Electric Heater.

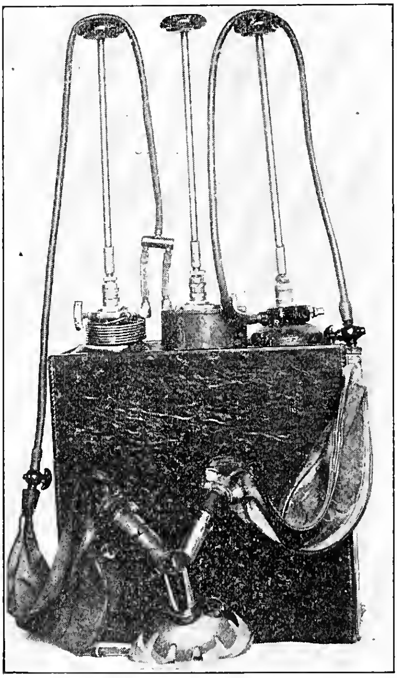


Fig. 39.—Gwathmey's Nitrous Oxid-Oxygen Apparatus.

be kept filled with nitrous oxid, and a puff of oxygen is given whenever indicated by cyanosis or active reflexes.

While this apparatus has been used in thousands of cases with satisfactory results, from the description of the apparatus and the method of administration given above it can be readily perceived that, unless the strictest attention is given to the administration, flaws will occasionally occur to mar the fixed plane of anesthesia that is to be aimed for. A possible objection outside of this consideration is the fact that the gases are not warmed except by the rebreathing of the patient, although they are thus properly moistened.

Davis' Method.—Griffith Davis' apparatus embodies all the good features of the Gatch apparatus, and, in addition, all the nitrous oxid is passed through a warming apparatus before it enters the mixing chamber.

Coburn has devised an apparatus for the administration of nitrous oxid and oxygen, according to the principles enunciated by Gatch, but with the addition of an electrical heating apparatus for warming the gases. Coburn's hospital stand is very neat and compact.

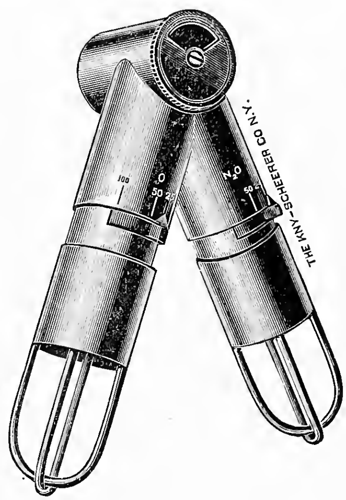


FIG. 40.—GWATHMEY OXYGEN Y-PIECE ADAPTEDF OR BENNETT'S, FURNISS', OR GWATHMEY'S INHALER.

Methods of Administration with Definite Quantities of Nitrous Oxid and Oxygen.—HEWITT'S METHOD.—Hewitt's apparatus consists of two bags, one of which is used for nitrous oxid and the other for oxygen; and a mask with valves, cylinders, and connections. Hewitt's technique consists in administering the gases in the following manner:

"The bags are half filled with their respective gases. When the gas is turned on, nitrous oxid and a small percentage of oxygen gain admission to the lungs. The bags are kept as nearly equal as possible in size, and partially distended throughout. The percentage of oxygen is gradually increased as the operation proceeds, but also occasionally admit a breath of fresh air." Hewitt limits the class of patients suit-

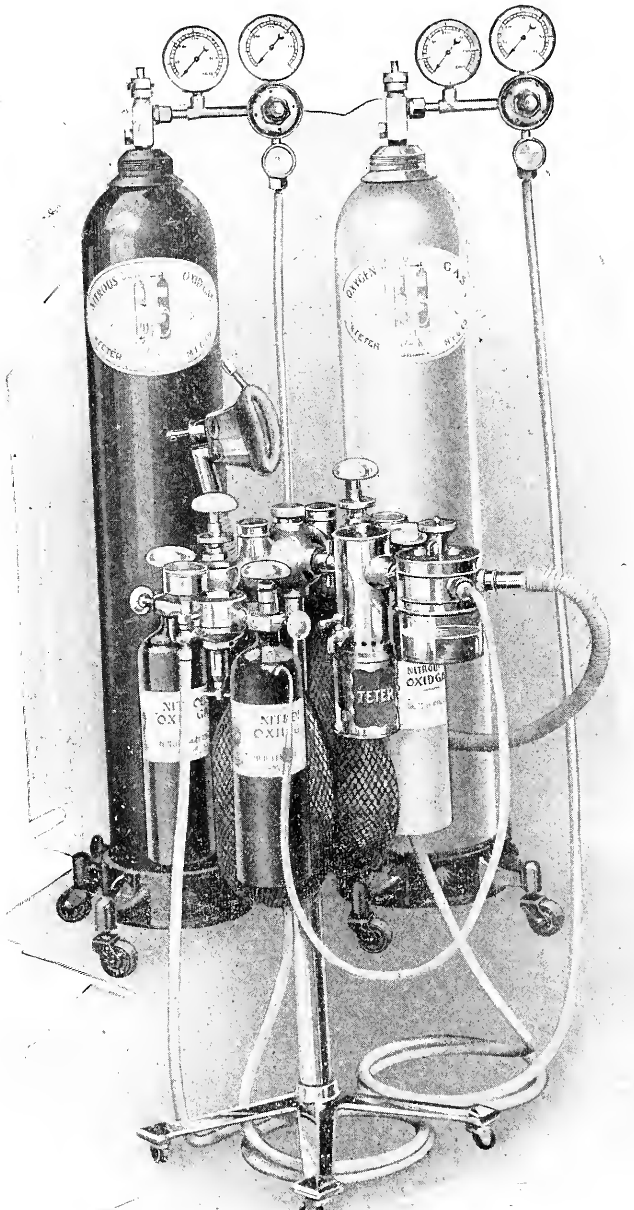


FIG. 41.—TETER NITROUS OXID-OXYGEN APPARATUS.

able for this apparatus to weak, anemic men and middle-aged women. His experience with this apparatus has not been such as to recommend its general adoption.

Gwathmey's Method.—The Gwathmey apparatus (Figs. 39 and 40) is a modification of Hewitt's with the valve on the nitrous oxid bag so arranged that rebreathing can be instituted at any time. Ether can also be added when necessary, and the nitrous oxid is heated by Brown's hot-water coil and cups. Ethyl chlorid can be given with the nitrous oxid and oxygen, if needed. The expiratory valve is regulated by a screw. Free expirations or forced expirations can thus be instituted at will by the anesthetizer. The technique is about the same as with the Teter apparatus.

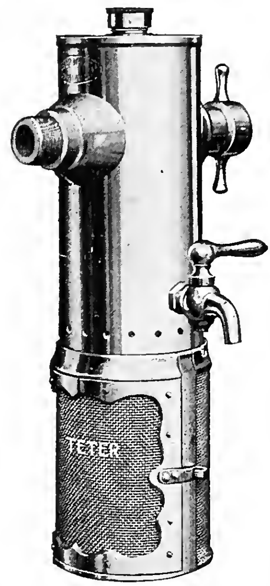


Fig. 42.—The Teter Vapor Warmer.

Teter's Method.—One of the best apparatus yet devised for the administration of nitrous oxid and oxygen for all purposes is the apparatus invented by Charles K. Teter, of Cleveland, Ohio. All the vapors inhaled by the patient are warmed and can be given through valves, or by the method of rebreathing, or a combination of these two methods, and at normal or positive pressure. The bags for the gas and oxygen are separate, and a definite amount of oxygen is constantly being mixed with the nitrous oxid. A certain amount of the expired gases is also constantly escaping through the expiratory valve. Warmed ether or chloroform can be added when needed. A more even plane of anesthesia is possible with this apparatus than with any other. A valve is placed upon the oxygen bag, but not upon the nitrous oxid, which allows continuous to-and-fro breathing. The following is the technique as given by Dr. Teter for the usual administration, and also for the administration through the nose.

Technique.—"Fill the nitrous oxid bag about two-thirds full; fill the oxygen bag so that it is pretty well distended and is under a little pressure. Just before placing inhaler over the patient's face, open the valve from the nitrous oxid bag. Now place inhaler in position, being sure that you have perfect coaptation to exclude all air. Start the nitrous oxid flowing from the cylinder into the bag; this should be so regulated as to keep this bag full all the time. After the patient has been breathing the pure gas for about ten to fifteen seconds, the oxygen valve should be opened to the second notch (which will be shown on the side of the valve cap and indicated by the ratchet), then keep increasing this one notch at a time, after three or four in-

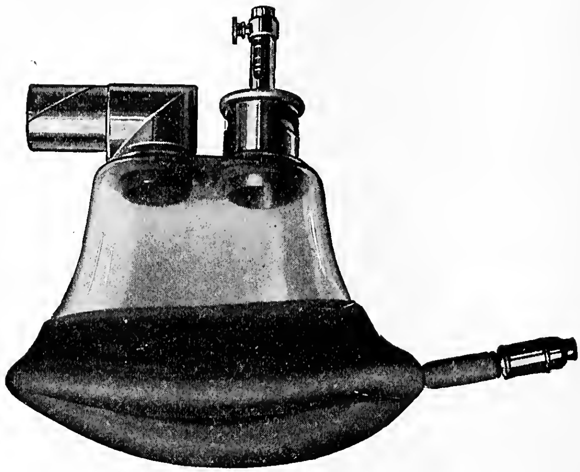


Fig. 43.—Teter's Face-Mask.

halations, until you have reached the fifth or sixth notch; do not turn this any further unless there are symptoms of asphyxia manifested. (The first manifestation of asphyxia would be blueness of the features, which would be noticed first in the mucous membrane of the lips, in the ears and eyelids). If there are asphyxial symptoms present, you should advance the oxygen valve still farther forward. It will be necessary to start the oxygen flowing from the oxygen cylinder into the bag after the patient has been breathing the mixture about forty seconds, in order to keep this bag well distended at all times, otherwise you would not be receiving the amount of oxygen indicated or desired. In order to keep the oxygen bag well distended the oxygen is allowed to flow very slowly from the cylinder, so

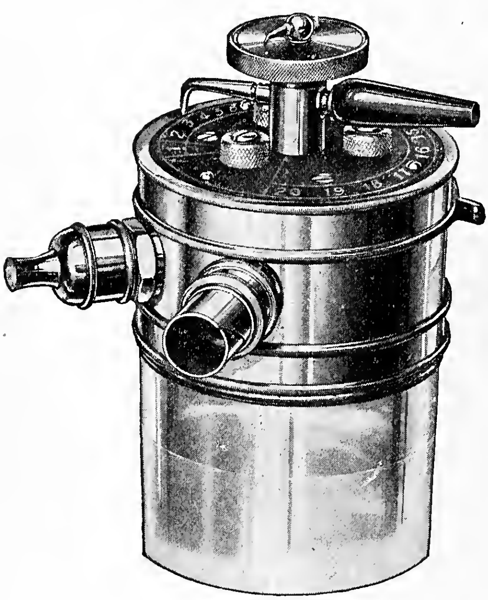


Fig. 44.—Teter Ether Attachment.

slowly that one will not be able to hear it, but enough to keep the bag well distended all the time. Practice is the only sure teacher, but one is soon able to adjust this properly.

"If your patient is not going under the effects of this mixture after

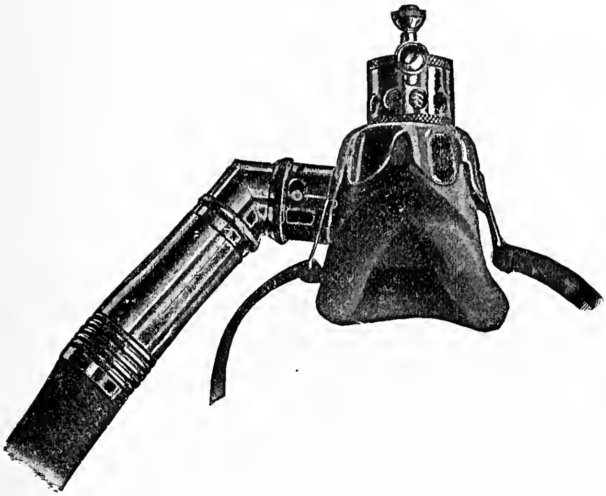


Fig. 45.—Teter Nasal Inhaler.

he has been breathing it for about forty seconds or less, he is inhaling too much oxygen, or there is an admixture of air. If the latter is the case, correct it; if the former, turn the oxygen valve back a notch or two for a few seconds, and, if he still does not respond, it may be that the oxygen is flowing too fast from the cylinder; if so, correct this, and your patient should pass into a sound and peaceful sleep. Of course, you will find some few patients that are exceptionally hard to

Fig. 46.—Teter's Auxiliary Tube for Administering Nitrous Oxid and Oxygen Through the Mouth. Used in connection with the nasal inhaler.

anesthetize, but by persistence all patients can be anesthetized with nitrous oxid and oxygen.

"By close observation on your part and being able to diagnose symptoms properly in order to know when to increase or decrease the amount of oxygen, you are enabled not only to induce any desired depth of narcosis, but are able to maintain it for any reasonable length of time

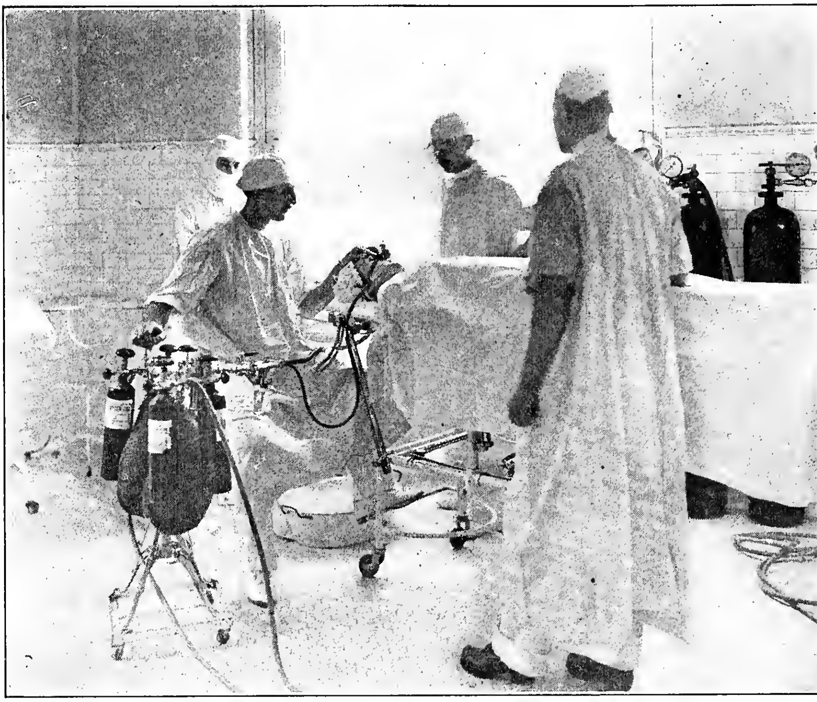


Fig. 47.—Teter Nitrous Oxid-Oxygen Apparatus with Nasal Inhaler in Use.

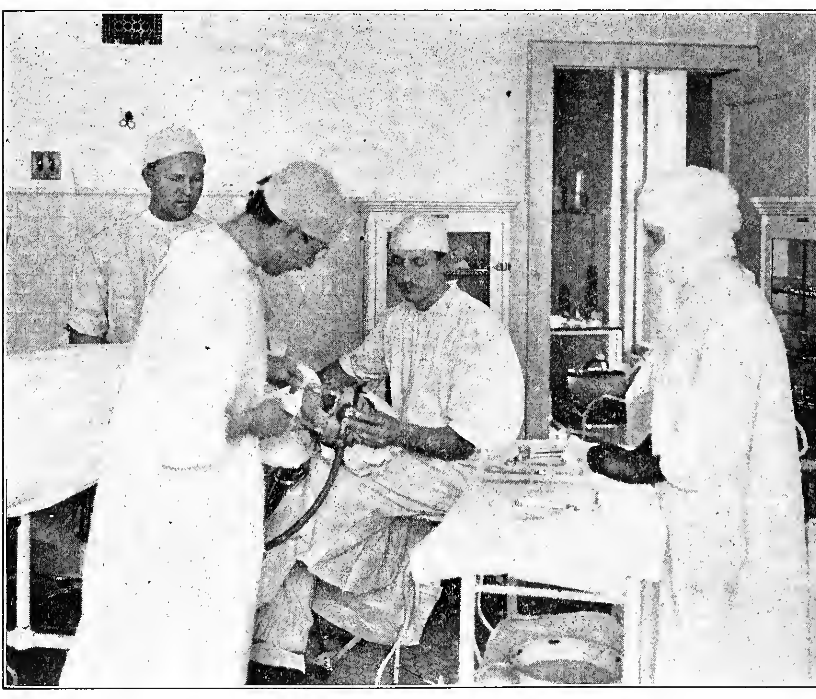


Fig. 48.—Teter Nitrous Oxid-Oxygen Apparatus with Nasal Inhaler in Use, with Surgeon Operating.

without ever admitting one breath of atmospheric air. In fact, you will be able to obtain and maintain better anesthesia without the admittance of air. You should not cause any jactitation of the muscles, or much if any cyanosis in producing anesthesia. . . . Do not be in too much of a hurry in bringing your patient under the influence of any anesthetic agent, but take some little time and give the system time to accustom itself to the new order of things. You will not only get much better results, but you will cause the anesthetic to be much safer by so doing."

Technique to be Followed in Administering Nitrous Oxid and Oxygen with the Teter Apparatus and the Teter Nasal Inhaler.—"Fill the respective bags as stated under the heading, 'Technique for the proper administration of nitrous oxid and oxygen when the face inhaler is to be employed.' Open the valve from the nitrous oxid bag, then adjust inhaler, taking the thumbs and spreading the lower part of rubber cap so that this will not press upon the alae of the nose, tending to close the nostril. This inhaler is so constructed that by proper adjustment it will fit any nose. In small children the top may be up as high as the forehead, but this will not matter so long as all air is excluded.

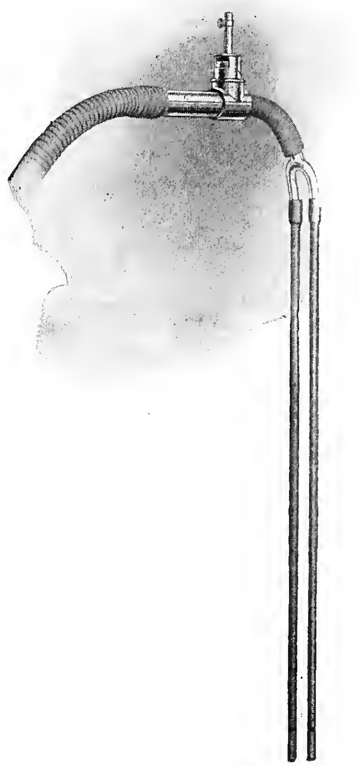


Fig. 49. — Teter's Nasopharyngeal Tubes for Nitrous Oxid and Oxygen.

"After adjusting inhaler, instruct the patient to breathe through the nose. If he will not do so, hold a piece of rubber over the mouth. (A quarter of a rubber ball the size of a large orange makes the best thing possible for this purpose.) Now allow the nitrous oxid to flow continually so as to keep the nitrous oxid bag full. After the first few inhalations turn the valve from the oxygen bag to the second notch and gradually increase this to the fifth or sixth notch, as the symptoms will indicate. After about one-half minute you should start the oxygen to flowing from the cylinder into the bag very slowly, so slowly that you will not be able to hear it, but enough to keep this bag well filled all the time.

"After inducing the desired depth of anesthesia, which should be accomplished in about two minutes, remove the rubber from the mouth. If the patient breathes through the mouth release the plunger in the inhaler, and it will descend upon the exhalation disk. This is done by loosening a set screw, which normally holds this plunger up and away from the exhalation disk. The inhaler is to be held firmly in position.

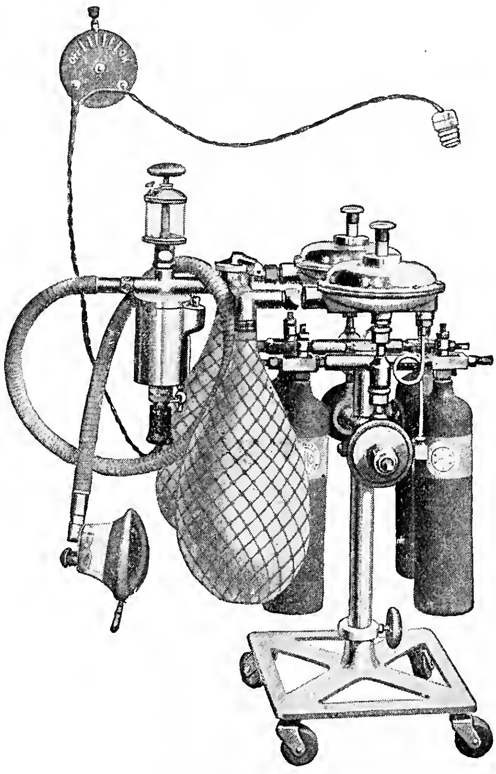


Fig. 50.—The Ohio Monovalve. Shown with warming device, including ether or chloroform cup.

Now the nitrous oxid is turned on more strongly from the cylinder, and the pressure thus formed in the bag will force the nitrous oxid through the nose, and, although the patient is inhaling and exhaling through the mouth, he is compelled to breathe the nitrous oxid, as it is under pressure greater by far than the atmospheric pressure. The oxygen bag is also allowed to fill with oxygen, and this is forced along with the nitrous oxid, according to symptoms indicating its need.

"It is out of the question to expect to maintain as tranquil an anesthesia by this method as is possible where we can exclude all atmospheric air and are not hampered in applying our agent, but we can keep our patient under the anesthetic for any length of time and free from all physical pain.

"If the patient continues to breathe through the nose, all that is necessary is to regulate the oxygen in accordance with symptoms displayed and continue to the completion of the operation."

Nitrous Oxid-Oxygen Endopharyngeally.—Connell has developed a very satisfactory method of administering nitrous oxid and oxygen, the technique of which is as follows:

After the patient is surgically saturated with the anesthetic, the delivery is shifted to the pharyngeal method by the nasal route. Each nostril is plugged by a collar of thick rubber tubing slipped over the nasal catheters. The pharyngeal rebreathing tube is then inserted, to which is attached a rebreathing bag. The quantity found most useful with this method is eight liters per minute, beginning with a five per cent oxygen mixture and increasing gradually up to a nine or ten per cent mixture by the end of the first hour. Where surgical relaxation is desired and protection against subconscious suffering is indicated, this is to be obtained not by dangerously increasing the oxygen starvation, but by adding ether as indicated. The rebreathing is used solely for economy. If the pharyngeal delivery is 22 liters, or five and one-half gallons, a minute, rebreathing may be dispensed with if the mouth be kept closed. (See Connell's Anesthetometer, p. 160.)

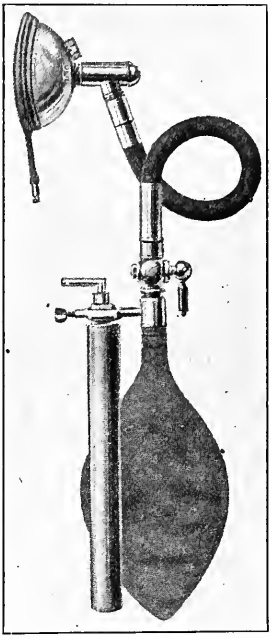


FIG. 51.—OHIO SMALL NITROUS OXID INHALER. May be easily carried to bedside or hospital ward; very satisfactory for short anesthesia.

The Ohio Monovalve.—The gas pressure as it leaves the cylinders is *automatically* reduced and controlled here.

In preparing to give the anesthetic, a cylinder of nitrous oxid and oxygen are both opened as far as the valves will permit. The gas passes through regulators which reduce the pressure to about two pounds, then through automatic valves, where it is further reduced to breathing pressure. The bags fill automatically, but when they are full the gas stops flowing. The bags are refilled as fast as the gas is consumed.

There is only one valve to handle. With it, pure nitrous oxid is given, and when it is turned beyond a certain point oxygen is mixed in fixed percentage. If turned still farther, the nitrous oxid is closed off and pure oxygen is administered.

If the patient is a deep breather, the gas can be given with increased force by simply turning a regulating device on top of the nitrous oxid and oxygen automatic valves. These are close to the one

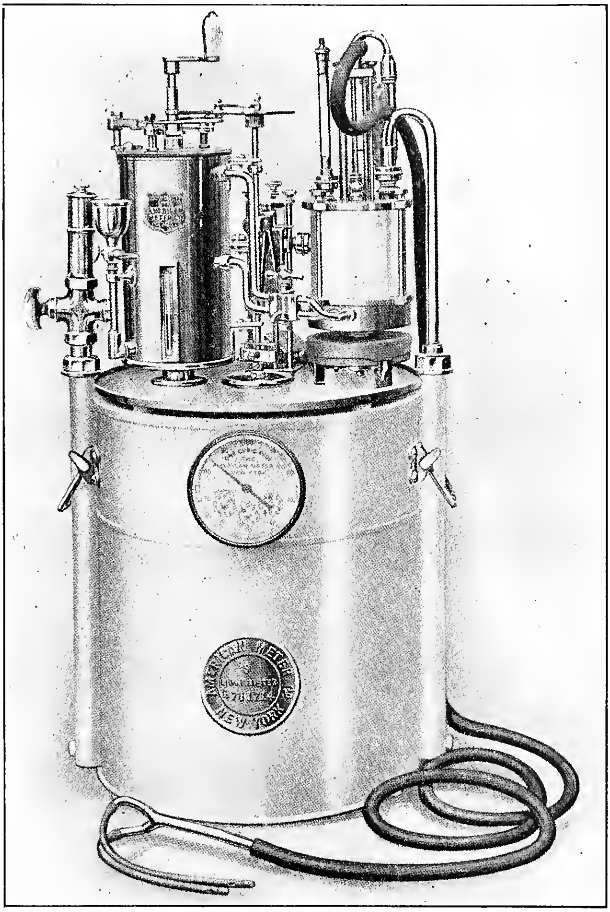


Fig. 52.— Connell's Anesthetometer.

valve referred to, and are so easy to operate that there is no danger of confusion.

The monovalve is made in two designs, one especially for offices and hospitals, where it is easily moved about on castors, and another design, which can be packed up and carried around from place to place.

Boothby and Cotton Apparatus.—The apparatus of Boothby and Cotton seems to mark a distinct step in advance. The apparatus is not portable, but is especially applicable for hospital use.

A PERFECTED APPARATUS[1] WITH NOTES ON ADMINISTRATION[2]

"Desirability of Constant Mixture and Necessity of Ether Addition.—All experimental and clinical work has emphasized the fact that a *constant* mixture (rightly proportioned for the particular case in hand) produces a smoother anesthesia than a mixture of varying composition; in other words, it has been shown that an intermittent and irregular supply of either gas does not conduce to a smooth surgical anesthesia.

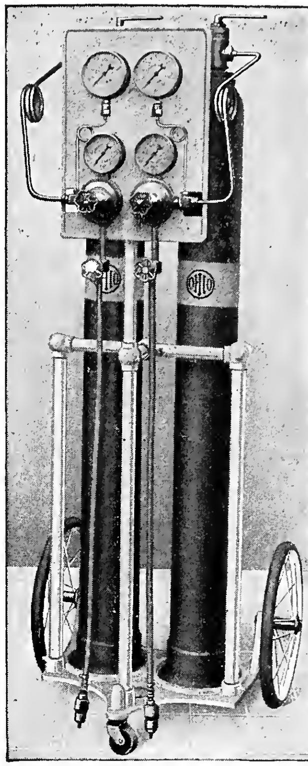


Fig. 53.—Pressure Gauges for Large Tanks of Nitrous Oxid and Oxygen.

"Hewitt was the first to develop an apparatus at all applicable for general surgical use. His methods of overcoming the pressures of the nitrous oxid and oxygen in the tanks is to use semi-elastic bags which are kept more or less full from the tanks by means of an intermittent flow of the gases controlled directly by hand valves. From these bags the flow of gas to the patient is regulated by a specially constructed and graduated valve that allows definite proportions of gas to pass from each bag, providing the pressures within the same are equal.

"In practice it has been found very difficult to keep the two bags evenly and equally distended, even if great pains and constant attention are being given by the operator to the manipulation of the hand valves; therefore, the pressure in the two bags varies and, consequently, the mixture actually received by the patient must of necessity be very varied.

"Fundamental Principles. Involved in Securing Constant Mixtures.—As a result of the inadequacy of any apparatus built on the principle of the Hewitt, we took up, now over a year ago, the study of the problem. We laid down four fundamental principles which were to be met, namely:

[1] See Figs. 54-55.

[2] Written by Frederic J. Cotton, First Assistant Surgeon, Boston City Hospital, and Walter M. Boothby, Assistant in Anatomy, Harvard Medical School, Assistant Surgeon, Mount Sinai Hospital (Boston, Mass.), Anesthetist to the Boston City Hospital.

"(1) There must be an absolutely *regular flow of each gas* at any rate desired, without the necessity of frequent valve manipulation.

"(2) The flow of the gases must be rendered *visible* so that their proportions can be approximately estimated at a glance.

"(3) An *efficient method of adding ether vapor* gradually yet rap-

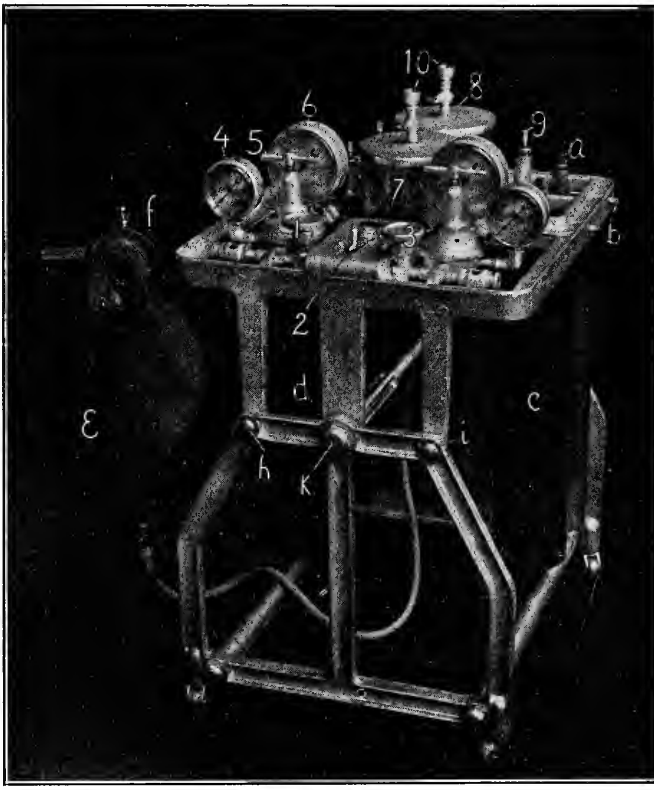


Fig. 54.—Boothby and Cotton Apparatus Set Up. (See page 169.)

idly up to any amount that even an extreme case may require must be available.

"(4) The face-piece must be so modified as to be absolutely *air-tight* and also practically self-retaining.

"Maintaining Regular Flow of Gases.—The first point, the crucial one, is to obtain an even flow of nitrous oxid gas from its liquefied form. This necessitates the use of an automatic reducing valve. The same is true of oxygen, although not in liquid form, in similar tanks under a pressure of 1,500 to 1,800 pounds to the square inch. The province of such a valve is to reduce these pressures to a working basis of 20 pounds to the square inch; a good valve should act automatically, and require no attention on the part of the anesthetist; furthermore, it does not freeze or become otherwise obstructed.

"This principle of the automatic reduction of high tank pressures is so fundamental that we consider it essential that this feature be actually an integral part of the apparatus and not secondarily attached

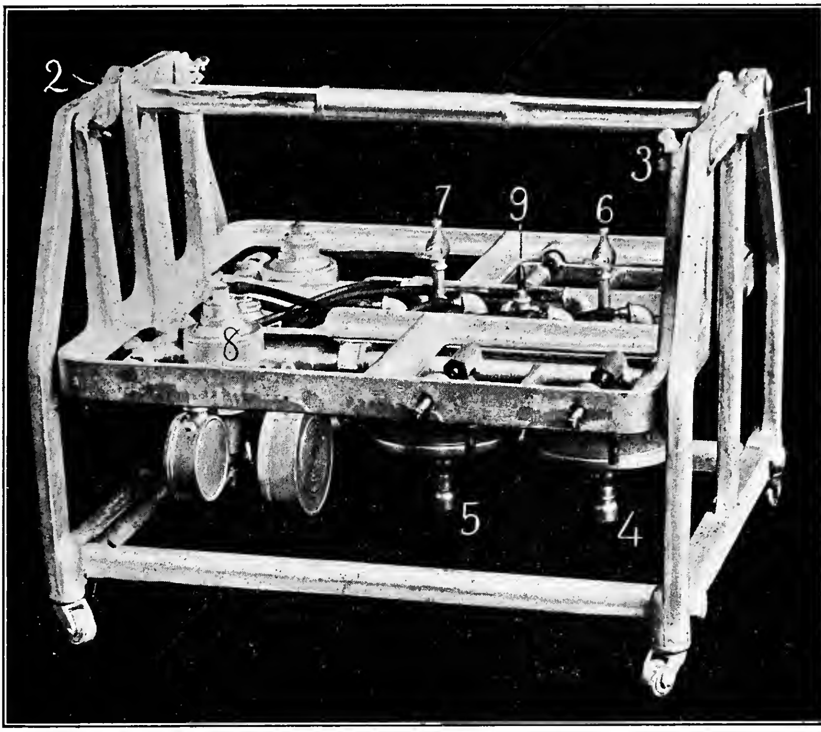


FIG. 55.—BOOTHBY AND COTTON APPARATUS FOLDED. (See page 170.)

to tanks which are then connected to an apparatus designed on the Hewitt type. For general use a tank of moderate size (containing 75 gallons of oxygen and 250 gallons of nitrous oxid) is the most practical and convenient; accordingly we have designed our apparatus for that size of tank (the smaller sizes can of course be used and are preferable for transportation in house operating).

"VISIBLE CONTROL OF FLOW OF GASES.—The second desideratum, namely, rendering the rate of flow of gases visible, so that the relative proportion of each gas may be estimated at a glance (also assuring the administrator of the fact that the desired flow is actually taking place) has been solved by having *each gas bubble separately through water into a glass mixing chamber.*

"The volume of gas delivered to the patient is controlled by means of a hand valve of fine adjustment acting against the *low* pressure delivered by the reducing valve. This is entirely independent of the automatic reducing valve. The hand-valves can be set to give any desired volume, which will continue unaltered for hours; a change in the rate of flow is obtained by simply turning the valve-handle a trifle till such volume per minute as is desired is seen to bubble through the water of the mixing chamber.

"The aim of the anesthetist is to determine, as early in the anesthesia as possible, the proportion of nitrous oxid and oxygen suited to the patient under his care. The greater his experience the earlier will he be able to do this with certainty. After this proportion is once ascertained the apparatus will deliver the same mixture as long as desired. After a brief experience one is enabled to approximate the desired proportion solely by the eye, thus rendering it easier to quickly obtain the constant mixture needed for the particular patient in hand. In difficult cases it greatly helps the anesthetist to determine whether the patient becomes rapidly cyanotic (and this is not a rare occurrence with beginners); the anesthetist can see at a glance that the cause of the difficulty is obstruction of the respiratory passages and not due to an insufficient proportion of oxygen in the mixture being administered to the patient.

"ADDITION OF ETHER VAPOR.—The third essential point, which consists of being able, gradually yet rapidly, to add to the respired mixture ether vapor (as much as an extreme case may need), has been met by providing a second chamber, containing ether. The gases, after leaving the mixing chamber, pass to a three-way valve by which they are allowed to pass by the ether chamber entirely, or are made to pass either partly or wholly over the surface of the ether, or they may be forced (if desired) to bubble *through* the ether.

"Thus *any amount of ether vapor required,* from the minutest trace to a relatively high percentage, *can be almost instantly obtained.*

"The possibility of gradually and yet rapidly increasing the strength of the ether vapor is a material advantage, for it allows the anesthetist to just 'catch' the patient within a few seconds after he gives a sudden warning of being 'light' by moving the legs, contracting the abdominal wall, or showing symptoms of impending vomiting. At such moments one may gradually but rapidly increase the ether percentage to that obtained by bubbling through the ether; after a few respirations the patient is seen to relax or the symptoms of impending vomiting disappear, at which time the ether should be entirely shut off. It is best, as a rule, at the beginning of trouble indicating a 'light' condition, to make no change in the rate of flow of the gas or oxygen, for when ether is administered a slight excess of oxygen is desirable; but, as soon as the impending trouble is overcome, the rate of oxygen may be slightly decreased, or that of nitrous oxid increased, depending on the amount of rebreathing desired. In all probability the new mixture will maintain a perfect condition of anesthesia for the rest of the operation, possibly without the necessity of again touching the valves.

"Because we have emphasized the necessity of having available an appliance by which strong ether vapor can be administered we must not be misunderstood; in at least one quarter of the cases no ether at all will be required; in perhaps another quarter about two minutes' inhalation of ether will be needed during the last stages of the preparation of the patient; in another small proportion an occasional addition of ether vapor for one or two minutes through the course of the administration will be found advisable; only very rarely and in rebellious alcoholic cases will more than a total of ten minutes' respiration of ether in addition to the gas mixture be needed for an hour's operation; and, even in these difficult cases, practically no more ether is needed after the first hour, no matter how long the operation is prolonged. Accordingly little or no nausea and vomiting follows a properly conducted nitrous oxid-oxygen-ether anesthesia in a great majority of cases.

"PRE-MEDICATION.—The cases run somewhat more smoothly, and perhaps with an average decrease in the amount of ether vapor needed, resulting in a more nearly ideal recovery, if moderate doses of morphin (gr. 1/8 to 1/4) and of atropin (gr. 1-120 to 1-100) are given hypodermically one-half hour before the beginning of the anesthesia.[1] At the Boston City Hospital this is a standing order, but if it is omitted for any reason we are not concerned except in the case of bad alcoholics. In other words, the preliminary injection of morphin is by no means essential, though it is desirable unless contradicted by some known peculiarity of the patient.

"NON-LEAKING FACE-PIECE.—The fourth point necessary for a nitrous oxid-oxygen anesthesia is to exclude even traces of air from leaking in between the mask and the face. This necessity holds true for every case and must be accomplished in spite of peculiarities of the facial contour or the presence of beard and whiskers. Boothby [2] recently described a collar that is not only air-tight but practically self-retaining. To those using this collar we call attention, elsewhere more fully dealt with, of the dangers of positive pressure; the expiratory valve must be so set that an outflow of the gases may occur whenever the pressure inside the masks exceeds 2 mm. of mercury, which is a pres-

[1] In the beginning, following the lead of Crile, we used scopolamin with the morphin. Often an efficient hypnotic, scopolamin has seemed to us too uncertain in its action to be worthy of routine use, and we have come to use atropin, which does at least reliably insure us against trouble from excess of mucus.

[2] *Boston Med. and Surg. J.*, 1912, *166*, 9, 328.

sure that is just sufficient to maintain the rebreathing bag full but not distended.

"REBREATHING REGULATED.—For an even anesthesia, and as an aid to the avoidance of surgical shock, a certain constant amount of rebreathing is of benefit; approximately the rate of flow of the gases should be such that from a quarter to a half of the volume of each respiration is of freshly added gas mixture. Such a proportion reduces to within reasonable limits the expense of gas-oxygen anesthesia; too much rebreathing is apt to be followed by post-operative discomfort, usually in the form of headache, and it may cause an increase of post-operative nausea and vomiting. Vomiting during the progress of the anesthesia is often an indication of excessive rebreathing for that particular patient, although in comparison with other patients it may not appear excessive; at all events increasing the volume per minute of the gas mixture frequently clears up the symptoms. Our observations on the effect of rebreathing, so far as they go, agree clinically with the laboratory findings of Henderson. Our observation of the blood pressure under nitrous oxid-oxygen (ether) anesthesia is that there is a distinct rise not only at the commencement but also throughout the operation. After the removal of the mask with its accompanying necessity for rebreathing, there is a distinct and rapid fall in the blood pressure. In two instances, both on very sick and debilitated

FIG. 56.—BOOTHBY AND COTTON FACE MASK.

patients, this fall was sufficient to abolish the radial pulse; the appearance of the patients and their mental attitude remained good; recovery was prompt and within one-half hour they were in fine condition and remained so.

"AVOIDANCE OF CYANOSIS.—*Surgical anesthesia is never obtained when the patient appears in the least degree cyanotic* on account of asphyxial spasm and rigidity. On the contrary the *patient must always be pink.* Any anesthesia accompanied by cyanosis is dangerous. Deaths under nitrous oxid-oxygen are doubtless due to conducting the anesthesia according to the erroneous idea of the necessity and safety of cyanosis; no deaths have been reported in which the patient's color was maintained pink.

"We have suggested that, in some cases, even when respiring a mixture of gas and oxygen in which the proportion of the latter is sufficient to maintain a pink color, the patient might be brought under too profound an influence of nitrous oxid, and the anesthesia be made dangerously deep. Our use of an absolutely air-tight face-piece has enabled us to demonstrate that such a condition occurs not infrequently. In fact, toward the end of a long operation it is often necessary to use equal parts of oxygen and nitrous oxid.

"The symptoms of an overdose of nitrous oxid in the presence of sufficient oxygen to keep the patient pink is, first, *stertorous respiration,* and second, the onset of an excessive secretion of mucus; unless the percentage of nitrous oxid is then decreased, the patient's face and hands take on a death-like pallor (not cyanotic) ; there is an absolute loss of all the facial reflexes; the respirations become shallow; and probably the blood pressure falls (that is, the temporal cannot be found so readily although the rate is not excessive). This condition, if pushed, would probably lead to death from paralysis of the respiratory center, though we know of no experimental evidence to support the hypothesis.

"The point we wish to make is that an excess of nitrous oxid may be given even with a proportion of oxygen sufficient to maintain the patient pink and the respirations normal; if a death-like pallor with the other symptoms noted should now supervene while respiring such a mixture, the patient is rapidly approaching the danger point of excessive anesthetization. In such a condition no time should be lost, for as yet we do not know how soon actual respiratory failure and death may occur. In brief, the mask should be removed, and, if necessary, artificial respiration instituted together with the administration of oxygen.

"The use of nitrous oxid for prolonged anesthesia is still in its infancy and its danger limits are not well understood; in consequence, for several years yet its effects must be carefully watched.

"WHEN ETHER SHOULD BE ADDED TO THE MIXTURE.—Although the patient is rapidly rendered unconscious (two minutes) by nitrous oxid-oxygen, yet it is nearly ten minutes before the body is sufficiently saturated with the nitrous oxid to permit the beginning of an abdominal operation. During this period, which may be occupied by the preparation and draping of the patient, we allow the anesthetist to depart somewhat from our rule in regard to avoidance of cyanosis; but even here we permit only the slightest degree of duskiness and never entertain the possibility of deep cyanosis. By the time the incision is made the patient must be actually pink and remain so throughout the operation. If then a mixture of nitrous oxid and oxygen with a proportion of the latter sufficient to keep the patient pink will not produce sufficient relaxation to meet the demands of the surgeon, the anesthetist must add ether vapor till relaxation is complete.

"For the best results close coöperation on the part of the surgeon and the anesthetist is essential. During the greater part of the majority of operations complete relaxation is not needed; when such relaxation is required by the surgeon he should so inform his anesthetist, who will be able within two minutes, by the proper administration of ether, to provide the same; as soon as such need is over the ether may be discontinued.

"Obstruction of the Air Passages.—A cyanotic condition of the patient, however, sometimes quickly develops even with an evidently liberal supply of oxygen as shown by the flow through the mixing chamber. In such cases the trouble is without question an obstruction of the air passages and must be quickly remedied. Contrary to the generally accepted opinion, cheek and tongue obstruction of the air passages is extremely common under nitrous oxid-oxygen anesthesia, and its prevention is absolutely essential. The most frequent cause is an obstruction of the nares together with a valve-like action of the lips or cheeks against the teeth that occurs in mouth breathing when there is muscular relaxation. A ready means of overcoming such a condition is to slip up under the face-piece or collar a piece of gauze or a thin ribbon retractor into the angle of the mouth to keep the lips apart and the cheek away from the teeth; or pieces of rubber tubing about six inches long, guarded by safety pins, may be introduced into the nares through the oro-pharynx. In rare cases the tongue may drop back and cause obstruction in spite of every effort to prevent the same by holding the jaw forward; in such cases a silkworm-gut stitch should be passed through the tongue and brought out under the collar, with a dental mouth prop placed between the teeth to prevent biting of the tongue. An absolutely free air passage for the gases must always be maintained; any slight obstruction, most commonly on inspiration, causes a labored respiration under which conditions a smooth anesthesia is impossible; besides it throws an extra exertion onto the patient.

"The theoretical benefit to be obtained from an increase of pressure is less than one per cent in efficiency; accordingly, a procedure embodying the dangers of collapse and of sudden death, with such a meager beneficent return, should not be used.

"In practice, therefore, the rebreathing bag should just become taut at the end of an expiration; this corresponds to a pressure of one or two mm. of mercury, which is sufficient to open the respiratory valve at the end of the expiration, and thus to allow the last part of the expired gases, that part which (as McKessen points out) contains the largest percentage of CO_2 to escape into the air.

"The experimental apparatus recently described by us, built on the principles enunciated above without regard to lightness and portability, has been most satisfactory and has met all expectations. We have reversed our former opinion as to the desirability of having an attachment for warming the gases and this attachment has been discarded.

"An apparatus to meet all requirements described above must have some size and weight. These items, however, have been reduced to their lowest terms by great care in the design and arrangement of the various parts. For the purpose of transportation the apparatus can be collapsed to a reasonable carrying size (height, 17 inches; length, 22 inches; width, 17¼ inches) by the simple removal of four lag bolts, set up with thumb screws, which allows the top half of the machine to swing down into the lower half; the center bar or axis acts then as a convenient handle and the framework forms a protecting cage for the valves and the glass chambers. To reduce the weight, the patterns have been made as small as is consistent with the strength requisite for hard hospital use and transportation for house operating, and the castings (except the valves) are made of aluminum alloy. The carrying weight is just under fifty pounds.

"Fig. I.[1] (1) Hand valve to regulate the volume supply of oxygen; it works against a low pressure of about 25 pounds to the square inch, therefore it can be set for, and will continue to deliver, any constant amount, and this can be estimated by seeing the rate of flow as the gas bubbles through the water in the glass mixing chamber (7).

"(2) Ether valve; when pushed over to the left the mixed gases from 7 go directly to the patient; when in the center (as illustrated) the mixed gases pass over the surface of the ether in chamber 8; when pushed over to the right the gases must bubble through the ether.

"(3) Hand valve; to control the volume of nitrous oxid in same manner as (1) regulates oxygen.

"(4) Low pressure gauge; the one on the left indicates the pressure of oxygen, and that on the right nitrous oxid, after being automatically reduced by the reducing valve.

[1] See Fig. 54, page 162.

"(5) Regulating handle on the reducing valve; this, after being set for the desired low pressure (20 lb.), does not need to be again touched.

"(6) High pressure gauge; to show the pressure in the supply tank.

"(7) Glass mixing chamber; contains water through which each gas bubbles separately, thus giving a ready means of estimating at a glance the rate of flow of both the oxygen and the nitrous oxid.

"(8) The ether chamber; by valve 2 the gases, after being mixed in 7, are allowed to pass around the ether chamber or made to pass partly or wholly over the surface of the ether, or forced to bubble through the ether, thus adding any desired amount of ether vapor to the respired mixture.

"(9) One of four valves; introduced so that any one of the tanks may be removed and replaced by a full one without interrupting the use of the apparatus.

"(10) Cups to fill the chambers with water and ether.

"(a) Valve on tank.

"(b) Screw by which each tank is clamped into its yoke.

"(c) One of the two nitrous oxid tanks on right side.

"(d) One of the two oxygen tanks on left side.

"(e) Rebreathing bag.

"(f) Mask with celluloid face-piece and the Boothby air-tight self-retaining collar.

"(h) Two of the four lag bolts which may be removed by unscrewing the thumb nuts on the inside to allow the top of the table to invert into the lower half.

"(i) Center axis on which the top half swings.

"Fig. II.[1] (1) Center axis on which the top half swings; the middle portion serves as a handle.

"(2) One of the four thumb nuts which are removed to invert the table.

"(3) Mixing and ether chamber protected by the frame when top is inverted for transporting.

"(4) Pet cocks for drawing off the water and ether from the chamber before inverting.

"(5) The under side of one of the automatic reducing valves.

"(6) The metal nipple to which the rubber tube is attached that leads to the rebreathing bag.

"Size: Height, 17 inches; length, 22 inches; width, 17¼ inches; weight, 50 pounds (aluminum castings)."

The Gwathmey-Woolsey Nitrous Oxid-Oxygen Apparatus.—The Gwathmey-Woolsey apparatus has been developed in accordance with the principles recognized as essential in the evolution of nitrous oxid and oxygen anesthesia, especially those utilized by Gatch and by Boothby

[1] See Fig. 55, page 163.

and Cotton. The gas supply is conveniently and efficiently furnished when equipped for portable use, first, by two one hundred gallon tanks of nitrous oxid which are in direct connection with the reducer at all times; second, by one forty gallon tank of oxygen, easily and quickly replaced when necessary.

The pressure of the nitrous oxid is reduced by an efficient reducer of small dimensions and light weight; that of the oxygen, by a very small valve. The gases are delivered under low pressure into a combination sight feed and warm water bath, where the administrator can see, on one side of a nickel partition, the nitrous oxid flowing, and on the other the oxygen. This sight feed enables the anesthetist to regulate the proportions of the gases very carefully.

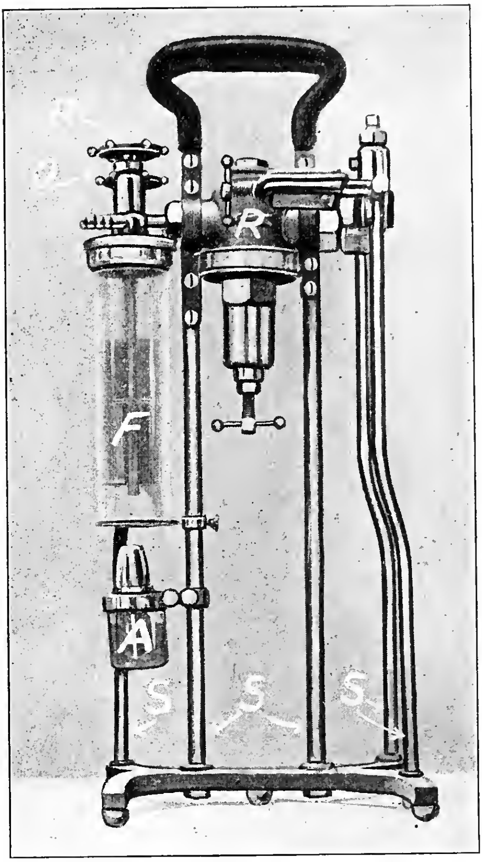


Fig. 57.—Gwathmey-Woolsey Nitrous Oxid-Oxygen Apparatus. R, reducing valve of nitrous oxid; R[1], regulating valve of nitrous oxid; O, regulating valve for oxygen; F, sight feed; S, supports.

This water sight feed is warmed by an alcohol lamp adjustable to its under surface, thus supplying heat and moisture, which are valuable assets in the administration of any anesthetic. From the sight feed, the mixed gases pass at the top through an exit tube to which is attached the rubber tube running to the rubber bag and mask. The gas cylinders are opened wide into the reducing valves, the flow from these valves being controlled by very sensitive wheels.

When the two nitrous oxid tanks and one oxygen tank are in place (enough for a two-hour administration), the total weight is under forty pounds. In hospitals where the supply is obtained from large tanks or from a generator in the cellar, the delivery hose from these sources may be attached to the apparatus.

The Gwathmey-Woolsey Mask.—The Gwathmey-Woolsey mask is an anatomical one made to fit the bones of the face. A rubber collar, devised first by Gatch and later used by Boothby and Cotton, is retained as an essential feature of the mask. The adjustment of this collar, to the absolute exclusion of all air, is considered one of the important features of the technique.

Ether.—In the small number of cases in which it is necessary to

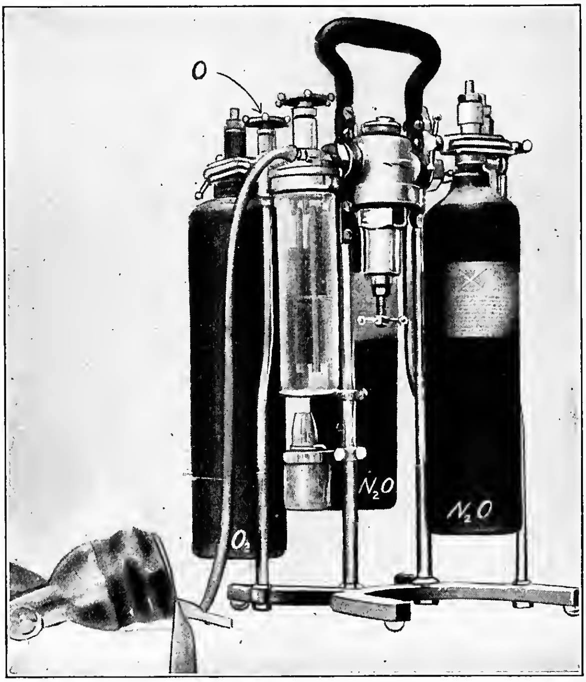


Fig. 58.—Gwathmey-Woolsey Nitrous Oxid-Oxygen Apparatus with Cylinders Attached. O, regulating valve for oxygen; O_2, oxygen tank; N_2O, nitrous-oxid tank.

give ether in combination with gas and oxygen it may be introduced by placing an ether chamber directly on the mask and between the mask and bag, as is usual with all gas-ether apparatus. The chimney piece of the Gwathmey gas-ether apparatus, to which the gas bag is attached, has been retained. This contains the inspiratory and expiratory valves upon a sliding cuff. With this cuff, the anesthetist can regulate the patient's breathing, through valves, partly through valves, rebreathing entirely, or, as is generally the case, rebreathing with the expiratory valve slightly open.

Positive Pressure.—Five mm. of mercury pressure in the rebreathing bag have been found a very great help in those subjects usually considered unsuitable for nitrous oxid and oxygen.

Endotracheal Insufflation.—The apparatus was especially devised for endotracheal work. It has been found most acceptable wherever endotracheal work is needed, the constant flow of the gases insuring an even anesthesia without danger. When used in this way, no bag is necessary, the connection being made directly with the tube in the trachea. The cases in which it has been used have been entirely satisfactory. The patient is anesthetized in the usual way, the catheter is inserted in the trachea, and a glass connecting tube is placed in the catheter, joining it with the rubber tube from the apparatus.

A mercurial manometer which automatically "blows off" at twenty-five mm. of mercury pressure is attached for endotracheal work. For the usual anesthesia, a safety valve set for a pressure of ten pounds protects the glass "sight feed."

Nasal Anesthesia for Oral Surgery.—For such operative procedure the bag can be dispensed with and the general principles outlined by Teter allowed to govern the technique. The Teter auxiliary tube for the mouth, to prevent spattering when the volume of gas is too great through the nasal passages, is also used. This method is entirely satisfactory in cases of adenoids and tonsils.

Analgetic Work.—With the nose-piece in position, a great many surgical operations, especially dental work, may be done with ease during the analgetic stage of nitrous oxid-oxygen anesthesia. The absence of the bag, or any impediment around the patient's head, is a very great advantage. The automatic action of the apparatus after once the flow of gases is started is a great help. It is now an acknowledged fact that dentists can do their work more acceptably to the patient and with greater satisfaction to themselves when using nitrous oxid and oxygen for painful dental work than without this help, or with only a local anesthetic.

Obstetrical Cases.—Guedel[1] reports a number of cases with apparatus for the self-administration of nitrous oxid and air in obstetrical cases. The analgetic properties of nitrous oxid and oxygen have not been tested in this field. It would seem, however, to be preferable to nitrous oxid and air by virtue of the absence of the slightest asphyxiation and the presence of a more prolonged stage of analgesia, the idea being to suppress all pain without completely subduing muscular effort. The nasal administration, although more wasteful than the usual method of mask with bag, is the most agreeable and most satisfactory method for these cases, inasmuch as it leaves the face entirely uncovered. The patient can thus answer questions, which is sometimes necessary in order to avoid passing from analgesia to anesthesia.

Technique of Administration for General Work.—The mask, with the cuff turned up, is placed upon the patient's face and held in

[1] *Indianapolis Med. J.*, Oct., 1911.

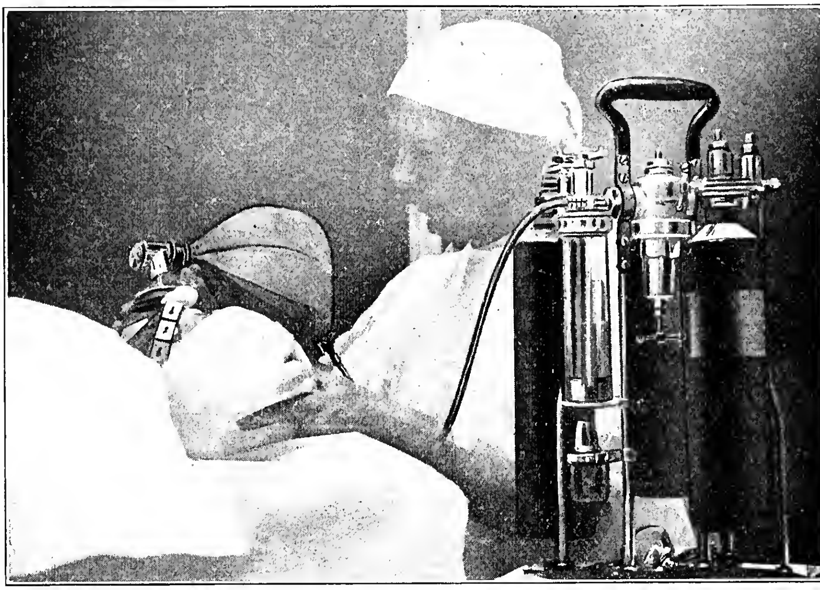


FIG. 59.—GWATHMEY-WOOLSEY NITROUS OXID-OXYGEN APPARATUS AS USED IN GENERAL SURGERY.

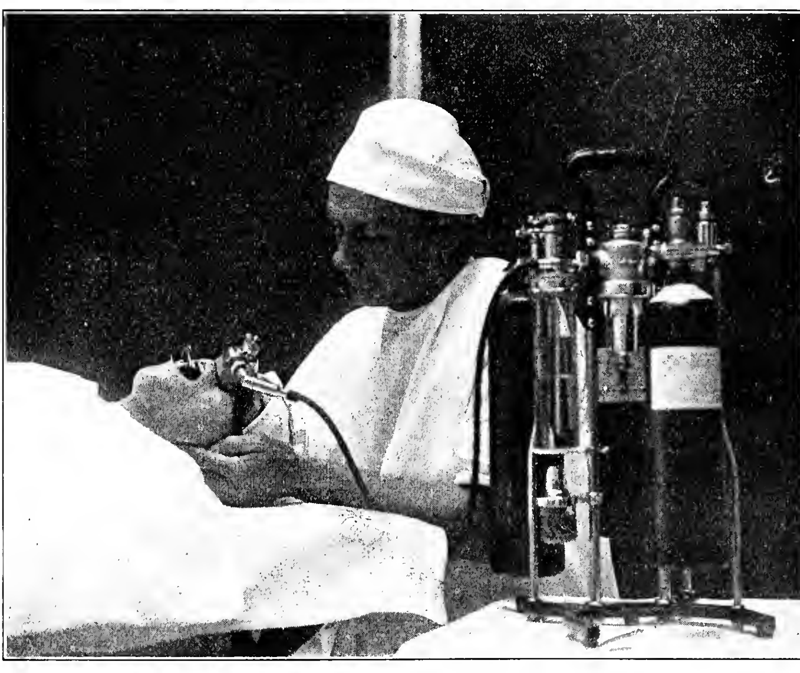


FIG. 60.—GWATHMEY-WOOLSEY NITROUS OXID-OXYGEN APPARATUS IN ADENOID AND TONSIL OPERATIONS.

position until unconsciousness ensues. The cuff is then turned down and fastened around the neck; it now becomes self-retaining. If the patient is a vigorous alcoholic or a nervous individual, the bag should be partly filled with nitrous oxid alone. When the gas is turned on, from two to six breaths, according to the patient, should be allowed through valves; the sliding cuff is then pulled out, and rebreathing instituted, the expiratory valve being left very slightly open, say one-sixteenth of an inch. As signs of anesthesia appear, oxygen should be allowed to bubble through in about the proportion that will be maintained throughout the operation. For the first five minutes the bag should be slightly overdistended, thus insuring a deeper anesthesia. After that, seven-eighths distention will meet all conditions. It is unnecessary to manipulate the valves after the patient has been anesthetized five minutes, a slight increase or decrease in the oxygen, or a slight increase or decrease in the nitrous oxid, according to the requirements of the patient, being all that is necessary. Quite often the patient will continue to be satisfactorily narcotized for ten or twenty minutes without the supply valves being touched. Five mm. pressure will relax resistant patients sufficiently for all surgical operations.

There is thus a continuous flow of nitrous oxid and oxygen, with continuous rebreathing. There is slight escape of the exhalations at all times. The patient's color reflex should be maintained, and duskiness should not be allowed. Stertor should be avoided whenever possible by the anesthetist sustaining the lower jaw with the hand or lessening the amount of nitrous oxid.

To summarize, the advantages of the Gwathmey-Woolsey apparatus are:

(1) Absolute and perfect control of the gases flowing at a low pressure.

(2) The gases are easily warmed whenever the patient's condition demands it.

(3) It is especially adaptable for endotracheal anesthesia, solving the problem of the administration of nitrous oxid and oxygen by this method.

(4) Small amounts of ether can be added whenever necessary.

(5) An even, automatic flow of gases, opening up a new field especially for using the analgetic properties of the gases.

(6) Small size and portability of the apparatus.

(7) The irritating impurities of the gases themselves, as well as small particles of rust from the inside of the cylinder, are washed out in the water filter sight-feed.

CHAPTER V

ETHER

HISTORY OF THE USE OF ETHER AS AN ANESTHETIC.

CHEMISTRY: The Term Ether; Properties of Ether; Anesthetic Ether; Precautions in Handling Ether; Sources of Impurities in Ether; Standards of Purity with Which Anesthetic Ether Should Comply; Rôle of Alcohol in Ether; Peroxids; Aldehyd; Physiological Action of the Impurities and Administration Means to Avoid Them.

SPECIAL PHYSIOLOGY: Effects Upon the Respiratory System; Effects Upon the Circulatory System; Effects Upon the Nervous System; Effects Upon the Muscular System; Effects Upon the Glandular System and Other Structures; Causes of Death from the Administration of Ether; Stages of Ether Anesthesia; Elimination; After-Effects.

ADMINISTRATION OF ETHER: The Open or Drop Method; The Mask; Ethyl Chlorid-Ether Sequence by the Drop Method; The Ethyl Chlorid Ether-Chloroform Sequence; The Ethyl Chlorid-Ether Sequence by the Closed Method; Chloroform-Ether Sequence; Anesthol; Anesthol-Ether Sequence by the Drop Method; The Ether Rausch; The Semi-Closed Method; Towel and Paper Cones; The Handkerchief Method; The Closed Method; The Nitrous Oxid-Ether Sequence; Technique of the Nitrous Oxid-Ether Sequence; Nitrous Oxid-Ether-Chloroform Sequence; The Vapor Method of Anesthesia; Warmed Ether Vapor.

VAPOR: The Open Method; Endopharyngeal Anesthesia; Oxygen-Ether Administration; Concentration of Ether Vapor; The Closed Method; Amount of the Anesthetic Used; Care of the Apparatus; Hints; Advantages; Treatment of Accidents.

INDICATIONS AND CONTRAINDICATIONS OF ETHER: Indications; Contraindications.

HISTORY OF THE USE OF ETHER AS AN ANESTHETIC

In 1795, ether was employed medicinally for the relief of asthma. About this time inhalation therapeutics seems to have been a medical fad for a short period, and ether and nitrous oxid were used to the exhilarating stage only. Although injuries received while under the influence were not felt, no one seemed to think of carrying the physiological effect of the drug beyond what is generally termed the second or excitement stage.

Twenty-three years later, in the English *Quarterly Journal of Science and Arts,* Faraday is stated to have said: "When the vapor of ether mixed with common air is inhaled it produces effects very similar to those occasioned by nitrous oxid. By the imprudent inspiration of ether a gentleman was thrown into a very lethargic state, which continued with occasional periods of intermission for more than thirty hours." Teachers, lecturers, and medical students had a general idea of the physiological action of ether when thus administered, and were in the habit of illustrating lectures by allowing inhalations to continue until the exhilarating effects were produced. This continued for the next thirty-four years, and ether frolics by students and others were indulged in. Occasionally, but accidentally, of course, the third, or surgical stage, was reached. Those who sustained injuries in these ether frolics did not complain, and, further, those who entered the third or surgical stage of anesthesia seemed, upon recovery, to have enjoyed the experience rather than otherwise.

These two facts were coupled together by Crawford W. Long, of Jackson County, Georgia, who in 1842 (302 years after its discovery and 47 years after it was first used medicinally) administered ether with the intention of prolonging surgical anesthesia while performing an operation. The anesthesia and operation were successful, and this procedure was practiced upon several different occasions by him and his assistants. Unfortunately he took no pains to acquaint the world at large of his discovery until Morton had successfully administered surgical anesthesia with ether in the General Hospital of Massachusetts, in Boston, four years later, October 17, 1846.

The first operation with ether in England occurred two months later, on Dec. 19, 1846, at the house of Dr. Boot, in Gower Street, London. J. Y. Simpson, in January, 1847, first employed ether in midwifery practice; he discovered that the labor pains were wholly abolished, the contraction of the uterus continuing. Thus painless childbirth was produced for the first time in the world's history.

The physiological effects of different percentages of ether and other narcotics, as determined by experiments on the lower animals, were first pointed out by John Snow in 1858, and later by J. T. Clover. Clover was also the first to demonstrate the very great advantages of the closed method of air limitation and to introduce the nitrous oxid-ether sequence.

The first committee to attempt definite scientific work was appointed in 1864, twenty-two years after ether was first used as an anesthetic.

Braun, a German physician, was the first to modify the Junker inhaler into one for giving ether as well as chloroform, either separately or in combination, and one of the authors of this book carried this vaporizing a step further by passing the vapors through hot water, thereby bringing them up to the temperature of the blood, and at the same time washing out various impurities. Gwathmey made experiments upon animals to discover the difference between the normal, warm and cold vapors of ether, and also between air and oxygen as the vapor carrier.

Contemporaneously with the writing of this book experiments were made by the authors, who succeeded in masking the odor. (See Chapter II, p. 91.)

CHEMISTRY

The Term Ether.—Ethers are organic chemical compounds of the general formula *R. O. R′*, where *R, R′* represent alkyl or aryl groups. Ethers are therefore the oxids of the alcohol radicals, and may be regarded as anhydrids of the alcohols, being formed by the elimination of one molecule of water from two molecules of the alcohols. They are related to the alcohols in the same way as the metallic oxids are related to the metallic hydroxids.

Ethers may be simple or mixed.[1] Simple ethers are the oxids of monovalent alkyls; that is, they contain two similar alcohol radicals. Mixed ethers are those with different radicals attached to the oxygen atom.

The term ether, as ordinarily used, signifies diethyl ether, ethyl ether, oxid of ethyl, "ethane-oxy-ethane," "hydrate of ethylene," ethylic ether, "hydrate of ether," "hydric ether," "vinous ether," or "sulphuric ether," the last two terms being survivals of an earlier nomenclature. The term must not be confounded with "compound anesthetic ether."[2]

Properties of Ether.—*Pure* ethyl ether is a colorless, very mobile, strongly refractive, neutral, inflammable liquid, possessing a penetrating but exhilarating odor and a sharp, burning taste. It has a specific gravity of 0.718 — 0.719 at 15/4°, and boils at + 34.6° under 760 mm. pressure of mercury. By intense cooling, ether forms an ice-like solid which melts at — 117° C. (Olszewsky). It is very volatile, and, if

[1] Compound ethers, or more properly *esters*, are hydrogen salts in which the typical acid hydrogen has been replaced by an alkyl, and may therefore be looked upon as alkyl salts of organic acids, since an alcohol and an acid radical are present.

[2] "Compound anesthetic ether" is a mixture of absolute ethyl ether and amyl hydrid (rhigolene), proposed by Richardson for the production of local anesthesia by means of cold. Accidents have occurred as the result of using this mixture as an inhalation anesthetic.

placed on the skin, it evaporates rapidly, producing cold and numbness. Ether is only slightly soluble in water (1 in 12 at + 22° C.), and it dissolves little water (about 1 in 34 at + 22° C.). It dissolves alcohol, benzin, and chloroform in all proportions. It is a good solvent for fats and some resins.

Anesthetic Ether.—This may contain ethyl alcohol (up to four per cent) and traces of acetaldehyd, acids, and water, although, for reasons given in the text, the last three mentioned should be entirely absent.

Precautions in Handling Ether.—Ether has a high vapor tension. When a vessel containing ether is left open to the air, the vapor rises sufficiently to displace the air or other gas overlying it, and then flows over the edge of the containing vessel. As the vapor is very heavy, being 2.6 times as heavy as the air, it falls to the table, shelf, or floor upon which the vessel rests. The vapor is very inflammable, and, when mixed with air, forms an explosive mixture, which is readily ignited by a flame. *Great care should be taken to avoid using ether near an open flame, as a lighted gas jet, burning candle, or stove, or in the neighborhood of a hot cautery. A cautery should never be used about the mouth or nose when ether is used as the anesthetic.* Several cases of severe burning have been recorded where these precautions were not taken.

It is important also to take the same precautions when pouring ether from one vessel to another. The heavy vapor will travel some distance along a floor, for example, before being sufficiently dissipated to be free from danger. Where ether is used with electric lights care should be taken that these are not arc lights, and, if they are incandescent bulbs, that there are no short circuits or sparks, as the vapor may be thus ignited.

Sources of Impurities in Ether.—All ether of anesthetic grade is now prepared from ethyl alcohol and sulphuric acid. The impurities to be suspected are therefore: (a) Those present in the two materials used; (b) those produced in the process; (c) those developed during storage.[1]

It is almost needless to call attention to the necessity of having ethyl ether as pure as human ingenuity can provide it. The methods used for purification and some of the means of detecting impurities are given in Appendix I. Many of the impurities are rarely found in anesthetic ether, as they are removed in the process of purification; and, when some of them are found, the trouble may usually be traced to substitution, accidental or otherwise, of commercial ether for that of anesthetic grade. Some manufacturers make anesthetic ether only, thus removing one source of possible human error. As in the case of

[1] The elimination of all the possible contaminants of ethyl ether, particularly those usually present in small amounts, has been discussed by Baskerville and Hamor in detail; see *J. Ind. Eng. Chem.*, *3*, 302, 307, 309, 316, 380, 391 and 395.

other chemicals, there are cases of sophistication, but these are comparatively rare.

Impurities from Materials Used in Manufacture.—The sulphuric acid used is of high grade, and usually contains no impurities which volatilize with the ether.[1] Rectified ethyl alcohol, 95 per cent, with 5 per cent water, is used. The process of rectification of the alcohol does not always remove amyl, propyl, or butyl compounds, or "fusel oil," and the essential oils characteristic of the source of the ethyl alcohol, which is commercially never free from aldehyds and traces of acetic acid. The source of the alcohol—that is, whether it is made from grain, molasses, sawdust, or what not—is immaterial, provided it has been properly rectified. Acetal, extractive matter (from barrels), and tannic acid are often present in the alcohol. Acetone and formaldehyd may also be present, but are to be suspected only when methylated alcohol is employed.[2] In the United States, alcohol denatured with ether is now allowed in the manufacture of ether, so there is little or no likelihood of the last mentioned contaminants. (See Appendix I.)

Contaminating By-products Introduced by the Process.—The crude ether distillate resulting in the manufacture of ether by the continuous process contains, together with water, alcohol and sulphur dioxid[3] as the principal contaminants, although small amounts of other impurities (as fusel oil, empyreumatic oily matter, ethyl acetate, aldehyd, acetic acid, acetal, acetone alone, or with furfurol) are generally present, these varying with the purity of the materials used in the manufacture and with the care with which the etherification is conducted.[4] These can be and are largely removed in the subsequent purification.

Impurities Developed in Storage of Ether.—The standards laid down by the various pharmacopœias of the world are not uniform. This is especially true for ethyl ether and chloroform. Some pharmacopœias call for an admixture of alcohol. This may come from its retention in the process of manufacture, or, as has been recommended, it may be added to the rectified ether up to 4 per cent. Other pharmacopœias call for an almost absolute ether (sp. gr., 0.720, 15/15° C.). The rôle

[1] Purchasers of ether have in the past complained of ether which contained sulphuric acid. Such contamination can be due solely to substitution of "commercial" ether.

[2] Guerin (*J. Phar. Chem.*, [7], *4*, 492) reported that he had detected acetone and formaldehyd in certain samples of anesthetic ether on the market in France (Dec., 1911); and this ether had evidently been prepared from alcohol denatured with methyl alcohol.

[3] It should be mentioned that the greatest yield of ether is obtained at 140–145° C., and that above this temperature much sulphur dioxid is evolved.

[4] Patch (*Proc. Am. Pharm. Assn.*, *54*, 337) found that a sample of ether sold as 90 per cent contained only 74 per cent; that two samples of U. S. P. strength possessed an acid reaction and yielded a residue; and one sample answering all other tests gave a brown residue.

of the alcohol will be discussed in another paragraph. If alcohol is added, then the impurities present in the alcohol are to be found in the ether supplied, but, of course, in correspondingly smaller amounts. Assuming that the ether is prepared pure with the exception of the vicariously allowable percentage of alcohol and its usual five per cent of water, there are changes which take place on keeping under certain conditions, namely, peroxidation, with the subsequent formation of acetaldehyd and acetic acid.[1]

Experiences of expert anesthetists, not accounted for by idiosyncrasy, obtained in the use of ethyl ethers supplied by various manufacturers in numerous surgical cases, caused Baskerville to carry out a series of elaborate investigations on the quality of the anesthetics supplied by various makers, and to determine what changes, if any, occurred in the drugs when kept under the conditions obtaining in everyday life.

Standards of Purity with Which Anesthetic Ether Should Comply.—All tests which have been reported in the literature were tried out. Many were found to be of no value and some to be misleading. Some pharmacopœial tests are unnecessarily rigid; some are open to improvements; others should be replaced entirely by improved methods of detection; and several new tests should be incorporated for detecting impurities not considered. Exhaustive investigation into modes of manufacture, validity of applicable chemical tests, as given in the pharmacopœias of every civilized nation, methods of administration, and clinical experience warrant the assertion that ethyl ether complying with the tests given in Appendix I for specific gravity, boiling point, odor, residue, activity, aldehyd, and peroxids will give the best results by whatever method the ether anesthesia may be induced.

It must be recognized that the demand for a good ether for anesthesia involves difficulties inherent in the practical application of chemical methods by hospitals and physicians. As stated in Appendix I, anesthetic ether should be provided in small containers, and it is impracticable, and should be unnecessary, to test the contents of each container before use; hence, reliance must be placed on the experience and integrity of the manufacturer and on the uniformity of his product. We have found that some ethers of the market vary from time to time, not only in specific gravity and absolute ether content, but also in impurities. It is incumbent upon him who uses ether to take proper precautions to prevent the development of storage impurities of which the manufacturer may have been innocent.

Rôle of Alcohol in Ether.—For various reasons a pure ether may be mixed with ethyl alcohol when it is to be used for anesthesia. Impurities then observed may be due in part to the alcohol used in dilution. Practically all ethyl alcohol contains some acetaldehyd.

[1] See Appendix I.

Ethyl alcohol serves, it is asserted, as a preservative for ether when the latter is properly stored. This, we believe, is without foundation in fact. Small amounts of ethyl alcohol interfere in no way with the application of ether in anesthesia. However, the presence of alcohol is unnecessary except when ether is administered by the "drop method." In this method the presence of alcohol prevents too rapid volatilization and consequent chilling of the mask with which the ether is administered and the freezing of the moisture of the breath or of the air therein, or the alcohol lowers the freezing point of the condensed water, thus preventing solidification of that water. Some administrators state that this freezing prevents the patient getting a full free flow of the vapor. A serious factor also is the chilling of the lungs by the cold vapor. Davis, of the Johns Hopkins Hospital, has made observations on the temperatures of a number of patients anesthetized with ethyl ether by the drop method and by warm vapors of ether.[1] In the former, the body temperature dropped 1° to 2° F., and in the latter, not more than 0.3° F. in any case. Alcohol occurring in ether is subject to oxidation, producing bodies in the following order: alcohol, aldehyd (aldehyd peroxid), acetic acid.

Some have maintained that pure ethyl ether free from alcohol is unsuitable for anesthesia, but it is a fact that the vapor from ether containing alcohol, when passed through water at 40° C., whereby the alcohol is removed, may be, and is being, used with great success for anesthesia.

Peroxids.—Ethyl ether of anesthetic grade contains peroxidized compounds after exposure to atmospheric oxygen for considerable periods of time, especially when it is stored in colorless glass vessels or in badly-stoppered tin containers. The latter is an unfortunately common practice in some hospitals. The extent of the oxidation is dependent upon the purity of the sample, the amount of air present, the nature of the container, the temperature conditions, and, in the case of glass vessels, the intensity of the light, which accelerates the oxidation.[2]

[1] Discussed in Appendix I. in detail.

[2] Baskerville and Hamor made the following experiments:

Ether was allowed to stand for 200 days in 150-c.c. tin containers, partly filled, stoppered as well as the mouth of the containers would permit, and exposed to varying temperature conditions inside of a window with southern exposure. The conditions of storage were similar to those which obtain in many laboratories and hospitals. None of the samples so exposed exhibited a peroxid reaction originally, but all contained small amounts of water and alcohol. The following results were obtained, using the vanadic acid and cadmium potassium iodid tests:

No. 1A (container one-fifth full): strong peroxid reaction; strongly acid.

No. 1B (container one-half full): marked peroxid reaction, but less pronounced than in No. 1A; strongly acid. (*Continued on p. 183.*)

Aldehyd.—Acetaldehyd is undoubtedly the commonest and most objectionable contaminant of anesthetic ethers, and its presence may account for some of the observations made in practice.[1] Several have found occasion to emphasize the objectionable presence of aldehyd in many ethers on the market.[2] It is one of the impurities most likely to be generated by exposing partially filled containers to varying atmospheric conditions for long periods of time. Ether should not be stored in glass vessels for any length of time without being tested for oxidation products before use, and the tin containers should be of such capacity that they need not be opened without being soon emptied. Any remnants in these containers, especially if they have been kept for some time, should not be used for anesthesia without purification. The careless practice observed in some large hospitals where the operating rooms are in more or less continuous service is to be looked upon with disapproval. The using of large containers of ether or chloroform, and placing them on a shelf where the drug is subjected to the conditions referred to, should not be countenanced by those in authority. It can scarcely be defended on the score of expense, as the cost of the anesthetic of this nature used in an operation is trifling in comparison with the other costs involved, and should not be counted when not only the comfort but the safety of the patient is taken into consideration.

Physiological Action of the Impurities and Administration Means to Avoid Them.—Since it is highly important that ether intended for

(*Continued from p. 182.*)

No. 1C (container four-fifths full): very faint peroxid reaction.

No. 2A (container two-thirds full): no peroxids present. This container was provided with a tightly fitting stopper. The neck of the can was cylindrical, whereas those holding the preceding were provided with a conical neck, and it was thus possible to cork the can more securely.

No. 2B (one-half full): no peroxids present. This sample was stoppered similarly to No. 2A.

No. 3A (one-tenth full): strong peroxid reaction.

No. 3B (one-third full): no peroxids present. This container was properly stoppered.

No. 3C (three-fourths full): no peroxids present. Container was well stoppered.

No. 3D (four-fifths full): no peroxids present. Container was properly stoppered.

Walton (*Can. Drug.*, *23*, 584) has reported that one out of eight samples of commercial ether examined contained hydrogen dioxid.

[1] Acetaldehyd vapor, when inhaled, produces asphyxia. Prolonged exposure to light and air gives rise to aldehyd in ether, and such treatment greatly affects the results of etherization. In one case of which we have record, a sample of ether which induced irritation of the respiratory tract during etherization was examined, and the only impurity found was acetaldehyd.

[2] Thoms: *Pharm. Ztg.*, 1894, 777; Warden: *Pharm. J. and Trans.*, 1885, 521; *Am. J. Pharm.*, *57*, 148; and Graham: *Proc. Penn. Pharm. Assn.*, 1906, 153.

anesthetic purposes should be carefully manufactured and properly stored, as prolonged exposure to light and air produces aldehyd and acetic acid, which greatly affect the results of etherization, causing coughing, suffocation, and even dangerous after-effects, such ether should always be tested for peroxids and aldehyd, and the presence of the latter should be rigorously guarded against, especially if the ether is to be administered by the drop method; or the ether, if so contaminated, should be administered by a method which eliminates these impurities before it is introduced into the animal system. This is accomplished by the Gwathmey method, as experimentally determined by Baskerville. Anesthetic ethers known to contain minimum amounts of aldehyd, ether known to contain excessive amounts (both offered on the market), and ether to which still larger amounts of aldehyd were added, were placed in the Gwathmey apparatus and severally operated as in practice, except that the vaporized ether, which the patient would have got, was condensed and examined. The aldehyd, acetic acid, and alcohol accumulated in the water, and the condensed ether (which the patient breathed) was free from the aldehyd and acetic acid, as shown by the most rigorous application of the tests recommended for their detection. (See p. 864.)

SPECIAL PHYSIOLOGY

The various factors which have been mentioned as exercising a modifying influence upon the physiological action of inhalation anesthetics in general are notably potent with reference to ether. Inasmuch as this agent is more commonly employed for general surgical purposes than any of the others, the effects of these modifying factors have been given most attention in the administration of ether. In the present stage of the development of this branch of surgery it is the exception rather than the rule to find an anesthetist giving ether alone, without the utilization of one or all of the modifying factors discussed under General Physiology. (See p. 30.) It is to be borne in mind, however, that the following consideration of the physiological effects of ether involves the administration of this agent without reference to sequence with other agents or to adjuvant medication, and without the utilization of other factors previously mentioned.

With ether, no less than with chloroform and the other inhalation anesthetics, the discussion of its effects upon specific parts of the organism is purely arbitrary, and is resorted to for purposes of convenience. It is to be borne in mind that this agent presents no exception to the general rule of the correlation of effects.

For a discussion of the course of ether anesthesia when all the modifying factors are considered, according to the most advanced technique, the reader is referred to Chapter VIII.

Effects Upon the Respiratory System.—It is unequivocably agreed that ether has a powerful stimulating effect upon the respiratory system during the earlier stages of its administration, as evidenced by the increased rate of respiration. As the administration proceeds, however, the direct action of the agent upon the respiratory center causes a slowing of the respiratory movements and a decrease in their depth, with final complete cessation of respiration, in consequence of paralysis of the center, as the administration is carried beyond the limits of safety. The rate, depth, and stertor of respiration thus become the safest guides as to the degree of anesthesia, as will be seen when the *stages* are discussed.

The respiratory system is affected before the circulatory, and for this reason it is possible to resuscitate the subject when respiration temporarily ceases from other causes than paralysis of the respiratory center.

Ether exercises a pronounced irritating effect upon the air passages, which gives rise to a free secretion of mucus.

For further details of the effects of ether upon the respiratory system the reader is referred to Anesthesia, p. 247.

Effects Upon the Circulatory System.—The effect of ether upon the *blood* has been made the subject of a large part of the experimental investigation of the physiological action of this agent.

Engelhardt,[1] in his experimental study of ether narcosis, was enabled to establish strictly definite relations between the concentration of the narcotic agent and the temperature of the vehicle in the effect of disintegration on human and animal red blood corpuscles. In these experiments 9.4 per cent sucrose solutions and salt solutions, such as 0.9 per cent sodium chlorid and 5.5 per cent magnesium sulphate solutions, were mixed with known quantities of ether. The higher the concentration of the narcotic agent, the lower the temperature at which the red blood cells were dissolved; *vice versa,* the weaker the concentration, the higher the temperature limit at which hemolysis took place. In animals, as well as in man, the disintegration-point corpuscles—i. e., the temperature at which the fluid changed its color through the breaking down of the theoretical corpuscular sheath and the escape of hemoglobin—was lowered by several degrees, after prolonged narcosis, with indifferent salt solutions. In the case of salt solutions containing ether, on the other hand, the red blood corpuscles which had been removed from the animal body during or after the narcosis were dissolved only at a higher temperature. In other words, the resistance of the red

[1] Engelhardt: "Neue Gesichtspunkte in der Beurteilung der Aethernarkose," *Mitt. a. d. Grenzgeb. d. Med. u. Chir., 13,* 1903-1904.

blood corpuscles against the narcotic agent was increased. Briefly, the red blood corpuscles of etherized animals, according to Engelhardt, have a lower "melting point" in indifferent salt solutions, whereas the "melting point" of the narcotized erythrocytes is increased in salt solutions which contain ether. The explanation for this increased resistance has not yet been discovered.

In his experimental investigations on the appearance of intravital coagulation and thrombosis in the vessels of internal organs after ether narcosis, Mulzer[1] was enabled to demonstrate a disintegrating effect of the ether vapors upon the cells. The primary factor consists in an injury of the red blood corpuscles through the anesthetic agent, which leads secondarily to agglutination and coagulation, with formation, or excretion, of fibrin.

With special reference to ether, twenty-five healthy animals, mostly rabbits, were anesthetized so deeply with ether such as is used for narcosis that the corneal reflexes were lost during the entire duration of the experiment. Some animals died during the narcosis, while others were subjected to vivisection, under deep narcosis, at the end of a definite period, and fresh specimens of their organs were prepared. In seven animals, which survived at most half an hour in the narcosis, nothing pathological was found, and the vessels contained only normal, undeformed, well-stained blood corpuscles. When the narcosis even slightly exceeded half an hour, more or less numerous blue-stained granules were found within the vascular lumina, especially in the subpleural small vessels of the lung, attached to the vascular walls. The red cells in the vascular lumen were, for the most part, perfectly normal only in the center, but deformed, granular, and disintegrated toward the vascular wall. In case the narcosis could be continued for three-quarters of an hour to one hour, there appeared fine blue threads, radiating from the blue granules or passing between them into the layer of the deformed red blood corpuscles. After a still longer duration of the narcosis the contents of certain vessels were seen to be distinctly arranged after the fashion of typical thrombi, granular-fibrillar masses alternating with layers of deformed or normal erythrocytes. Individual lumina of small vessels were entirely filled with granular and fibrillar masses, between which lay only some masses of reddish detritus, but no normal blood corpuscles. Occasionally distinct granules and very delicate threads could also be demonstrated in the capillaries of the pulmonary alveoli. Although these processes occurred chiefly in the finer vessels of the lung, they were also observed, although to a less marked extent, in the vessels of the liver and the kidneys.

[1] Mulzer: "Das Auftreten intravitaler Gerimmungen und Thrombose in den Gefässen innerer Organe nach Aether und Chloroform Narkosen," *Münch. med. Woch.*, 1907, No. 9, 408.

These blue-stained granular and fibrillar masses are regarded by Mulzer as granular and fibrillar fibrin. As the primary factor, he assumes a lesion of the red blood corpuscles through the circulating ether, which acts as a blood poison. This leads secondarily, favored by a variety of other causes, to agglutination and coagulation, with formation, or excretion, respectively, of fibrin. The number of the red blood corpuscles is very considerably diminished, after the narcosis, and the changes in the configuration of the erythrocytes plainly indicate the destructive influence of the narcotic agent.

Bloch,[1] who investigated the effects of ether upon the hemoglobin and the red blood corpuscles during ether narcosis in man and in rabbits, considers it as certain that any narcosis causes an organic change of a certain number of red blood cells in consequence of the chemical absorption of the anesthetic agent into the blood. Provided the operative intervention is not too long and is conducted under proper concentration of the ether vapor, without too great a difference in temperature at the surface of the lung, the lesion does not exceed the degree of a "physiological" injury of the erythrocytes. Otherwise the hemoglobin escapes entirely from the red cells under disintegration of the cellular lecithin sheath, only the stroma remaining behind; or the hemoglobin may escape in part, rendering hemoglobin débris of various forms visible. These erythrocyte ruins are retained in the liver, spleen, and other organs, and are in part utilized again. The lost blood corpuscles are replaced by compensatory function of the bone marrow, from which new erythrocytes pass into the blood, according to Bloch, whose statements are based upon the counting of the blood corpuscles and the determination of the hemoglobin.

In an experiment upon a rabbit blood corpuscles with polychromatophile degeneration, microcytes, macrocytes, masses of stellate figures, etc., were found by means of Jenner's blood stain, so that Bloch does not regard it as altogether impossible that ether narcosis may ultimately produce the blood picture of pernicious anemia.

As the most tangible evidence of the destructive power of ether upon the blood, hemorrhagic transudates into the body cavities were found in animals which had been killed by the narcosis. Individual differences, as emphasized by Bloch, must be assumed to exist in different animal species, and even in different animals of the same species.

Stursberg[2] studied the behavior of the blood pressure, under the

[1] Bloch: "Neuere Untersuchungen über die Einwirkung von Aether auf Haemoglobin und rote Blutkörperchen während der Narkose an Menschen und an Kaninchen," *Deut. Ztschr. f. Chir.*, 1909, *97*, 132.

[2] Stursberg: "Ueber das Verhalten des Blutdrucks unter der Einwirksung von Temperatureizen in Aether und Chloroform Narkose und seine Bedeutung für Entstehung der Nachkrankheiten." *Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1911, *22*, 1.

action of temperature stimuli, in ether narcosis, as well as its bearing on the origin of post-anesthetic diseases. He found that the action of cold upon the skin is followed by a contraction of the peripheral arteries, and hence a rise of blood pressure with increased blood supply to the internal organs. This behavior of the vascular reflexes, in his opinion, certainly plays an important part in the origin of diseases due to catching cold. He investigated the behavior of dogs in ether narcosis under the action of cold produced by plunging the animal into a cold bath. It was found that in ether narcosis this vascular reflex behaved as in unnarcotized animals. In chloroform narcosis, on the other hand, the refrigeration of the skin is not followed by extensive vascular contraction with hyperemia of internal organs. Ether narcosis, therefore, involves certain conditions for after-diseases due to cold which do not exist in chloroform narcosis. Accordingly any chilling of the skin is to be carefully avoided in ether anesthesia.

Ether acts as a *direct heart stimulant* during the early stages of its administration, and when, during the course of deeper narcosis, the subject is allowed to return to a lighter degree, the pulse is accelerated, and blood pressure is slightly raised or remains constant. Ether becomes a cardiac depressant only in the later stages of anesthesia, or when a toxic amount is employed. Because of its depressing effect, under these circumstances, upon the vasomotor center, there is general arterial dilatation, with slowing of the pulse and a slight fall of blood pressure. In fatal cases of ether toxemia cardiac failure follows failure of respiration.

While the circulation may be stimulated or depressed by surgical shock or other means, in the vast majority of cases of ether anesthesia it is dependent upon the respiration. Blood pressure is maintained at the highest level during full surgical anesthesia by giving the smallest dose possible to obtain this state. An overdose of the anesthetic, or an obstruction in the airway, rapidly increases shock, with consequent fall of blood pressure and with rapid and feeble pulse. While the heart may be arrested in diastole by ether, a fatal case of reflex inhibitory arrest has never been reported. The circulation is immediately affected by the handling of important nerves and blood vessels, but the heart usually resumes the normal rhythm as soon as this ceases. The auricles, as a rule, are more affected than are the ventricles, as indicated by a weakened auricular contraction and increased ventricular relaxation.

Effects Upon the Nervous System.—The first effect of ether upon the nervous system is one of stimulation. Like chloroform, however, with increasing dosage, it produces progressive paralysis of the central nervous system, the phenomena affecting the centers in the following order:

(1) The higher cerebral centers, involving the intellectual faculties;

(2) The lower cerebral centers, involving sensation and motion;

(3) The spinal cord, involving sensation and motion;

(4) The medullary centers, involving vital function.

Sensation is not lost with equal rapidity throughout the body, the back and the extremities being involved first, the genital organs and rectum next, and the parts supplied by the trigeminus last.

The effects of ether upon the nervous system, as observed clinically, are given under the Stages of Anesthesia.

Effects Upon the Muscular System.—During the early administration of ether, when the stimulating action of the agent is generally manifest, the muscular system is affected no less than other parts of the organism. The entire muscular system may be thrown into a state of tonic contraction, or, as pointed out by Hewitt,[1] there may occur a fine tremor, designated as the "ether tremor." As the administration proceeds, general muscular relaxation ensues. It is to be borne in mind, however, that spasm of various parts of the muscular system, particularly of the masseter, the tongue, the laryngeal muscles, the muscles of the neck, chest, and abdomen, may occur during the course of ether anesthesia, giving rise to respiratory embarrassment and other complications.

The clinical significance of the effects of ether upon the muscular system is considered under Stages of Anesthesia.

Effects Upon the Glandular System and Other Structures.—The action of ether upon the glandular system is of clinical importance with reference to the course of the administration, but particularly with regard to the influence upon the after-effects. Because of the stimulating and irritating effects of ether upon the mucous membranes of the upper air passages, trachea and bronchi, there is always a hypersecretion of mucus, which, in some instances, amounts to what has been called *mucus-inundation.* This may give rise to fatal asphyxia, and is presumably one of the causes of post-anesthetic bronchitis and pneumonia.

The irritating effect of ether affects the salivary glands, giving rise to an excessive secretion of the fluid. When this is swallowed, post-anesthetic vomiting is apt to occur. Coincidentally with hyperactivity of the mucous glands of the respiratory tract and of the salivary glands, there is apt to be overactivity of the mucous glands of the stomach and intestines, causing retching and vomiting during and after the administration.

The action of ether upon the liver and kidneys has called forth considerable investigation, both clinical and experimental.

Gröndahl,[2] studying the effects upon the *kidneys,* found, in 75 ether

[1] Hewitt: "Anæsthetics," 363 (1912).

[2] Gröndahl: "Wirkung der Aethernarkose auf die Nieren," *Norsk Magazin for Laegevidenskaben,* 1905, No. 5; *Deut. med. Woch.,* 1905, No. 25, 1005.

narcoses, where the urine had been examined before the narcosis, albumin present in 27 cases (36 per cent), always associated with cylinders, excepting in three instances. The albumin frequently did not appear until the second day, and promptly subsided in the majority of the cases. The high percentage of albuminuria is referred by Gröndahl to the fact that, in general, these patients had undergone severe and prolonged operations. Albuminuria appeared at the end of the first day in 20 per cent of the cases, and, at the end of the second day, in 16 per cent. The average duration of the albuminuria was from seven to nine days. It was influenced by the age of the patients, the time of the operation, and the amount of ether used. In case of repeated narcosis the albuminuria appeared after each narcosis, but with diminishing severity. Ether accordingly, in Gröndahl's opinion, does not cause an intoxication-nephritis.

According to Rathery and Saison,[1] ether inhalation, single or repeated, is capable of producing certain lesions of the liver and the kidneys in rabbits, although by no means invariably. The renal lesions are less frequent and less severe than in the corresponding experiments with chloroform. The liver, on the other hand, seems to be even more sensitive toward ether than toward chloroform, for it is often changed more seriously after ether inhalation.

Thompson [2] summarizes his observations upon the effects of ether upon renal activity as follows:

"(1) During ether narcosis the volume of urine secreted is affected in two ways. In the majority of experiments there is a decrease, in a few an increase. The latter is probably an early or light effect, the former a pronounced effect. The depressing effect is, however, more marked than with chloroform, and complete arrest occurs more readily.

"(2) The after-effect is less marked but similar to that of chloroform. The maximum outflow of urine occurs about three hours after removal of the anesthetic.

"(3) The output of nitrogen with ether corresponds more closely with its influence on the outflow of urine than is the case with chloroform. In the later stages of the anesthesia, where the urine volume is decreased, the excretion of nitrogen is diminished almost exactly to the same degree as the urine volume. In the group of catheter experiments the excretion of nitrogen fell to 26.03 per cent, the quality of urine to 25.4 per cent of the normal amount.

"(4) The effect of ether narcosis on the circulation of the urine dif-

[1] Rathery, F., and Saison, M.: "Lésions éxperimentales du foie et du rein à la suite d'inhalation d'éther au lapin," *Compt. rend. Soc. de. biol.*, L. 18, 5, 211 (1910).

[2] Thompson, W. H.: "Anæsthetics and Renal Activity," *Brit. Med. J.*, March 17, 1906.

fers also from that of chloroform. With the former the urine, when diminished in volume is, as a rule, more concentrated (contains more nitrogen). The converse was the case with chloroform. The effect of ether is therefore *primarily vascular.*

"(5) In ether narcosis, when the curves of urine outflow, kidney volume, and blood pressure are compared, although there is not complete parallelism, there is, on the whole, a closer correspondence than is the case with chloroform. This statement does not apply to the arrest of urinary secretion, which occurs more readily, and with a relatively higher blood pressure, in ether than in chloroform narcosis.

"(6) The escape of leucocytes into the urine, after full ether narcosis, is more marked than with chloroform, probably indicating a higher degree of stasis in the glandular capillaries. Dilatation of capillaries and escape of leucocytes have been noted by previous investigators, after ether inhibition, in the case of other vascular areas than renal.

"(7) An increased excretion of chlorids is seen after ether inhalation, but is much less, and of shorter duration, than in the case of chloroform.

"(8) Temporary albuminuria appears in dogs in a much larger proportion of experiments with ether than with chloroform.

"(9) Reducing substances, not sugar, which were not present in the normal urine, appeared in a small number of the experiments after ether narcosis."

From experiments upon dogs, Grube[1] attributes the glycosuria observed during ether narcosis to a disturbance of the heat regulation of the organism. He is of the opinion that the reduction in temperature is produced by the radiation from the skin, as a result of the vasodilatation caused by the ether.

Nicloux[2] conducted an interesting series of experiments upon guinea pigs with reference to the passage of ether from the mother to the fetus. The following conclusions were arrived at: The ether passes from the mother to the fetus; the fetal *liver* contains more ether than the maternal liver, presumably due to the relative richness of the former in lecithin. Chloroform shows exactly the same behavior. This transition is in every way comparable to the behavior of alcoholic substances, which involve the blood corpuscles and the plasm in the same proportion. Nicloux[3] was also able to demonstrate the passage of considerable quantities of ether into the *milk* in ether narcosis. The animal serving for these experiments was a goat. The cause is referred by Nicloux to the

[1] Grube: *Arch. ges. Physiol., 138,* 601.

[2] Nicloux, M.: "Passage de l'éther de la mère au fœtus," *Compt. rend. Soc. de biol.,* 1908, *64.*

[3] Nicloux: "Passage de l'éther dans le lait," *Compt. rend. Soc. de biol.,* 1908, *64.*

affinity of ether for fats. Analogous investigations have shown the passage of chloroform into the milk.

Fabre and Verrier[1] report, as contributions to the knowledge of the influence of ether narcosis upon the lactation, two observations upon nursing mothers, who were put under ether for the performance of minor operations (ruptured perineum and anal fissure). The secretion of milk was in no way modified in these two cases, and the infants were put to the breast on the day of the operation without untoward results.

In the discussion of these observations Raucher stated that in his experience with several cases the action of the anesthetic on the secretion of milk was *always negative.* There is, accordingly, no reason to put off a necessary operation on a nursing mother. The child is not usually put to the breast on the day of the operation, but more to let the patient rest than for fear of a secretion of inferior milk. On the following day the nursing may be resumed.

Causes of Death from the Administration of Ether.—Because of the relative safety of ether, the causes of death from its administration have not been made the subject of such extensive experimental and clinical investigation as has chloroform.

It is generally conceded that, in fatal ether toxemia, respiration fails before circulation. Respiratory failure may result from paralysis of the respiratory center, or as the result of an overdose, or it may occur quite independently of this, from obstruction of the air passages from any cause. Fatal reflex respiratory shock may supervene as the result of the surgical procedure, and is more apt to occur, in consequence of reflex muscular spasm, during the lighter stages of anesthesia than during full surgical narcosis.

According to Hewitt,[2] "The all-important point concerning respiratory failure in moderately healthy patients under ether is that, *however such failure may arise, the circulation at the moment when breathing ceases is sufficiently satisfactory for remedial measures to be almost invariably successful.* The heart is not likely to fail unless restorative measures be too long delayed."

According to Henderson,[3] primary cardiac death may occur under ether. Primary cardiac failure can be induced, easily and with certainty, simply with ether. Failure to recognize this in the past has been due, he asserts, mainly to the fact that dogs have hitherto been the principal experimental animals, and dogs rarely exhibit the phenomena. Cats, on the other hand, and many human subjects, after being rendered

[1] Fabre and Verrier: "Influence sur la lactation de l'anesthésie par l'éther," *Bull. de la Soc. d. Obstét. et de Gynécol.*, May, 1912, 552.

[2] Hewitt: "Anæsthetics," 367 (1912).

[3] Henderson, Yandell: "Primary Heart Failure in Normal Subjects under Ether," *Surg., Gynecol., and Obstet.*, Aug., 1911, 161.

acapnic, are liable to die of primary cardiac failure under ether. They are hypersusceptible to ether in the same manner that acapnic dogs and acapnic persons are hypersusceptible to chloroform. Henderson believes that these forms of death, and, in fact, by far the greater number of all deaths under anesthesia, are fundamentally due to acapnia resulting from the excessive pulmonary ventilation of the stage of excitement.

Stages of Ether Anesthesia.—When ether is administered according to the most modern technique (see Administration, p. 199), the subject, as a rule, quietly passes into the stage of surgical anesthesia, as if falling into a profound sleep, from which the recovery is so uneventful that it may be likened to the awakening from normal slumber.

It is always to be borne in mind, however, that there may be individual variations from the usual course of events, even with the most careful technique. When the anesthetist, for any reason, fails to employ the various auxiliary measures now in use, the stages of anesthesia are quite well marked. Four stages may be observed, which are as follows:

First Stage, or Stage of Light Anesthesia.—In the last edition of his "Anæsthetics" (1912, pp. 362-363) Hewitt states that, in consequence of the pungent and rather disagreeable odor of ether, "it is impossible to avoid completely all unpleasant sensations at the commencement of the inhalation." This is so easily and so completely accomplished by the preliminary administration of an alcoholic solution of oil of bitter orange peel (see p. 91), that it seems almost unnecessary to give in detail the phenomena otherwise noted during the first stage.

This stage usually occupies the first two minutes of the inhalation. Respiration is accelerated. Blood pressure is slightly increased, the pulse is full and bounding, and the color reflex is heightened. If the vapor is administered in too great concentration, there may be holding of the breath, swallowing, closure of the glottis, a feeling of suffocation, muscular rigidity, coughing, and turning of the head from side to side. The pupils are dilated. The special senses are disturbed, though the order in which they are affected has not been definitely determined.

Second Stage, or Stage of Excitement.—With ether, as with chloroform, this stage, so far as the excitement is concerned, should not occur. It is obviated in part or in full by the utilization of modern technique, which calls for the adaptation of the method to the individual case. In any event, this stage is marked by the more or less abrupt loss of consciousness, with the consequent interference with memory, volition, and intelligence. The subject, however, responds to stimuli, and may give evidence of apparent consciousness. Words and sentences become more and more incoherent, and crying, singing, or laughing, shouting, and struggling may initiate a typical stage of excitement. As the anesthesia deepens, marked rigidity of the muscles, clonic or tonic contractions, partially of certain muscles, notably the muscles of the jaw and larynx, appear. The pupils continue to be dilated and mobile. Mucus and saliva are now freely secreted. The face is flushed, and, unless care is exercised in keeping the airway clear, cyanosis may occur. Perspiration now appears over the face and other parts of the body. The pulse is still accelerated, full and bounding. Respiration may now become irregular, and apnea may occur, the cessation of breathing lasting for variable lengths of time. The "ether-tremor," to which reference has been made, sometimes occurs during this stage, the patient shaking with quite noticeable violence. This is more apt to occur as the subject is emerging from than when going under the influence of the anesthetic. In either event this phenomenon disappears with the deepening of the anesthesia. Vomiting occurs, if at all, during the transition from the second to the third stage. The muscles particularly concerned in respiration are now no longer subject to reflex stimulation, and, as the subject passes into the third stage, they become so flaccid that there is no longer danger of serious interference with respiration from this cause.

Third Stage, or Stage of Surgical Anesthesia.—The recognition of this stage of anesthesia is important, inasmuch as the subject is not in condition for operative interference until this time. The indications of normal surgical anesthesia may be briefly stated as follows:

(1) *Respirations* regular, deep, and softly stertorous.
(2) *Muscles* of extremities lax.
(3) *Color* of face, ears, and lips about normal.
(4) *Pupils* reactive to light.
(5) *Lid reflex* weakly present.
(6) *Coughing reflex* absent.
(7) *Phonation* absent.

It is to be borne in mind that there may be greater or less variation from the indications of what may be called normal surgical anesthesia, but this is not sufficient to obscure the recognition of this stage.

The respirations are now regular, full, and generally audible. A soft stertor may be considered normal, but if breathing becomes strongly stertorous it is an indication of some obstruction in the airway. The respirations are the principal guide as to the depth of narcosis. When the regular, automatic, respiratory action is obtained, this should be maintained, bearing in mind slight variation in different individuals. A decrease in the depth and amplitude of respiration indicates a return to consciousness, and calls for an increased amount of the anesthetic. An increase in stertor should be modified by changing the position of the lower jaw or head.

Cyanosis is not present in normal anesthesia.

The heart action is accelerated, compared with the normal, during this stage, and the pulse is full, bounding, and regular, usually varying from 80 to 110 per minute. As the anesthesia progresses the face may become more flushed than normal. Blood pressure, as a rule, remains constant.

The pupils, when no preliminary medication is used, may be slightly dilated (from 3½ to 4½ mm.),[1] or they may contract to normal, remaining so throughout this stage. The eyeballs are generally fixed, though they may be rolling.

Relaxation of all the muscles now occurs, the continuance of this stage depending upon the further conduct of the administration. (See Administration, p. 199.)

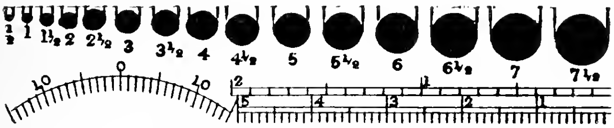


Fig. 61.—The Pupillometer.

The third stage of anesthesia may change in the direction of (1) *return to consciousness,* or (2) *deepening narcosis,* or the beginning of the fourth stage.

The indications of returning consciousness may be summarized as follows:

(1) Respiration weak.
(2) Pallor of face.
(3) Swallowing movements.
(4) Pupils dilated.
(5) Lid reflex return.
(6) Lachrymation excessive.
(7) Phonation returns.

These phenomena call for an increased amount of the anesthetic.

Fourth Stage, Stage of Deepening Narcosis, or Stage of Overdose.—The indications of the onset of this stage may be summarized as follows:

(1) Respirations weak.
(2) Dusky appearance of face (cyanosis).
(3) Pulse soft, feeble, irregular.
(4) Pupils dilated; no reaction to light.
(5) Eyeballs fixed and dry.
(6) Eyelids separated.

The first indications of impending overdose, ordinarily noted by the administrator, are the irregular pulse and the quiet feeble respirations. The muscles become flaccid. Blood pressure is markedly decreased.

[1] It may be noted here that the average ether pupil, as measured by the pupillometer, is larger than the average chloroform pupil (see p. 308).

When ether is given in an overwhelming dose, the heart may be paralyzed immediately after paralysis of respiration.

Elimination.—Nicloux [1] investigated the elimination of ether, after the narcosis, and found that the quantity of ether amounts to about 150 mg. per 100 c.c. of blood, immediately after the cessation of the inhalation; then the amount of ether in the blood rapidly diminishes, so that only one-half of the above quantity is demonstrable at the end of five minutes. Only traces of ether can be detected after two hours, and none is left after four hours.

As compared to the elimination of chloroform, the elimination of ether must be designated as very rapid.

These findings are in keeping with the observations of other investigators.

After-Effects.—The after-effects of ether narcosis may be considered under two heads, viz.: (1) Immediate, and (2) Remote.

Immediate After-Effects.—It has been stated that if ether is administered according to modern methods, with the utilization of preliminary and accompanying factors, the subject emerges, as a rule, from the anesthetic state as if from normal sleep, feeling no ill effects so far as the anesthesia is concerned. Under other circumstances, however, even with the most careful technique, the recovery period may be marked by retching, nausea, and vomiting. Hematemesis sometimes occurs, and very rarely hemoptysis is encountered.[2] Transient mental disturbances, amounting in some instances to mania and dementia, have been reported. Muscular excitement may be noted for a brief period, and in rare instances choreiform movements have been known to last for two or three weeks. Cerebral hemorrhage, with resulting hemoplegia, has been noted in persons with arteriosclerosis. Pulmonary complications ("ether-bronchitis" and "ether-pneumonia") are among the most frequent early after-effects.

Remote After-Effects.—The remote after-effects of ether narcosis are not of such frequent occurrence and severity as follow the use of chloroform. Many interesting observations have been made, however, particularly with reference to the results of the action of ether upon the various organs.

The studies of Ross and Hawk [3] consisted primarily of an inquiry into the influence of diet and of a subnormal body temperature upon post-anesthetic glycosuria. The subjects used were dogs, and the anes-

[1] *Loc. cit.*

[2] Hewitt: *Loc. cit.*, 375.

[3] Ross and Hawk: "Further Studies on the Metabolic Influence of Ether Anæsthesia," from the Laboratory of Physiological Chemistry of the University of Illinois, Dec., 1911.

thesia was brought about either by means of specially prepared, so-called "dehydrated," ether,[1] or by ether U. S. P. Two methods of administration were employed: one a compressed air method in which the apparatus concerned was similar to that of Gwathmey; whereas, in the other instance, the ordinary *cone* method was utilized. In a portion of the experiments a specially devised apparatus was employed to maintain the normal temperature of the animal during the anesthesia period. In each instance this period was two hours in duration.

When fed diets, principally meat, containing from 3.3-4.1 grams of carbohydrate per kilogram body weight, the dogs gave *no evidence of post-anesthetic glycosuria under any conditions,* i. e., with either type of anesthetic, either method of administration, or after a pronounced lowering of the body temperature. When the carbohydrate portion of the diet was entirely replaced by meat, *post-anesthetic glycosuria was observed in every instance,* irrespective of the character of the anesthetic, the mode of its administration, or the course of the body temperature. All urines were examined qualitatively by means of copper and bismuth reduction tests, and quantitatively by means of fermentation and polarization.

Grube [2] investigated the influence of ether narcosis upon the body temperature and the carbohydrate metabolism. According to his observations, the glycosuria which follows upon the ether narcosis in dogs, often also in man, can be prevented by counteracting the simultaneous lowering of the body temperature, which is produced by the vasodilator effect of the ether, combined with the arrest of muscular activity.

The conclusions of Hawk,[3] after careful animal experimentation with reference to the effects of ether upon the urine, are as follows:

(1) An initial diuresis proportional to the length of anesthesia follows ether narcosis, varying from thirty minutes to four and one-half hours.

(2) Ether anesthesia invariably caused the animal to lose weight upon the day of the narcosis.

(3) The fractions of urine first voided after ether anesthesia possessed specific gravities ranging from 1.024 to 1.042, as compared with the normal specific gravity of 1.015 to 1.019.

[1] This ether was later found by Baskerville to contain even more acetaldehyd than the ether U. S. P. used. Consequently, it may be concluded that the usual or even excessive amounts of acetaldehyd present in anesthetic ether play little or no part in the production of post-anesthetic glycosuria.

[2] Grube: "Ueber den Einfluss der Aethernarkose auf die Körpertemperatur und den Kohlehydratestoffwechsel," *Pflüger's Arch. f. d. ges. Physiol.,* 1911, *138,* 601.

[3] Hawk, P. B.: "On the Diuresis Following Ether Narcosis," *J. Med. Res.,* 1908-1913, 203.

Seelig[1] summarizes the result of his investigations concerning ether as follows:

(1) Ether inhalation always produces a more or less marked glycosuria in dogs which are fed on meat.

(2) The glycosuria is always demonstrable during the narcosis, but lasts only a short time beyond it.

(3) Persistent carbohydrate-feeding prevents the occurrence of glycosuria in dogs.

(4) Suppression of an existing ether glycosuria, through subsequent intravenous oxygen infusion, is not feasible.

(5) The glycosuria is associated with hyperglycemia.

(6) The glycogen contents of the liver are greatly diminished after ether narcosis.

(7) No glycosuria occurs when the ether inhalation is combined with a simultaneous intravenous infusion of oxygen, provided that correct dosage of oxygen is administered.

(8) Intravenous introduction of CO_2 does not give rise to glycosuria.

Röhricht[2] examined the urine of 100 patients who had been operated upon under ether narcosis, as to the appearance of glycosuria, with positive findings in twelve cases. He arrived at the conclusion that neither the operative traumatism nor the quantity of the ether administered and the duration of the narcosis stand in a direct causative relation to the resultant glycosuria; but that this must be interpreted as a consequence of an injury to the organism through the inhaled ether. The exact nature of this injury is problematical, Röhricht finding no sufficient explanation in the fat-infiltration of the liver, or in the chemical and mechanical action of ether on the blood, or in an influence upon the nervous organs. In his opinion, several partly unknown effects of the ether must coincide in order to produce the glycosuria. A glycosuria-producing property of the ether can hardly be imagined in the absence of an individual predisposition. In his opinion, advanced age has a certain bearing upon the occurrence of post-narcotic glycosuria. Undoubtedly, however, the ether narcosis may be the cause of an abnormal composition of the urine.

In a study of acetonuria following ether anesthesia Hamblen[3] found, in 120 cases etherized by the cone method, acetonuria developed in 88.5 per cent. In the same number anesthetized by the drop method only 26 per cent showed acetonuria. (For further discussion of this subject, see

[1] Seelig: "Ueber Aetherglykosurie und ihre Beeinflussung durch intravenöse Sauerstoffinfusionen," *Arch. exp. Pathol,* 1905, *52,* 481.

[2] Röhricht, R.: "Klinische Beobachtungen über Glykosurie nach Aethernarkosen," *Beitr. zur klin. Chir.,* 1906, *48,* 535.

[3] Hamblen: "The Occurrence of Acetonuria Following Ether Anesthesia," *Univ. Penn., Med. Bull.,* June, 1909.

Chapter IX, Treatment Before, During, and After Anesthesia, p. 365, section on "Post-Anesthetic Toxemia.")

Engelhardt [1] affirms a specific toxic action of the narcotic agent, more particularly ether, and the affections of the lungs are referred by him to cytolytic or hemolytic processes (aside from pulmonary edema through overdosage, and coarse aspiration-pneumonia). The onset of pulmonary changes, after ether narcosis, depends, in his opinion, upon the "melting point" of the red blood corpuscles and the quantity of ether absorbed by the erythrocytes and the blood-plasm on the one hand, and upon the temperature of the body on the other hand. As the small quantity of anesthetic which has passed into the blood can rarely be ascertained, he emphasizes that this cell-dissolving action represents the highest degree—the only one that can be tested experimentally, however—of the injurious influence of the narcotic agent upon the body cells. In support of his argument, he mentions the fact that a decrease in the number of post-operative pneumonias is noted in narcosis with morphin-scopolamin as well as in spinal anesthesia.

In discussing post-operative pulmonary complications and thromboses after ether narcosis, Otte [2] says that excellent results were obtained in regard to pneumonia, bronchitis, secretion of mucus, and thrombosis. The narcotic was repeatedly administered in the presence of pulmonary complications, such as tuberculosis, asthma, or bronchitis, without any essential aggravation of the bronchitis, or rise of temperature. *As a very important and useful aid in ether narcosis, as well as in all other inhalation narcoses, he recommends systematic inhalations of warm water-vapor, before and after the narcosis, preferably with an admixture of thymol and salicylic acid.*

ADMINISTRATION OF ETHER

The Open or Drop Method.—The administration of ether alone by the drop method, and continuously on an open mask, is not as desirable as certain other methods. Many surgeons and anesthetists, however, prefer this method to any other, and for this reason the best procedure of administration will be fully described, but not until the necessary preliminaries have been considered.

The Dropper.—It is better to drop the ether from the original container than to pour the contents into some patented or other dropper. No container holding over 100 grams, or, at the most, a quarter of a

[1] Engelhardt: "Zür Entstehungsursache postoperativer Pneumonien," *Centr. Chir.*, 1907, No. 4, 89.

[2] Otte, A.: "Ueber die postoperativen Lungenkomplikationen und Thrombosen nach Aethernarkosen," *Münch. med. Woch.*, 1907, No. 50, 2473.

pound, should be used. Internes and others using original tin containers as droppers often neglect to cut out the top and replace the same

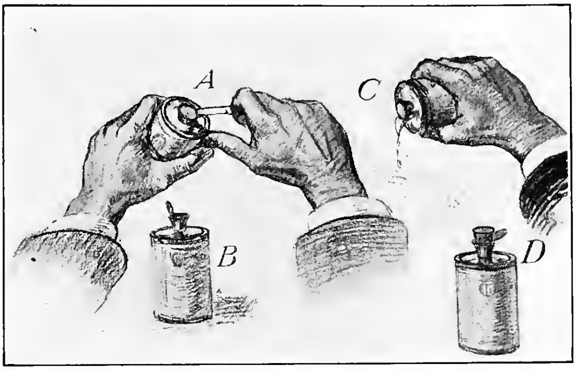


FIG. 62.—DROPPER FROM ORIGINAL CAN, OLD FORM.

with a cork after perforating this top to admit of its use as a dropper. In this way quite as much ether may be wasted as is used. It is more important to maintain the original purity of the ether used. Four good methods for making a dropper out of an original tin container are as follows:

First: Bend a safety pin as shown in the illustration, then pass it through the cap on the neck of the ether can, when the free end may be again straightened. Then clasp safety pin and drop from either end.

FIG. 63A.—CHLOROFORM AND ETHER CONTAINERS FOR THE DROP METHOD.

Second: A number of pin holes are made in the top of the neck of the can. A small piece of surgical gauze is now placed over these holes and twisted so as to come to a point. This gauze prevents the ether from squirting out of the can. When the can is not in use a small piece of surgeon's plaster may be placed over the pinholes to prevent excessive evaporation; or, preferably, the top may be cut out and a clean velvet cork inserted. It is inadvisable to use the remainder of this ether, even with these precautions, if it has to be kept for any length of time, say, for a week or more. (See page 868.) However, there are occasions when only small amounts of ether are used

FIG. 63B.—CHLOROFORM AND ETHER CONTAINERS FOR THE DROP METHOD.

in an operation, and many short operations may quickly follow each other. In such event the container may be used until the ether is consumed.

Third: When a new can is to be used, or the cans above described are to be used again, a safety pin, one inch long or more, bent in the middle at right angles, is placed by the side of the cork, and pin and cork are inserted into the can. (Fig. 63B.) The rate of flow of ether may be regulated perfectly by pressing the thumb against the protruding part of the bent pin. The cork should be firmly inserted to avoid its being pushed out by this pressure. The cork may oftentimes be used again. This, of course, depends upon its condition.

Fourth: Notch the cork very slightly, place a small piece of gauze in the notch and insert in the neck of the can, after cutting out the top. Mechanical obstructions, such as pieces of cork, may, however, interfere with the flow of ether. The cork should not be used again.

FIG. 64.—ETHER CONTAINER WITH DROPPER.

An excellent tin container, so arranged for dropping ether, has recently appeared upon the market. The illustration (Fig. 64) is self-explanatory.

Ether is also now obtainable in glass ampules, so constructed that, by snipping the tip thereof, they may be used as droppers; or the neck

FIG. 65.—GLASS CONTAINER FOR HOLDING ETHER.

may be cut off and the contents poured into a vaporizer. The ampules are made by one company of actinic and by another of anactinic glass; the latter protects the ether from decomposition by light (Fig. 65).

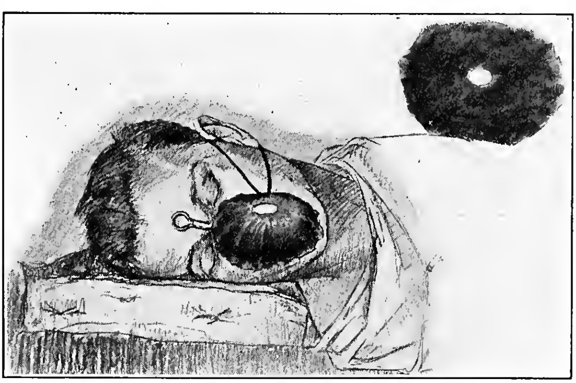


FIG. 66.—LUMBARD'S RUBBER. ETHER BLANKET AND ELASTIC MASK HOLDER.

The Mask.—The usual mask consists of a wire frame and metal hoop for holding the gauze in place. When an ordinary ether mask is used without towels, gauze, or something else around the mask, much of the vapor is blown into the air by the patient's breath, the surgeons, anesthetist, and nurses getting the full benefit of it, and, in a private house, the disagreeable, penetrating odor will linger almost as long as if the cone had been used. The patient gets the cold vapor that sinks through the mask. Everyone suffers in consequence of this crude and antiquated method.

The prevention of waste and the administration of the ether in the most acceptable way by this method are accomplished as follows:

The mask is covered with as many thicknesses of gauze as possible without interference with free respiration (from 1/16 to 1/8 of an inch in thickness). The patient thus receives a more perfect vapor than if only one or two layers of gauze are used, consequently there is much less irritation to the respiratory passages.

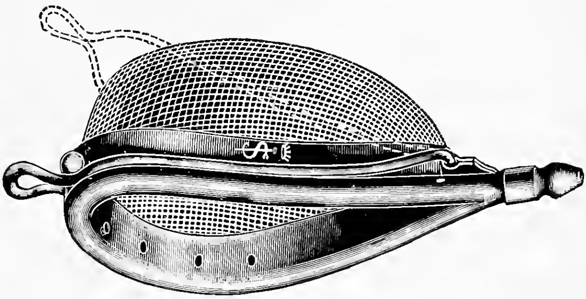


Fig. 67.—Yankauer-Gwathmey Drop and Vapor Mask.

The Yankauer Mask.—The Yankauer mask, of closely woven wire over which are stretched several layers of gauze, is one of the best masks for the drop method of ether or chloroform.

The Ferguson Mask.—The best mask yet devised for the drop method for ether alone is that devised by Ferguson. It consists of a wire frame, so flexible that it can easily be adjusted to the face by bending the wire between the fingers. It is covered with several thicknesses of gauze, which are held in place by a wire band. The unusual feature consists of a wire frame surrounding this gauze mask, over which is stretched a canton flannel bag, with a small hole either in the middle or on the side, depending upon whether the patient is in the dorsal or lateral position. This outer covering of canton flannel prevents the blowing of the ether vapor all over the room. The best feature of this mask is that it gives the patient a warmer vapor. It is really semi-closed, a certain amount of rebreathing taking place, but not as much as is usual with a rubber bag. As the mask is not air-tight, it is in a measure automatic, and does not require so intimate a knowledge of the physiological action of ether to maintain the surgical level called for by the operation. The patient is not subjected to cold ether vapor, as with the cone or ordinary mask, and consequently comes out of the anesthetic in a better condition.

The Mayo brothers, of Rochester, Minn., have probably used the drop method of ether for a longer period of time and had a larger number of administrations than any other surgeons. They report between 14,000 and 20,000 administrations. The following is their method:

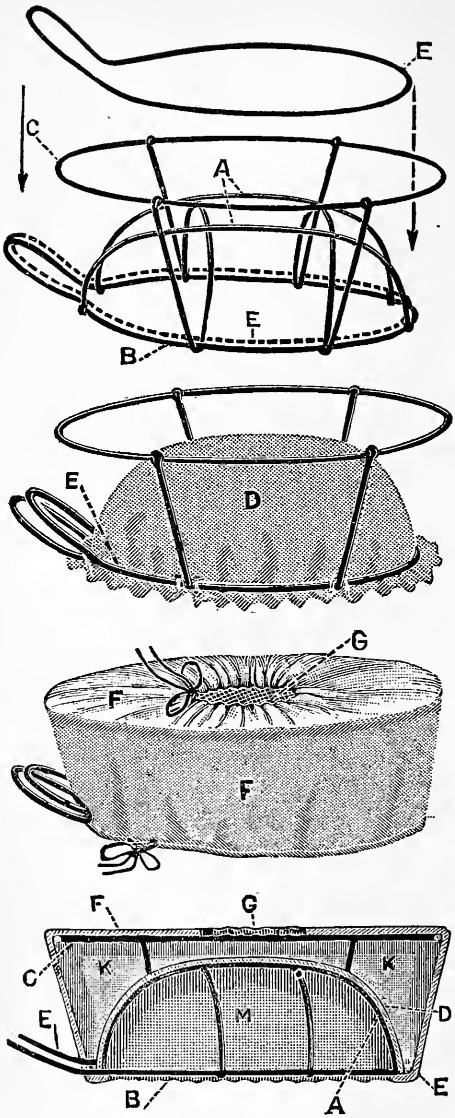


Fig. 68.—The Ferguson Mask. A, B, C, E, wire frame; E, retaining wire; D, gauze; F, canton flannel hood; G, opening in hood for air; also used to drop anesthetic on to D; K, open chamber; M, under surface of the mask next to patient's face.

"All patients are anesthetized on the operating table in the operating room, while preparation of the patient is going on at the same time. This is one of the important factors in producing a rapid surgical narcosis.

"An acute cold is a contra-indication to any anesthetic, but as soon as the cold becomes chronic there is not much danger from etherization, and, instead of operating during an acute cold and giving chloroform (unless in an emergency), we wait a few days until the acute attack has passed, and then they are as good subjects for ether as for any other anesthetic. Chronic bronchitis is often improved by an anesthetic.

"Use a four-ounce ether can and fit an ordinary cork with a groove on either side into its mouth, fill one groove with absorbent cotton and let it extend out of the can about one inch. One can regulate the drop easily by the manner in which the point is clipped. We usually fix two cans, one with a large dropper, and use it until the patient is fully under the anesthetic, and then change to the other can with the small dropper, and continue its use during the operation. The inhaler used is the improved Esmarch, with two thicknesses of stockinet (frame boiled and stockinet changed after each patient). We drop as slowly and carefully in giving the ether as though it were chloroform, until the patient's face is flushed, and then a few layers of surgeon's gauze are added, and the ether is given a trifle faster until the patient is surgically etherized; then return is made to the same covering as at the start, and the regular drop continued throughout the operation. A patient can be brought under ether in this way in from three to five minutes, and, when ready, patients do better if the operation is started at once.

"As it requires very little ether to keep a patient surgically etherized, one can change to the small dropper during the operation. A much deeper narcosis is required to start an operation or to make the incision than later on when the operation is in progress. Patients should be prepared for each stage of the anesthesia with an explanation of just how the anesthetic is expected to affect him; 'talk him to sleep,' with the addition of as little ether as possible. We have one rule: patients are not allowed to talk, as by talking or counting patients are more apt to become noisy and boisterous. Never bid a patient to 'breathe deep,' for in so doing a feeling of suffocation is sure to follow, and the patient is also apt to struggle."[1]

Davis gives the following as his method of administration of ether by the drop method:[2]

"Place a piece of rubber protector over the patient's eyes to shield them from the ether vapor. Protect the face with a moist towel or gauze which extends over the rubber tissue and around the chin. Use a wire frame mask similar to the Esmarch chloroform inhaler, only larger, in order to give more space under the inhaler for the mixture of air and ether. Cover the wire frame with one or two layers of stockinet or several layers of gauze. The gauze should be thrown away and the wire frame boiled after each administration.

"Apply the mask to the patient's face and administer the ether drop by drop, very slowly at first, then gradually increasing as the patient is able to take the stronger vapor. When the patient cannot respond to questions, a moist towel or gauze is wrapped snugly around the mask, leaving a small area in the center for the free passage of air through the gauze. By this method the air is prevented from escaping around the edges of the mask, and is made to pass through the ether-laden gauze. The ether should not be dropped down faster than the patient can comfortably breathe it in. Never be in a hurry to put the patient to sleep. Do not let an impatient operator worry or hurry you on, as the welfare of the patient depends upon the slow and gradual ratio of the increasing concentration of the ether-vapor. The patient will become unconscious in two or three minutes, and should be ready for the operator in ten minutes. After the patient has become completely anesthetized very

[1] Magaw, Alice: "A Review of 'Over Fourteen Thousand Surgical Anesthesias,'" *Surg. Gyn. and Obst.*, Dec., 1906, 795-799.

[2] Davis, S. Griffith: "The Administration of Ether by the Drop Method," *Md. Med. J.*, May, 1907.

little ether, dropped slowly, but continuously will suffice to maintain the proper condition. Having reached surgical anesthesia, the further efforts of the anesthetist should be devoted to observing the respiration, pulse, pupils, and the patient's general condition, and to prevent him from passing into that dread stage of respiratory paralysis. The respiration should be quiet, with perhaps a very slight snore. Panting and rapid breathing, or irregular stertorous breathing, indicate that the patient needs more air."

Ethyl Chlorid Ether Sequence by the Drop Method.—Using an ordinary Esmarch inhaler, with a lozenge-shaped aperture cut in the

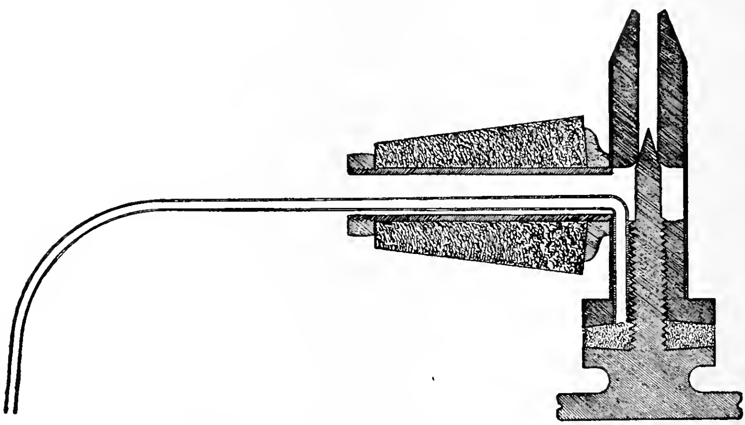


FIG. 69.—DAVIS DROPPER FOR INSERTION IN ORIGINAL CONTAINER.

rubber tissue which is placed over the gauze covering the mask, encircle the mask with a towel so as to have more or less rebreathing. Commence dropping the ethyl chlorid upon the mask until the patient reaches unconsciousness. Now begin dropping ether. If the patient swallows, or shows any signs of returning consciousness, continue dropping the ethyl chlorid until this disappears, then recommence with the ether. Continue in this way until full surgical narcosis is reached, when the ethyl chlorid may be discontinued. The ether may now be continued by the drop method, as already outlined, or ethyl chlorid may be sprayed intermittently for five to ten seconds on the mask until the second stage is reached, when a switch may be made to ether. If signs of consciousness ensue, ethyl chlorid must be continued to be intermittently sprayed, the ether at the same time being dropped upon the mask.

The Ethyl Chlorid-Ether-Chloroform Sequence.—The change to chloroform should not be made until the patient is in full ether anesthesia. The anesthetist should then allow the reflexes to become slightly active and the chloroform should be commenced very gradually. The change to chloroform should be made if there is profuse secretion of mucus and saliva following the ethyl chlorid and ether.

The Ethyl Chlorid-Ether Sequence by the Closed Method.—The ethyl chlorid anesthesia may be induced, as fully given in the chapter upon Ethyl Chlorid, and a switch can then be made to ether by revolving the ether chamber. It is safer and better from every standpoint to admit the ethyl chlorid from the bottom of the bag instead of near the patient's face. Two to five c.c. of ethyl chlorid are usually sufficient to obtain the anesthesia desired before turning on the ether.

The advantages of the ethyl chlorid-ether sequence are, principally, the rapidity of induction and freedom from the second, or struggling, stage of anesthesia. This sequence is usually much quicker than the nitrous oxid-ether sequence.

Whenever the open or closed method of ethyl chlorid-ether is used, ether can be either dropped or turned on very gradually much earlier than in the nitrous oxid-ether sequence.

Warning! With the ethyl chlorid-ether sequence it is unnecessary to carry the patient to full surgical narcosis. The anesthesia induced by ethyl chlorid is usually quiet and without either cyanosis or stertor. There is, however, *a possibility of danger in the initial stages from sinking the patient too deep. Whenever the lid reflex is entirely abolished a change should be made.* It is unnecessary to wait for the cornea to become insensitive. Ethyl chlorid-ether sequence is especially indicated for children, and for nervous individuals, who might be frightened by a mask or bag being placed over the face.

Chloroform-Ether Sequence.—When morphin has been given as a preliminary, and the induction is preceded by the use of a few drops of farina cologne or an alcoholic solution of oil of bitter orange peel, a remarkable difference in all the reflexes may be noted as the patient goes under the anesthetic. The induction will, under these circumstances, proceed to the second stage with chloroform. When this stage is reached, give one drop of ether every thirty seconds for one or two minutes, then alternate the drops of ether with the chloroform, and, finally, as the third stage is reached, continue with ether unless the reflexes become active, when a few drops (3-8) of chloroform can be given and the ether continued. This is the safest way to induce anesthesia when ether is the terminal anesthetic, for the simple reason that the struggling stage will not occur if careful attention is given to the small details. Ether thus replaces chloroform at what is known as the dangerous stage of anesthesia. During the last few minutes of the anesthesia chloroform may again replace the ether. In this way the patient comes out of the anesthetic without noticing the odor of ether.

The change from ether to chloroform must take place when the reflexes are slightly active, and in the following manner: Commence with one drop of chloroform every ten seconds and note whether the reflexes are deepened or not, then change to two drops, and then to three drops every ten seconds. It will be found that the patient can be kept lightly under in this way, and between the second and third stages without causing any nausea or vomiting, provided some preliminary medication has been given.

Anesthol.—Neef's[1] definition of anesthol is "chloroform modified to increase its safety without impairing its anesthetic usefulness." For a full discussion of anesthol see Chapter XX.

The Anesthol-Ether Sequence by the Drop Method.—In the anesthol-ether sequence, as well as in the ethyl chlorid-ether sequence, a factor of safety is preliminary medication with morphin. The New York German Hospital's system is to give about 1/4 of a grain of morphin one-half hour before narcosis. Hellman,[2] anesthetist to the German Hospital, prefers pantopon, 1/3 of a grain three-quarters of an hour before the operation, and repeats this just before the operation. In certain selected cases he gives 1/100 grain of hyoscin with the first dose. Hellman states that, while he thoroughly dislikes morphin before anesthesia, in pantopon he has a safe and reliable aid.

Neef states:[3] "The odor of the anesthetic may become markedly repugnant to those who have previously been under its influence, and assurance on this point may help to bring about a prompt decision. A few drops of a 10 per cent emulsion of Persian oil of rose in deodorized alcohol on the mask is an efficient way of eliminating this disagreeable element in the induction of anesthesia."

Using an ordinary chloroform or some similar mask, the anesthesia is commenced with one to three drops of the oil of orange, which is then followed by the anesthol and continued with ether. This is, in the authors' opinion, safer than the chloroform or ethyl chlorid-ether sequence, and much safer than the continuous use of ether by the drop method for the following reasons:

First: Anesthol is less "smelly" than chloroform or ether, and for this reason no doubt is less irritating to the upper air passages.

Second: The anesthesia is induced a little quicker than by chloroform.

Third: Both experimental and clinical experience justify the statement that next to nitrous oxid it is probably the safest induction anesthetic.

The administration is conducted as follows: With the mask encir-

[1] Neef, F. E.: "Surgical Essentials," *Am. J. Surg.*, April, 1912.

[2] Hellman, A. M.; "The Use of a New Opium Preparation Before Anesthesia—A Preliminary Note with a Report of 50 Cases," *J. Am. Med. Assn.*, Jan., 1912, n. s. 7, No. 1, 39-45.

[3] *Loc. cit.*

cled by a towel, the anesthol is administered drop by drop, say one drop the first ten seconds, two drops the next ten seconds, etc. As soon as the patient becomes accustomed to the anesthetic vapor the drops may be rapidly increased. If the patient's breathing is shallow a few drops of ether from time to time will stimulate and keep up the respiratory function. As the stage of primary anesthesia or unconsciousness is reached, the ether must be pushed as rapidly as the condition of the upper air passages of the patient permits. If ether is given at this time, drop by drop, and there is no swallowing reflex, it should be continued; otherwise, if there are swallowing reflexes, anesthol may be continued for ten or twenty seconds and then the ether recommenced.

If there is objection made by the patient to the vapor strength, as indicated by the turning of the head or holding of the breath, the mask may be slightly lifted from the face and then replaced. If there is marked pallor of the face, and the pulse is weak during the induction stage, the anesthol should be immediately replaced by ether. Cyanosis should not be allowed during the induction period. If this occurs a rearrangement of the air passages by moving the head to right or left, or by supporting the chin, or raising slightly the lower jaw, or, in elderly people, supporting the alæ of the nose, will correct this trouble. The usual amount of anesthol necessary to induce anesthesia when morphin has been given is 15 to 25 c.c.

The average time, when morphin or some preliminary medication has been given, is five minutes; without this preliminary, it is eight minutes. When properly given the morphin-anesthol-ether sequence is induced in over 90 per cent of cases with no stage of excitement whatever. The induction stage must not be prolonged too long, as vomiting is apt to occur.

After the change has been made to ether, if it is desirable to deepen the anesthesia for any reason, instead of crowding the ether and thereby producing unnecessary salivation, a few drops of anesthol will quickly and safely deepen the anesthesia, without the salivary gland activity that would be produced by an amount of ether sufficient to obtain the relaxation called for.

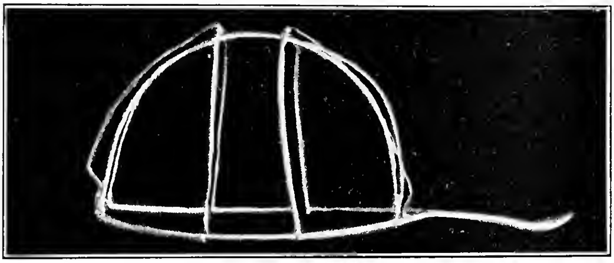
A glance at the statistics for the anesthol-ether sequence will fully convince anyone of the safety and desirability of this sequence. At the German Hospital, in the year 1905, 149 cases were given anesthesia by this method, increasing in number each year until the year 1911, when there were 919.

The Ether Rausch.—Coughlin [1] recently described the "ether rausch." We quote voluminously from Coughlin's article.

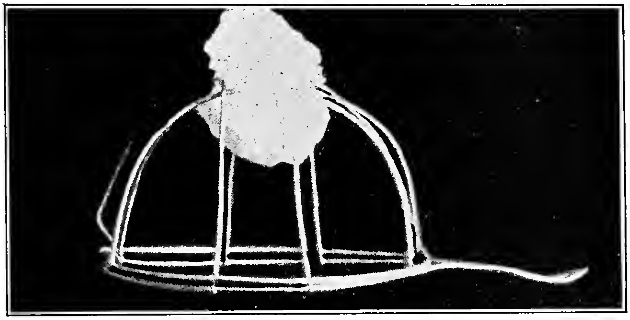
The ether rausch, according to Coughlin, was used in this country twenty-five years ago. Lindner, of Dresden, has used it more than five

[1] **Coughlin, William T.:** *J. Am. Med. Assn.*, **July 1, 1911, 17, 18.**

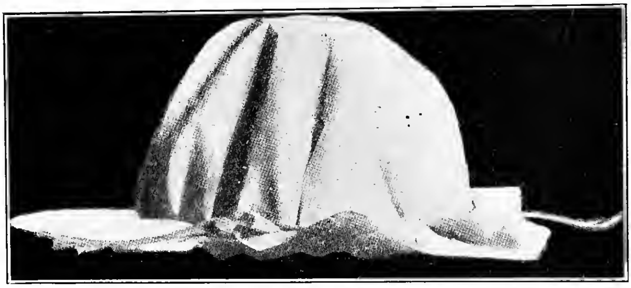
thousand times. Coughlin is using it at the College Clinic, St. Louis University Medical School. He reports two hundred cases, in some of which he acted both as the anesthetist and operator. The only fail-



A. Wire Frame of the Mask.



B. The Pad of Gauze in Position.



C. The Frame Covered with Oiled Silk.

Fig. 70.—The Ether Rausch.

ures were in patients who refused to proceed beyond the first two or three inhalations. He recommends it for all minor surgical operations that can be better done if the patient feels no pain, such as opening abscesses, setting fractures, reducing dislocations, and removing ingrowing toe-nails. From his experience he states that it is contraindicated in any operation which requires more than five minutes' time, or in those in which general relaxation is necessary. Pale, flabby children, chronic bronchitis, emphysema, marked arteriosclerosis, or diseases of the pulmonary or cardiovascular system also contraindicate its use. Coughlin thinks it is preferable to any local anesthetic for the special cases outlined. In many cases of great local inflammation the injection of a hypodermic needle gives almost as much pain as the relief it affords during the actual incision. The ordinary Esmarch inhaler is not satisfactory, as it does not allow enough ether to be introduced at one time to produce general anesthesia without very great irritation of the upper air passages. The mask, therefore, must be a large one; large enough to fit the outside of the face. Air must be rigidly excluded as far as possible. An ordinary Derby hat has been frequently used by Coughlin for this purpose. It is placed over the patient's face with the saturated ether gauze attached to the crown by a safety pin. Wet towels are placed around the undersides of the hat, thus excluding all air. The mask generally used, however, is a very large wire frame, the margin of which fits closely the outer margin of the face. A pad of gauze is placed at the top of this mask, which is then saturated with ether and then the wire frame is covered with oiled silk, the points of contact with the mask and face being filled in with the wet towels. The patient is told that the only unpleasant feature is the smell of the ether. He is now requested to raise his arm and to keep it raised as long as possible. After placing the mask over the face the patient is told to breathe deeply. At about the twelfth inhalation the arm wavers and begins to fall. The mask is removed and at once the operation is begun and quickly finished. The patient may be cyanosed at first, but this quickly disappears, and he comes out of the anesthetic quietly. In the particular case related by Coughlin the patient was eating dinner twenty minutes after the operation was concluded.[1]

The Semi-Closed Method.—The drop method of ether just described can be changed quickly into the semi-closed method in the following manner:

Have the mask with towels arranged according to Davis's method for administering drop by drop.

Place another towel around the mask and face and then place an additional towel over the opening in which the ether is dropped. This will insure, more or less, to-and-fro breathing. The upper towel can be removed from time to time, when half a dram to one dram of ether may be poured upon additional pieces of gauze placed upon the top of the mask. The upper towel is now to be quickly replaced.

The rebreathing will continue for two to four minutes, when ether may be again added and the towel replaced as before. This procedure is

[1] As ethyl chlorid has a longer stage of analgesia than any other inhalation anesthetic theoretically, at least, it should be preferable to ether for the *"rausch."*

indicated when, for any reason, it is hard to maintain a proper degree of anesthesia by the ordinary drop method.

Towel and Paper Cones.—These cones are still used in a great many hospitals, and one of the best methods of making them is described by Miller (Providence, R. I.) as the Handkerchief Method, and is fully illustrated.

The Handkerchief Method of Administering Ether.—"This is the result of a search for a simple, clean, and otherwise practical appliance for the administration of ether by the internes of hospitals. It has been used with satisfaction in over 20,000 cases.

"The appliance consists of: (1) an open cone; (2) a ring of sheet metal; (3) a handkerchief and diaphragm of gauze.

"The cone is made from three sheets of newspaper folded to form a strip six inches wide. (Fig. 71 A.) This strip is folded upon itself to form a funnel which, when flattened out, has a breadth of six inches. (Fig. 71 B.) The funnel is covered with a clean towel which measures about eighteen by twenty inches. The towel is placed on a flat surface. The newspaper funnel is placed upon the towel with one end of the funnel at the middle of the towel. The towel is folded about the outside of the funnel. (Fig. 71 C.) The long end of the towel is pushed through the funnel (Fig. 71 D) and folded over the end of the funnel. (Fig. 71 E.) The short end of the towel is folded inside the funnel. (Fig. 71 F.)

"A strip of $\frac{28}{1000}$ sheet brass, silver plated, two inches wide and fifteen inches long, is formed into a ring which is adjustable in size. (Fig. 71 G.) The ring is sterilized by boiling.

"A diaphragm composed of eight layers of No. 1 sterile surgical gauze is placed over one end of the cone. (Fig. 71 H.) The metal ring is adjusted to a size a little smaller than the inside of the cone. It is placed over the diaphragm and pushed inside the cone, carrying the diaphragm to the full depth of the ring. (Fig. 71 I.) The ring is pulled open as far as possible, fixing the diaphragm in the cone. (Fig. 71 J.) There is thus formed a chamber, its sides formed of the thin sheet of metal, its floor formed of eight layers of gauze, and its roof free. The roof of this chamber is the distal end of the cone. A handkerchief of No. 1 sterile surgical gauze is well shaken out and placed in the chamber. (Fig. 71 K.) The two sides of the chamber are drawn together and held by a safety pin passing through the two sides of the cone close to the metal ring. (Fig. 71 L.) At the proximal end of the cone is an air space four inches deep. The temperature in this space during an ordinary administration of ether is about 88° F. (Fig. 71 M.)

"Before beginning the administration of ether with this cone, the gauze handkerchief is drawn partially out from the chamber, leaving a clear airway at one end of the chamber. (Fig. 71 L.) On the gauze

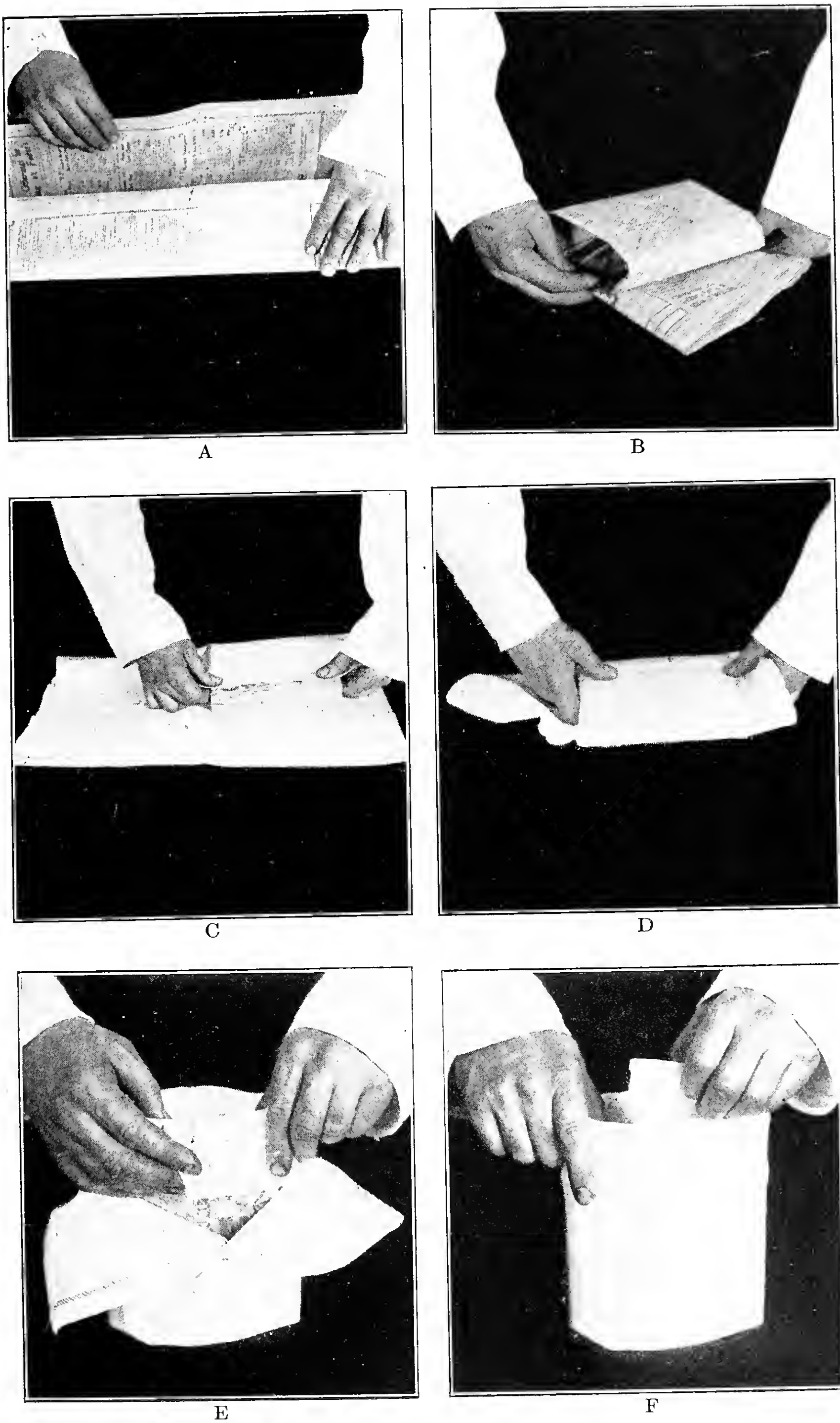


Fig. 71a–f.—The Handkerchief Method.

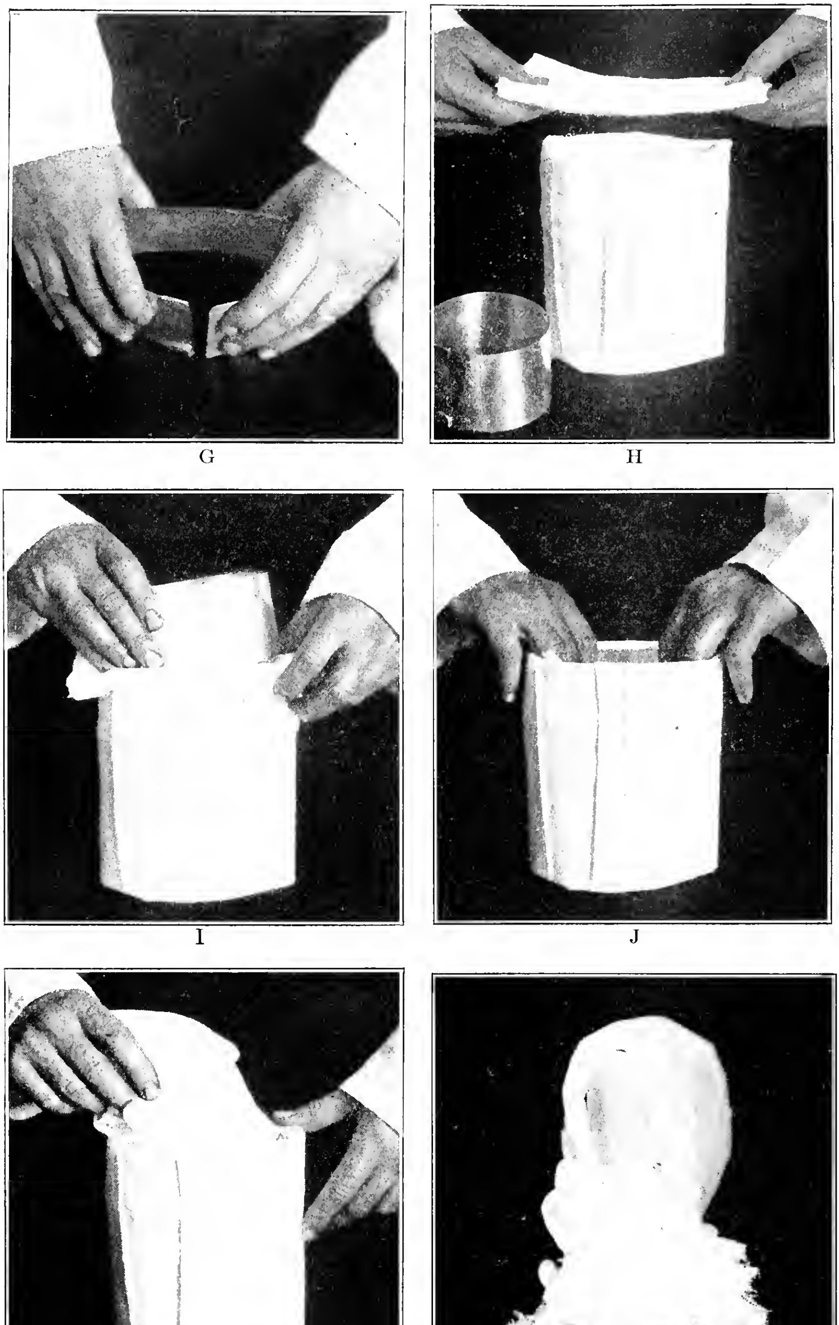
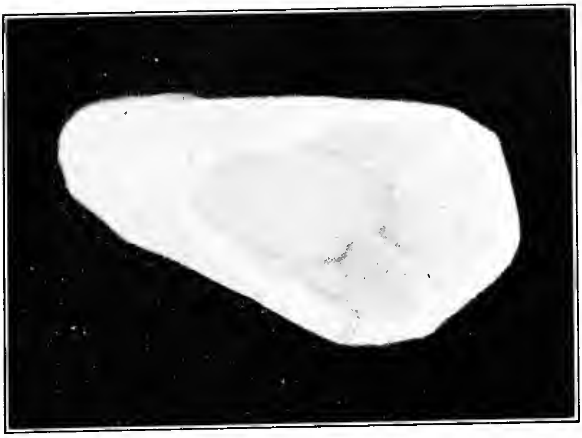
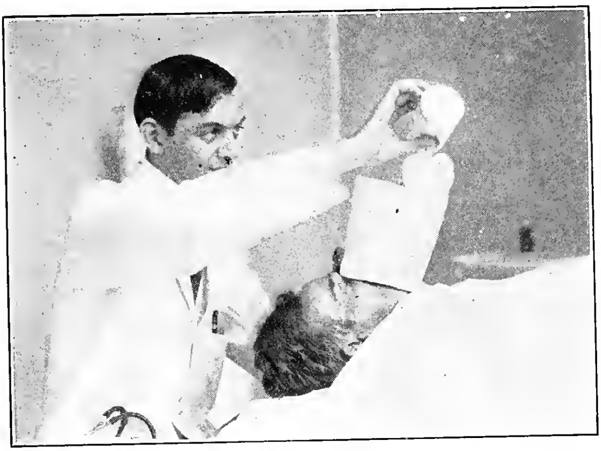


Fig. 71g–l.—The Handkerchief Method—Continued.



M



N

O

FIG. 71M–O.—THE HANDKERCHIEF METHOD—Continued.

diaphragm are placed a few drops of the oil of orange. The proximal end of the cone is fitted to the patient's face, and he is allowed to take several breaths through the cone. Ether is then added to the gauze handkerchief, drop by drop, until the patient has become accustomed to the vapor. (Fig. 71 N.) Then the gauze handkerchief is pushed into the chamber, so as to completely fill it, and ether is added gradually until anesthesia is complete. (Fig. 71 O.)

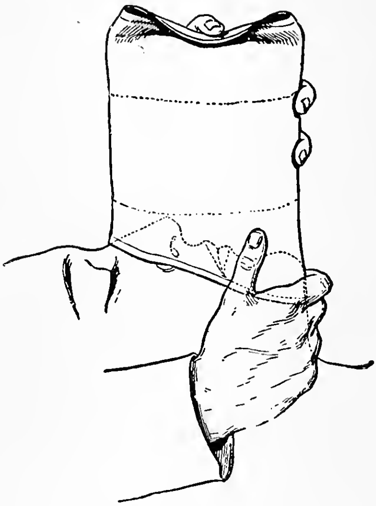


Fig. 72.—Cone Adjusted to the Face. There is ample air space above, and nose space below the frame. Right hand supports the chin, to prevent relaxation of the jaw and prolapse of the tongue. Left hand folds the top of cone to increase the amount inspired. (Gallant: *Med. Record*, Dec., 1899.)

"If this proceeding is carried out slowly there is no coughing, choking, or feeling of suffocation. The supply of air necessary for respiration is not interfered with, and the amount of ether vapor inspired is imperceptibly increased.

"During the operation ether is added constantly, drop by drop, or poured on the handkerchief frequently in small quantities, at the distal end of the cone, or through the proximal end, on removing the cone momentarily from the patient's face. The handkerchief is frequently taken from its chamber and shaken out. In this way the evaporating

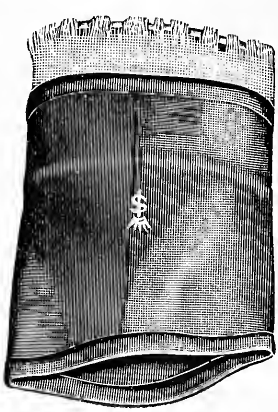


Fig. 73.—Allis Inhaler with Soft Rubber Cover for Semi-open Method.

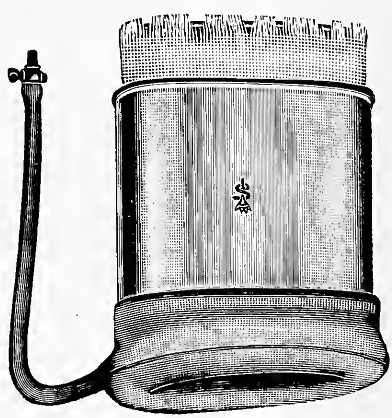


Fig. 74.—Allis Inhaler, Metal with Rubber Cushion for Face and Gauze Diaphragm.

surface is kept free and the amount of ether remaining on the handkerchief is frequently noted. The eyes are not covered.

"The handkerchief method has the following theoretical advantages: (1) simplicity; (2) cleanliness; (3) continuous administration of ether; (4) evaporating surface at some distance from the patient's face; (5) no interference with free air supply; (6) warmed ether vapor; (7) steady, constant control over the amount of ether vapor inspired; (8) economy; no ether is wasted by soaking into the cone, or by running down the neck of the patient.

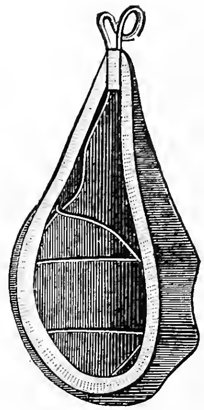


Fig. 75.—The Esmarch Inhaler.

"This method has also the following practical advantages:

"(1) Inexperienced anesthetizers have been quickly taught to use the method satisfactorily.

"(2) Anesthetizers who have been accustomed to the use of other methods have all preferred the handkerchief method after a short trial.

"(3) Patients who have taken ether badly in other ways have been smoothly anesthetized by the handkerchief method."

When using these cones, or any other semi-closed or closed method of ether, it is always best to begin the administration with an open mask by pouring one or two drops of the oil of orange and then proceeding to the drop method as described by Dr. Davis. As the patient reaches surgical anesthesia, change to the cone mask, upon which has been placed one or two drams of ether; continue adding the ether from time to time as the condition of the patient demands.

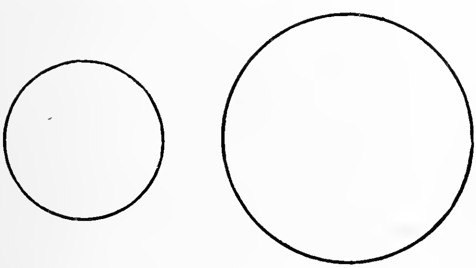


Fig. 76.—Comparative Size of Bores of Inhalers (Luke).

The Closed Method.—The closed method of administering ether was the immediate precursor of the gas-ether sequence. It was developed in England in 1872, and has been employed successfully in thousands of cases since that time. Dr. Clover was the first to develop an apparatus that received extensive recognition. As the method of administration is the same with any mask and bag, regardless of the name of the inhaler, directions will be given suitable for any apparatus that may be used.

Any inhaler for the administration of the nitrous oxid-ether se-

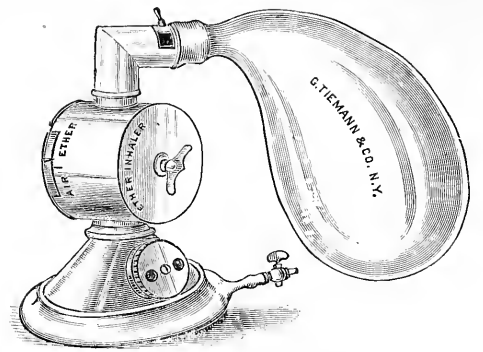


FIG. 77.—BENNETT'S NITROUS OXID-ETHER APPARATUS: ETHER INHALER.

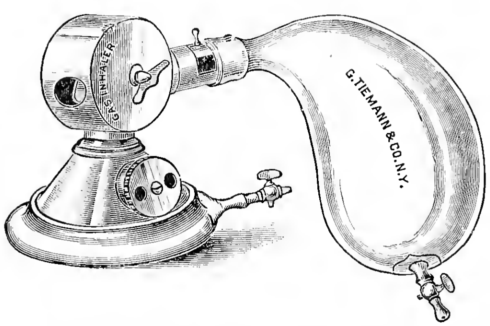


FIG. 78.—BENNETT'S NITROUS OXID-ETHER APPARATUS: GAS INHALER.

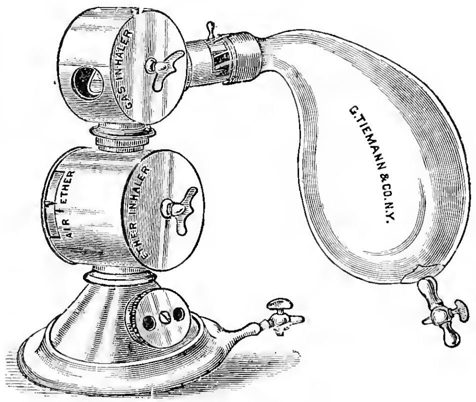


FIG. 79.—BENNETT'S NITROUS OXID-ETHER APPARATUS: GAS AND ETHER INHALER.

quence should have a large bore. The two illustrations taken from Luke make further comment unnecessary.

The Nitrous Oxid-Ether Sequence.—The nitrous oxid-ether sequence, which consists in giving one or two bags full of gas and, while the patient is unconscious, gradually turning on the ether, was probably introduced into this country by Thomas Bennett, of New York City.

THE BENNETT INHALER. — This apparatus consists of a face-piece with a rubber cushion, a gas cylinder and a cylinder for holding the valves used in administering gas, and two bags. The apparatus can be taken apart and used for the closed administration of ether alone, or for gas and air, or for the gas-ether sequence. Nearly all of the gas-ether apparatus in America are probably modifications of this inhaler.

THE GWATHMEY INHALER. — The Gwathmey inhaler, for the administration of the nitrous oxid-ether sequence, is a modification of the Bennett inhaler. It consists of a face-piece with expiratory valves, one cylinder for the passage of gas alone or through ether, or the continuance of the administration with ether alone by the closed method, and a chimneypiece containing an inspiratory and expiratory valve. These valves can be easily pulled out of the way by a sliding collar, so that to-and-fro breathing

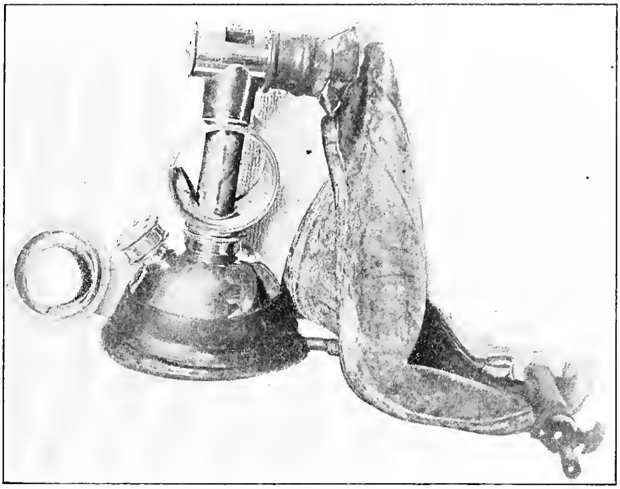


Fig. 80.—The Gwathmey Inhaler Open.

can be instituted at any time. A rubber bag is attached to this chimneypiece. At the other end of the bag a rubber tube with a stopcock connects the bag to the gas cylinder. If the Gatch method of administration of gas and oxygen is to be used, a Y-piece connects the nitrous oxid and oxygen cylinders to the bag. The apparatus is reduced in weight and bulk to nearly one-half that of the Bennett apparatus, having one cylinder and one bag. The object of the nitrous oxid-ether sequence is to avoid the first and second stages of ether narcosis with its preliminary excitement, struggling, coughing, holding the breath, swallowing, and all other disagreeable and disgusting effects that were formerly connected with this stage of etherization, and to enter immediately into the third stage for surgical anesthesia. The patient is thus enabled to take advantage of one of the safest general anesthetics

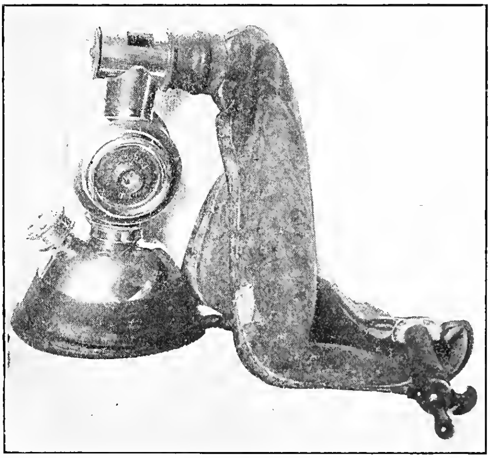


Fig. 81.—The Gwathmey Inhaler Closed

in the most agreeable manner possible, and with the least physical and nervous strain. It is the exception for the patient to show any excitement whatever, and deep anesthesia is generally reached in about three minutes.

THE FURNISS GAS-ETHER INHALER.—This inhaler consists of exactly the same number of pieces as the Gwathmey inhaler, and differs only in

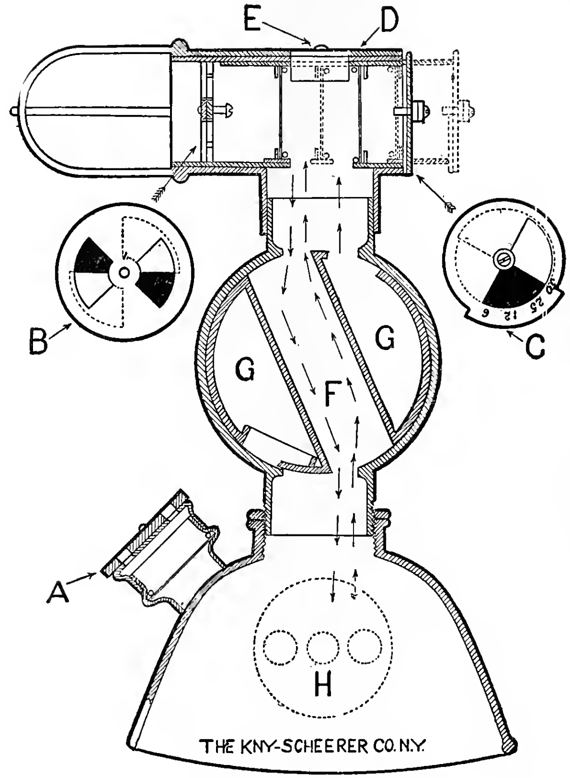


FIG. 82.—GWATHMEY NITROUS OXID-ETHER APPARATUS.

minor details. In purchasing any apparatus for the administration of nitrous oxid and ether in sequence, the purchaser should bear in mind one general rule governing the safety of the method of administration, and that is the size of the aperture through which the patient breathes. (See Fig. 76.)

As the technique for the administration of the gas-ether sequence is practically the same for all three inhalers, general directions applicable to all three inhalers follow.

The distinctive feature of the Gwathmey gas-ether inhaler is that, as the ether chamber is turned on, the ether can escape into the bag only —the opening toward the patient's face being still closed. This continues until the ether chamber is one-half on, at which time it begins to show at the opening toward the patient's face. The patient thus gets a more uniform and diluted ether vapor than if both openings of the ether chamber appeared at the same time. This makes it possible to make the change to ether without the patient swallowing or showing other recognition of the change.

THE DAVIS INHALER.—This inhaler is for the gas-ether sequence or the ethyl chlorid-ether sequence; the ether in every instance is given by the drop method. The apparatus is a perfect one for the purposes for which it is used. Davis was probably the first in America to get out an apparatus for the administration of ether by the closed drop method.

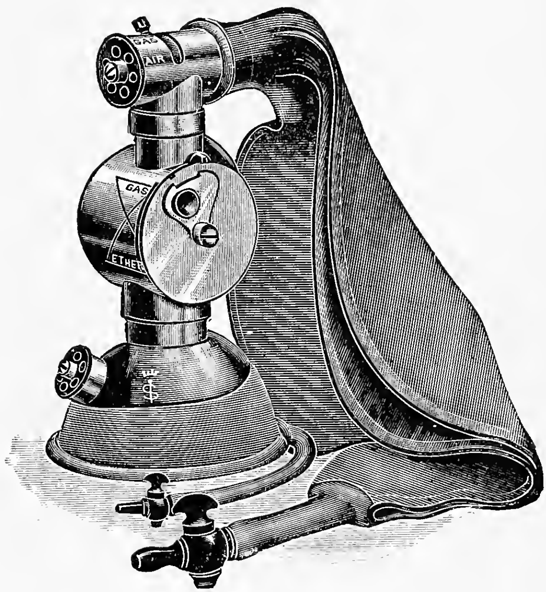


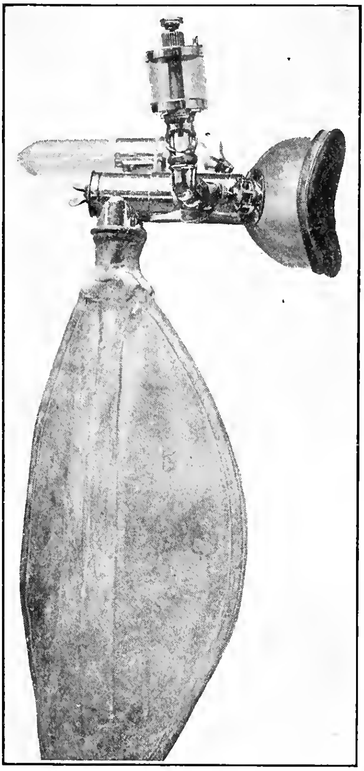
FIG. 83.—THE FURNISS NITROUS OXID-ETHER APPARATUS.

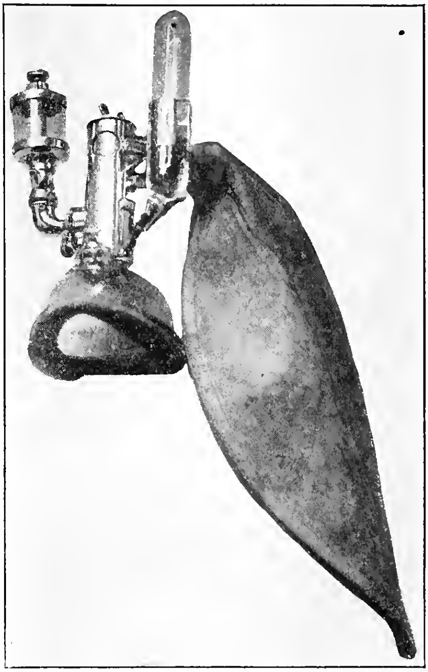
Technique of the Nitrous Oxid-Ether Sequence.—First: Fill the rubber bag with gas. It is well to have the gas bag attached to the nitrous oxid cylinder throughout the operation, so that a change can be made in the gas mixture or additional nitrous oxid added to the bag at any time.

Second: Place two to four drams of ether in the ether chamber. Be careful to have the ether chamber so arranged that the odor will not penetrate the face-piece or other chambers of the inhaler.

Third: See that the air cushion on the face-piece is partly inflated. If this cushion is too tightly inflated it will not be as effective in excluding the air as when it is only partly inflated.

Fourth: Place the mask gently upon the patient's face, having first removed all pillows. Have the patient breathe through the valves or airway once or twice before turning on the gas. When the gas is turned on, it should enter the inhaler quietly. (It will not do this if the bag is overdistended.) Have the patient breathe one bag of gas through valves. Then turn to to-and-fro breathing, and, if necessary, refill the bag again with gas. The patient will now be unconscious, provided no air has been allowed to enter the inhaler between the face and mask or any other part of the apparatus. Now begin turning on the ether very, very slowly. If the patient coughs, swallows, or holds the breath, turn off the ether and allow a little rebreathing, and then begin with the ether again. If the patient still rebels, more nitrous oxid should be added in the bag. When the ether chamber is on full the patient should be in deep surgical anesthesia, which should be in from two to three minutes, depend-





Figs. 84 and 85.—The Davis Apparatus, Showing Inhaler for Ethyl Chlorid-Ether Sequence by the Closed Drop Method.

ing upon the patient. Surgical anesthesia is usually indicated by a slight snore. A breath of air may now be admitted by raising the mask from the face on inspiration and replacing again so as to catch the expiration of the patient in the bag. The expired air thus passes through the ether chamber and keeps the bag full of warm ether vapor. A breath of fresh air may be admitted every two to six breaths, according to the condition of the patient. One or two drams of ether poured from the container into a minim glass should be added every two and one-half minutes. This may be necessary for the first five or ten minutes; after that, a dram every three minutes will be all that is necessary with the majority of patients.

In very cold weather it is always best to place the inhaler upon a radiator or stove or in front of a register, or to dip it in hot water before commencing the anesthesia.

Caution! With any closed inhaler never allow the bag to become deflated, otherwise the patient attempts to breathe from the vacuum, and a tremendous strain is immediately thrown upon the respiratory and circulatory systems, resulting in shock and collapse, if unnoticed.

Nitrous Oxid-Ether-Chloroform Sequence.—For all operations lasting over one hour it is well to change to chloroform or ether on an open mask for the last ten or fifteen minutes. The change to chloroform should be made when the reflexes are slightly active. Very small amounts of chloroform will be necessary to maintain the narcosis. If at any time the patient becomes pale or shows signs of shock from any cause, ether by the drop method should be immediately substituted for the chloroform. The indications for a change from the closed method to the open would be rapid respirations or marked cyanosis. Deep anesthesia is easily and safely maintained with ether by the closed method.

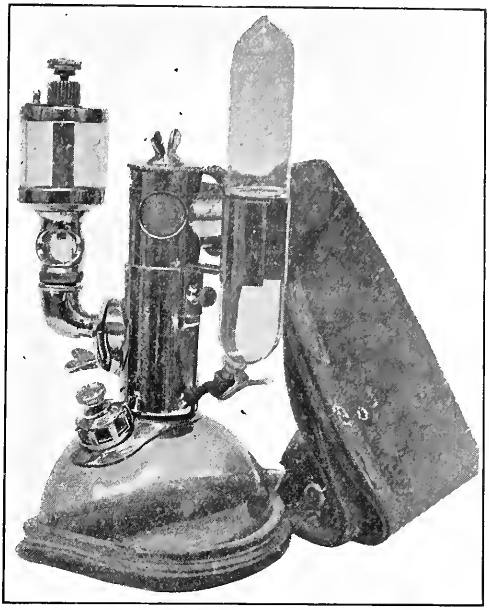


FIG. 86.—DAVIS APPARATUS FOR GAS-ETHER OR ETHYL CHLORID-ETHER BY DROP METHOD.

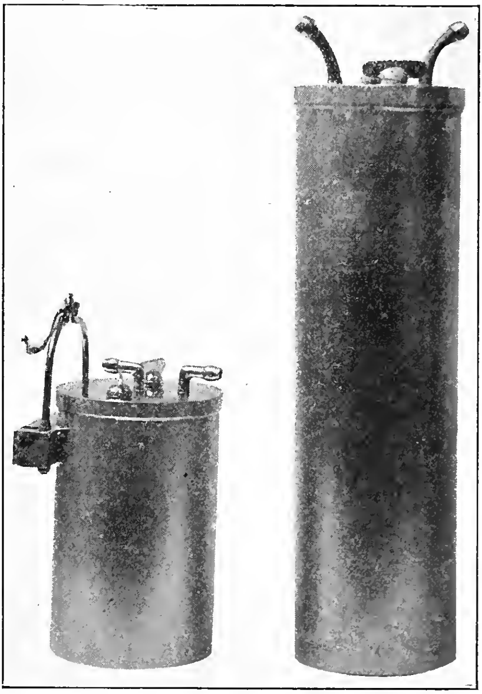


FIG. 87.—DAVIS HEATERS FOR ETHER OR NITROUS OXID AND OXYGEN.

The pulse is usually full and bounding, the respirations are deep, and the face is flushed. Unless the change to chloroform is made toward the close of the operation, the patient does not usually come out of

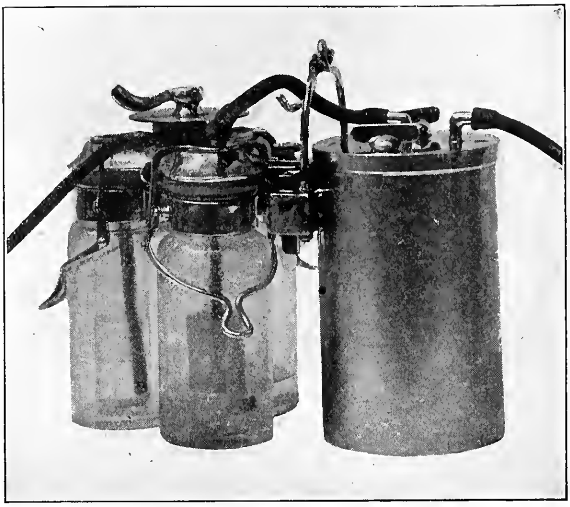
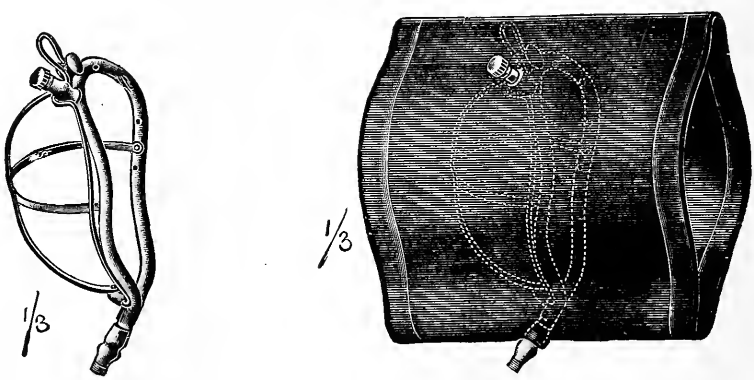


FIG. 88.—DAVIS HEATER WITH THE GWATHMEY THREE-BOTTLE VAPOR INHALER.

this method of anesthesia as quietly as if this change had not been made. There does not seem to be the danger attached to the administration of chloroform in this way after the circulatory and respiratory



A. B.

FIG. 89.—VAPOR MASK. A. The mask, one-third size. B. Rubber covering for the mask, which helps to prevent cooling and waste of the anesthetic.

centers have been stimulated by the nitrous oxid and ether. The change to chloroform may be made immediately after reaching full ether anesthesia if for any reason it is desired to give the smallest amount of ether and at the same time avoid the dangers of the initial stages of chloroformization.

The Vapor Method of Anesthesia.[1]—The vapor method is one in which air, oxygenated air, oxygen, or other gas passes either over or

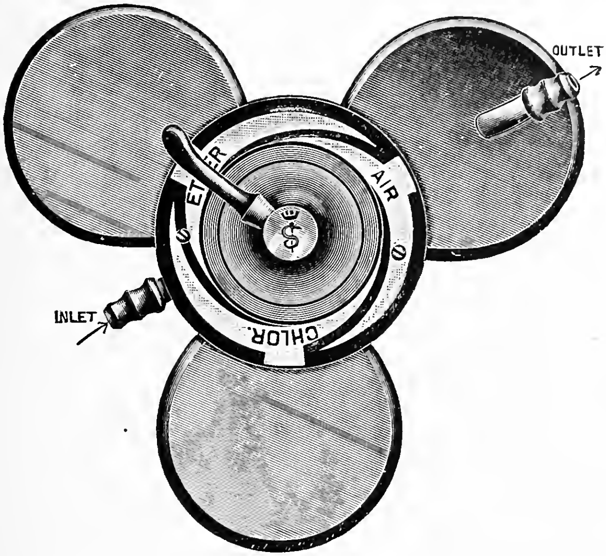


Fig. 90.—Top of Three-Bottle Vapor Inhaler.

through the anesthetic agent, or the anesthetic is allowed to drip into the current of air and is thus *vaporized before being delivered to the patient.* The term distinguishes it immediately from the drop method, where the *anesthetic* is placed upon gauze or other material and is *vaporized by the patient.*

When the vapor is carried by tube to the pharynx or trachea it is called endopharyngeal or endotracheal insufflation, the word insufflation meaning "the blowing of powder (or gas) into a cavity." [2]

Endopharyngeal, endotracheal, and rectal anesthesia are modified forms of the vapor method of admin-

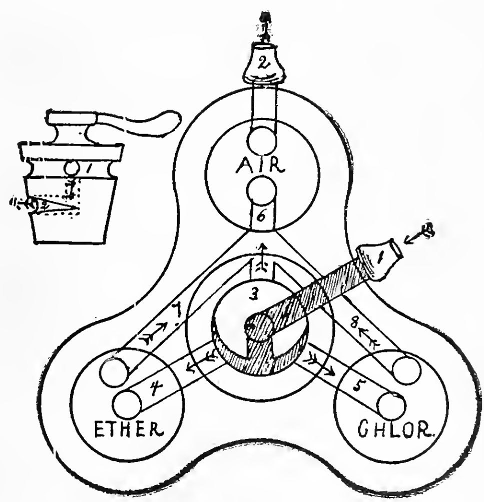


Fig. 91.—Diagram of Top of Three-Bottle Inhaler.

[1] For a discussion of the vapor method by chloroform, see Chapter VII.
[2] Gould: "Medical Dictionary."

istration. Junker's small chloroform bottle, operated by a hand atomizer, was probably the first vapor apparatus. The reasons for the evolution of the administration of ether from the drop and cone to the vapor method have been aptly described as follows: "Until within a very few years ether has suffered from an evil reputation with patients despite its indescribable beneficence. This reputation has been due in no small degree to the

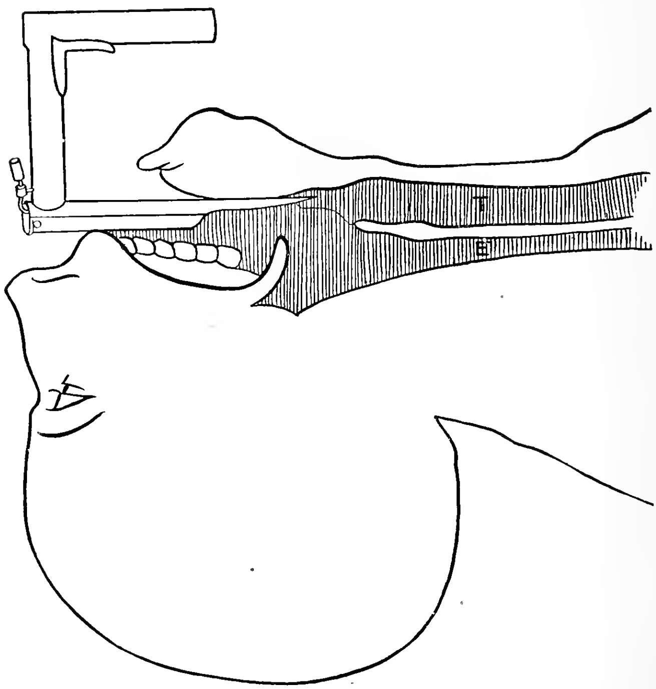


FIG. 92.—JACKSON'S SPECULUM IN POSITION FOR THE INTRODUCTION OF THE ENDOTRACHEAL CATHETER. Note the position of the patient's head. (See p. 428.)

manner of its administration. The liquid ether has been poured or dropped on a sponge or other absorbent material, and the sponge placed in a glass, metal, or rubber container called a cone. This in turn was placed more or less insistently and abruptly over the mouth and nose, and inhalation of the suffocating fumes forced until unconsciousness ensued. Such a proceeding had everything to make it intolerable to the sufferer, and was endured only to afford escape from a greater horror—the pain of operation."

Warmed Ether Vapor.[1]—Ether vapor may be delivered to the patient warmed to room or body temperature, as conditions demand, by so many different methods that there is no longer a question of the pa-

[1] For detailed discussion of warming the anesthetic vapor, see p. 71.

tient's inhaling a warmed vapor. The value of employing warmed ether vapor is, however, still doubted by some practitioners.

When the closed vapor method is used the temperature of the ether vapor is increased to from ten to twenty degrees, so that, when inhaled,

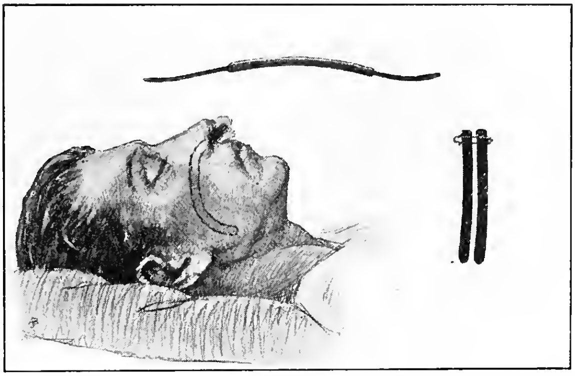


Fig. 93.—Endopharyngeal Tubes for Maintaining Insufflation Anesthesia. (Lumbard.)

the vapor is practically at room temperature. With the open method the ether vapor is usually warmed by being passed over or through hot water. The condition of the patient, the season, and the locality determine whether or not the vapor should be warmed. A patient whose vitality is exhausted, and who may be already in a state of shock, needs artificial heat from every source to prevent a further decrease in body

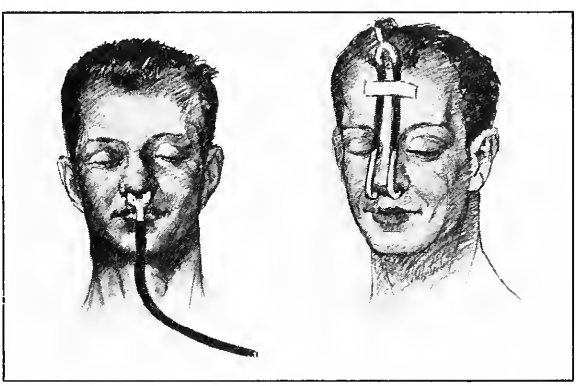


Fig. 94.—Glass Nasal Tubes for General Anesthesia. (Lumbard.)

temperature. On the other hand, it would be entirely unnecessary to heat the vapor for any ordinary operation during very hot weather.

Between these two extremes there is a mean of temperature (usually room temperature), at which experience has taught that all requirements of safe anesthesia are met.

It may be of interest in this connection to note the experience of other observers.

Lawen [1] is convinced that chilling is one of the essential contributing

Fig. 95.—Junker Inhaler. (1) Uncovered mask and hand pump attached. (2) Vapor mask covered. (3) Tubes for mouth work. (4) Sponge holder.

factors to post-operative complications. In twenty-seven reported cases with an apparatus for warming the fumes, the results were excellent.

Joss [2] finds that ether cools the air inhaled 33° to 44° below the temperature of the room. The cooled air undoubtedly lowers the re-

[1] *Münch. med. Woch.*, Oct. 3, 1911, *58*, No. 40, 2097.

[2] *Mitteil. Grenz. Med. und Chir.*, Jena, 1911, *22*, 528.

sisting powers of the cilia of the ciliated epithelium lining the upper air passages, when these passages become chilled. Infection is more liable to find its way into the finer air passages, as salivation increases under the chilled anesthetic.

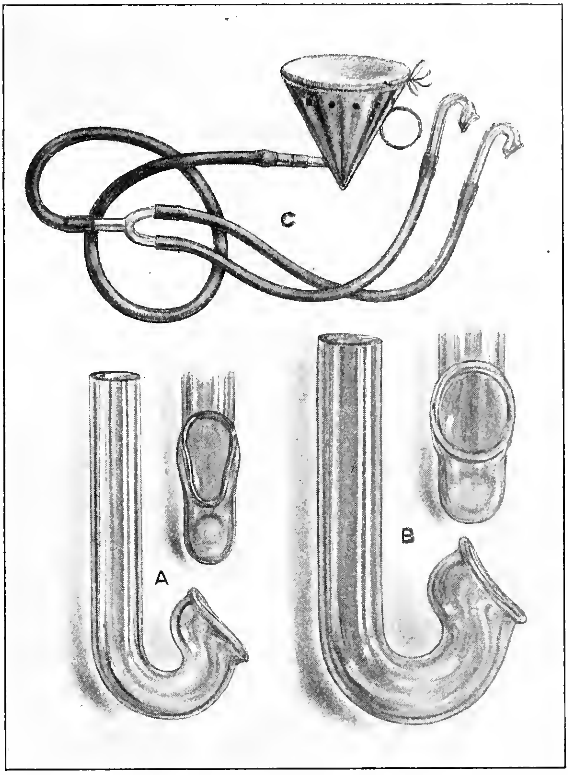


Fig. 96.—Lumbard's Glass Nasal Tubes (A and B). Same Attached to Drum for Drop Method of Ether-Chloroform (C).

Hervey,[1] after demonstrating that ether is warmed when inhaled by the patient, sums up his experience with warmed ether as follows:

"(1) The administration of ether vaporized at a distance from the patient, the so-called closed method, is a distinct advance, whether warmed or not.

"(2) The vapor acts with increased rapidity proportional to its warmth.

"(3) Placid breathing, resembling natural sleep during anesthesia, is often an index of nerve competence, and this efficiency is weakened and disturbed by algid anesthetic irritations.

[1] *N. Y. Med. J.*, Feb. 15, 1913.

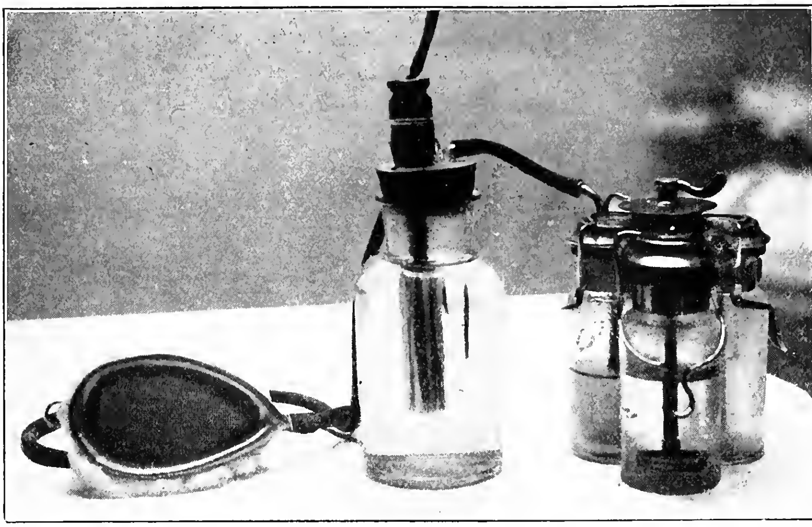


FIG. 97.—THREE-BOTTLE VAPOR APPARATUS CONNECTED WITH ELECTRIC HEATER AND VAPOR MASK.

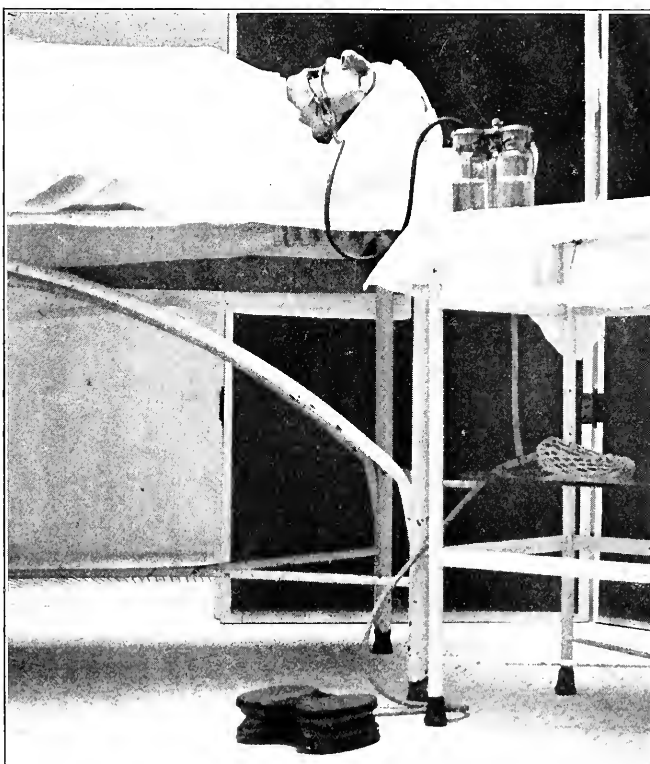


FIG. 98.—FOOT PUMP ATTACHED TO THREE-BOTTLE VAPOR INHALER The vapor passes through hollow tubes welded to mouth-gag.

"(4) Ether amounts will average less than by other methods, as shown by statistics of hospital expense.

"(5) Patients awaken with less distress and with a marked favorable difference in appearance.

"(6) It is suitable for extreme infancy and old age.

"(7) Dryness of the throat is never complained of unless oxygen has been added.

FIG. 99.—GWATHMEY METHOD OF ADMINISTERING WARMED VAPOR THROUGH THE NOSE.

"(8) Cold produces the so-called irritation of ether, contributing to nausea, vomiting, and shock, delays the return to nutrition,—disturbing the stomach by ingestion of ether-laden secretions,—and annoys the patient by leaving a lingering after-taste on the breath, due to impairment of the eliminative functions of the mucous membranes.

"(9) The vapor warmed in some way loses a portion of its odoriferous strength and persistence, to the relief alike of anesthetist, surgeon, and patient."

He also states that "it requires no expert observer favorably to contrast the natural and placid breathing of a patient anesthetized by warm vapor with that of one whose membranes are swollen and awash from the irritation of algid inhalations."

VAPOR

The Open Method.—When the open method is indicated the vapor mask is used. The latest model consists of a close-fitting mask, the base of which is a hollow tube with perforations inside so that, as the vapor is pumped either by foot or by an electric motor, or passed from an oxygen or air tank through the apparatus, the patient inhales a certain known percentage of the anesthetic and gets only this percentage, regardless of the depth or rate of respiration. The upper part of the mask is modeled after the Yankauer, and is made of wire gauze. The mask is

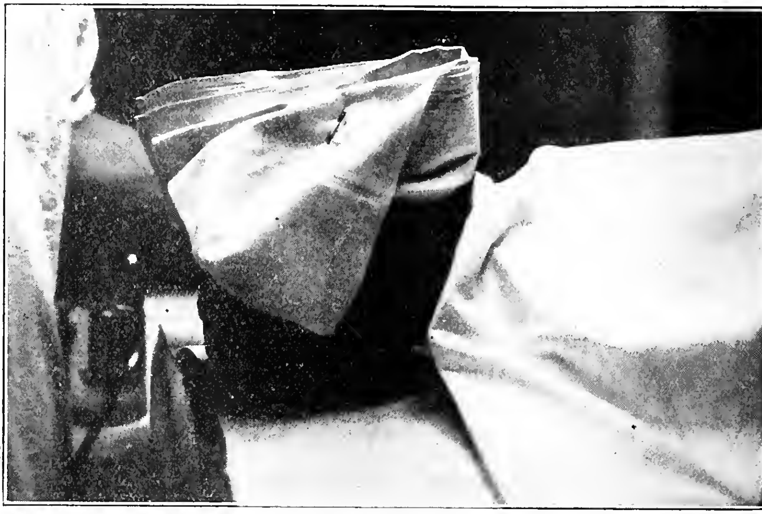


FIG. 100.—ETHER VAPOR MASK ENCIRCLED BY A TOWEL HELD IN PLACE BY A SAFETY PIN.

FIG. 101.—SAME AS FIGURE 100 WITH OUTER FOLD OF TOWEL DROPPED AS PATIENT REACHES SURGICAL ANESTHESIA.

usually surrounded by a towel, the object of which is to decrease the amount of ether vapor blown away, to reduce the quantity, and to increase the safety, by warming the vapor by the slight amount of rebreathing thus obtained.

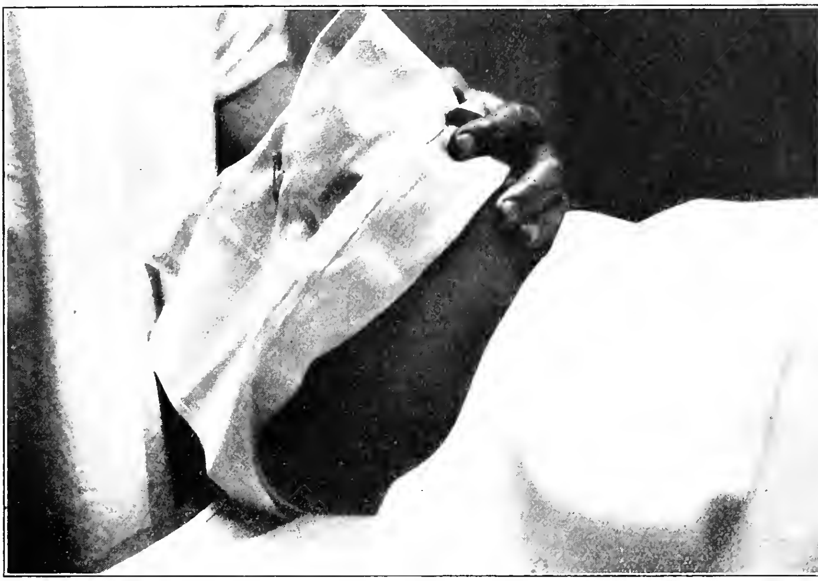


Fig. 102a

Fig. 102b.

Figs. 102a and 102b.—Methods of Holding Jaw Forward so as to Maintain an Open Airway.

Where the mouth is necessarily open during long operations upon the nose or mouth, the mouth gag with hollow tubes attached or a hollow tube may be substituted for the vapor mask just referred to. or pharyngeal tubes may be used.

Small children and weak anemic men or women can be easily anesthetized by the open method of vapor alone. Ordinarily it is best to commence by the drop method and switch to the vapor as the patient reaches surgical anesthesia. If, however, the vapor alone is to be relied upon, the anesthetist proceeds as follows: Air is pumped vigorously

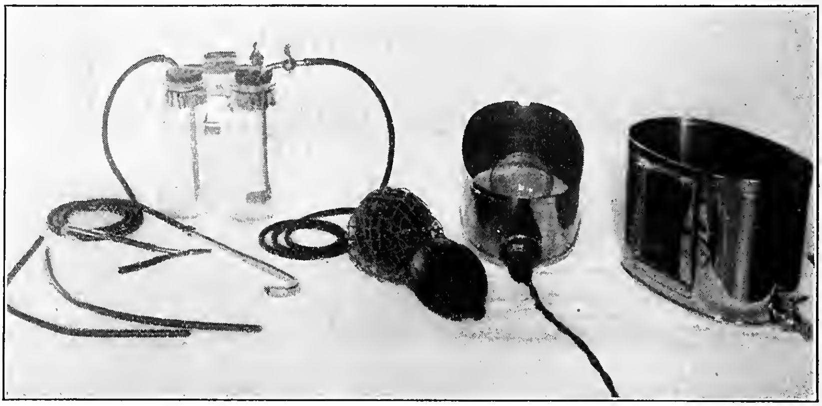


FIG. 103.—PINNEO'S ETHER VAPOR APPARATUS, DISCONNECTED.

through the bottle marked air or water. The index should now be gradually turned toward chloroform. If the patient coughs, sneezes, or holds his breath, the index should be turned back again and a fresh start made. Continue in this way until the patient is well under the anesthetic, when ether may be substituted for the chloroform in the same manner. If the patient is a child, and if there is a suggestion of status lymphaticus or other contraindication to chloroform, ether may be placed in the small chloroform bottle, and the gradual change to ether, as just described for chloroform, made. As the patient becomes accustomed to this mild vapor the stopcock may be very gradually turned to the larger ether bottle.

For strong, vigorous adults or alcoholics ether from the small bottle may not be sufficient to get the patient under quietly and easily. In this instance the vapor may be supplemented by drops of chloroform or ether upon the vapor mask. After the patient is well under surgical anesthesia it will be easy to hold him with the vapor alone.

Most elderly patients do better with the combination of ether and chloroform than with any other anesthetic. When this is so, the index must be turned to a place between ether and chloroform and such a combination of these drugs maintained as will satisfy all given requirements.[1]

Pinneo has devised a very useful apparatus for vapor anesthesia, the vapor being heated by an ordinary electric bulb.

Endopharyngeal Anesthesia.—Karl Connell was the first to report a large number of cases by this method. We quote voluminously from his paper on automatic pharyngeal anesthesia:

Fig. 104.—Pinneo's Ether Vapor Apparatus in Use.

"In view of the objections to the endotracheal delivery, I have been led to seek a method which would overcome the necessity of intubation and the dangers of a badly supervised delivery, yet preserve the feature most desired for routine anesthesia, to wit, an automatic, even, accurate, and effective delivery of the anesthetic agent. In the pharyngeal insufflation method of large volumes of dilute anesthetic agent deep into the pharynx, I believe we have such a method. The delivery is established after full surgical relaxation has appeared by face-mask methods. Speaking now of ether vapor in air delivery, the essential feature of this pharyngeal method is that a volume of air is insufflated by positive pressure into the lower pharynx, a volume sufficient to provide entirely for each inspiration, without any air being inhaled by nose or mouth, and a volume bearing a known percentage of ether vapor in the greatest dilution which will hold that patient evenly and safely anesthetized for the operation in hand.

[1] For additional literature relating to the subject of vapor anesthesia, see Cullom: *J. Am. Med. Assn.*, Sept. 21, 1912, 1114; Hervey: *N. Y. Med. J.*, Nov. 9, 1912; and Pinneo: *J. Am. Med. Assn.*, Nov. 23, 1912, 1862.

"The delivery is accomplished by preference through two catheters inserted one through each nostril a distance, on the average, of 12 cm.

"The proper distance to insert each catheter is the distance measured

Fig. 105.—Pinneo's Mouth Tube for Continuous Vapor Anesthesia.

Fig. 106.—Endopharyngeal Insufflation and Mouth Tube Combined.

off on the tube from its eyelet, from the auditory meatus to the ala nasi on that side. This carries the tube well into the lower pharynx, but not into the esophagus.

"The catheters selected for the adult are size 18, F, soft rubber, velvet eye, with accessory eyelet. These are attached to a Y metal delivery tube with bent prongs for convenience of placement and to prevent angulation and to hold the catheters in place. This Y tube accurately fits the nose and forehead, and is held in place by adhesive plaster strapped across the brow.

"The volume insufflated is such as to entirely supply the needs of inspiration without extraneous dilution. This requires 18 liters of air per minute for the average adult, into which is vaporized the ether."

The essentials of endopharyngeal anesthesia, according to Connell, are as follows:

"First: The ether tension in the arterial blood to the sensorium is the determining factor of anesthetization.

"Second: This tension is established by maintaining in the alveolar air during preliminary narcosis an ether content of from 30 to 45 per cent by weight to air under conditions at sea level, an equivalent in pressure of from 119 to 182 mm. of mercury. During the early stage of anesthesia, say for the first twenty to forty minutes, this tension must be maintained by percentages scaling from 26 down to 15 per cent. After the establishment of anesthetic saturation of the body, it is maintained at about the latter percentage, the equivalent of an ether pressure of 48 mm. in the alveolar air.

"Third: These figures probably hold for the entire animal kingdom, the variable factors seen in ordinary etherization being these: Firstly, the rapidity with which the body is brought to complete anesthetic saturation, as determined by the efficiency with which the ether tension in the alveolar air is maintained by fresh delivery, by diffusion, and by tidal movement; secondly, the rapidity of blood circulation; thirdly, the bulk of the particular body to be saturated and the capacity of that body for storage and destruction of the ethyl radical.

"Fourth: The zones of anesthesia above and below this saturation or anesthetic tension point are already well established for man. With absolute certainty as to the outcome, man may be placed in an ether atmosphere of the percentage of ether or vapor pressure required to produce deep, medium, or light anesthesia.

"Fifth: The zone of surgical relaxation, i. e., an ether pressure of 45 to 50 mm., is a zone for many hours devoid of danger by ether intoxication.

"When one links these evident advantages of a full and continuing knowledge of the dose delivered, with the advantage of an even, automatic, unwearying, impersonal machine delivery of the anesthetic agent and its menstruum, the combination works for ideal anesthesia.

"For anesthesia to be maintained automatically, at the same time safely, with uniform success, requires that three factors be under the control of the operator or anesthetist: Firstly, that complete preliminary relaxation of the individual be secured; secondly, that the anesthetic agent and its menstruum be so delivered as to be freely available for respiration; thirdly, that the delivery be of such volume as to entirely supply the needs for respiration, as well as of such accurately measured and known percentage or tension of anesthetic as to hold a given individual safely and evenly anesthetized.

"For delivery to become automatic the anesthetic agent and its menstruum must be made freely available for inspiration by the delivery passing the chief obstruction, namely, the base of the tongue. Full preliminary anesthesia is best accomplished by face-mask methods, since man will not tolerate the introduction of pharyngeal or endotracheal tubes when conscious, nor breathe quietly in the subconscious stage of preliminary anesthesia the irritating vapors, i. e., 30 to 45 per cent of ether by weight, needed for establishment of complete anesthesia. These vapors to be inhaled quietly must be inhaled by the subconscious patient in such a way as to arouse no unusual impressions. Attempting to blow vapors of the strength needed for the induction of anesthesia into the pharynx or trachea results in straining, coughing, gagging, and the swallowing of air. Only when the patient is completely relaxed can insufflation methods be instituted. This period of face-mask delivery occupies six to twelve minutes for the most advantageous relaxation. If the operative procedure is now to occupy more than five or ten minutes, automatic insufflation may be established with decided advantage.

"Of course, it is to be distinctly understood that in the administration of anesthetics by the aid or means of automatic contrivances intelligent supervision is at all times necessary."

Connell[1] compares endotracheal and endopharyngeal anesthesia in the following manner:

"The ideal place to deliver ether vapor in air is, without question, directly into the trachea by insufflation through a loose endotracheal catheter after the method of Meltzer. For effective delivery, for complete and certain aëration, for even and controllable anesthetization, for freedom from shock and from the sequels of ether anesthesia, this method is not surpassed.

"Time does not permit me to elaborate on these nor on the various accessory advantages of this method, namely: the ability to maintain, when desired, positive pressure on the interior of the lung, to exclude mucous and other foreign material from the bronchial system, and to maintain an ideal artificial respiration if accident arises.

"The one and only hindrance to the establishment of the endotracheal delivery as a routine method of anesthesia is the act of intubation.

[1] Extracts from paper read by invitation before the first annual meeting of the American Association of Anesthetists, Minn., June 18, 1913.

"This alone, with its possible dangers, its ever-present delays, and occasional difficulty of intubation will, no doubt, effectively block the general adoption of this very useful and effective mode of delivery as a routine method of anesthesia."

Endopharyngeal anesthesia is not so thoroughly effective in control over aëration or over positive pressure, nor so effective in excluding foreign material from the larynx as the endotracheal delivery.

Oxygen-Ether Administration.—According to the investigations of some authorities, the apparent advantage by the administration of oxygen is in the exact and equal dosage at all times.

Hewitt states:[1] "There is little if any advantage to be gained by this system of anesthetizing, except in certain special cases. We have seen that in vigorous subjects some degree of air limitation is actually advantageous in conducting etherization. When we pass, however, from the vigorous subject, at one end of the scale, to the exhausted and feeble individual at the other, we have not only to be careful to provide a sufficient supply of air with the anesthetic, but we may even find it necessary to replace air by oxygen in our administration. Generally speaking, when respiratory embarrassment is present to such a degree that there is duskiness or actual cyanosis, ether is, as we have seen, contraindicated. In certain exceptional and desperate cases, however, in which defective blood oxygenation coexists with such a degree of cardiac derangement that the risk in giving a general anesthetic is that sudden syncope may arise from a very slight degree of respiratory embarrassment, ether may be the only permissible anesthetic, and under such exceptional circumstances as these the administration is best effected in conjunction with oxygen."

Others do not agree with Hewitt that little or no advantage is to be gained by the administration of oxygen with ether. On the other hand, we have every reason to believe that the after-effects of ether are considerably diminished by the combination with oxygen instead of air. Sufficient data are not at hand for us to speak authoritatively upon this subject. The administration of oxygen with ether is one of the simplest and at the same time safest procedures possible. Attach any vapor inhaler to the ordinary large hospital oxygen tank and allow the oxygen to pass through the ether, and this vapor to then pass through the water bottle and thence to the patient. A very simple apparatus for the administration of ether and oxygen can be quickly made as follows:

Procure two wash bottles holding about six ounces. Have the rubber stoppers perforated to hold small glass tubes, as in the ordinary wash bottle that accompanies any oxygen tank used in hospitals. The first bottle should be filled with four ounces of ether, the second bottle

[1] Hewitt: "Anæsthetics," 340.

with four ounces of water. Allow the oxygen-ether vapor to pass through the water bottle by a rubber tube connecting the two bottles. The efferent tube should then pass on to the patient. This vapor may be administered through the apex of an ordinary cone, the cone to be made more or less air-tight by towels wrung out in hot water placed around the margin of the cone and on the patient's face. We again refer to chart (page 668) of a patient anesthetized with oxygen and ether, showing the even pulse, temperature, respiration, and blood pressure. The only objection to the impromptu apparatus is the fact that the oxygen or ether cannot be increased or decreased separately, as in the Gwathmey or some similar apparatus especially made for that purpose. When using this method the patient should be anesthetized by the nitrous oxid-ether or oil of orange-ether sequence or the chloroform-ether sequence, and after reaching the surgical stage a switch should be made to the oxygen-ether combination. The pulse will be found to be full and bounding, the respirations deep and regular, and the color index marked. Sufficient air will be let in by such a mask to slightly dilute the oxygen. The oxygen-ether combination has not been tried out by the closed method except in very short cases, and is not recommended. Few complications will arise to give the anesthetist uneasiness when the oxygen-ether combination is administered with a suitable apparatus and by the open method, already described.

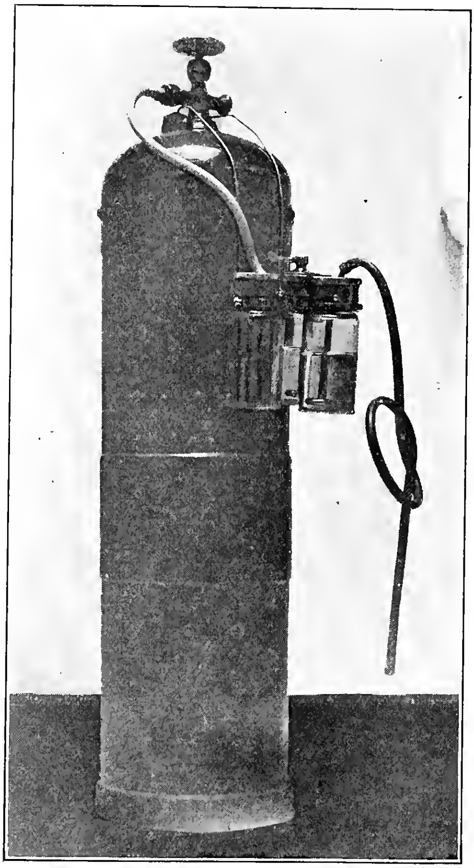


Fig. 107.—Three-Bottle Vapor Apparatus Attached to Oxygen Tank.

Concentration of Ether Vapor.[1]—Dreser has made laboratory experiments regarding the percentages of respirable ether vapor. Different accurate mixtures, placed in rubber bags, were inhaled by a number

[1] *Johns Hopkins Hosp. Bull.*, Jan., 1895, No. 6.

of men. All agreed that 8 per cent ether vapor was irrespirable, that 9 per cent caused contraction of the glottis, that 7 per cent caused irritation and cough, that 6 per cent was slightly irritating but not irrespirable, and that 5 per cent was usually respirable. Dreser concluded that: "A person in a conscious state should not inhale ether vapor exceeding 7 per cent. Now when a patient by inhaling a weaker concentration of ether vapor has been made insensible, to such a degree at least as to show no more reflex action, this very state will favor the injurious effect of the stronger concentration upon the lungs. As long as the

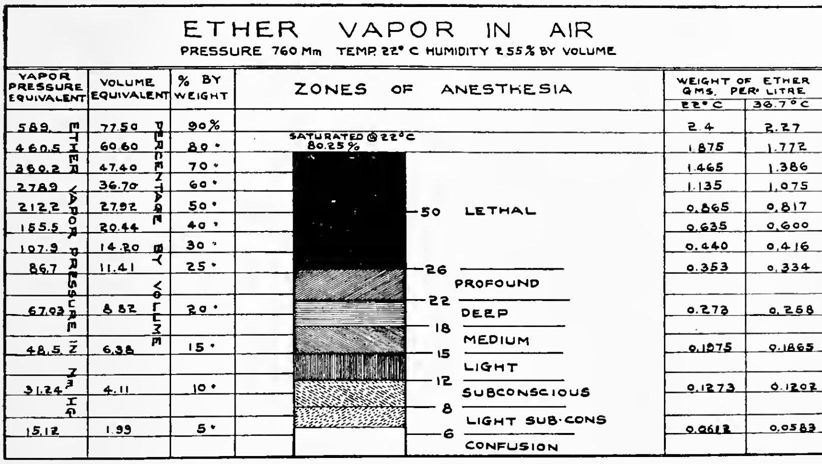


FIG. 108.—CHART I, SHOWING THE NECESSARY PERCENTAGE OF ETHER VAPOR FOR THE ENDOPHARYNGEAL OR ENDOTRACHEAL ADMINISTRATION.

patient is conscious, the reflex contraction of the glottis prevents the irrespirable gas or vapors from entering the finest air passages." The anesthetist should take care that the lungs of the narcotized patient are not injured. In a closed inhaler the percentage of carbonic acid met with in these experiments, even with healthy persons, was never high enough to produce the slightest narcosis, "therefore the percentage of carbonic acid met with in the air of the masks could not be looked upon as having a paralyzing or narcotizing effect."

Karl Connell[1] was the first to develop the accurate percentages of ether necessary for surgical anesthesia when given by the vapor method either endopharyngeally or endotracheally. These charts represent a composite of three hundred cases of surgical anesthesia at the Roosevelt Hospital charted after a working experience had been gained on a previous series of about six hundred cases.

Chart I indicates the zones of ether anesthesia in terms of weight

[1] Extracts from a paper read by invitation before the first annual meeting of the American Association of Anesthetists, Minn., June 18, 1913.

of ether to air delivered under working conditions. The volumetric equivalent and ether vapor pressure equivalent are tabulated in parallel columns, as is the absolute weight of ether per liter in the air at delivery and at body temperature.

These zones are for practical working guidance in surgical etherization, and are not absolute. The zones above the 15 per cent level gradually lower toward that level as the anesthetic tension of about 48 milli-

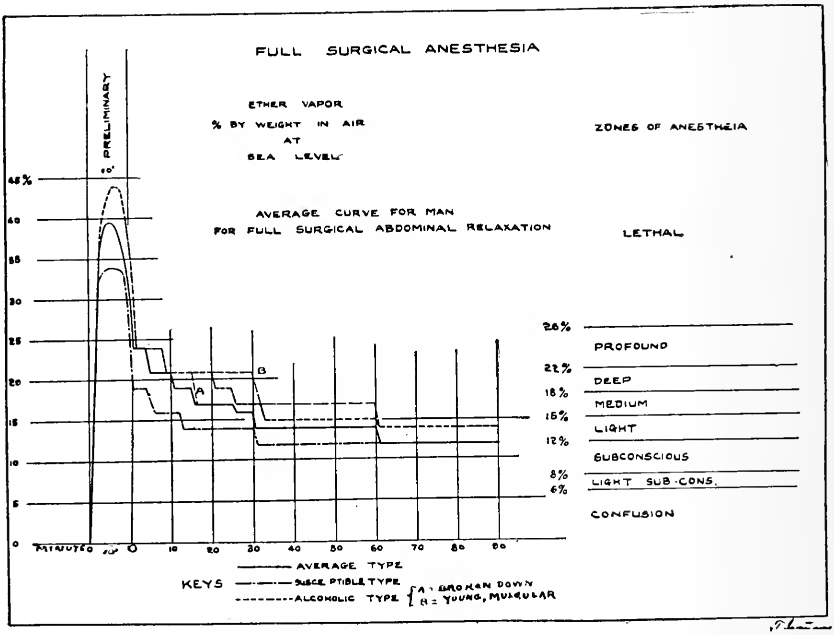


Fig. 109.—Chart II, Showing the Most Advantageous Ether Pressure.

meters of the entire body is attained. At the end of an hour of full anesthesia even the zone of deep anesthesia for a considerable length of time might result lethally. For example, when a dog, after anesthetic saturation, is carried in the zone of profound anesthesia by endotracheal delivery, respiratory effort ceases in about an hour, only to begin again when the ether tension is lowered. Such dosage would result fatally if provision is not made for artificial respiration. These zones are the same whether the delivery be by face-mask or by insufflation.

Chart II shows the most advantageous ether pressure to maintain in the pulmonary air, charted in terms of weight of ether in air under usual working conditions at sea level.

The percentages above 15 per cent during the preliminary and early stage of full surgical anesthesia are needed to establish the proper anesthetic tension in the arterial blood to the sensorium pending such time as the entire circulating and fixed tissues of the body are brought to uniform tension. As seen on the chart, there is a difference of 20 to 30 minutes between the length of time such saturation takes in a man of the young, robust, or alcoholic type to the much shorter time taken to saturate the small, relaxed woman or child. All types, however, when the general tension is once established, run on the same base line. This, for complete anesthesia, is between 14 per cent and 15 per cent by weight of ether, yielding a tension between 45 and 51 millimeters. The absolute point is not as yet fully established, but is probably about 48 millimeters. In fact, it would seem from preliminary observation that this tension is basic not alone for all types of man, but also for the entire animal kingdom. Below this level the operative case may be carried where only light anesthesia is desired, or when the operation reaches such a stage that protection against shock influence is no longer needed (i. e., that very effective protection conferred by full ether anesthesia), or where the anesthetist desires the patient to enter the zone of slow ether desaturation and recovering consciousness. This recovery zone may be so gauged that in short operations the patient leaves the table practically conscious and, even after long operations, in full possession of all pharyngeal reflexes.

Saturation of the arterial blood and sensorium is complete in the curve shown, to the extent of full surgical anesthesia, in about two minutes for each liter of circulating blood, being complete in medium-sized children in six minutes, and in the adult in twelve minutes. Operations, even major procedures, may be begun before full relaxation is established or at the peak of the preliminary curve, say at the end of six minutes in a docile adult. Yet where it is desired to fully protect the patient against shock-producing and inhibitory influences, it is desirable to wait for full surgical relaxation, i. e., about ten to twelve minutes.

While the arterial blood to the sensorium may be fully charged by high percentages within ten minutes, yet the general body of an adult is not brought to full tension, approximating 48 millimeters, by the delivery curve shown, for from forty to sixty minutes. Desaturation proceeds even more slowly, although marked changes of deadened or awakened sensibility may be seen within three minutes by increase or decrease of ten millimeters of ether vapor pressure in the air delivered. This sensitiveness is more pronounced before the anesthetic tension of the entire body is established. Partial recovery is more rapid than deepening anesthesia by changes of equal degree before saturation is complete. After the anesthetic tension is established, anesthesia may be more rapidly deepened than diminished, an observation readily explicable on physical and chemical grounds.

The patient may be carried in the zone of profound anesthesia or deep, medium, or light anesthesia at will. With the data at present in hand, the most advantageous anesthetization by ether can be plotted in advance for the type of individual and for the nature and stage of the operation, and maintained after the initial stage entirely automatically, and, were it desirable, without the presence of any anesthetist. The ether intoxication may be reduced to a small factor and shock influence effectively blocked.

Conclusions.—The percentages of ether needed by man are well established, and the most advantageous anesthesia may be plotted in advance. These percentages are probably basic for the animal kingdom.

Fig. 110.—Administration of Warmed Ether Vapor by the Closed Method.

A curve plotted for man for advantageous etherization rapidly ascends in the preliminary stage to 30 to 45 per cent by weight of ether in air, after five minutes it falls, reaching 26 per cent by the tenth minute, when surgical relaxation is well established. Through the next half hour it scales downward, reaching 15 per cent in 30 or 40 minutes. It runs on or about this base line for some hours, descending when the zone of recovery is desired to be entered.

The Closed Method.—When the closed method is decided upon, any mask and bag used in the gas-ether sequence may be employed. A rubber tube from the three-bottle vapor inhaler in this instance will be attached to the stopcock of the bag. The expiratory valve will be left slightly open so as to have the escape of a small amount of air at all times, while at the same time constant rebreathing is maintained. The inspiratory valve of the inhaler should be out of commission. Air should be constantly forced in, and the bag kept about nine-tenths full so that no effort either to inhale or exhale is exacted of the patient.

With vigorous pumping a bead of 1/8 to ¼ of an inch in height will be maintained in the ether bottle. Continuous pumping must be maintained throughout the administration of the anesthetic. Toward the close of the anesthesia the tubes from the pumping apparatus and of the mask should be detached from the three-bottle vapor inhaler and attached to the warming apparatus, and the patient's lungs thus thoroughly aërated before the mask is removed from the face, the bag to be 2/3 inflated as before. This should be done from five to ten minutes before the completion of the operation so that by the time the operation is

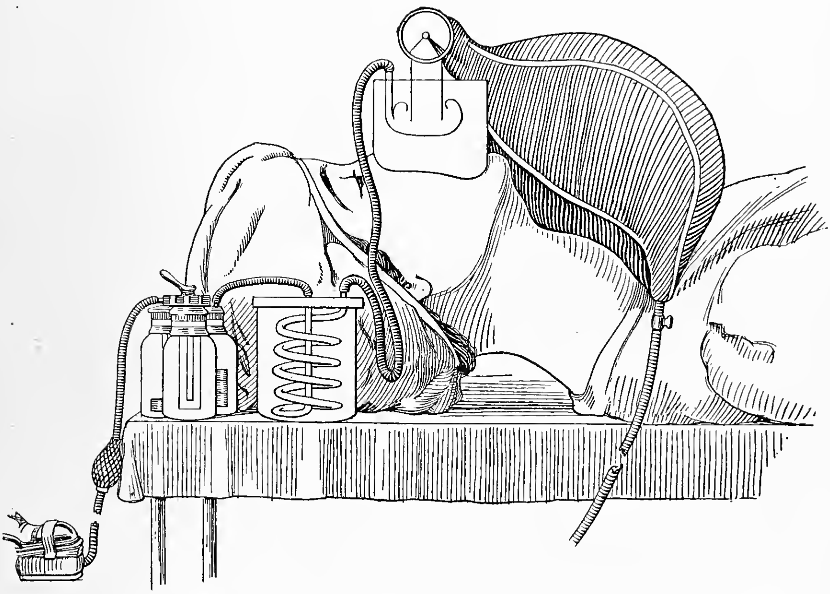


Fig. 111.—Diagrammatic Sketch of the Nitrous Oxid-Ether Vapor Sequence.

finished the patient's reflexes will all be present and he will be practically from under the influence of the anesthetic.

Amount of the Anesthetic Used.—With the closed vapor method usually two (rarely three) ounces of ether per hour are required; if three ounces are used the first hour, one ounce will suffice the second hour. With the open method, three to four ounces of ether are necessary to maintain complete relaxation.

Care of the Apparatus.—All the ether and chloroform remaining in the apparatus should be thrown away. The water bottle should be emptied and the bottles detached from the apparatus (this last procedure in order to save the rubber washers). The mask and bag should be thrown into the sterilizer and boiled as are other surgical apparatuses, or they should be thoroughly rinsed in carbolic 1-40 or bichlorid solution and then rinsed in cold water. If a tube or mouth gag is used, it should also be thoroughly boiled after each operation.

Hints.—The principal care of the anesthetist with any vapor apparatus is to see that there is no leakage either at the bottles or face-piece or bag, also that no kinks occur in the rubber tubing or that pressure is not made on the tube by assistants or nurses.

Advantages.—The following are the advantages of the vapor method:

First: The small amount of the anesthetic used, two to four drams for a thirty-minute operation, or two or three ounces of ether per hour.

Second: The technique is easily acquired.

Third: Objectionable mucous râle is usually entirely absent.

Fourth: In over ninety per cent of cases there are no unpleasant after-effects.

Fifth: A continuous plane of narcosis is easily maintained.

Sixth: An intermitting narcosis which is wrong in principle is avoided.

Seventh: The passage back and forth over the dangerous vomiting center is usually made easily.

Treatment of Accidents.—When respiration ceases the first thing to do is to give the patient a quick, hard slap upon the chest. If this does not start the respiration, the next movement is to place the hands upon the side walls of the chest and press very hard several times in succession. If the patient does not begin to breathe immediately the following procedures must be followed and in much quicker time than it takes to give the directions:

First: Insert a mouth gag and pull the tongue well forward.

Second: Lower the head, and while this is being done pressure upon the side walls of the chest must be continued. As soon as the patient is lowered to the Trendelenburg position, grasp the arms just above the elbows, and press them vigorously to the sides and then draw the arms backward and sideways over the head, at the end of this movement making considerable traction. Repeat this movement about 15 times to the minute. At the same time have an assistant dilate the sphincter ani. Another assistant can be vigorously massaging the precordial region while artificial respiration is being kept up. If there are a sufficient number of nurses or assistants standing around, bandages starting at the feet and continued to the thighs with the idea of expressing the blood in the extremities to the body is sometimes beneficial. If these procedures do not give some definite result within two minutes, the Lewis pendulum swing should be attempted.

If respiratory arrest is due to mucus or saliva, the anesthetic must be discontinued, a mouth gag inserted, and the upper air passages swabbed out with a sponge placed upon a long sponge holder.

If the fourth stage is brought on by hemorrhage or shock from handling important nerves or blood vessels, and the respiration is still good and a dilute ether vapor has been given, a Trendelenburg position with bandaging of the lower limbs and intravenous saline infusion will usually rectify this condition. If the fourth stage is anticipated from certain events, it may be sometimes prevented by a hot rectal saline infusion. It is not unusual where the patient is in an extreme condition to start a hypodermoclysis at the time the operation is commenced.

According to American statistics, one death occurs in 5,623 administrations of ether by the drop or vapor method. This means that death is due to gross carelessness or ignorance.

In extremely rare and unusual cases of status lymphaticus, in which the organs may be diseased and anomalous, such as a very small heart with a large aorta and enlargement of the tongue, it is quite conceivable that the heart may be paralyzed before the respiration ceases. When paralysis occurs from this condition it is usually during primary anesthesia. If the anesthesia is continued for 15 minutes or over, compensation occurs and a death after that time could hardly be attributed to this cause.

INDICATIONS AND CONTRAINDICATIONS OF ETHER

Indications.—Hewitt states that in "healthy and moderately healthy subjects the risk connected with the administration of ether is very slight, the reported fatalities having almost invariably taken place in exhausted or markedly diseased individuals."

The senior author agrees with Hewitt as to the risk connected with the administration of ether.

With the modern methods of administration, and with the combinations and sequences which make it possible to adapt the anesthetic to the patient, the indications for ether almost parallel the indications for operation, except, of course, for very short surgical interventions.

Ether is especially indicated to continue the narcosis in operations about the mouth or nose, such as excision of the tongue or lower jaw, where there is considerable shock.

Ether by the vapor or drop method is indicated for adenoid and tonsil cases, and wherever the status lymphaticus is suspected. Wherever a deep anesthesia is desired, ether by the closed method is indicated, as for amputations, dislocations, genito-urinary operations, laparotomies, excision of the breast, amputation of the cervix, vaginal and supravaginal hysterectomy, and in all conditions of shock and collapse.

Contraindications.—The first objection to any method of administration of ether is where the patient has suffered intensely from a previous administration of this drug, and expresses a decided dislike for the odor and after-effects. Such idiosyncrasies must be respected. The senior author knows of one death caused by disregarding this rule. The history of this case is appended.

Patient, female, aged 35 years. Operation, removal of ovarian tumor. The anesthetist was warned not to use ether, as nausea and vomiting of an exaggerated type had followed a previous administration of this agent. The anesthesia was begun with chloroform, but as surgical anesthesia was reached pulse, respiration, and color seemed to indicate a change. A few drops of ether were placed upon the mask to stimulate the patient. Almost immediately vomiting ensued. Upon deepening the anesthesia vomiting ceased, and a smooth narcosis ensued to the end of the operation. Ether was used from time to time as needed. As the patient came out of the anesthetic vomiting started again, and continued, with intermissions, for forty-eight hours. The character of this vomiting was so violent that a retention stitch was broken and a small piece of intestine was caught in the wound. When the dressings were removed the tissues along the line of incision appeared tense and swollen. Upon reopening the wound, the gut was found to be gangrenous, and this portion was removed under an anesthetic. In spite of good nursing, peritonitis and death followed.

Nitrous oxid and oxygen would probably have saved the life of this patient.

Kocher[1] states that respiratory disturbances and pathological changes in the respiratory organs, with dyspnea, are contraindications of prime importance. Ether, he holds, causes more suffering and more lasting damage to the respiratory organs than can be attributed to chloroform.

In lung and kidney disease, bronchitis, phthisis, dyspnea, and emphysema, and in ophthalmic operations, patients do better with some other anesthetic than ether.

In aneurism and atheroma ether is contraindicated. It is also contraindicated in acute attacks of asthma or bronchitis. In chronic bronchitis or asthma ether introduced cautiously and given by modern methods is perfectly safe. In any condition with high blood pressure ether is contraindicated.

Mortimer[2] states that ether should not, as a rule, be given to infants and young children, in whom it excites much mucous secretion which may embarrass breathing or lead to bronchitis.

Elderly people do not usually take ether well, because of the degenerate state of the respiratory and circulatory systems. Heavy smokers and people whose mouths and throats are in an unhealthy state, who are likely to cough and secrete much mucus and to have enlargement of the tongue and upper air passages, are considered by Mortimer[3] as unfavorable subjects for ether.

[1] "Text-Book of Operative Surgery," 50.
[2] "Anesthesia and Analgesia," 55.
[3] *Loc. cit.*

Ether is contraindicated if an actual cautery, a lamp, or any kind of electrical spark is to be employed.

Most writers state that ether is contraindicated in operations upon the brain, because of the desirability of having the field of operation as free from blood as possible. Many surgeons, however, prefer the drop, or vapor, method of ether in all operations upon the brain. Similarly, exophthalmic goiter is stated as contraindicated, but many surgeons prefer ether by the open method for this operation.

CHAPTER VI

ETHYL CHLORID

CHEMISTRY: Chemical History; History of Its Use as an Anesthetic; Uses; Preparation; Properties; Storage and Containers; Impurities Which May Develop in Ethyl Chlorid; Detection of Impurities in Ethyl Chlorid.

PHYSIOLOGY: Effects upon Respiratory System; Effects upon the Circulatory System; Effects upon the Nervous System; Effects upon the Muscular System; Effects upon the Glandular System; Causes of Death under Ethyl Chlorid Anesthesia; Stages of Anesthesia; Elimination; After-Effects; Comparison with Other Anesthetic Agents.

INDICATIONS AND CONTRAINDICATIONS.

ADMINISTRATION: Experimental Data; Methods of Administration; Open Method; Semi-closed Method; Closed Method; Combinations and Sequences.

BIBLIOGRAPHY.

CHEMISTRY

Chemical History.—Ethyl chlorid ("sweet spirit of salt"; *æthylum chloratum; æther chloratus; æther hydrochloricus seu muriaticus;* hydrochloric ether; chloro-ethane; monochlorethane; *chloræthyl; leichter salzather; ether chlorhydrique;* chelen or chelene; kelen or kelene; anodynone; antidolorin; ethylol; loco-dolor, etc.) was first obtained in alcoholic solution by Basil Valentine (*pseudo-*).[1] Sweet spirit of salt was

[1] He described its preparation thus (*Diederholung des grossen Steins der uralten Weisen,* ed. Petræus, p. 72): "This I also say that when the spirit of common salt unites with spirit of wine, and is distilled three times, it becomes sweet and loses its sharpness." In his "Last Testament" (*Basilius Valentinus,* ed. Petræus, p. 786) he also says: "Take of good spirit of salt which has been well dephlegmated and contains no watery particles one part; pour to this half a part of the best and most concentrated spiritus vini, which also contains no phlegma or vegetable mercury." Valentinus goes on to state that this mixture must be repeatedly distilled, and then "placed in a well-closed bottle and allowed to stand for a month or until it has all become quite sweet and has lost its acid taste. Thus is the spiritus salis et vini prepared, and may be readily extracted."

In 1739 Johann Pott demonstrated that sweet spirit of salt could be obwell known to the later chemists. Glauber, for example, referred to it in 1648.

In 1749 [1] Ludolff stated that, on heating alcohol with sulphuric acid and sodium chlorid, a distillate was obtained which, when treated with lime, yielded an ether, but he endeavored in vain to obtain a similar compound by the action of hydrogen chlorid (muriatic gas) on alcohol. Baumé was also unsuccessful in this direction, but Woulfe [2] obtained the preparation in this way, and it was afterwards prepared and sold by an apothecary in Germany under the name of "Basse's hydrochloric ether" (1801).

History of Its Use as an Anesthetic.—Flourens [3] drew attention to the anesthetic properties of ethyl chlorid in 1847, and Heyfelder, in the following year, first administered the vapor for surgical purposes. Unsatisfactory symptoms often accompanied its administration at that time, these effects being attributed to imperfection in the manufacture and the consequent presence of impurities. The use of the agent as a general anesthetic was abandoned until 1895, since which time it has rapidly gained in favor. This is principally attributable to the improved methods of administration and to an increase in the knowledge of its properties and physiological action; and last, but not least, to improvements in its manufacture.

Ethyl chlorid may be regarded as ethyl alcohol (CH_3CH_2OH), in which the OH has been replaced by Cl; hence the formula CH_3CH_2Cl, which was established by Colin and Robiquet.[4]

Alcoholic muriatic ether is a solution of ethyl chlorid in an equal amount of alcohol by volume. It has been used as an internal stimulant in doses of 0.6 to 1.8 c.c.

Uses.—So far ethyl chlorid has not been used technically, although Palmer [5] called attention to its advantages (and disadvantages) as an industrial refrigerating agent. In medicine it is used for (a) general anesthesia (by inhalation); (b) local anesthesia (by external application, in effect, refrigeration); (c) diagnostic and therapeutic purposes. Its physiological action will be referred to later.

Preparation.—As noted, ethyl chlorid may be regarded as ethyl alcohol (C_2H_5OH) in which the hydroxyl has been replaced by chlorin.

tained by the action of butter of arsenic or butter of antimony (arsenic or antimony trichlorid) on spirit of wine, and other chemists found that other metallic chlorids might be employed for the same purpose. Rouelle, in 1759, found that ethyl chlorid results from the action of sulphur chlorid, phosphorus pentachlorid, aluminum chlorid, ferric chlorid, stannic chlorid, etc., on alcohol.

[1] *Die in der Medicin siegende Chemie . . .*, Erfurt, 1746-9.

[2] *Phil. Trans.*, 1767, 520.

[3] Hewitt: "Anæsthetics," 1907, 11.

[4] *Ann. chim. phys.* (2), *1*, 343.

[5] *Eng. Digest*, *5*, 262.

Ethyl alcohol is the raw product from which it is usually made, although ethyl chlorid results in the regulated chlorination of ethane,[1] and on treating acetic and other ethers with hydrogen chlorid by the action of hydrochloric acid on ether in sealed tubes,[2] and by the action of chlorin on ethyl iodid. In actual practice ethyl alcohol is mixed with hydrogen chlorid, which acts as a desiccating agent itself,[3] or dehydrating agents, as zinc chlorid[4] or phosphorus pentoxid[5] are added to remove the water produced. If these agents were not added the reversible reaction would reach an equilibrium. This equilibrium may be avoided by increase of pressure.[6]

Impurities from Materials Used.—If pure hydrogen chlorid be used there is little danger of impurities being introduced from that source. The quality of the alcohol used, however, is very important. If denatured alcohol, especially if wood alcohol be the denaturant, or one of the denaturing substances, then methyl chlorid will likely be pro-

[1] Darling: *Ann., 150,* 216; Schorlemmer: *Compt. rend., 58,* 703.

[2] Berthelot.

[3] Ethyl chlorid may be prepared by distilling ethyl alcohol (5 parts), sulphuric acid (2 parts), and sodium chlorid (12 parts) together, or by passing dry hydrogen chlorid into absolute alcohol; but it is said that the action of hydrochloric acid upon alcohol gives a poor yield of chlorid unless zinc chlorid is added to the alcohol before passing in hydrochloric acid (Groves: *J. Chem. Soc.,* 1874, *27,* 637). Groves found that when hydrochloric acid gas was passed into a boiling solution of zinc chlorid (2 parts) in 95 per cent ethyl alcohol (3 parts), the yield was nearly theoretical. He purified the product by washing with water.

[4] Kruger [*J. prakt. Chem.* (2) *14,* 193] recommended that a mixture of one part of zinc chlorid in 82 parts of ethyl alcohol should be saturated with hydrochloric acid gas in the cold, and then heated to the boiling point. Hydrochloric acid gas being conducted into the mixture during distillation, as the process is carried out, a reflux condenser prevents the alcohol vapor from coming over, and the zinc chlorid is said to act by abstracting water from the alcohol, the nascent ethylene combining with hydrogen chlorid to form ethyl chlorid, according to Schorlemmer (*J. Chem. Soc.,* 1876, 308). On the action of hydrochloric acid on alcohol, alone and in the presence of zinc chlorid, see also Robiquet and Colin: *Ann. chim. phys.* (2), *1,* 343; Regnault, *ibid.* (2) *71,* 355; Kuhlmann: *Ann., 33,* 108; and Lowig, Pogg.: *Ann., 45,* 346. On velocity of the reaction, see Kailan: *Monatsh.,* 1907, *28,* 559. The formation of ethyl chlorid in this process is partly due to the action of hydrogen chlorid upon alcohol, and partly to the union of this nascent ethylene with hydrogen chlorid.

[5] The practice of some American manufacturers is to use phosphorus pentoxid as the dehydrating agent.

[6] The process of Mennet and Cartier (French Patent, 206, 574, June 23, 1890) relates to the production of ethyl chlorid. An autoclave of 150 liters capacity is used, into which a mixture of 95 kg. of hydrochloric acid (21° Be.) and 34 kg. of 93–95 per cent ethyl alcohol is maintained at 50 atmospheres pressure and at 130° C. for about 28 hours. The pressure is then diminished to 42 atmospheres, and finally the autoclave is cooled. See also Hager's *Handbuch d. pharm. Praxis,* 1910, *1,* 189.

duced. This gas (b.p., —24° C.), while very soluble in ethyl chlorid, may easily be removed by rectification. Aldehyds form compounds with hydrogen chlorid. Any acetic acid present is liable to form acetyl chlorid, and the higher alcohols, as propyl, butyl and amyl, produce their corresponding halogen derivatives. It is desirable, therefore, to use only absolute alcohol of the highest degree of rectification.

An examination of seven different makes of ethyl chlorid obtainable in London in 1905 showed that all the branded samples were pure, as was also one unbranded sample. The report of this investigation [1] states that ethyl chlorid should be free from water, foreign chlorids, acids, aldehyds, ether, alcohol, and organo-metallic substances.

Purification.—Ethyl chlorid is purified [2] by passing the vapor through water, dilute caustic solution, and then concentrated sulphuric acid. This treatment is intended to free it from alcohol,[3] hydrogen chlorid,[4] and water. Redistillation is sometimes practiced. This rectification serves to remove other alkyl chlorids, the methyl going off in the first fractions of the distillate, and the higher compounds remaining in the residue.

Properties.—Ethyl chlorid is a colorless mobile liquid at low temperatures and is exceedingly volatile. It possesses a sweetish taste and a pungent, yet fragrant, "ethereal" odor. It is inflammable, burning, when ignited, with a smoky green-edged flame, producing fumes of hydrogen chlorid; hence care must be exercised in using it near an open flame or a hot cautery. It even decomposes when very close to a hot bulb or an incandescent electric light.

Ethyl chlorid does not freeze at —29° C.; it possesses a boiling point of +12.5° C.[5]; and its specific gravity is 0.92138 at 0° [6], 0.9176 at +8° [7], 0.9510 at +12° [8], and at +25° [9] the vapor has a specific gravity of 0.91708. Its vapor density is 2.22.

Water dissolves about one-fiftieth of its weight of ethyl chlorid and acquires a sweetish, ethereal taste. Ethyl chlorid is readily soluble in ethyl alcohol and ethyl ether, and neither solution should give a reaction with silver nitrate solution, as ethyl chlorid itself does not react with silver nitrate at ordinary temperatures. Ethyl chlorid dissolves phosphorus, sulphur, fats, oils, and many resins. It combines with many

[1] *Lancet*, 1905, ii, 1631.

[2] *Pharm. J.* (4), *15*, 694.

[3] Acetyl chlorid decomposes to acetic and hydrochloric acids with water.

[4] And other bodies forming acids with water.

[5] Regnault: *Jahresber.*, 1863, 67.

[6] Pierre: *Compt. rend.*, *27*, 213. Darling (*Jahresber.*, *21*, 328) found a density of 0.9252 at this temperature.

[7] Linnemann: *Ann.*, *160*, 195.

[8] Ramsay: *J. Chem. Soc.*, *35*, 470.

[9] Perkin: *J. prakt. Chem.* (2), *31*, 481.

metallic chlorids—for example, antimony pentachlorid and ferric chlorid —to form crystalline compounds.

Storage and Containers.—Owing to its extreme volatility, ethyl chlorid cannot be kept in ordinary bottles, except at a temperature be-

FIG. 112.—SEALED TUBES OF ETHYL CHLORID. These contain 3 and 5 c.c. for use in various inhalers for general anesthesia.

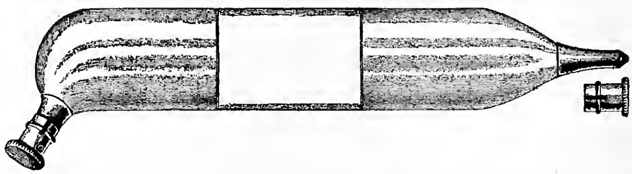


FIG. 113.—DOUBLE-END ETHYL CHLORID TUBE. This possesses the advantage of enabling the operator to utilize the spray whose emerging angle will be most convenient. They are put up in 10 and 30 gm sizes.

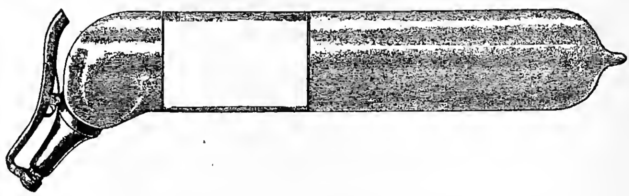


FIG. 114.—AUTOMATIC CLOSING TUBE FOR ETHYL CHLORID. These are made to hold 10, 30, and 60 gm of ethyl chlorid and are used for local and general anesthesia. They may be graduated. The tube is glass, but the automatic cap is made of a noncorroding metal.

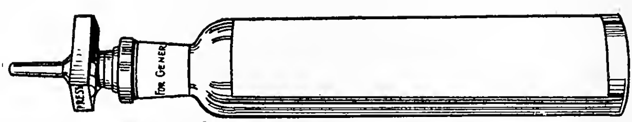


FIG. 115.—AUTOMATIC CLOSING TUBE FOR ETHYL CHLORID. It is graduated in cubic centimeters for discharging any desired amount and containing 60 c.c.

FIG. 116.—FLEXIBLE SPRAYING NOZZLE. This is detachable, made of soft German silver tubing, and enables the operator to reach any tooth and to enter the nose, throat or external auditory canal to apply ethyl chlorid as a local anesthetic.

low +10° C., and even then the stopper must be tight-fitting and very well secured, and the bottles should preferably be stored in an inverted position. Ethyl chlorid is now supplied on the market in sealed or mechanically capped glass or metal tubes of convenient forms, wherein the ethyl chlorid is held under pressure. Automatic closing tubes are preferable for local anesthesia, and there are at least five different types of these on the American market, each manufacturer using his special form of container, some of which are described here. Ethyl chlorid is also furnished by certain manufacturers in plain capped tubes.

Containers of ethyl chlorid should be kept in a dark, cool place, remote from lights or fire; and no empty tubes should be refilled with a

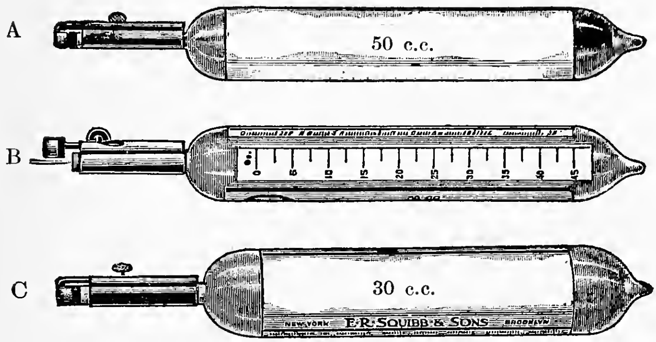


Fig. 117.—Ferguson's Ethyl Chlorid Tubes for General and Local Anesthesia.

A.—50 c.c. tube of ethyl chlorid intended for general anesthesia only. The capillary is gauged so as to deliver the proper amount of ethyl chlorid in the right time to produce a satisfactory narcosis. It is graduated and has a large capillary bore. It is not adapted for producing local anesthesia.

B.—50 c.c. tube open, showing the graduations.

C.—Tubes containing respectively 30 c.c. or 60 c.c. of ethyl chlorid are made for local anesthesia only. The capillary on each is of the same size, and is gauged so as to deliver the minimum amount of ethyl chlorid compatible with a good local anesthesia, thereby preventing waste. These tubes differ from the 50 c.c. tube in capacity and size of capillary bore, and are not adapted for producing general anesthesia except in the case of infants or young children, and very susceptible subjects.

Open the tube by pushing the thumb button forward as far as it will go in a direction parallel with the long axis of the tube. Do not press down on the button, as by doing so the capillary tube may be broken. When through using, remove the thumb from the button and allow the spring to bring the cap back in place; the tube is thus closed instantaneously and tightly. If any foreign matter becomes lodged on the end of the capillary tube, interfering with its free working, gently wipe it off with the finger, at the same time grasping the tube in the hand to cause pressure by body heat and to drive the obstructing particles out. Never try to free it with a needle, pin or other instrument.

fresh lot of the compound, since such an economy may result in spreading infection.

Glass as Compared with Metal Containers.—It is maintained by some that ethyl chlorid decomposes when exposed to air and sunlight; hence that the drug should be kept in metal containers. It is further claimed that, inasmuch as ethyl chlorid is inflammable, there is less danger of breaking in accidentally dropping the metal container. In opposition to this, it may be said that, in filling any container, no air remains in it on account of the great volatility of ethyl chlorid. Furthermore, in drawing off a portion of the contents of a tube, pressure is produced within the tube which is constant for each temperature, it matters not how much liquid ethyl chlorid is present, so long as there is some liquid there; hence no backward pressure is created, whereby air may be sucked into the tube. Undoubtedly light facilitates the decomposition of ethyl

Fig. 118.—The Gebauer Container for Ethyl Chlorid.

chlorid by oxygen, but it has not been shown that light produces any change in ethyl chlorid when oxygen is absent. Assuming that the ethyl chlorid is pure, there is another objection to the use of a metal

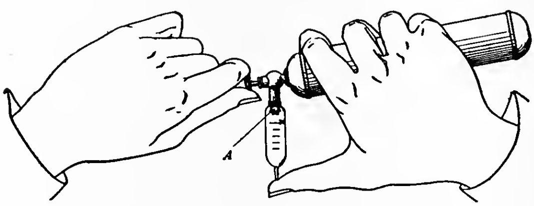


Fig. 119.—Technic of Ethyl Chlorid Measure-Dropper. Attach the measure-dropper to an ethyl chlorid tube; holding the tube in a horizontal position with the apex of the dropper pointing down, open the valve in the tube by gradually turning the screw to the right, allowing the ethyl chlorid to fill the chamber in the dropper, at the same time holding the thumb over the opening in the apex of the dropper as shown in cut. When the graduated chamber in the dropper is filled to the desired amount, close valve again.

Now hold the tube with the apex of the dropper pointing downward about two or three inches directly above the gauze in the inhaler and remove the thumb. The ethyl chlorid will now issue from the dropper in forms of drops, which are directed upon the gauze in the inhaler. As a general rule 3 to 5 c.c. will suffice to anesthetize a person for a short operation, but there is no fixed rule as to the quantity of ethyl chlorid required, since some will take more than others. The anesthetist must be guided entirely by the symptoms of his patient as to the duration and quantity of the ethyl chlorid required. If it is observed that 3 c.c. will not suffice to anesthetize the patient, one simply opens the valve again in the tube and lets 1 or 2 c.c. more of ethyl chlorid flow into the graduated chamber of the dropper and proceeds as before. If the ethyl chlorid does not drop fast enough from the apex of the dropper, it can be made to drop faster by placing the thumb or finger over the opening in the neck of the dropper marked "A". With a little practice the dropping may be regulated.

container, namely, inability to tell how much of the preparation is within the tube and how much has been or is being used in the anesthesia. This has been met by having a graduated (3 c.c. capacity) dropper made of glass, which may be attached to the metal container. The design of such a dropper is shown in Figure 119.

Impurities Which May Develop in Ethyl Chlorid.—Uncertain results have been encountered by several who have used ethyl chlorid for general anesthesia and these have been attributed in some cases to impurities that were present and were later detected chemically.[1]

The original product must not have been properly purified, for the conditions essential for the decomposition of ethyl chlorid itself involve oxygen, and, as animadverted, oxygen has no opportunity to enter the receptacle in which ethyl chlorid is dispensed. The presence of small amounts of water may bring about a reverse change in ethyl chlorid, with the formation of ethyl alcohol and hydrogen chlorid. The latter may readily be detected by spraying some of the drug into a clear silver nitrate solution. The appearance of a turbidity indicates free hydrogen chlorid, as pure ethyl chlorid does not thus react with silver nitrate.

Detection of Impurities in Ethyl Chlorid.—The impurities likely to occur in ethyl chlorid are (a) those which it brings with it from the manufacturer and (b) those resulting through careless storage. While the exact nature of all of these is unknown, yet ethyl chlorid, complying with the requirements of the pharmacopœias as given below, is entirely suitable for the purposes for which it is intended. On account of its volatility, the examination of ethyl chlorid presents more difficulties than are encountered in the cases of ethyl ether and chloroform; and it is indeed fortunate that it may be easily prepared in a state of comparative chemical purity.

The *Pharmacopœia of the United States*[2] prescribes the following tests for purity:

1. "If 10 c.c. of ethyl chlorid, while cold, be dissolved in alcohol, and a few drops of silver nitrate T. S. be added, no turbidity should be produced (*absence of hydrochloric acid*).

2. "If 10 c.c. of ethyl chlorid be agitated with 10 c.c. of cold water and the supernatant stratum of ethyl chlorid be evaporated spontaneously, and if a few drops of potassium dichromate T. S. be added to the remaining aqueous liquid, followed by some diluted sulphuric acid, and the mixture be boiled, no odor of aldehyd should be developed, and a greenish or purplish color should not be produced in the liquid (*absence of alcohol*).

3. "On allowing ethyl chlorid to evaporate from clean, odorless blotting paper, which has been saturated with it, no unpleasant odor should remain upon the paper (*absence of sulphur compounds*, etc.)."

The *British Pharmacopœia* requires that it should leave no residue on evaporation and that an aqueous or alcohol extract should have no acid reaction with blue litmus paper. The *Deutsches Arzneibuch*[3] requires

[1] Hawley: *J. Am. Med. Assn.*, 1906, *47*, 502.
[2] 8th decennial revision, 32.
[3] 1910, 37.

also that "during evaporation, and, thereafter, no garlic odor should be apparent (phosphorus compounds)." The *French Codex,*[1] while giving the incorrect specific gravity, states it should be free from ethyl bromid and iodid. The *Pharmacopœia Helvetica*[2] requires that, when its vapors are led through water, the water must not give an acid reaction with litmus nor a reaction with silver nitrate.

All the tests seek to eliminate acids.

PHYSIOLOGY

One of us (J. T. G.) has not employed ethyl chlorid, either in the laboratory or in the operating room, to such an extent as to warrant the consideration of this agent from the point of view of personal experience. In the pages which follow, therefore, the reported work of other investigators is freely and almost exclusively utilized.

Effects Upon the Respiratory System.—The effect of ethyl chlorid upon the lungs, according to Müller,[3] is pathological rather than physiological. Cole[4] found that, when given in the form commercially known as *somnoform* (see p. 818), ethyl chlorid markedly increased the size and rate of contraction and the tone of the diaphragm, which remained in a state of strong tonic contraction, the heart still beating strongly.

Embley[5] found, from his experiments upon animals, that, as the blood pressure fell, respiration ceased, and, as the blood pressure rose, the respiration returned. He does not, therefore, agree with other investigators in the view that respiration may be paralyzed by ethyl chlorid independently of fall of blood pressure, in ordinary administra-

[1] 1908, 249.

[2] 1907, 27.

[3] Müller, B.: "Narkologie," *1*, 454.

[4] Cole: *Proc. Physiol. Soc.*, June 15, 1903; *J. Physiol.*, *29*, 25.

[5] Embley: *Proc. Roy. Soc.*, *78*, 31 (1906); *Pharm. J.* (4), *24*, 650; *Lancet*, April 20, 1907. The solubility of ethyl chlorid vapor in water at normal pressure and +21° C. is 253.36 per cent by volume (0.678 per cent by weight); and the solubility in blood is approximately 500 per cent of vapor by volume at 38° C. The heart muscle is paralyzed by ethyl chlorid just as it is by chloroform and in contrast with ethyl ether, but the quantity of ethyl chlorid vapor in air required is nineteen times as great as that of chloroform to produce similar results. On the vascular system the net result is dilatation, but the degree of paralysis is strikingly less than that produced by chloroform, even when the latter is present in less than one-tenth of the quantity of air inspired. A strength of 5 to 7 per cent of ethyl chlorid vapor in the air required appears to be the limit of safety from danger of syncope in dogs for prolonged and continuous administration, and the conclusions arrived at by Embley are considered to apply to man. For the administration of ethyl chlorid he advises employing a gasometer containing the proper mixture of air and ethyl chlorid vapor.

tions. Respiratory arrest is preceded by a remarkable prolongation of the respiratory pause. In none of Embley's experiments was the heart arrested before respiration. The integrity of the respiratory mechanism in ethyl chlorid narcosis, he holds, is dependent upon the maintenance of blood pressure.

Respiratory frequency is not affected as a rule; but McCardie [1] states that ethyl chlorid quickens and deepens respiration.

Effects Upon the Circulatory System.—According to Müller,[2] the solubility of ethyl chlorid in water is slight and the solution very loose, for which reasons the blood-serum takes up only a slight amount. It is not much more soluble in blood-serum than in pure water. A small amount is, however, taken up by the blood corpuscles. On account of its slight solubility in blood-serum, very highly concentrated mixtures of air and ethyl chlorid must be carried to the lungs, for, in consequence of the loose solution, the vapor is at once given off from the blood, the patient awakening promptly unless such highly concentrated mixtures are administered.

Embley,[3] who investigated the pharmacology of ethyl chlorid, found that the solubility of the vapor in water at normal pressure and 21° C. is 253°, 36 per cent by volume (0.678 per cent by weight); and the solubility in blood is approximately 500 per cent of vapor by volume at 38° C.

Camus and Nicloux [4] found that ethyl chlorid is taken up by the blood with great rapidity, and that it is also eliminated very rapidly.

All authorities are agreed that in full surgical narcosis with ethyl chlorid a very great fall in blood pressure is noted. Even when given for a short time, according to McCardie,[5] a fall of blood pressure takes place.

Embley [6] says: "The effect of ethyl chlorid upon the heart muscle, as is the case with chloroform, is paralytic, but the quantity of ethyl chlorid vapor required in the air is nineteen times as great as that of chloroform to produce comparable results." He further states that the effect of ethyl chlorid upon the arterioles isolated from the central nervous system is relaxation. (In this respect also it is similar to chloroform, but the amount required is vastly greater.) The effects upon the vasomotor mechanism also are parallel with the action of chloroform. From his experimental work Embley found that the action of ethyl

[1] McCardie: "The Position of and Mortality from Ethyl Chloride as a General Anesthetic," *Brit. Med. J.*, March 17, 1906, 616.

[2] Müller: *Loc. cit.*

[3] Embley: *Proc. Roy. Soc.*, *78*, 31 (1906); *Lancet*, April 20, 1907; *Pharm. J.*, *24*, 650.

[4] Camus and Nicloux: *Compt. rend.*, *145*, 1437.

[5] McCardie: *Lancet*, Oct. 7, 1905; *Brit. Med. J.*, March 17, 1906.

[6] Embley: *Loc. cit.*

chlorid on the vascular system caused dilatation. The degree of paralysis, however, is strikingly less than that produced by chloroform, "even when the latter is present in less than 1/10 of the quantity of the air inspired."

Embley concludes: (1) That vagus inhibition of the heart occurs very readily in ethyl chlorid vapor of a strength of ten per cent and upward when administered in the air inspired; (2) that sudden fall of blood pressure occurred during the administration of ethyl chlorid vapor in a strength ranging from ten to twenty per cent, owing to vagus inhibition of the heart. If thirty per cent is administered, fall of blood pressure is due to weakening of the cardiac arterial musculature; (3) that cardiac inhibition is not so serious from ethyl chlorid as it is from chloroform. It requires nineteen times more ethyl chlorid to produce a given degree of cardiac depression than is required of chloroform, while it requires only four times as much to produce cardiac arrest by vagus stimulation; hence, inhibition sets in relatively more rapidly. Herein rests the relative safety of ethyl chlorid.

Webster,[1] who experimented upon animals with ethyl chlorid, ethyl bromid, and ethyl iodid, says: "The difference of any action between the chlorid, bromid, iodid and *somnoform* is one of degree only and this degree seems to depend upon the volatility of the drugs." With small doses he found that there was a slight rise in blood pressure, followed by a return to normal, whereas, with larger doses, the pressure rapidly fell.

Buxton [2] states that flushing of the face, due to dilatation of the peripheral vessels, is always associated with ethyl chlorid inhalation, and may account, in part, for any fall of blood pressure that takes place. When large doses of ethyl chlorid are employed the circulatory changes are secondary to the respiratory changes.

Effects Upon the Nervous System.—Müller holds that the blood carries the gas into the cerebrum and to the ganglion cells, into the fluids of which the ethyl chlorid passes, and is taken up by the cholesterin-lecithin mixtures. This results in paralysis of the cells. But, as the solubility in the cell-juice is slight, only a small amount of ethyl chlorid enters into the cell, insufficient, in short narcosis, to paralyze all the cells. Although the centers of pain-sensation may be paralyzed, the quantities do not always suffice to paralyze the more resistant centers against narcotic agents; as a result, the reflexes, the muscles, and so forth are not completely paralyzed, inhibited, or relaxed in the anesthesia. It is only after the ethyl chlorid vapors have been inhaled for some time that larger amounts of these vapors collect in the central elements of the ganglion-cells, in the cholesterin-lecithin mixtures (which dissolve larger

[1] Webster: *Bio-Chem. J., 1,* 328 (1906).
[2] Buxton: "Anæsthetics," 256.

quantities of ethyl chlorid than water or blood-serum), inducing a total paralysis of the centers.

The action upon the nerve tissue was studied by Cantelupe, who found that ethyl chlorid exerted a double action; on the one hand a direct chemical action, and on the other an indirect action, due to cerebral anemia through paralysis of the vasomotor center. The fibers of the white substance, in the cerebrum as well as the cerebellum, are found to present slight degenerative changes, which are interpreted as the expression of the nutritive changes of the nerve-cell, and therefore also of its nervous process, and which still persist at the period of awakening. Such changes may be purely functional, and therefore curable.

Effects Upon the Muscular System.—Muscular rigidity may be present during the stage of excitement. In some cases, according to Hewitt,[1] muscular relaxation accompanies stertor, but there is more often some rigidity. This rigidity in some subjects may be so general as to culminate in opisthotonos. The strong tendency to contraction of the masseter muscles has been noted by all administrators of this ethyl chlorid.

Effects Upon the Glandular System.—It is held by various observers that the gastric and intestinal functions are slightly influenced; the secretions of the liver and the kidneys are diminished.

Causes of Death Under Ethyl Chlorid Anesthesia.—From the foregoing discussion of the effects of ethyl chlorid upon the organism we may agree with the statement of Hewitt[2] that ethyl chlorid may prove fatal in two distinct ways, *viz.:* (1) by *simple overdose, ethyl chlorid toxemia, or ethyl chlorid syncope;* (2) by *intercurrent respiratory embarrassment* (*asphyxia*).

The prominent features of simple overdose, as noted by Hewitt, are: pallor, pulselessness, arrest of breathing, wide dilatation of the pupils, general muscular flaccidity and separation of the lids. Cardiac arrest quickly follows.

In death from asphyxia with ethyl chlorid the intercurrent respiratory embarrassment, according to Hewitt, may depress a circulation already depressed by the agent. The prominent features in this instance are: spasm about the jaws, mouth, tongue, larynx, or respiratory muscles. Respiratory arrest, with some cyanosis, supervenes, followed by cardiac arrest.

(For the mortality of ethyl chlorid, see Appendix on Statistics.)

Stages of Anesthesia.—The stages of ethyl chlorid anesthesia are a little different from those of the other pulmonary anesthetics.

The *first stage* is an analgesic stage which commences after two or three breaths of the anesthetic, and which lasts over thirty seconds.

[1] Hewitt: "Anæsthetics," 439.

[2] *Ibid.*, 455.

This is the stage before stertor and other signs of anesthesia appear. It is sufficient for opening an abscess, but the operator is taking the risk of causing pain unless he works rapidly.

The *second stage* is a true anesthetic stage which lasts from one to three minutes after removing the mask from the face. In fact, the anesthetic stage is sometimes deepened after the removal of the mask, owing to the absorption of the ethyl chlorid from the lower air passages. On account of the spasm of the masseter, as frequently happens during this stage, it is necessary that a dental prop be inserted between the teeth in *all* cases, and not only when intra-oral operation is contemplated.[1]

The *third stage* is again one of analgesia. It lasts from 30 to 40 seconds, during which no sensation is felt, but the patient may talk or move slightly. Just before the patient becomes conscious, swallowing occurs for some little time. The first sense to return is hearing, and the next is sight.

The *fourth stage,* when the administration is continued too far, corresponds to that of other inhalation anesthetics under the same circumstances, *viz.,* the bulb is affected, causing cessation of respiration, arrest of the heart, and death.

In prolonged ethyl chlorid narcosis, Müller distinguishes four stages, as in all narcoses. The first and second stages are very brief. The reflexes, however, are lost, and the pupils present exactly the same behavior as in other narcoses. In the brief narcosis, on the other hand, the pupils continue to react, nor are the other reflexes lost.

Herrenknecht,[2] whose experience with ethyl chlorid as a narcotic agent was so entirely satisfactory that he earnestly endorsed its employment, distinguished four stages of narcosis, as follows: (1) The prenarcotic analgesic stage; (2) the stage of excitement; (3) the stage of deep sleep; (4) the post-narcotic analgesic stage.

The *first stage,* according to Herrenknecht, is chiefly characterized by the diminishing frequency of the pulse and respiration, the deepening of the respiration and the onset of moderate muscular tension. The eyeballs are almost invariably turned upward. The patient is still conscious, however, and aware of the fact that he is being operated upon, although there is not the least sensation of pain. The hearing is still completely preserved in this stage.

The *second stage,* or stage of excitement, occurred only rarely in the experience of Herrenknecht, and was limited to habitual abusers of alcohol and to very nervous and excitable patients. As a prophylactic measure, he always administered morphin, or preferably morphin-

[1] Boyle: "Practical Anesthetics," 126.

[2] Herrenknecht: "3000 Aethylchloridnarkosen," *Münch. med. Woch.,* 1907, No. 49, 2421.

scopolamin, to patients of this type, prior to the narcosis; and more ethyl chlorid was injected into the mask, in order to hasten the third stage.

The *third stage* is characterized by muscular relaxation, and complete loss of reaction to external stimuli; the conjunctival and corneal reflexes have disappeared; the patient appears as if quietly asleep.

The *fourth stage* resembles the first, except that the patient conveys the impression of being wide awake; there is no noteworthy pain. The fourth stage is hardly ever absent, not even when the third stage has not been reached and the supply of ethyl chlorid has been stopped after the onset of the first stage. The end of the fourth stage is recognized by the movements of defense on the part of the patient, and the manifestation of pain on operative interference.

The signs of complete anesthesia under ethyl chlorid are: (1) A quick, deep, and regular respiration; (2) eyeballs fixed or rolling; (3) face usually slightly flushed; (4) muscular relaxation or rigidity; (5) pupils widely dilated; (6) absence of conjunctival and corneal reflexes.

A continuous, safe narcosis is not easily maintained with the present methods. Much cyanosis is a signal for the admission of air or the temporary discontinuance of the anesthetic. Respiratory embarrassment and spasm of the jaw are common in muscular subjects. Increasing stertor is a signal for more air.

The best guide is probably the respiration. If the anesthesia is very deep, cessation of the administration is indicated. It is to be borne in mind that anesthesia is deepened after the administration is discontinued, owing to the absorption of the agent from the lower air-passages. The pulse is usually slow.

The *signs of an overdose* are: (1) Unusually widely dilated and fixed pupils; (2) very great pallor; (3) intermittent respirations or gasping for breath.

Elimination.—Experiments were performed by Lotheissen,[1] to determine if ethyl chlorid was still demonstrable in the expired air some time after the narcosis. For this purpose, the expired air was passed through a pure concentrated alcoholic solution of potassium hydroxid into water, which was then heated and mixed with a solution of silver nitrate, in order to test for the presence of chlorin. The reaction never occurred when the inspired ethyl chlorid was expired through this apparatus; whereas it appeared at once after the direct introduction of even small traces of ethyl chlorid vapor. Upon the basis of these observations, Lotheissen concluded that ethyl chlorid was not breathed out again in the undecomposed state, the chlorin, at least, disappearing from the expired air. But as this air did not possess the odor of mus-

[1] Lotheissen: "Aethylchlorid Sauerstoff Narkose," *Arch. klin. Chir.*, 1910, *91*, 65.

tard-oil, Lotheissen was of the opinion that a chemical change occurred; perhaps the formation of ethyl thiocarbimide (C_3H_5NS), for the lungs have a strong reducing power. At any rate, the ethyl chlorid does not remain fixed for any length of time, so that it cannot exert a prolonged narcotizing effect, which means a great advantage in case of threatened asphyxia.

The excretion of ethyl chlorid [1] takes place mostly through the lungs; especially in brief narcosis nearly all the vapors are again eliminated by the lungs relatively rapidly on account of the looseness of the solution in the blood. The kidneys and other glands enter only very slightly into consideration in brief narcosis, essential amounts of ethyl chlorid being eliminated by those organs only in prolonged narcosis. The very slight solubility in the blood-serum also induces the complete absence of gastric affections, nausea, vomiting, etc., after brief narcosis, for the small quantities in the blood are at once eliminated and do not pass into the gastric juice, or do so only in very minute amounts, devoid of any effect. In prolonged narcoses, larger amounts enter the blood and are also secreted into the gastric juice, giving rise to nausea or even vomiting after awakening. The solubility in the cholesterin-lecithin mixtures, which are formed in the protoplasm of the cells, is also less than with chloroform or ether, for example, so that no such quantities can accumulate in the cells. When the inhalation of new vapors in the narcosis ceases, no new quantities are taken to the cells, but the quantities contained in the cells are reëliminated. However, this elimination can take place only in the quantities which the blood-serum is capable of dissolving. As the cholesterin-lecithin mixtures of the ganglion cells dissolve ethyl chlorid, and therefore accumulate the same during the narcosis, in considerably larger quantity than the blood-serum is capable of dissolving, the narcosis will naturally continue until the last quantities of ethyl chlorid have been eliminated from the ganglion cells. In a brief narcosis, these accumulated quantities are very trifling in amount; after a prolonged anesthesia, however, they reach a certain amount beyond which one must not pass or the patient will die. As ethyl chlorid is only slightly soluble in cholesterin-lecithin mixtures—less than chloroform, for example—this quantity is smaller than what is stored up in the ganglion cells. Nevertheless, after prolonged narcosis, this quantity of ethyl chlorid will suffice to produce after-effects, in the form of vertigo, headache, etc.

After-Effects.—Concerning the after-effects of ethyl chlorid upon the animal organism, König [2] states that the result of the examination of the urine of the animals for albumin proved negative in all his experiments. Examinations were made a few hours after the narcosis, and on

[1] Müller: *Loc. cit.*

[2] König, R.: "Die Chloraethylnarkose," *Arch. klin. Chir.* 1912, *99*, 147.

the next day. This serves to show that the ethyl chlorid exerts no injurious action upon the blood corpuscles and the kidneys, leaving no noteworthy after-effects in this respect.

The after-effects occurred in so far, however, as all the animals were found to undergo a more or less considerable loss of body weight, usually about 100 gm., within 8 to 10 days. Several animals suffered from diarrhea. Rabbits which were narcotized repeatedly, on successive days, or every other day, recovered very slowly from the narcosis; they were extremely drowsy and weak, a considerable time elapsing before the normal condition was reëstablished. This observation, as well as the loss in body weight, combined with severe diarrhea, permits the conclusion that ethyl chlorid hardly leaves the organism so rapidly as is generally assumed to be the case. Perhaps there occurs a chemical change, namely, a decomposition of the ethyl chlorid in the lung, which organ is said to possess a strong reducing power. It is probable that this was suggested by Lotheissen, who asserted after his experiments that at least the chlorin must disappear from the expired air, as it is no longer demonstrable in the same. König points out that Lotheissen's experiments and conclusions are not tenable, and that these investigations in no way prove a retention of chlorin in the organism.

Clinically, the after-effects vary according to the preparation of the patient, the length of the administration, and the method employed. It is conceded by all unbiassed observers that vomiting is one of the commonest after-effects, occurring in from 15 to 20 per cent of cases. Nausea associated with headache occurs in even a greater percentage. The nausea is the same as in ether narcosis, but of shorter duration. It seldom lasts over 15 minutes; in exceptional cases, however, it has lasted 30 hours.[1] Hysterical symptoms may appear in young girls and erotic patients. Erotic thoughts and dreams may occur with this anesthetic as with nitrous oxid and oxygen. (*It is for this reason that the anesthetic should never be administered except in the presence of a third person.*)

Fainting and collapse are sometimes observed. Jaundice has been reported in a few cases, showing the effect upon the liver. Albuminuria is absent except in prolonged cases. Fatty degeneration of the kidneys and liver has been noted after repeated administrations. These symptoms may come on in from one to six hours after the administration and may continue for several hours. Collapse is more liable to follow ethyl chlorid than any other anesthetic.[2] This is the principal reason why attempts have never been made at a prolonged anesthesia with this drug. Symptoms of asphyxia appear only with too highly concentrated vapors, or when the inhalation is continued after the onset of prolonged slumber; i. e., when the so-called *narkosenbreite* (extent of narcosis) is exceeded.

[1] Hewitt: *Loc. cit.*, 446. [2] *Ibid.*

Comparison with Other Anesthetic Agents.—The narcotic power of ethyl chlorid, when administered by inhalation, mixed with air, is similar to that of ether, and weaker than that of chloroform. Because of the rapidity with which it abolishes consciousness, and the evanescent effects (fugaciousness) of the agent, unless these are forestalled, it is more comparable to nitrous oxid than to either chloroform or ether.

Maass,[1] who is an opponent of ethyl chlorid narcosis, maintains that, in regard to its absolute danger, ethyl chlorid should be ranked as at least equal to chloroform, for like the latter it may cause heart-death. Relatively, ethyl chlorid is more dangerous than chloroform, in so far as its desirable as well as undesirable effects are characterized by the rapidity of the onset and the almost instantaneous development to a climax; while the risk of a fatal overdosage is rendered imminent by the smallness of the permissible dose, as well as the impossibility of working in great dilution with air. For this reason, the successive use of ethyl chlorid and chloroform is by no means advisable, as the prepared or suggested injury through the brief ethyl chlorid anesthesia will develop to such an extent in the following chloroform-narcosis, by the summation of the stimuli, as it were, as to endanger the patient's life to an alarming degree, especially as the disturbances concerned in the summation all affect the circulatory system. In a similar way, Maass also considers the beginning of ether narcosis with ethyl chlorid as an added danger. Ethyl chlorid cannot even remotely concur with nitrous oxid, where the effect of the latter suffices, for this gas is very much less dangerous than ethyl chlorid. It is better to employ ether, he holds, when nitrous oxid or local anesthesia is not sufficient. The respiration and the heart action are apt to be overwhelmed very suddenly, the ethyl chlorid attacking the body so vehemently that it succumbs before the system can accommodate itself to its action.

Ethyl chlorid is appropriate for use in the act of parturition, because the patient's exhaustion permits the production of a relaxed state approaching analgesia with small doses of an anesthetic sufficient for the application of forceps. Another special indication for ethyl chlorid is in war surgery, because soldiers who have been anesthetized with ethyl chlorid awaken sooner and more completely, and thus become fit for transportation, than those who have received ether or chloroform. Furthermore, ethyl chlorid involves less danger of shock than chloroform, for wounded soldiers suffering from both physical and mental exhaustion.

The advantages of ethyl chlorid as compared with other liquid inhalation, or aliphatic anesthetics, consist in the rapidity with which it produces anesthesia, and the usually complete absence of after-effects,

[1] Maass: "Chloraethyl als Inhalationsanaesthetikum," *Therap. Monatsh.*, 1907, 303.

when *properly employed.* On the other hand, ethyl chlorid can in no way replace either chloroform or ether, where prolonged loss of sensation is required, its great toxicity strictly forbidding the exceeding of a maximum dose of 5 c.c.

Upon the basis of his experience, Herrenknecht [1] concludes that ethyl chlorid is the least dangerous narcotic which we possess at present, not even excepting nitrous oxid. However, it is not applicable for prolonged narcoses, because the scope of the narcosis is evidently not a wide one in the case of ethyl chlorid, and is therefore easily surpassed. It is naturally dangerous when too much is given in a short time of such a highly efficient agent, capable of so rapidly inducing narcosis. The inhalation should be interrupted with the onset of muscular relaxation and disappearance of reflexes. According to animal experiments, and the experience of other observers with patients, respiration usually stops first with ethyl chlorid, followed by failure of the heart action. Hence, immediate artificial respiration, perhaps combined with cardiac massage, will probably always prevent a threatened death, as the very volatile compound promptly escapes from the body. In spite of the large number of his ethyl chlorid narcoses (3,000) Herrenknecht has never yet been obliged to resort to artificial respiration or stimulation with camphor.

Hewitt [2] thinks that ethyl chlorid is far more dangerous than nitrous oxid and distinctly more dangerous than ether, the reason for this being stated as the considerable fall of blood pressure which takes place. Regarding its safety, Boyle [3] says ethyl chlorid cannot be compared with nitrous oxid and oxygen, and rates its dangers as equal to those of chloroform. Luke and Ross [4] state that this drug is safer as an anesthetic agent than ether, chloroform, or ethyl bromid, but that it must not be considered as safe as nitrous oxid.

Behr [5] indicates, as special advantages of ethyl chlorid, the relative harmlessness of the drug when used in suitable doses, its pleasant odor, which facilitates its employment, more especially for children, also the absence of a feeling of suffocation and the diminution of the stage of excitement, the rapid induction of anesthesia, the speedy return to consciousness, and, finally, the total absence of after-effects.

INDICATIONS AND CONTRAINDICATIONS

Indications.—In this discussion of the indications for the use of ethyl chlorid no reference will be made to the administration of this

[1] Herrenknecht: *Loc. cit.*
[2] Hewitt: "Anæsthetics," 1907, 135, 444.
[3] Boyle: "Practical Anæsthetics," 1907, 141.
[4] Luke and Ross: "Anæsthesia in Dental Surgery."
[5] Behr: *Berl. klin. Woch.*, 1911, No. 2, 67.

agent as a preliminary to ether or chloroform, this phase of the subject being considered under each respective combination or sequence.

Children, according to all the writers consulted in this connection, are the best subjects for the administration of ethyl chlorid. It has been used as a routine anesthetic for children five days old and upward,[1] being especially well borne by infants from a few weeks to a few months old. Children of any age, up to about eight years, take this anesthetic, as a rule, without difficulty, losing consciousness and becoming quiet in about ten seconds, and giving a satisfactory anesthesia of a minute or a minute and a half. It is preferred by some [2] to any other agent for circumcisions, for example, and for the majority of short operations in children under eight years of age.[3] In dental operations upon children, where not more than two teeth are to be extracted, and for removal of tonsils and adenoids, it is advocated.[4]

Luke and Ross,[5] Cantlie,[6] Mortimer,[7] and many others, consider ethyl chlorid preferable to nitrous oxid for short operations upon very young subjects.

Adults present no special indications for ethyl chlorid anesthesia. This agent may be given satisfactorily, however, to very aged and anemic subjects,[8] but great care is advocated [9] in such cases, the recumbent position being insisted upon. In patients whose general condition is satisfactory, and when the administration is skilfully conducted, ethyl chlorid may safely be employed.[10]

For short operations, where greater muscular relaxation is required than is obtainable by nitrous oxid, or where a deeper narcosis is desired, for short examinations or operations in gynecological work, and in brief operations in obstetrical practice, ethyl chlorid may be satisfactorily employed.[11]

Contraindications.—The earlier advocates of ethyl chlorid acknowledged practically no contraindications to its use. Girard, for example, according to McCardie,[12] held that circulatory troubles and respiratory affections did not contraindicate its use; neither age nor sex, nor alcohol-

[1] Mortimer: "Anesthesia and Analgesia," 50.

[2] Knight, H. Astley: "Notes on Ethyl Chloride," *Brit. Med. J.,* March 17, 1906, 618.

[3] McCardie: *Loc. cit.*

[4] Cantlie, James: "Anesthetics and Surgical Technique."

[5] Luke and Ross: "Anesthesia in Dental Surgery," 92.

[6] Cantlie: *Loc. cit.,* 171.

[7] Mortimer: *Loc. cit.,* 50.

[8] Luke and Ross: *Loc. cit.,* 92.

[9] Buxton.

[10] Hewitt: *Loc. cit.,* 441 (1907).

[11] McCardie: *Brit. Med. J.,* March 17, 1906, 617.

[12] *Ibid.*

ism, nor other intoxications forbade its administration. The only doubtful factor was the state of the urinary organs.

In a general way it may be stated that robust, athletic, and alcoholic subjects and confirmed smokers present contraindications to the use of ethyl chlorid, as do likewise persons suffering from chronic or acute diseases. Any obstruction to swallowing renders ethyl chlorid dangerous. Respiratory affections, whether due to contracted or small air passages, to marked pharyngeal catarrh, or to diseases of the lungs involving marked respiratory embarrassment, particularly in the presence of bronchorrhea, are contraindications to the administration of this agent. Feeble heart action, with a probability of fatty degeneration, is given as a contraindication.

It is generally conceded that ethyl chlorid is not suitable for operations, long or short, during which absolute muscular relaxation is desired.

ADMINISTRATION

Experimental Data.—According to König,[1] a careful examination of the available literature concerning the dosage of ethyl chlorid shows the remarkable fact that, up to the present time, no exact dosage has been stated. Very imperfect methods have been employed, which by no means permitted an accurate dosage of the ethyl chlorid in the inspired air. The quantity of the *liquid* narcotic used is not decisive for the course of the narcosis, but the decisive factor consists in the amount of narcotic *vapor* which is mixed with the air breathed by the patient, or the laboratory animal; in other words, the vapor tension of the inspired air. The quantity of narcotic taken up by the blood and the tissue juices, König asserts, is dependent upon the ethyl chlorid contents of the inspired air; the higher the latter (up to a certain degree), the more is taken up by the blood from the inspired air. When constantly new air saturated to the same degree with ethyl chlorid is supplied to the individual, just as much as has already been excreted from the blood will be taken up again. The contents of the blood in ethyl chlorid, therefore, will be adjusted to a certain standard which is dependent upon the contents of the inspired air in these vapors.

In view of the fact that the dose of ethyl chlorid required for narcosis (meaning the smallest dose at which narcosis just begins) is not known, König endeavored, in a series of experiments, to establish the amount of the smallest narcotizing dose, by the use of accurately measured quantities. It was also important to obtain in all cases a complete narcosis, that is, a narcosis with less of the corneal reflex and relaxation of the muscles. Furthermore, the longest possible duration of the nar-

[1] König: *Loc. cit.*, 147.

cosis was aimed at, in order to study the effects of ethyl chlorid in extensive narcoses, such as are absolutely necessary for operative purposes.

The animals serving for these experiments were frogs and rabbits. The latter were selected for the reason that they are best adapted to experimental investigations, and also because all the experiments for the determination of the narcotizing dose of an anesthetic agent have been almost exclusively performed upon rabbits. The ethyl chlorid of Henning (Berlin) and the preparation of Kahlbaum (Berlin) were used for these experiments. In order to grade the dose with accuracy, it was, of course, necessary for the preparations to be absolutely pure. The purity was determined by passing the ethyl chlorid vapors into water, and ascertaining that this water neither reddened blue litmus paper nor became at once opaque upon acidulation with nitric acid and addition of silver nitrate.

A number of experiments were performed on rabbits, using a mask, in order to employ the customary method of narcosis in the human subject. The idea was to obtain a short but deep narcosis, with muscular relaxation and disappearance of the corneal reflex. The customary procedure was therefore exactly followed, meaning that doses of 2 to 5 c.c., averaging 4 c.c., of ethyl chlorid, were administered at the beginning of the narcosis, which was then continued with smaller quantities, 1 to 2 c.c. These narcoses were invariably associated with extreme restlessness on the part of the rabbits. The most violent tonic-clonic spasms appeared constantly, and were usually increased to an enormous intensity. The extremely rapid onset of the narcosis was characteristic of the experiments with the mask; the corneal reflex was usually lost as soon as one minute later, and deep narcosis with complete muscular relaxation set in. But there again at once appeared the rhythmic twitching, typical for rabbits, independent of the respiration, frequently limited to the extremities, but often involving the entire body of the animal. Chewing spasms, and, in consequence, salivation, as well as opisthotonos and exophthalmos, were almost invariably demonstrable. Respiration was always extremely irritated. There was severe dyspnea, rapidly increasing to such a degree, with concentrated vapors, as to terminate at last in arrest of breathing. On immediate removal of the mask, and institution of artificial respiration, the breathing promptly returned spontaneously (with the exception of one case), and the animal soon awoke. The awakening always took place very rapidly, after one or two minutes, as a rule, as soon as the animals were supplied with fresh air. Otherwise the narcosis took the usual course of prenarcotic excitement and increased muscular tonus; muscular relaxation in the stage of deep narcosis; and another postnarcotic increase of the muscular tonus, with a certain analgesia. The pupils were usually dilated, and the eyeballs were prominent, causing marked exophthalmos. Frequently distinct cyanosis was demonstrable. These symptoms were due to vasomotor paralysis. Arrest of respiration invariably preceded the stoppage of the heart action, showing that ethyl chlorid, on account of its first stimulating and then paralyzing action upon the respiratory center, is not an indifferent narcotic, although the dangerous asphyxia can usually be prevented, or removed, by suitable precautionary measures.

The most important results of König's experiments, from the standpoint of the therapeutic employment of ethyl chlorid, are as follows: The smallest narcotizing dose of ethyl chlorid, for cold-blooded animals, is about 2 volume per cent (1.85 vol.); for warm-blooded animals, about 4 or 9 volume per cent, respectively. The fatal dose cannot be accurately stated. In cold-blooded animals death was caused with a dose of about 15 volume per cent. The narcotization-zone of ethyl chlorid is extremely wide. Although the facts established upon rabbits cannot all be unconditionally referred to man, the efficient doses for man must be nearly the same as that for rabbits.

Methods of Administration.—The authors of this volume are convinced, from a review of the literature of ethyl chlorid employed as an inhalation anesthetic, that the best possible method for the administration of this agent has not yet been evolved. Theoretically, the best and safest method of administration is with warmed, moistened, and oxygenated vapor of ethyl chlorid. So far as we are aware, this method has not been employed in full, no one having experimented with warmed ethyl chlorid vapor. Under Combinations and Sequences (p. 276) it will be seen that this agent has been employed with oxygen. An apparatus could easily be devised for administering the vapor warmed, moistened and oxygenated, and in definite amounts, in known percentages of the combined vapors. With these modifications of technique, and with the preliminary use of an alcoholic solution of oil of bitter orange peel, as indicated, doubtless many of the objections to ethyl chlorid as a general anesthetic might be overcome. Its field of usefulness might likewise be widened.

Hewitt[1] calls attention to two important points in connection with the administration of ethyl chlorid which help to explain the incidence of dangerous symptoms. "In the first place," he says, "ethyl chlorid narcosis is, by the method now in use, so rapidly induced that it is usually difficult or impossible to recognize any stages or degrees in the administration. In the second place, the appearance of the patient during full narcosis is unattended either by cyanosis or pallor—symptoms which with nitrous oxid and with chloroform respectively indicate that a sufficiently large quantity of the drug has been given. When these two points are borne in mind it will readily be seen that, unless proper care is taken, the limits of safety may readily be overstepped, and that

[1] Hewitt: *Loc. cit.*, 1907, 442.

the patient may be plunged, with few if any intervening symptoms, from a safe to a dangerous degree of narcosis. If cyanosis is present it is due to 'overcrowding.'"

Open Method.—The open method of administration has nothing to commend it save its seeming safety, which, to the superficial observer, lies in a large intake of an unlimited supply of air together with unknown quantities of ethyl chlorid.

An ordinary chloroform mask is placed over the patient's face and ethyl chlorid is administered drop by drop, or a small stream of ethyl chlorid is *intermittently* sprayed upon the mask until anesthesia ensues. The anesthesia produced in this way seems to be perfectly safe, but certainly no more so than the anesthesia produced by Ware's mask.

Anesthesia produced by the open method has been kept up from thirty to forty minutes. Care must be taken to stop its administration immediately upon rigidity or spasm. As long as the respirations are free and clear, there is seemingly no danger from this method.

Collapse is less liable to occur after prolonged anesthesia with the open method than with the closed.

Milne,[1] who reports 600 cases of ethyl chlorid anesthesia, 300 by the open method and 300 by the closed method, from his experience, advocates the open method.

Malherbe's[2] method of administration is as follows: A handkerchief is held in the palm of the right hand, which is hollowed out to receive it. Into this hollow a jet of chlorid of ethyl is sprayed, 2 to 4 c.c. The "compress" is then firmly applied over the mouth and nose of the patient, who is instructed to breathe deeply. The head and lower jaw are supported with the left hand. "It is absolutely necessary," he says, "not to allow any air to be breathed." Anesthesia is complete in 30 to 40 seconds. If the operation is protracted, he renews the dose, claiming that 15 c.c. is sufficient for 15- or 20-minute operations. He also reports, from a colleague, 93 operations, lasting from 8 to 48 minutes, the patients varying from very young infants to two patients over 80 years of age.

Semi-Closed Method.—Martin Ware[3] has reported one or two thousand cases without a fatality. The apparatus which he used consists of a rubber face-piece, into which a tube three to five inches long is inserted; a few layers of gauze are placed between the tube and mask. A stream of ethyl chlorid is directed on the gauze intermittently, thus ap-

[1] Milne: "The Administration of Ethyl Chloride by an Open Method," *Brit. Med. J.*, 1911, 1051.

[2] Malherbe: "Chloride of Ethyl as a General Anesthetic," *Med. Press and Circ.*, 1911, *91*, 461.

[3] Ware, Martin: *Med. News*, Aug. 3, 1901; *Med. Rec.*, April 6, 1901.

On ethyl chlorid in general anesthesia, see A. M. Dodge: *Boston Med. and Surg. J.*, Feb. 25, 1909, 234. Leighton (*St. Louis Med. Rev.*, Feb. 16, 1907) considers the combination ethyl chlorid-ether an ideal one.

proximating the drop method of chloroform; a layer of hoarfrost quickly forms, due to the freezing of the watery vapor of the expired air. As this frost covers the gauze, a hissing noise is heard as the patient goes into the third stage of anesthesia. If the gauze is entirely covered with ice, the mask should be immediately removed upon inspiration and replaced again upon expiration.

Ware stated that relaxation can be readily secured in children, and also in alcoholics, when a preliminary injection of morphin is given. With neurotics, relaxation is very difficult to secure. He estimated the

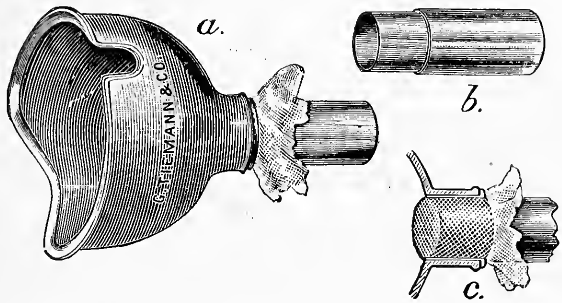


Fig. 120.—Martin Ware's Apparatus for Administering Ethyl Chlorid.

failures at five per cent. By failure was meant a prolonged period of excitation, and, while the patient was seemingly narcotized, the possibility of causing muscular rigidity by painful manipulations.

Closed Method.—In order to obtain the best results from ethyl chlorid, it is necessary to employ a rubber bag large enough to receive three or four full expirations, and some arrangement for allowing the ethyl chlorid to enter the bag below so that there may be a very gradual mixture of the ethyl chlorid with the expired air. The connections between the mask and the bag must be large enough not to interfere with respiration in the slightest way. This being so, the small tubes containing 3 to 5 c.c. of ethyl chlorid may be easily attached to a stopcock of any gas-ether apparatus. A rubber tube large enough to hold the glass ethyl chlorid tube securely (admitting the small glass apex of the ethyl chlorid container well into the caliber of the tube) may be attached to the bag as shown in the illustration (Fig. 121). A piece of cotton or gauze must be placed between the end of the glass tube and the bag so as to prevent any glass entering the bag. After the bag has been inflated by the respirations of the patient, this tube may be broken between the thumb and first two fingers of the anesthetist's hand and the ethyl chlorid allowed to go into the bag. When the closed method is followed, one or two cubic centimeters of ethyl chlorid is sufficient for children, and for feeble and anemic adults. Five cubic centimeters will be found sufficient, as a rule, for adults, alcoholics, and athletes.

Whether the patient is in the recumbent or sitting position, the head *must* be on a line with the body, thus insuring an absolutely free airway. No pillows should be allowed under the head unless some deformity, such as accompanies rheumatism, will not permit of the head going back. If the operation is one in which the mouth is to be opened, such as extraction of teeth, adenoids, and tonsils, and excision of the tongue, a mouth gag must be inserted *before* the administration commences, otherwise difficulty may be experienced in opening the mouth. It sometimes happens that, even with full surgical narcosis, the masseter muscle may be firmly contracted, making it almost impossible to

Fig. 121.—Ethyl Chlorid by the Closed Method.

pry the teeth apart. The duration of an administration given by the closed bag and inhaler can be expected to be from one to three minutes.

The administration is conducted as follows:

Upon expiration, the mask is firmly applied to the face; upon inspiration it is raised slightly, say from 1/8 to 1/4 of an inch from the face, and *reapplied immediately*, so as to catch the full expiration. In from three to five respirations the bag will be full, when it must be held firmly in place upon the face. The ethyl chlorid tube is now broken and, if at the end of a minute the patient is not completely under the influence of the anesthetic, the end of the bag can be tilted up slightly, when the ethyl chlorid will mix more intimately with the inclosed air. In full surgical anesthesia the muscles are relaxed, with the exception of the masseter, as stated before. The pulse is full and bounding and increased in rapidity. The respirations in an ideal anesthesia are also full and regular but not as full as with nitrous oxid and oxygen, or with ether by the closed method. Usually there is some stertor, the eyes may be fixed and turned downward, the pupils dilated and the lid reflex abolished. There is no cyanosis or jactitation. If too large a dose is given or the inhaler is held on the face too long, there may be a rigidity or opisthotonos. The color should be pink; if cyanosis or spasm is present the mask must be taken off the face and again reapplied.

The average time required to induce anesthesia is one minute. If an anesthesia of from five to fifteen minutes is required, a breath of air should be given and the inhaler reapplied about every four to six respirations, with the occasional spraying of a little ethyl chlorid into the inhaler.

The method last described, of introducing ethyl chlorid at the bottom of a closed bag through a stopcock, was first proposed by Hewitt.

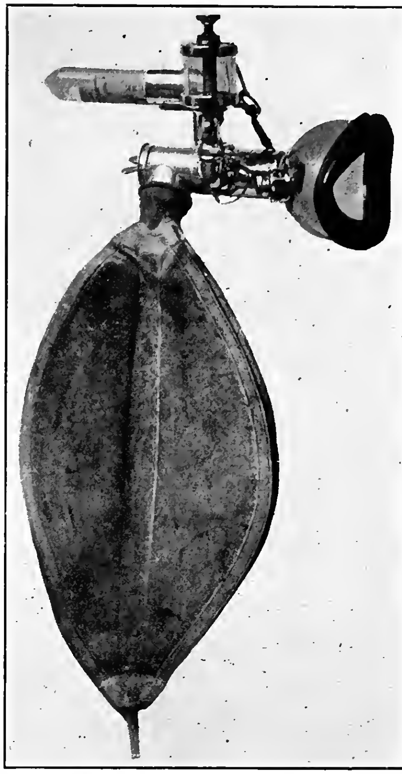


FIG. 122.—DAVIS ETHYL CHLORID-ETHER-INHALER: CLOSED DROP METHOD.

Hewitt,[1] from the experimental work of König, and from his own clinical observations, concluded that, "as with other anesthetics, the effects produced by ethyl chlorid primarily depended upon its vapour tension in the atmosphere presented to the patient. But the last-named observations tend to show that there is no definite percentage mixture the continuous inhalation of which will produce satisfactory results. With percentage mixtures sufficiently weak to be respirable without discomfort an unsatisfactory type of anesthesia results; while with mixtures sufficiently concentrated to produce narcosis satisfactorily the initial sensations are so unpleasant as to prescribe such initial vapour concentration. So far as our present knowledge extends," he continues, "it would seem that, with this anesthetic, the best results are to be obtained by a rational and cautious use of the close system of anesthetization, the vapour being gradually but increasingly added to the to-and-fro respiratory current till anesthesia takes place. We have yet to ascertain whether any special concentration of vapour should be aimed at, after consciousness has been destroyed, and, if so, how such concentration may be secured. We have also to determine by future research the relative influences of the oxygen limitation and the carbonic acid retention which are involved in close methods of administering ethyl chlorid."

[1] Hewitt: *Loc. cit.*, 431.

From his experience Hewitt found that if ethyl chlorid is administered to adults from an open or semi-open inhaler large quantities of the drug will be needed to bring about even partial anesthesia, the third stage not being attained in many cases. He found that unsatisfactory anesthesia was obtained when attempts were made to administer, by the valveless method, percentage mixtures of ethyl chlorid and air, that is, without rebreathing. When half the amount was given by the valveless system and the other half by rebreathing, the results were still unsatisfactory. He next tried a definite ethyl chlorid and air mixture diluted with a further unknown quantity of air by the valvular system,—the pure mixture, of known composition, being breathed by the same system, the remainder of the mixture being breathed by the close system. The results were again unsatisfactory, swallowing and shallow breathing characterizing the administration. A measured quantity (5 c.c.) of ethyl chlorid was next given by means of a Clover inhaler, to which was attached a bag containing 10,000 c.c. of air. The expirations were at first allowed to escape but were retained during the second half of the administration. This method proved more satisfactory than any of the preceding. His final experiments were with the following procedure: "(1) *Placing 3,000 c.c. of atmospheric air in a bag;* (2) *allowing the patient to commence rebreathing this air; and* (3) *gradually diffusing therein a measured amount of ethyl chlorid contained in a small glass tube connected with the bottom of the bag." With this method the results were satisfactory in thirteen cases in which he first tried it, but subsequently it was found to be somewhat less satisfactory than when the patient's own expired air, as opposed to fresh air, was used to partially fill the inhaling bag before the introduction of the ethyl chlorid."*

For further information relative to the administration of ethyl chlorid, see additional bibliography at end of chapter.

Combinations and Sequences.—Somnoform.—Somnoform is a mixture of 5 per cent ethyl bromid, 60 per cent methyl chlorid, and 35 per cent ethyl chlorid. It is not so stable as ethyl chlorid, having a greater tendency to decompose, and, like the latter drug, causing headache and vomiting. It is very seldom used in this country, pure ethyl chlorid being preferred by the majority of those who advocate ethyl chlorid for any purpose.

Anesthol.—Anesthol, which was first employed by Willy Meyer,[1] in 1898, is a clear, transparent fluid of a very agreeable odor. It is a

[1] Meyer, Willy: "The Improvement of General Anesthesia on the Basis of Schleich's Principles. With Special Reference to Anesthol," *J. Am. Med. Assn.*, Feb. 28, 1903; *ibid.*, March 7, 1903. *Also* "The Improvement of General Anesthesia on Basis of the Principle of Adapting the Boiling Point of the Anesthetic to the Temperature of the Body (Schleich)—Ten Years' Experience at the German Hospital," *Med. Rec.*, Aug. 15, 1908.

combination[1] of 17 per cent of ethyl chlorid, 35.89 per cent of chloroform, and 47.19 per cent of ether. It has a specific gravity of 1.045, which, as Meyer points out, is very close to that of blood (1.056-1.059). Its boiling point is 104° F (40° C.). For a further exposition of the principles involved in the making and use of this preparation see Chapter XX.

Meyer's observations with this anesthetic, administered by means of the drop method and an Esmarch inhaler,[2] are as follows:

"1. Surgical anesthesia is established in the majority of cases in about eight minutes. If morphin is previously administered, even this time is very frequently reduced by a few minutes.

"2. The stage of excitation, if it sets in at all, is of very short duration.

"3. Complete anesthesia having been gradually induced, the pulse is full and slow—of the chloroform-anesthesia type—and respiration regular, not stertorous.

"4. In no instance has there been an increase in salivation or bronchial mucus during narcosis.

"5. The face presents a healthy color. There is no pallor nor cyanosis.

"6. If too little of the anesthetic is given, the patient will begin to gag or vomit, as with chloroform; if too much is administered, respiration will become shallow, and eventually, if still more is poured on the mask, stop altogether, but the pulse will not be interfered with. In other words, the respiratory and not the circulatory center is first affected by an *overdose*. . . . The tendency throughout the narcosis is toward recovery from the effect of the anesthetic, not toward a profound anesthesia. . . .

"7. After the anesthetic has been stopped, the patient soon comes to, sometimes even while still on the operating table. If he sleeps

[1] Sollman: "Pharmacology," 437. "The claim that anesthol is a chemical compound, and that its composition does not alter on evaporation, seems to be unfounded."

[2] Neef ("Practical Points in Anesthesia") states that at the German Hospital it is the practice to employ a Schimmelbusch mask, covered with flannel, over which impermeable cloth, with a lozenge-shaped fenestrum the size of a ten-cent piece, is placed. He also states that it requires 15-20 c.c. for induction, and 40-60 c.c. for narcosis. It is now the routine custom at this institution to administer a hypodermic of morphin, 1/12 to ¼ gr., one-half to three-quarters of an hour before anesthesia. Cardiac collapse occurs during induction, if at all. This is indicated by weak pulse and pallid face. A change to ether by the drop method will quickly remedy this. When stimulants are needed at any other time, a few drops of ether may be added. With anesthol the volume of the pulse may be expected to decrease about one-third in the course of an hour, and as much as one-half in a two-hour anesthesia. "Crowding" is the cause of salivation or cyanosis during anesthesia, and of excessive vomiting afterward.

longer, it is usually on account of the previously administered morphin.

"8. Vomiting occurs in a small percentage of cases after return to consciousness. It is, however, not of a prolonged or distressing type.

"9. Untoward after-effects,[1] such as bronchitis, pneumonia, nephritis, are not seen as a result of anesthesia with this mixture. A pre-existing catarrh of the bronchi or inflammation of the kidneys may, of course, become somewhat aggravated for a few days, but never to the extent that may happen after the inhalation of other gaseous substances. These complications certainly are never produced by this anesthetic.

"10. Patients afflicted with serious valvular cardiac lesions, chronic pulmonary affections, atheromatosis, diabetes, profound anemia, or other complications of serious character have stood this preparation most satisfactorily; contrary to what one would be justified in expecting in such cases, a better circulatory and respiratory condition was induced during anesthesia.

"11. The total quantity used is generally small. Our narcotizers very often carry a patient through an anesthesia lasting from one to two hours, with two to three ounces."

For further information, especially in reference to the chemistry of anesthol, see Chapter XX.

Ethyl Chlorid and Oxygen.—Lotheissen[2] proposes an improvement of ethyl chlorid narcosis by means of the simultaneous inhalation of ethyl chlorid and pure oxygen. For this purpose, he constructed an apparatus which is a modification of the Roth-Dräger apparatus, for hospital practice; also a smaller, cheaper apparatus which can be easily transported to the patient's dwelling. This new method of ethyl chlorid narcosis has been used by him for five years past, without unfavorable experiences, in about five hundred anesthesias. The usual duration of anesthesia was ten minutes, only a small number being longer than twenty minutes. The average quantity of ethyl chlorid administered per minute amounted to 1 to 2 c.c. with 1½ liters oxygen. In cases concerning habitual users of alcohol, in whom anesthesia could not be obtained within two or three minutes, a few drops of ether were added, resulting in a mixed narcosis of ethyl chlorid and ether with oxygen. In Lotheissen's experience, it is not advisable to pass to chloroform or its mixtures after the beginning of the narcosis with ethyl chlorid. In order to avoid asphyxia, in consequence of concentrated vapors, the oxygen is allowed to escape before the ethyl chlorid is inhaled. The pulse-rate and respiratory frequency are not affected, as a rule. Vomiting is less common than with other narcotics. After-effects are always trifling and transitory. Although Lotheissen admits hardly any contraindications, he does

[1] Torek, F.: "Anesthol Poisoning Causing Acute Yellow Atrophy of Liver After Operation for Ileo-colic Intussusception," *Am. Surg. J.*, 1910, *52*, 489-492.

[2] Lotheissen: *Loc. cit.*

not employ the ethyl chlorid-oxygen narcosis in those cases where it is advisable to avoid general anesthesia.

Rosenthal and Berthelot [1] have found that a mixture of oxygen and ethyl chlorid, instead of ethyl chlorid alone, produces very satisfactory anesthesia, even to one hour's duration. In 1906 they stated that all the experiments had been conducted upon animals.

Ethyl Chlorid and Nitrous Oxid.—Ethyl chlorid has been given by one of the authors (J. T. G.) with nitrous oxid and oxygen in a number of cases, thus securing complete relaxation, otherwise unobtainable with the latter combination. Ethyl chlorid may be sprayed into the inhaler or through an inspiratory valve. The only objection to using ethyl chlorid in this way is the fact that considerable vomiting occurs immediately after the removal of the mask.

Ethyl Chlorid with Ether.—The ethyl chlorid-ether sequence is given in the same way as the nitrous oxid-ether sequence, that is, with any of the closed inhalers. As the patient gets well under the ethyl chlorid, the ether is turned on gradually. The technique of the administration is as follows:

Attach a tube containing 3 to 5 c.c. of ethyl chlorid to the stopcock of the bag by a rubber tube. As the patient fills the bag three-fourths full, break the neck of the tube of ethyl chlorid and thus allow the ethyl chlorid to enter the bag. As the patient sinks under the ethyl chlorid, turn on the ether very gradually.

Ethyl Chlorid with Chloroform.—Ethyl chlorid should not be administered preliminary to chloroform, inasmuch as both of these agents are respiratory depressants, both are cardiac poisons, and both act quickly. They have been used in this way, but this sequence should be avoided because it is dangerous.

BIBLIOGRAPHY

Blumfield: "Recent Work in the Field of Anæsthetics." *The Practitioner,* 1903, 420.

Braine, Carter: "The Administration of Anæsthetics in Dental Surgery." *Brit. Dent. J.,* Oct., 1904, 717.

Buxton, Dudley: "Operations on the Upper Passages from the Anæsthetist's Point of View." *The Practitioner,* Jan., 1905, 77.

Chaldecott, J. H., and Stephenson: "Ethyl Chloride as a General Anæsthetic in Eye Work." *The Ophthalmoscope,* April, 1904, 129.

Daniells, G. W. B.: "The Administration of Ethyl Chloride." *Brit. Med. J.,* 1904, 949.

De Prenderville: "Advantages of Ethyl Chloride Anæsthesia." *The Lancet,* 1904, 978.

[1] Rosenthal and Berthelot: *Compt. rend., 146,* 43.

Flemming, A. L.: "Ethyl Chloride: A Few Practical Remarks." *Bristol Med. Chir. J.*, Sept., 1904, 228.

Hatch, R. M.: "Chloride of Ethyl as a Dental and General Anæsthetic." *Brit. Dent. J.*, Oct., 1903, 638.

Hewitt, F. W.: "Anæsthetic Effects of Ethyl Chloride." *The Lancet*, 1904, 1408 and 1486.

Hilliard, Harvey: "Ethyl Chloride as an Anæsthetic in General Practice." *The Practitioner*, Feb., 1905, 203.

Luke, T. D.: "The Use of Ethyl Chloride as a General Anæsthetic." *Edinburgh Med. J.*, 1903, 425.

Lynch, Jerome M.: "The Choice of an Anæsthetic in Anal Surgery." *Va. Med. Semi-Monthly*, July 24, 1908.

McCardie, W. J.: "Ethyl Chloride as a General Anæsthetic." *The Lancet*, 1903, 952 and 1198.

Seelig, M. G.: "Combined Ethyl-Chloride and Ether Anæsthesia." *St. Louis Courier of Med.*, Feb., 1905.

Ware, Martin W.: "One Thousand Personally Conducted Cases of Ethyl Chloride Narcosis." *J. Am. Med. Assn.*, Nov. 8, 1902.

CHAPTER VII

CHLOROFORM

Chemistry: History; History of Its Use as an Anesthetic; Properties; Uses; Preparation of Chloroform; Impurities Liable to Be Present in Chloroform; Stability of Chloroform; Decomposition of Pure Chloroform; Rôle of Alcohol in Anesthetic Chloroform; Character of Containers; Stoppers for the Containers; The Changes Which Anesthetic Chloroform Undergoes When a Current of Oxygen Is Conducted Through It; The Decomposition of Chloroform Vapor Upon Exposure to Gas Light, etc., During Administration; Effect of Agitation Upon Anesthetic Chloroform; Standards of Purity for Anesthetic Chloroform.

Special Physiology: Effects Upon the Respiratory System; Effects Upon the Circulatory System; Effects Upon the Nervous System; Effects Upon the Muscular System; Effects Upon the Glandular System and Other Structures; Causes of Death from the Administration of Chloroform; Stages of Anesthesia; Elimination.

Indications and Contraindications: Indications; Contraindications; After-Effects; Comparison with Other Agents.

Administration of Chloroform: Drop Method; Other Methods of Administration; The Roth-Dräger Oxygen and Chloroform Apparatus; Vernon Harcourt's Inhaler; Junker Apparatus; Braun's Inhaler; Gwathmey Three-Bottle Vapor Inhaler.

CHEMISTRY

History.—Chloroform, $CHCl_3$ (trichlormethane, methenyl trichlorid, dichlorinated chlorid of methyl, perchlorid of formyl, formyl trichlorid), was independently discovered in 1831 by Guthrie, Soubeiran, and Liebig,[1] yet it has been asserted that there are indications of an earlier acquaintance with the compound. For example, we are told by Hutman,[2] on the authority of Johannes Porta [3] and Sir Walter Scott,[4]

[1] A fuller historical account may be had in Appendix II, p. 871.

[2] *J. Chim. med.* (3), *4*, 476.

[3] "Magna Naturalis," 1619. It should be mentioned here that in 1589 Gianbattista Porta used an essence made from hyoscyamus, solanum, poppy and belladonna, enclosed in a lead vessel, for producing sleep by inhalation of the vapor.

[4] "Letters on Demonology and Witchcraft," 1830.

that chloroform was known in former times and was then employed as a means of producing insensibility. Investigation shows that this statement is based upon misinterpretation.[1]

History of Its Use as an Anesthetic.—In March, 1847, Flourens announced to the Academy of Sciences of Paris that chloroform exercised on the lower animals an anesthetic action analogous to that of ether. In the same year Doctor (afterwards Sir) J. Y. Simpson, looking for a more convenient and less objectionable anesthetic than ether, consulted Mr. Waldie, a chemist of Liverpool, who suggested that he use chloroform. In November, 1847, he read a paper entitled "Notice of a New Anæsthetic Agent as a Substitute for Ether in Surgery and Midwifery." From this time on its use spread rapidly.

In January, 1848, Hannah Greener, the first victim to chloroform, died at Winlaton near Newcastle, Dr. Meggison being the chloroformist. It may be appropriate to relate exactly under what circumstances she died. The operation was for an ingrown toe-nail. The girl was seated in a chair and only a few whiffs of chloroform were administered, and she died. She was only eighteen or twenty years of age. The history of this first case is given in detail for the reason that so many of the physiological principles relating to chloroform, as we know them to-day, were violated on that occasion, namely:

First: It was administered with the patient in an upright posture.

Second: It was administered for a minor operation.

[1] Most ancient authors who pretend to treat of the wonders of natural magic give recipes for calling up phantoms by the inhalation of certain gases from burning medicated mixtures, generally of oils, and by the use of suffumigations of strong herbs (Hibbert's "Apparitions," 120). The ancient Egyptians, Assyrians, and Chinese were familiar with many vegetable substances (*e. g.*, *cannabis indica*) capable of producing ecstatic, sedative, and anodyne effects (Snow's "Chloroform and Other Anæsthetics," 1858; Bernard's "Leçons sur les anesthésiques et sur l'asphyxie," 1875; Lyman's "Artificial Anesthesia and Anesthetics," 1883; and Dastre's "Les anesthésiques," 1890). From the "Odyssey" (iv., 220) we learn that Helen "cast a drug into the wine whereof they drank, a drug to lull all pain and anger and bring forgetfulness of every sorrow." Herodotus refers to the custom of the Scythians of inhaling the fumes of a kind of hemp; Disscorides (*De Med. Mat.*, iv., 76) makes mention of the practice of boiling in wine the root of the *Atropa Mandragora* and of administering some of the decoction prior to surgical operations; and Pliny (xxxv., 94) refers similarly to the powers of the mandrake. Mandragora appears to have been used to some considerable extent (Galen, lib. vii., 207; Lucian, "Demosthenes Ecomium," 36); it was employed in compounding the "spongia somnifera" of Theodoric. The Bible and the Talmud also contain references to ancient practices of inducing sleep by artificial means. However, excepting the use of Memphis marble and vinegar as a local anesthetic by the Romans, carotid compression and (later) mesmerism, vegetable narcotics only were used to assuage suffering and for the induction of unconsciousness until the foreshadowing of the modern system of anesthesia by the discovery of nitrous oxid.

Third: It was administered to a patient with high nervous tension.

Fourth: It was probably administered in a concentrated dose.

Fifth: To a young, vigorous woman. There would be no justification for such a fatality with our present knowledge.

Ten years after its introduction as an anesthetic, Dr. John Snow published his classical work on "Chloroform and Ether Anæsthesia," giving among other things an exact percentage of chloroform and apparatus for administration of the same.

In 1879 the first committee on the British Medical Association met and condemned the use of chloroform. In 1890, the second Hyderabad committee met and concluded that chloroform was a comparatively safe drug when properly used. In 1901 the British Medical Association committee published a second report condemning the indiscriminate use of chloroform. In the same year Dr. Frederick Hewitt issued a second edition of his work on anesthetics, stating (page 497) that with a compound sequence (N_2O-Ether-$CHCl_3$) it is possible to proceed to deep chloroform anesthesia with safety and smoothness.

In 1904 one of us (J. T. G.) read a paper at a meeting of the Surgical Section of the New York Academy of Medicine, showing that the value of chloroform was more than doubled when used with oxygen instead of air, and also stating that this combination was, theoretically at least, safer than ether and air.

In 1906 [1] one of the authors of this book (J. T. G.) read another paper before the American Medical Association, drawing attention to the remarkable difference between warm and cold chloroform vapor, and giving reasons why chloroform should be preferred in the Southern States, Cuba, Philippines, and in any of the tropical countries.

Properties.—Chloroform is a colorless, limpid liquid, possessing a sweet but somewhat burning taste and an agreeable "ethereal" odor. When absolutely pure, it possesses a density of 1.49887 at 15/4° and boils at +61.2° C. Pure chloroform decomposes under certain conditions, which will be referred to later, and should never be used for anesthesia. *Anesthetic chloroform* does and should contain 0.25 to 1.00 per cent of ethyl alcohol, which acts as a preservative. Therefore anesthetic chloroform may have a specific gravity of not less than 1.476 at 25/25°.[2]

[1] "A Plea for the Scientific Administration of Anesthetics," *J. Am. Med. Assn.*, Oct. 27, 1906, *47*, 1361-1364.

[2] The anesthetic chloroform on the American market varies in specific gravity from 1.4730 to 1.4827 at 25/25°, usually in close proximity to 1.476, the minimum density permitted by the *Pharmacopœia.*

The samples of chloroform of German manufacture examined by Baskerville and Hamor (*loc. cit.*) varied in specific gravity from 1.487 to 1.492 at 15/15°, although one sample possessed a density of 1.497 at this temperature.

The specific gravities of the chloroforms recognized as official by the pharmacopœias of various countries are given in the following table: (*Continued on p.* 284)

When pure, chloroform is not combustible; but when mixed with alcohol, it burns with a smoky flame edged with green. Chloroform is slightly soluble in water (0.822 gm. per 100 gm. water at 20° C.) and it imparts to it a sweet taste. It is miscible in all proportions with absolute alcohol, ether, benzene, and petroleum spirit. It is soluble to a limited extent in aqueous alcohol. It may be made into an emulsion with water by means of saponin. Chloroform is an important technical solvent; it dissolves fats, certain components of india-rubber, resins, sulphur, phosphorus, iodin, various alkaloids, many alkaloidal salts, as well as many other organic compounds.[1]

Uses.—Chloroform is used in medicine as an anesthetic,[2] stimulant, antispasmodic, counterirritant, antiseptic;[3] as an antidote in cases of

(*Continued from p.* 283)

DENSITIES AT 15° ACCORDING TO VARIOUS PHARMACOPŒIAS

1.480	1.489	1.490	1.497	1.498	1.500	1.485–1.489	1.485–1.490
Spain Portugal Mexico	Switzerland	Greece	Chili	France	Roumania	Germany Denmark Hungary Norway Sweden Finland	Belgium

1.485–1.495	1.490–1.500	1.490–1.493	1.490–1.495	1.498–1.500	1.499–1.500	Not below 1.476 at 25°
Japan	Austria	Italy	Great Britain	Holland	Russia	United States

The chloroform constants according to various editions of the *United States Pharmacopœia* are as follows:

Date	Density at 15°	Boiling Point
1851	1.49	142° F.
1869	1.490–1.494	140° F.
1873	1.480	142° F.
1882	1.485–1.490	60–61° C.
1893	Not below 1.490	60–61° C.

[1] See, in this connection, Pettenkofer: *Jahresber.*, 1858, 363; Schlimpert: *Ibid.*, 1859, 405; Nowak: *Archiv Pharm.* (3), *3*, 281; Hesse: *Pharm. J.* (3) *4*, 649.

[2] Sir James Simpson: "New Anesthetic," 1847, 7; *Illust. London News*, Dec. 4, 1847, 370-2; E. B. Simpson: *Century, 25*, 412; *Liv. Age, 66*, 720; *J. Med. Sci.*, Sept., 1847; *Ednb. Medico-Chir. Soc.*, Nov. 11, 1848; J. Y. Simpson's "Anesthesia," 1849, 93, 145, 182, 193, 203.

[3] As an antiseptic, chloroform prevents the growth of micro-organisms, but it does not affect the action of soluble ferments (*J. Soc. Chem. Ind.*, 1886, 331). On the antiseptic applications of chloroform, see Robin: *Compt. rend.*, *30*, 52; Augendre: *Ibid.*, *31*, 679; Barnes: *Pharm. J.* (3), *5*, 441; Salkowski: *Chem. Report.*, 1888, 166; and *Pharm. J.* (3), *18*, 315, 356, 855.

strychnin poisoning, and as an analgesic; technically in electrotechnics, rubber industry, and photography; and in dentistry as a solvent.

Preparation of Chloroform.[1]—Chloroform is made from alcohol, acetone, or "methylated spirit," by treatment with chlorid of lime ("bleach"), other hypochlorites, or electrolysis of a halogen salt in the presence of the first mentioned substances. It is also made from carbon tetrachlorid by reduction, the tetrachlorid, as a rule, being previously made from carbon disulphid.

Impurities Liable to Be Present in Chloroform.—The impurities liable to be present may be from the variety of materials used in the manufacture of chloroform just noted, and changes the product is liable to undergo on keeping, which will be considered later from chemical and physiological standpoints.

Impurities from the Manufacturer.—These are usually the so-called "organic impurities," which are found in considerable amounts in a chloroform which has been made from poorly rectified spirit, acetone, or carbon tetrachlorid (the sources), if impure chemicals have been employed in the manufacture or subsequent rectification and purification, or if the chloroform has not been properly purified. These impurities, even though some may not be of much importance from a physiological standpoint, must still be given attention, since an impure chloroform is likely to become altered through oxidation during storage, notwithstanding the fact that pure ethyl alcohol has been added.

The possible impurities of this class are as follows: Excess water; excess alcohol; acetone; methyl alcohol; carbon tetrachlorid; tetrachlorethylene, hexachlorethane, etc.; aldehyds; amyl, propyl, and butyl alcohols, and compounds; ether[2]; acids (sulphuric, hydrochloric, formic, acetic); metallic chlorids; ethyl chlorid; ethylene chlorid; ethylidene chlorid[3]; ethyl acetate; oils ("empyreumatic," "pyrogenous," "chlorinated"); fixed and extractive matter.

Purification in Manufacture.—Some of the impurities are washed out with water, others are removed by treatment alternately with concentrated sulphuric acid and sodium carbonate. This product is then further purified by fractional distillation. The details of treatment would be out of place here, however. Interesting facts appear in Appendix II, page 871.

Impurities Liable from Improper Storage.—Although the rationale of their development will be discussed in later paragraphs, the

[1] Further details are given in Appendix II, p. 871.

[2] From 1865 to 1875, ether was considered as one of the general contaminants of chloroform.

[3] About 1880, ethylidene chlorid was regarded as a general impurity of chloroform.

possible impurities of this class may be conveniently enumerated here. They are: Acetaldehyd; acetic acid; formic acid; carbonyl chlorid; hydrochloric acid; hydrogen dioxid; chlorin; chlorinated derivatives of alcohol oxidation products.

These impurities are dealt with specifically in Appendix II on page 871.

PHYSIOLOGICAL CONSIDERATIONS IN RESPECT TO IMPURITIES.—Huchard[1] has said, "Pure chloroform, well given to a patient prepared for it, almost never kills." Serious results have occurred from the use of anesthetic chloroform containing foreign substances, and although the grades at present sold as chloroform for anesthesia hardly contain sufficient impurities which can be held responsible *per se* for deaths which have occurred during narcosis, yet the presence of these products may account for some, at least, of the disagreeable after-effects so often noticeable following the administration of some chloroform.[2] Consequently, anesthetic chloroform should comply with the most rigid tests,[3] and the preparation which conforms with these requirements, and at the same time is comparatively less likely to decomposition than others also answering the same tests, should at all times be preferred to a cheaper but less stable grade. According to the investigations of Feigl and Meier,[4] the customary chemical examination of a sample of anesthetic chloroform is not conclusive, but requires confirmation by biological tests. Most important, however, is clinical experience.

In regard to the fatal results which have been obtained in practice following the use of chloroform vapor for the induction of anesthesia, a considerable percentage of cases, especially those where death has ensued immediately upon first inspiration, may not be due to the action of chloroform at all.[5] However, Simpson[6] enumerates a number of cases

[1] *J. des. Pract.*, May 31, 1902.

[2] We have private information as to ill effects from chloroform supplied by certain dealers.

[3] The pharmacopœial tests are, in general, insufficient, and samples of chloroform may comply with the tests prescribed by various pharmacopœias, and yet important differences may be shown to exist among them by means of other tests. These facts have been brought out by Langaard (*Therap. Monatsh.*, May, 1902). Our opinions will be found in this book.

[4] *Biochem. Z.*, 1906, 316. Feigl and Meier marked out the blood-pressure curves on a drum by means of a kymograph; healthy dogs were made to inhale equal quantities of chloroform of different makes through a tracheal canula. The results obtained showed that the different brands of chloroform, although they appeared almost identical by the chemical tests, differed considerably in their liability to cause a diminution in blood pressure and to cause arhythmia of the pulse beat.

[5] See, in this connection, Nussbaum: *Handb. d. allg. p. spec. Chir.*, 1867, 612; Lawrie: *Lancet*, 1890, *i*, 149.

[6] *Brit. Med. J.*, 1870, *i*, 199.

antedating the general introduction of anesthesia which may be classed as "chloroform deaths." [1]

In all indubitable cases the nature of the chloroform administered certainly plays an essential rôle; this fact is supported by convincing evidence, even though the percentage of deaths caused by chloroform administered during operations is unaccountably different in different years, times, and places. We can only attribute the existing diversity of opinion on the subject to the degrees of purity of the anesthetic used, the different modes of administration, the varying lengths of the time of anesthesia, the varying severity of the operation, and the state of the patient.

According to almost all authorities, the first danger from the use of chloroform consists in an interruption of respiration,[2] and it has been said that only after the observation of the pulse had superseded that of respiration did chloroform deaths become more frequent.[3] Experience has therefore clearly shown that every obstacle to respiration must be removed; the presence of irritating contaminants in the anesthetic must, as a consequence, be guarded against.[4] In France Sedillot,[5] who laid the greatest stress on the purest chloroform, did not have to record a single death; but in nine-tenths of all the chloroform deaths on record not a word is said in regard to the article employed, and consequently an important factor for forming an opinion is entirely excluded.[6]

[1] Sansom ("Chloroform," London, 1865) put the average mortality at 0.75 per 10,000; Richardson (*Med. Times and Gaz.*, 1870) at 2.8; and Morgan (*Med. Soc. Va.*, 1872), at 3.4.

[2] Metcalfe (*Trans. N. Y. Acad. Med.*, *1*, 145) stated in 1850 that his experience, extending then to 800 administrations, went to substantiate the fact that the use of impure chloroform causes headache, nausea, and bronchial irritation.

[3] Hewitt: *Proc. Roy. Med. and Chir. Soc.*, 890.

[4] Occhini [*Pharm. J.* (3), *8*, 988] came to the conclusion that the tolerance of chloroform can be assured by the preventive use of ammoniacal inhalations. Although chloroform and ammonia have a mutually antagonistic action on the heart, according to Ringer (*Practitioner*, 1881, 19), such a method is unnecessary if pure chloroform of anesthetic grade is properly administered to a patient prepared for it.

[5] *Bull. Soc. Chir.*, *7*, 1881.

[6] Some exceptions may be noted here. Dr. Hunter McGuire, surgeon in the Confederate Army during the Civil War, at one time remarked that chloroform had been administered 40,000 times in his corps alone without a single death, and he attributed the result largely to the splendid grade of chloroform which the Union Army had supplied him (almost all the chloroform used by the Confederate Army was captured from the Federals, although some of English manufacture came through a blockade.)

In 1882 Preston [*Pharm. J.* (3), *12*, 982] recorded that there had occurred 53 deaths in 152,260 administrations, and that in these 53 cases the impure chloroform had something to do with the fatal results. Atthill (*Brit. Med. J.*, DuBois-Reymond[1] appeared to have experimentally demonstrated that impure chloroform is dangerous. Therefore, to the rules for administering chloroform so often given, he considered that one omitted by all but Sedillot and his school should be added, namely, that the quality of the chloroform be carefully determined and only the very best chloroform procurable be employed for anesthesia.

There can be no question but that DuBois-Reymond obtained results which indicated rather a difference of degree than of kind between the action of pure and impure anesthetic chloroform. He insisted that the impurities act as cardiac depressants;[2] but, as was noted at

1892, *i*, 110) stated that he had administered chloroform in over two thousand cases, and considered that it is essential for its safe use that the chloroform be pure; he mentioned that the chloroform in general use at that time was often impure.

Chisholm (*Sci. Am. Suppl.*, No. 642, 10,259), who had in 1888 a record of 10,000 cases of general anesthesia with chloroform and no deaths, recorded his experiences, but made no mention whatsoever of the purity of the chloroform used.

[1] *Brit. Med. J.*, 1892, *1*, 209.

[2] The report of the Hyderabad Commission shows that deaths from chloroform are more frequently due to its checking the power of respiration than to arrest of the heart's action; see, in this connection, *Lancet*, 1890, *1*, 149, 421, 486, 1140, 1369; 1890, *2*, 356. Indeed, Lawrie states (*Chloroform*, 1901, 15) the doctrine that chloroform has no direct action on the heart must be considered as finally established. This is supported by the results of the biochemical observations of Feigl and Meier (*Biochem. Z.*, 1906, 316), who concluded that narcotic doses of pure chloroform have little or no action on blood pressure, the heart, or the circulatory system in general; and that these effects, when observed, are usually due to accompanying impurities in commercial alcohol. Some observations, however, seem to indicate that chloroform has an action on the circulatory system, although in these cases the purity of the anesthetic was not always considered. Cf., for example, Filehne and Biberfeld: *Z. f. exper. Path. u. Therap.*, 1906, *3*, 171; these investigators discuss the advisability of adding volatile analeptics to chloroform to prevent the reduction of blood pressure. Also, Busquet and Pachon (*Compt. rend. Soc. biol.*, *66*, 90) reported fibrillation of guinea-pig's heart under the influence of chloroform; Schaeffer and Scharlieb (*Proc. Physiol. Soc.*, 1903, 17) have insisted on the specific nature of the action of chloroform on cardiac muscles; and Embley and Martin (*J. Physiol.*, *32*, 147) have found that the action of chloroform in the blood in such quantities as may occur with inhalation of 1 to 3 per cent of vapor in air paralyzes the neuromuscular mechanism of the blood vessels. Tissot (*Compt. rend.*, *142*, 234) reported that more than 70 mg. of chloroform per 100 c.c. of arterial blood often causes death. It appears that chloroform forms a loose combination with hemoglobin; for a discussion of the physical chemistry of anesthesia, wherein this is discussed, see Moore and Roaf: *Thompson, Yates and Johnston Lab. Rept. Liverpool*, 1905-6, 151-94.

Waller (*Nature*, *76*, 403) "tested purified chloroform against the concentrated residue of its impurities, and found the former to be more powerful than the latter"; he did not, however, lay any stress upon the fact that anesthe time,[1] it does not appear that by their removal *pure* anesthetic chloroform[2] ceases to hamper circulation.[3] That the impurities are ordinarily very slight DuBois-Reymond admitted, but he contended that, although really infinitesimal in quantity, they act strongly in chloroform solution. From his experimental investigations and deductions, we learn that there are undoubted impurities which are able to intensify and hasten the lethal properties of chloroform, but we cannot definitely assert just what these are. We know, however, what the general likely impurities of anesthetic chloroform are; and, if proper precautions are taken to guard against their presence, untoward symptoms should not follow the proper administration of anesthetic chloroform.

Stability of Chloroform.—There has been not a little variety of opinion among chemists as to the nature and products of the decomposition of chloroform, especially the changes which chloroform undergoes upon exposure to air; in fact, this discordance dates from the introduction of chloroform as an anesthetic and prevails to-day. This condition is ascribable to the many influencing factors occasioned by the degree of purity of the chloroform which may have been under examination, the extent and nature of its exposure; but it is principally due to the failure to consider, and therefrom to correctly interpret, the rôle of the general variable, alcohol, and with it the accompanying moisture.

Decomposition of Pure Chloroform.—The products of the decomposition of "pure" chloroform, according to various investigators, may be thus summarized:

thetic chloroform can be of variable quality. Tunnicliffe (*Pharm. J.*, (4), *18*, 515) subjected samples of anesthetic chloroform to mechanical shaking for several days, then exposed them for a considerable time to direct July sunlight, and finally allowed them to evaporate in the laboratory to one-half bulk; the residual portion did not differ at all from pure chloroform in its toxic action on cardiac muscle.

[1] *Brit. Med. J.*, 1892, *1*, 236.

[2] "Chloroform Pictet" was taken as the example.

[3] See (1) *supra*, and also Charteris and MacLennan: *Brit. Med. J.*, 1892, *1*, 679, who believed that differently manufactured chloroform, although conforming to the tests specified by the *British Pharmacopœia*, might have different actions, and that possibly some of the dangers were due to the employment of impure chloroform—not by any means an original idea, yet one unique, coming as it did as the expression from a therapeutic standpoint. Therefore, they tested this assumption by administering six different makes of chloroform to guinea-pigs and found that there was a very evident difference in action exhibited by the different chloroforms, five of which were of standard British manufacture. Thus, with "chloroform Pictet" and one chloroform prepared from pure ethyl alcohol, recovery was quicker than with chloroform from rectified spirit, and three other makes from ethyl alcohol, and, further, during recovery no rhythmic tremors were observed.

Chlorin; Hydrogen chlorid	Morson; Maisch; Hager.
Carbonyl chlorid	Rump; Regnault.
Carbonyl chlorid; Hydrogen chlorid. . . .	Schoorl and Van den Berg; Dott.
Carbonyl chlorid; Chlorin.	Brown; Schacht and Biltz; Adrian.

The formation of carbonyl chlorid alone has been definitely agreed upon. Free chlorin[1] can only result from the photochemical decomposition of carbonyl chlorid: $COCl_2 \rightleftarrows CO+Cl_2$.

The decomposition of chloroform has been universally conceded to be an oxidation process. The extent of the oxidation is dependent upon the nature of the container, the amount of air present, the purity of the sample, and the intensity of the light to which it is exposed.[2]

It is likely that, in the cases where chlorin has been identified as an indication of incipient alteration of chloroform, hydrogen dioxid was the real cause of the reactions observed.

Rôle of Alcohol in Anesthetic Chloroform.—With regard to the changes which occur in anesthetic chloroform, that is, chloroform containing alcohol, during exposure to air and light, there also existed a decided diversity of opinion,[3] principally owing to the fact that no examinations were made during the course of the various investigations, so far as we are aware, for the presence of the oxidation products of alcohol in such chloroform. Some have even regarded the presence of absolute alcohol in chloroform as deleterious.[4] The whole subject

[1] *Vide* Baskerville and Hamor: *J. Ind. Eng. Chem.*, *4*, No. 4.

[2] It is generally accepted that chloroform is unaffected by light alone, and that light, although it accelerates oxidation, is not a necessary factor in the process. However, several investigators appear to have inclined to the view that light favors decomposition. In this connection, see Coehn and Decker: *Ber. 43*, 130; and Weigert: *Ann. Physik,* 1907 (4), *24,* 55. The influence of light on the reversible reaction, $CO+Cl_2 \rightleftarrows COCl_2$, seems to be purely catalytic. The rôle of any water is that of a true chemical catalyst. The decomposition of pure chloroform is accelerated by light, and carbonyl chlorid is formed with increased readiness in the presence of acids. Lowry and Magson (*Trans. Chem. Soc.*, *93,* 121) observed that the formation of carbonyl chlorid is evidently accelerated by the presence of acids.

[3] DuBois-Reymond (*Sci. Am. Suppl.*, No. 839, *13,* 413) considered that alcohol was of no use when impurities were present and was not necessary when the chloroform was pure; and Helbing and Passmore (*Helbing's Pharm. Record,* March, 1892) concluded from the few experiments which they made on the decomposing influence of sunlight on chloroform in the presence of concentrated sulphuric acid that the value of the addition of absolute alcohol to pure chloroform was questionable. These investigators *assumed* that the chloroform which they termed *pure* contained no alcohol.

[4] *Pharm. J.*, *7,* 345. Mialhe found that chloroform acquired "caustic properties" when mixed with a small quantity of absolute alcohol, and concluded that chloroform used in medical practice which caused vesication of the lips and nostrils contained a certain quantity of anhydrous alcohol, the presence of which was suspected by Soubeiran and Gerdy. Mialhe thought that the alcohol might act by combining with and coagulating the albuminous fluids of the body.

was therefore carefully investigated by one of us (C. B.)[1] It was also hoped to throw light on, if not fully explain, the rôle of alcohol[2] and other substances in the so-called preservation of chloroform, a satisfactory explanation of which had been wanting.

Those who have investigated the part played by alcohol in preserving chloroform, up to the present time have held that either chloroform decomposes in the presence of alcohol and that alcohol takes care of the decomposition products, or that the alcohol acts as a "catalytic retarding agent" (Stadlmayr).

We have definitely shown that the products of the oxidation of anesthetic chloroform are primarily the oxidation products of alcohol, and that no decomposition of chloroform itself occurs while the oxidation of alcohol proceeds. When the oxidation of alcohol reaches a maximum, decomposition of the chloroform goes on, as in the case of pure chloroform, with the exception that chlorinated derivatives of the oxidation products of alcohol may result. The decomposition of the chloroform itself is retarded, even prevented, so long as oxidation of the alcohol proceeds, and the retardation is consequently dependent upon the amount of alcohol present. The preservative action of alcohol, first suggested by Squibb in 1857 and later (1863) by Brown, independently, is essentially that of a "shunt," and any substance soluble in chloroform and readily oxidizable will exert an inhibitory effect on the oxidation of chloroform itself; for example, sulphur and many other substances.[3]

[1] *Loc. cit.*

[2] The amounts of alcohol stated as permissible in the various official chloroforms intended for anesthetic purposes are as follows:

Belgium	1.0 per cent.
Denmark	1.0 per cent.
Sweden	0.5—1.0 per cent.
United States	0.6—1.0 per cent.
France	0.005 part by weight.
Italy	0.5 per cent.
Switzerland	1.0 per cent absolute.

[3] "Inorganic Preservatives." Boettger (*Bull. de therap.*, May 15, 1864) found that chloroform which had undergone decomposition by exposure to sunlight might be purified by agitation with sodium hydroxid, and stated that when chloroform was placed in contact with sodium hydroxid it might be preserved indefinitely. Newman and Ramsay (*Lancet*, Jan. 23, 1897) recommended a similar treatment, namely, the use of lime, both for purification of decomposed chloroform and as a preservative. Brown (*Pharm. J.*, *61*, 669; *Mon. Sci.*, *53*, 423), however, found that the method of Newman and Ramsay was unsatisfactory. These compounds act by combining with the decomposition products of chloroform. They do not prevent decomposition.

Allain (*Chem. Ztg.*, *19*, 310) learned that sulphur, purified by digesting for 24 hours with ammonia, and then carefully washed and dried, would effectually prevent the decomposition of chloroform. (In a sample saturated with sulphur, after exposure to sunlight for four months, no impurities could be detected and

All compounds which have been found to serve as preservatives of chloroform are reducing agents, and the effect is only due to their capacity for oxidation.

Character of Containers.—Anesthetic chloroform should preferably be furnished in vials, ampules, or bottles of high-grade anactinic

the sample produced a ''normal anesthesia''). Temoin (*Pharm. central.*, *45*, 872; *Chem. and Drug.*, *64*, 973) reported that chloroform to which 0.4 per cent of sulphur had been added underwent no alteration on keeping, even when exposed to light. This was verified by Dott [*Pharm. J.*, (4), *2*, 249], who also experimented successfully with morphin, gallotannic acid, and hypophosphorus acid.

''Organic Preservatives.'' Masson [*J. pharm. chim.*, (6) *9*, 568] found that poppy-seed oil exerted a marked preservative action on chloroform. A specimen containing 0.1 per cent was exposed to direct sunlight for 21 days, at the end of which time there was no decomposition; and one with 0.2 per cent of the oil, kept in ordinary light, showed no decomposition in three years. From Masson's own observations on the preservative powers of alcohol (Masson considered that the preservative action of alcohol on chloroform was demonstrated by the condition of the samples at the *Pharmacie Central*, in 1899, where specimens containing only 0.1 per cent and exposed in yellow glass bottles in a window to diffused light were found to have kept perfectly after standing for ten years), one would conclude that he considered it perfectly satisfactory.

Breteau (''French Patent,'' 1905, 353, 858) devised a method for the prevention of the alteration of chloroform in the air and light, and of indicating finally the decomposition, which consisted in adding to the chloroform from 5 to 10 thousandths parts of one of the following bodies: pith of elder, cork of coniferæ; and 3 to 5 thousandths parts of guaiacol, ionone, spermaceti, cholesterol, terpineol, citronellic acid, geranic acid, etc. He stated that the elder pith might be impregnated with a solution of a material colorless in chloroform, and dry, this material, as Congo red, undergoing a change of tint under the influence of the decomposition products of chloroform. Congo red was stated to be very desirable, since it turned blue, and gradually decomposed, when the alteration was decided. Later Breteau mentioned the following substances as preservatives of chloroform in addition to those previously mentioned: ethyl alcohol and ethyl ether, nitrobenzene, methyl and amyl salicylates, thymol, and coniferin. As indicators, he stated that cellulin and gelatin might be used in addition to dyestuffs and that the indicator might also consist of a dyestuff which changed color in the presence of the decomposition products of chloroform (''First Addition to French Patent,'' 353, 858, 1905, dated June 30, 1905). Still later he stated that the indicator might be interposed between the chloroform and the stopper of the container, or might be fixed to the stopper, or might even form the stopper. Cinnamic acid and inosite-mono-methyl ether were added to the list of preservative agents (''Second Addition to French Patent,'' dated Nov. 18, 1905, 358, 858).

Breteau and Woog (*Compt. rend.*, *143*, 1193) found that, by the use of 2 to 4 parts per 1,000 of oil of turpentine, purified spermaceti, menthol, terpineol, citronellol, geraniol, amyl and methyl salicylates, guaiacol, thymol, safrol, ionone, or methyl-protocatechuic aldehyd, chloroform could be preserved in white glass bottles in diffused light. A number of indicators show the acidity of chloroform undergoing incipient decomposition before it is sufficiently developed to affect silver nitrate.

glass,[1] containing about the quantity sufficient for one narcosis, and at the most not more than can be used within several days. If, for any particular reason, chloroform is ordered in a large container, it is advisable, immediately after opening it, to subdivide the entire remaining contents into two-ounce bottles, taking care to fill the small bottles completely. In no case should chloroform be gradually withdrawn in small quantities from large bottles or carboys. When it is found necessary to store anesthetic chloroform it should always be kept in a cool, dark place, in well-filled, or, better still, completely filled, tightly stoppered bottles of anactinic glass.

The keeping qualities of anesthetic chloroform may be seriously affected by the character of containers. The question of keeping anesthetic chloroform in tin containers has been much agitated in the United States War Department, and within the last ten years this department has decided in favor of the tin container. We (C. B.) believe that glass containers are more conducive to the maintenance of purity for several reasons. First, in cleaning the vessels before filling, any foreign matters present may be readily observed and the bottles properly cleaned. Second, in the case of tins, some of the flux used in soldering may be introduced and thus impart an acid reaction to the chloroform. Hydrochloric acid accelerates the decomposition of chloroform. The introduction of this flux is also a problem in ether manufacture which requires the utmost care. Third, we have been informed [2] that "moist chloroform in the presence of a metal will slowly form traces of CH_2Cl_2 and probably . . . that it is possible to distill pure, dry chloroform in a metal container and produce a decomposition, as shown by the following formula:

$$4CHCl_3 + Cu_2 = C_2Cl_6 + 2CH_2Cl_2 + Cu_2Cl_2.$$

This reaction, however, takes place so slowly that it would never be noticed except in the handling of a material on which superlative efforts have been expended for years in order to get the last extreme of purity." Moreover, "all chloroform contains traces of CH_2Cl_2."

Stoppers for the Containers.—The *Pharmacopœia of the United States* formerly required the use of glass-stoppered bottles,[3] but subse-

[1] The glass should show no alkaline reaction when the bottle is filled with distilled water containing several drops of phenolphthalein solution and heated at 100° C. for six hours. On the action of alkalies on chloroform, see Berthelot, *Bull. Soc. chim.*, (2), *29*, 4; André, *Compt. rend.*, *102*, 553; de St. Martin, *ibid.*, *106*, 492; and Mossler, *Monatsh.*, *29*, 573. It appears to be well established that potassium hydroxid in alcoholic solution will slowly decompose chloroform.

[2] By a prominent manufacturer in a private communication.

[3] All of the manufacturers of chloroform in this country use brown glass ("anactinic") bottles. Of the eight different makes of German chloroform that have come into our hands, only two were contained in colorless bottles.

quently changed this to well-stoppered bottles, thus allowing the use of cork stoppers, a practice which has become general in this country.[1]

Two objections have been urged against the employment of cork stoppers:

First, the chloroform penetrates the cork after some time, especially during the agitation incidental to shipment, causing shrinkage and perhaps leakage.[2] The second objection is that organic matter is extracted from the cork, and the chloroform fails when the sulphuric acid test, a test used for the detection of fusel oil, chlorinated decomposition products, etc., is applied. To obviate these difficulties certain manufacturers of chloroform have adopted the plan of covering the bottom of corks with tin foil, a procedure which so far has been found to be satisfactory, but which may be open to some of the objections to tin containers. Other manufacturers use a paper or parchment covering, and still others select only the best corks and extract them thoroughly with chloroform before use.

The Changes Which Anesthetic Chloroform Undergoes When a Current of Oxygen Is Conducted Through It.—Among the anesthetic mixtures the combination of chloroform vapor with oxygen was used shortly after the introduction of chloroform as an anesthetic, and it has recently been reintroduced into practice by Neüdorfer, Kreutzmann, and others. It is stated by anesthetists that oxygen does not antagonize the action of chloroform on the heart or nerve centers, but that it protects the patient from the dangers which result when chloroform is administered while his blood is in a condition of undue venosity [3] and that it prevents any intercurrent asphyxial condition. Gwathmey has stated positively [4] that oxygen increases the value of all inhalation anesthetics as regards life.[5]

[1] In Germany, however, glass-stoppered bottles are used by prominent producers of anesthetic chloroform.

[2] Allain [*J. pharm. chim.* (3), *9,* 571] and Masson [*ibid.,* (6), *9,* 568] have recommended that, when chloroform is kept in cork-stoppered bottles, a lute of "bichromate gelatin" should be used to prevent leakage. This is unnecessary when a proper stopper is used, and the employment of lutings on the stoppers has led to differences between the manufacturer and consumer in the past.

[3] Buxton: "Anæsthetics," 4th ed., 299.

[4] *Med. Rec.,* Oct. 8, 1910, 616. On chloroform-oxygen narcosis, see also Ziegner: *Münch. med. Woch., 57,* 2585.

[5] It has been maintained, however, that chloroform undergoes alteration in this procedure. Falk (*Deut. med. Woch.,* 1902, 862) attempted to demonstrate that the passage of oxygen through chloroform (the purity of this was not described, but it was evidently of the grade specified by the German Pharmacopœia) produces chemical changes in the anesthetic. He reported that, after the passage of oxygen for 20 minutes, changes could be recognized in the residual chloroform, in some cases hydrochloric acid and in others an acid having reducing properties (acetic acid, resulting from the oxidation of the alcohol in the chloroform used?) having been recognized. The quantities produced were

We have investigated the changes which anesthetic chloroform undergoes when a current of oxygen is conducted through it. We have found that no serious oxidation occurs during the period of anesthesia, and that the oxidation which does occur has to do only with the alcohol present. Furthermore, it was determined that the oxidation products were entirely removed when the chloroform vapor was swept by the oxygen current through water.[1]

The Decomposition of Chloroform Vapor Upon Exposure to Gas Light, Etc., During Administration.—The occurrence of untoward symptoms during the administration of chloroform in rooms in which gas is burning,[2] or where there are other varieties of naked flames,[3] or strong electric light[4] has been reported; consequently authorities have warned

found to be greater the higher the temperature and degree of illumination. This work is partially contradicted by the clinical results obtained by anesthetists, and by the observations of Willcox and Collingwood (*Brit. Med. J.*, Nov. 5, 1910) on the administration of oxygen bubbled through absolute alcohol. They stated that the administration of oxygen bubbled through absolute alcohol is a marked cardiac stimulant. It is especially important to note that they found the administration pleasant and non-irritating to the patient—that it caused no ill-effects to the lungs or bodily system.

[1] Baskerville and Hamor, *loc. cit.* Anesthetic chloroforms containing 0.56 to 1.00 per cent of alcohol and 0.03 to 0.05 per cent of water were used. Oxygen was allowed to flow through 3½ to 4 ounces of chloroform in the Gwathmey apparatus at such rates that about half remained in the vaporizer after 3½ to 10½ hours. The vapors were cooled by a suitable condenser and collected. The examination of the residue and condensed chloroform showed the following:

Acidity (acetic acid):	
Chloroform used	None.
Residue in container	0.00015 gm. in 100 c.c.
Condensed chloroform	None.
Sulphuric acid test:	
Chloroform used	Negative.
Residue in container	Marked reaction.
Condensed chloroform	Negative.

[2] One of the earliest references to the decomposition of chloroform by exposed flames is in the *China Med. Missionary J.*, Dec., 1888, 160. Iterson, Fischer, and Zweifel drew attention to this decomposition in 1889, and in that year Patterson narrated personal experiences (*Practitioner, 42,* 418). See also *Lancet,* March 12, 1898; *Birmingham Med. Rev.*, Aug., 1892; but especially, Schumburg, *Apoth, Ztg., 13,* 758; Gerlinger, *ibid., 17,* 314; and Eisenlohr and Fermi, Ber., 1892, 585. Soubeiran and Liebig had observed that a mixture of chloroform and alcohol in equal measures burns with a smoky flame and pungent odor.

According to Ramsay and Young (*Jahresber.*, 1886, 628), the vapor of chloroform, when passed through a red-hot tube, yields hexachlor-benzene, perchlorethane, and some perchlorethylene.

[3] Oil lamps and candles. Waddelow, *Pharm. J.* (4), *6,* 324.

[4] Buxton ("Anæsthetics," 1907, 180) states that he observed that chloroform decomposes when a powerful electric lamp is held over the inhaler. Cf. Schoorl and Van den Berg (*Pharm. Weekblad, 43,* 47), who show that air is necessary for such decomposition.

against the performance of surgical operations by gas light.[1] As to just what products are formed there is a difference of opinion. Iterson[2] considered that there occurred a combination of the chloroform vapor with the combustion gases, whereas Hartman[3] and Waddelow[4] observed an odor of chlorin. Von Langenbeck considered that chlorocarbonic acid was formed, and Breaudat found hydrochloric acid and an acrid oil.

At all events, when a mixture of chloroform vapor and air is decomposed by a flame, irritating compounds are formed.[5]

Effect of Agitation Upon Anesthetic Chloroform.—Tunnicliffe concluded that when chloroform is initially pure, except for added alcohol, it remains free from pharmacological deterioration under the ordinary conditions of military transport, providing that the bottles are kept closely stoppered and protected from strong light. Baskerville subjected several samples of chloroform to intermittent agitation for over two hundred hours in a Spiegelberg shaking apparatus and learned that:

(1) When anesthetic chloroform is subjected to agitation accompanied by shock, the alcohol present undergoes oxidation, the extent of this being dependent upon the amount of air present, the nature of the agitation, especially its violence and length, and the light exposure. The experiments were all made in daylight at about 20° C.

(2) Impurities decomposable by sulphuric acid are formed under such conditions, these resulting both from oxidation of the alcohol and, when unprotected cork stoppers are used, from the extraction of organic matter from the stopper or luting. "Chlorinated decomposition compounds" may form, although we are inclined to attribute the response had for their presence to oxidation products of alcohol in this case.

Since these conclusions apply to anesthetic chloroform of the present *United States Pharmacopœia* degree of purity and strength, care should be exercised to see, when such chloroform is shipped for considerable distances, or is to be kept in stock on shipboard, that a minimum amount of air is present.

Standards of Purity for Anesthetic Chloroform.—There have been instances of sophistication of anesthetic chloroform,[6] and these, while

[1] E. g. Von Langenbeck: *Pharm. Ztg.*, April 6, 1889, 221.

[2] *Ibid.*

[3] *Ibid.*

[4] *Loc. cit.* See also Wardleworth, *Pharm. J.* (4), *14*, 376.

[5] *Lancet*, 1899, *1*, 1728; *Therap. Gaz.*, 1899, 601; Breaudat's "Dict. de physiologie." Cf. Ragsky, *J. prakt. Chem.*, *46*, 170.

[6] Baird (*Proc. Mass. Pharm. Assn.*, 1906, 59) examined six samples of chloroform in 1904 and found one adulterated.

rare, have been cases mainly of substitution of commercial chloroform.[1] The purity of the drug may be endangered through lack of chemical control in the manufacture or from careless storage. It is quite evident that every sample cannot be tested. Reliance must be placed upon the integrity of the manufacturers. Confidence in the product, however, may be enhanced by chemical examinations of shipments from time to time. Manufacturers and users will find that compliance with the tests given in Appendix II will insure a drug suitable for anesthesia.

SPECIAL PHYSIOLOGY

The difficulties encountered in the study of the effects of chloroform upon the organism have been attributed by Gill [2] to the *isolation of the phenomena of the physiological action of this agent*—in other words, to "the arbitrary separation of prominent phenomena from their intimate surroundings." Conclusions should not be drawn from an individual phenomenon, but from a set of phenomena, or a "state." Gill cites, as an illustration, the phenomenon of pallor, which is a direct manifestation of reflex stimulation of the vasomotor center. It is also a direct result of primary cardiac syncope, and, again, it is a secondary result of stomachic inhibition of the respiratory center. The fallacy of drawing conclusions from pallor alone, without the aid of the accompanying phenomena, is obvious.

In considering the special physiology of chloroform, as well as of the other inhalation agents, for purposes of convenience the phenomena have been grouped according to the part of the organism chiefly involved. It is to be borne in mind, however, that the effects of chloroform upon one system of organs cannot be entirely dissociated from its effects upon other systems, and that a given result may be produced by different causes, or by a combination of causes.

Inasmuch as the physiological action of inhalation anesthetics in general is based largely upon observations made concerning the effects

[1] This appears to have been practiced as late as 1885 in this country, since Davenport [*Am. J. Pharm.*, (4), *16*, 111] reported that fourteen out of fifteen samples of chloroform examined by him in that year were the crude article. Chloroform of inferior grade, frequently encountered about 1880 [see Perrin: *Pharm. J.*, (3), *9*, 614; and Championnière, *ibid.*, (3), *12*, 623], especially in France, is now rarely represented as being of anesthetic grade. This is largely due to the stringency of many of the pharmacopœias, but is in part to be ascribed to the experience and integrity of the manufacturers. It sometimes happens, however, that chloroform is declared to be impure by surgeons, following a fatality from its use in particular, when this is not the case. For an example, see the experiences of Blum: *Pharm. J.*, (4), *19*, 103.

[2] Gill, Richard: "$CHCl_3$ Problem," 1906, *2*.

of chloroform, the discussion of the special physiology of this agent may entail a certain amount of repetition.

Effects Upon the Respiratory System.—The effects of chloroform upon the respiratory system are secondary to, and largely dependent upon, the effects of this agent upon the circulation, low arterial tension being a very important factor. The respiratory system, even to the extent of complete cessation of breathing, is also affected through the action of chloroform upon the nervous mechanism of respiration.

When concentrated chloroform vapor is administered, asphyxial symptoms immediately appear, free breathing being suspended from reflex closure of the larynx. With a low percentage of chloroform, according to the experiments of Collingswood and Buswell,[1] chloroform quickly produces apnea of a pronounced character. This is not due to diminution of carbon dioxid in the blood, for it can be produced by chloroform mixed with expired air. Chloroform diminishes the excitability of the respiratory center to the carbon dioxid stimulus.

Buckmaster and Gardner [2] have given a number of plethysmographic tracings to show the lung ventilation during chloroform anesthesia with different percentages of chloroform and ether, and also analyses of the blood gases. They show that with unimpeded respiration under anesthesia by chloroform given at a slight positive pressure, the ventilation of the lung takes place at a lowered level. During a narcosis in which respiration continues, the lung ventilation is diminished in the first three minutes by about sixty per cent of its original value, and by a similar amount after prolonged anesthesia. They consider that the carbon dioxid content of the blood is reduced below a threshold value by any state of hyperpnea prior to administration of the drug, and this diminution in carbon dioxid content plus the diminished excitability of the respiratory center would suffice to retard or abolish the activity of the center. Gas analyses actually show that with a deep and rapid respiration there is a marked fall in the carbon dioxid content of the blood. They also bring forward evidence to show that the diminution in oxygen content of the blood during chloroform narcosis is not due entirely to diminished alveolar ventilation, but to the action of the drug on the red corpuscles. For further effects of chloroform upon the respiratory system see Stages of Anesthesia, p. 306.

Effects Upon the Circulatory System.—The effects of chloroform upon the circulatory system have been made the subject of extensive investigation, from both the experimental and the clinical points of view.

The action of chloroform upon the *blood,* when administered by inhalation, has engaged the attention of a number of investigators. It is

[1] Collingswood and Buswell, *Proc. Physiol. Soc.*, 1907, 34.

[2] Buckmaster and Gardner, *London Roy. Soc.*, Nov. 16, 1911; *Nature, 88,* 131.

conceded to have a practical bearing upon the administration of this agent.

Gill,[1] in discussing the relation between chloroform and the blood, emphasizes the point that this relationship is twofold. The negative action of the chloroform causes deoxygenation by diminishing the normal supply of air to the alveoli; its physiological, or physicochemical, action is indirectly the cause of the suspension of the functions of the cerebral centers. The quantity of chloroform vapor that is absorbed may, therefore, be limited to the amount of oxygen requisite to be abstracted from the blood. Inasmuch, however, as the blood, which is directly affected by the physiological action of chloroform, is a variant, and as its actual condition necessarily influences the result that appears in it, it follows, as Gill contends, that each individual example requires its own anesthetic degree of chloroform action. Any undue interference with the proper function of the respiratory apparatus tends, by increasing the deoxygenation of the blood, to intensify the action of chloroform.

According to Carlson,[2] the osmotic concentration of the blood is increased during chloroform anesthesia in proportion to the depth and duration of the anesthesia. This is probably due chiefly to the amount of the anesthetic dissolved in the serum.

The action of chloroform on the reducing power of the blood has been studied by Lambert and Garneier.[3] When defibrinated blood is treated with a current of air containing chloroform vapor, the reducing power of the blood is sometimes increased at once, always after an hour, and this increased reducing power is not due to the dissolution of chloroform in the blood. When, however, defibrinated blood and similar blood containing chloroform are made to circulate respectively through the two lobes of a fresh liver, the glycogen disappears more rapidly in the lobe through which the blood containing chloroform circulates, and at the same time the reducing power of this blood increases more rapidly than that of pure blood, and in a higher degree than corresponds with the glycogen that disappears. It follows, therefore, that the increased reducing power is not due simply to a more active formation of sugar or to a diminution in its rate of consumption.

Tunnicliffe and Rosenheim[4] studied the action of chloroform on the *heart* by adding saline fluid perfused through the heart by Locke's method. The depressing action on the heart produced by chloroform was found to be very marked. It was delayed, however, when, in addition to the saline fluid, lecithin was added. The quantity of chloroform

[1] Gill: *Loc. cit.*, 254.

[2] Carlson: *Am. J. Physiol.*, *21*, 161.

[3] Lambert and Garneier: *Compt. rend.*, *132*, 493.

[4] Tunnicliffe and Rosenheim: *Proc. Physiol. Soc.*, 1903, 15.

which seriously affected the heart was practically identical with that in the blood in fully narcotized animals.

Schaefer and Scharlieb [1] have insisted on the specific nature of the action of chloroform on *cardiac muscles*. The state of the heart called paralytic dilatation is regarded by them as one of excitatory inhibition; excitation of the terminal inhibitory mechanism is, however, distinguished from excitation of the vagus and its endings, and can be brought about by chloroform when the vagus endings are thrown out of action by atropin. The high development of the inhibitory mechanism in the heart explains why it, of all muscular tissues, should be most profoundly affected.

It is of special interest to note that in the frog chloroform produces contraction of the blood vessels, and not dilatation, as most observers have stated. In the frog used, the central nervous system was destroyed, either entirely or with the exception of the cerebrum.

The action of chloroform on the *blood vessels* has been studied by Embley and Martin [2] with reference to the kidneys and bowels. They found that chloroform, in the blood in such quantities as may occur with the inhalation of one to three per cent of the vapor in the air, paralyzes the neuromuscular mechanism of the blood vessels. This partly, at least, accounts for the fall of blood pressure which results. These findings are not contradictory to those of Schaefer and Scharlieb, but rather supplement them.[3] Vessels in different parts may react in different ways to the same poison in different doses. The dilatation is mainly confined to the splanchnic area.

It is now generally conceded by clinical observers that a dilatation of the entire cardiovascular system follows the inhalation of chloroform. The fall of blood pressure is thus accounted for.

Tissot [4] has studied the proportion of chloroform in the organism during anesthesia. In animals rapidly anesthetized by chloroform the amount present in the blood may exceed 50 mg. per 100 c.c., and may reach 70-80 mg. If the anesthesia is slowly induced, it sinks to 45 or even 35 mg. *More than 70 mg. per 100 c.c. of arterial blood often causes death.* In the brain the chloroform is in equilibrium with that in the blood. If a fatal result ensues, at the moment of the heart's arrest the amount in the venous blood is more than in the brain, but afterward the amount in the brain is often higher than in the venous blood. *The amount in the venous blood is always less than in arterial blood.* The length of the period of anesthesia, proportion of chloroform in the brain, and the rapidity of blood circulation are important factors.

[1] Schaefer and Scharlieb: *Proc. Physiol. Soc.*, 1903, 17.
[2] Embley and Martin: *J. Physiol.*, *32*, 147.
[3] Schaefer and Scharlieb: *Loc. cit.*
[4] Tissot: *Compt. rend.*, *142*, 234.

Meyer and Gottlieb[1] have directed attention to the narrow margin between a therapeutic dose and an overdose of chloroform. They found that in deep narcosis, with compensated heart action, the blood content of chloroform is 0.035 per cent, whereas in the blood of a dog anesthetized to the point of cardiac failure, the chloroform content was 0.058 per cent. The reason for this narrow margin, they hold, is that, in spite of the fact that respiration ceases first, the heart is the organ primarily affected. This explains why artificial respiration often fails unless the pressure upon the chest is sufficiently forcible to expel the chloroform-laden vapor from the left ventricle. Otherwise the heart continues to be poisoned. The left ventricle, which is principally affected in heart failure, was found by Pohl, according to Meyer and Gottlieb, to contain 0.22 per cent of chloroform, whereas the right heart contained only 0.02 per cent. These investigators found, in some of their experiments, that chloroform could be detected in the blood seven hours after cessation of the anesthesia. The danger comes, not from the amount of chloroform contained in the blood, but from its hypersaturation with the vapor at some one time.

Abel[2] found that in the stage of complete anesthesia the brain contains three times more chloroform than an equal weight of blood; blood containing 0.015 per cent, and brain substance 0.0418 per cent. The serum of the blood contains very little chloroform during anesthesia, the greater part that is taken up and carried by the blood being bound to the red and white corpuscles.

The effect of chloroform upon the *heart* itself has been the subject of much investigation and wide diversity of opinion. By some[3] it has been maintained that primary cardiac paralysis occurs only with high percentages of vapor; by others[4] it has been claimed that permanent stoppage of the heart is no more likely to occur with high percentages than with low ones. These views have been challenged by those[5] who hold that the heart is never primarily affected, its action being maintained until respiration has ceased. Despite these diverse findings, it is now almost unanimously agreed that chloroform, administered to the degree of surgical narcosis, acts as a direct heart sedative or depressant, and that death occurs as a result of this action.

The indirect action of chloroform upon the heart has also given rise to diversity of opinion, particularly with reference to the question of fatality. Whether this action is the indirect result of the irritation by the vapor upon the sensory nerve-endings within the upper air and pul-

[1] Meyer and Gottlieb: "Experimentelle Pharmakologie."
[2] Abel: *Bull. Johns Hopkins Hosp.*, Jan., 1895.
[3] Snow: "On Chloroform and Other Anæsthetics," 1858.
[4] Comm. Royal Med. and Chir. Soc.; also, Glasgow Comm. (1879-1880).
[5] First Hyderabad Commission, 1891.

monary passages, giving rise to stimulation of the cardio-inhibitory center, or whether it is a direct result of the effects upon this center of the anesthetic circulating in the blood, has not been determined.

The entire subject of cardiac inhibition has been studied experimentally by Embley.[1] He found that cardio-inhibitory effects are common with atmospheres containing more than two per cent of chloroform vapor. The degree of inhibition increased with increasing percentages of the vapor. His findings with reference to fatal cardiac inhibition are not in keeping with those of the Hyderabad Commission.[2] Embley held that slowing or complete inhibition of the heart's action did not occur in animals in which he divided the vagi, and that in order to bring about complete and permanent cardiac inhibition more injury to the heart is necessary than occurs in slight chloroform anesthesia. The Hyderabad Commission, on the other hand, held that animals may be killed by vagus excitation. As Hewitt has pointed out, the possibility and extent of the application of these and similar observations to human subjects are yet to be determined.

The vasomotor center is primarily stimulated by chloroform, and does not become paralyzed by the direct action of the agent until the stage of deepening narcosis, when death is imminent.

The cause of death from the administration of chloroform has been made the subject of so much experimental and clinical investigation that it has been thought advisable to consider this phase of the action of this agent upon the organism under a special heading.

Effects Upon the Nervous System.—According to the consensus of opinion, based upon clinical observation, chloroform produces a progressive paralysis of the central nervous system, the order in which this results being as follows: (1) The higher cerebral centers, involving the intellectual faculties; (2) the lower cerebral centers, involving sensation and motion; (3) the spinal cord, involving reflex action; (4) the medullary centers, involving vital function.

For purposes of convenience the above order will be followed in the ensuing brief discussion of the effects of chloroform upon the nervous system. For further data on this subject see the Stages of Anesthesia, p. 306.

Effects Upon the Muscular System.—The effects of chloroform upon the muscles of the heart and blood vessels have been discussed under Effects upon the Circulatory System.

Muscular spasms are prone to characterize the ordinary administration of chloroform, this tendency being the greater the more vigorous is the muscular development of the subject. The muscles of the extrem-

[1] Embley: "The Causation of Death During the Administration of Choloroform," *Brit. Med. J.*, Apr. 5, 12, 19, 1902.

[2] *Loc. cit.*

ities, abdomen, chest, larynx, neck, and jaws are particularly apt to be involved in tonic spasms during the earlier stages of chloroform anesthesia. As anesthesia progresses to the deeper stages, muscular relaxation follows spasm, as a rule. Sometimes, however, clonic spasms of certain muscles, particularly of the fingers (piano-playing movements), may be noted, the extremities may be involved in slow, coördinated movements, or jerky adductor movements of the arms may occur, presumably as the result of clonic contractions of the muscles of the chest. Spasmodic tongue retraction may occur, giving rise to stertor and stridor.

(For the important significance of the muscular phenomena of chloroform anesthesia see Stages of Anesthesia, p. 306.)

Effects Upon the Glandular System and Other Structures.—The mucous, salivary, and sweat glands are stimulated to hypersecretion during light chloroform anesthesia.

Nicloux and Fourquier demonstrated that chloroform has a special affinity for fat, for liver, kidney, spleen, and nerve tissue, and for striped muscle. According to these investigators the liver of the fetus is even more materially affected than is that of the mother.

Thompson [1] conducted a large number of animal experiments, which led to the following conclusions with reference to the kidneys:

(1) The volume of urine secreted by the kidneys is affected, as a rule, during chloroform narcosis, in two ways. In the early stages, when the anesthesia is light, the quantity is frequently increased, whereas, during full anesthesia, the secretion is always diminished, and may be suppressed.

(2) The after-effect is invariably a great increase, which may reach to four times the normal volume for the same period of time. The maximum outflow may occur about three hours after removal of the anesthetic.

(3) The total excretion of nitrogen is, as a rule, greatly increased. The averages taken from experiments with diminished urine volume show that during the anesthetic period the excretion of nitrogen fell to eighteen per cent of the normal, whereas the quantity of urine in the same series fell only to thirty-five per cent of the normal. In a minority of the experiments with increased urine volume, the total nitrogen per period was also increased, but to a much less extent than the volume of urine in the same experiments.

(4) The urine secreted during chloroform anesthesia is almost invariably more dilute (contains a lower percentage of nitrogen) than the normal urine. This holds good even when the volume of urine is diminished. Hence it is inferred that chloroform affects not only the blood

[1] Thompson: "Anæsthetics and Renal Activities," *Brit. Med. J.*, Mar. 17, 1906.

flow through the glomerules, but also the secretion of nitrogenous solids in the tubules, the latter being even more marked than the former.

(5) There is a general but not accurate correspondence between urine outflow, kidney volume, and blood pressure. The relationship between the first and second is closer than that between the first and third.

(6) In prolonged narcosis, with marked diminution of urine volume, there is a considerable exudation of leucocytes in the renal tubules, which subsequently escape with the urine. The condition is probably produced by more or less vascular stasis in the glomerular vessels.

(7) The excretion of chlorids is much increased both during and after chloroform narcosis. In the fourth period, after the removal of the anesthetic, the amount in the urine of the dog may be ten times the normal quantity.

(8) Albumin appears in a small proportion of experiments after chloroform inhalation.

(9) Reducing substances other than glucose are almost invariably increased. The nature of the reducing substance has not been definitely determined.

Chloroform, according to Apperly's[1] observations, affects the cells of the liver, interfering with the metabolism of fats. The poisonous fatty acids, which cause an acid intoxication, are thus thrown out into the blood. The cells lining the tubules of the kidneys are so damaged that their excretory function is interfered with. As acute infections, especially of the peritoneum, cause changes in the same organs, chloroform should not be given in these cases.

According to Delbet[2] and his co-workers, chloroform has a special affinity for the adrenals and checks their functioning. These effects are responsible, they hold, for operative shock and for sudden quiet death in coma after an operation. Delbet injects 0.0004 or 0.0006 gm. epinephrin subcutaneously at the beginning of the operation, thus rendering anesthesia more regular, diminishing operative shock, and lessening the frequency of sudden post-operative fatalities. If prostration continues, another dose of epinephrin is given the next day.

Levy's[3] investigations seem to prove that epinephrin may be safely injected just before induction, or during deep anesthesia, but that a certain definite risk is taken when injection is made during light chloroform anesthesia.

For further discussion of the effects of chloroform upon the glandu-

[1] Apperly, R. E.: "Effect of Chloroform and Ether on Liver and Kidneys in Health and Its Significance in Certain Infective Conditions," *Brit. Med. J.*, Sept. 14, 1912, *2*, 2698.

[2] Delbet: *Revue de Chirurgie*, 1912, No. 4, 32.

[3] Levy: *Brit. Med. J.*, Sept. 14, 1912.

lar system, see sections on Elimination, p. 309, and After-Effects, p. 310.

Causes of Death from the Administration of Chloroform.—In summing up the action of chloroform upon the organism, Hewitt says[1]: "So far as we have gone, then, it would seem that we have in chloroform a drug which is a powerful protoplasmic poison; which, when given in toxic quantities, leads to death of the organism, not because it paralyzes respiration—for, were it merely a respiratory depressant, artificial respiration would be invariably successful in averting death—but because, as recent researches have shown, it markedly depresses the circulation. It is this circulatory depression which renders it difficult to resuscitate patients. The fact that an overdose of chloroform generally paralyzes respiration before the heart's action finally ceases must not be allowed to overshadow the more important fact that, prior to and during the respiratory failure, the heart has, in many cases, ceased to circulate blood through the organism. Whether in true chloroform toxemia the fatal circulatory failure is principally (a) a failure of cardiovascular origin due to chloroform directly affecting the musculature of the vascular system *as a whole;* whether it is principally (b) a failure of cardiac origin, the chloroform directly affecting the *cardiac muscle relatively more than the walls of the arteries and arterioles;* whether it is principally (c) a failure due to the action upon the *nervous mechanism which controls cardiac action;* or whether it is principally (d) due to a paralysis of the *vasomotor mechanism*—we cannot at present positively say."

According to Gill:[2] "In narcosis which runs its course uncomplicated by vasomotor, stomachic, or (primary) cardiac disturbance the ultimate cause of death is oxygen-starvation. The respiratory muscles tend to become exhausted, and their failure to act forms a proximate cause: the action of the heart also tends to fail, and cardiac syncope, indirectly induced by the negative action of the agent when in the form of vapor, becomes the intermediary means of the causation of death. The question which fails first, the heart or the action of the respiratory machine, will be decided by the initial condition of the former. If the heart be abnormal, and, in consequence, less able than normally to withstand increased pressure in its right ventricle, it will fail before the respiration. But if the heart be normal, the action of the respiratory machine will cease before the pulse disappears, because the power of resistance possessed by the respiratory muscles is known to be less than that of the heart."

Luke and Ross[3] attribute chloroform deaths to *cardiac syncope* arising from the following:

[1] *Loc. cit.,* 1912, 126.
[2] Gill, Richard: "The $CHCl_3$ Problem," *2, Physiological Action,* 284.
[3] Luke and Ross: "Anæsthetics," 3rd ed., 192.

(1) *Reflex stimulation of the vagus,* causing inhibition of the cardiac pulsations (during light anesthesia).

(2) The *depressant action* of the chloroform on the medullary center of the heart, the vasomotor center, the intrinsic ganglia, and the myocardium itself (in deep anesthesia from overdose).

(3) *Cessation of respiration by:* (a) Direct obstruction from laryngeal stertor, or from the falling back of the tongue; (b) Direct retardation and arrest of the pulmonary circulation, first in the capillaries and later in the larger vessels, due to the direct local action of chloroform; (c) Interference with the respiratory center in the medulla, and the subordinate centers in the spinal cord.

Stages of Anesthesia.—Under the caption, Factors Which May Be Said to Modify the Physiology of Anesthesia as Ordinarily Induced (p. 62), attention is directed to the fact that, in the experience of one of us (J. T. G.), the phenomena observed during the administration of inhalation anesthetics are modified, to a more or less pronounced degree, by certain procedures now employed by a number of anesthetists. This modification is particularly to be noted in the sequence of events commonly described as stages of anesthesia. It is to be borne in mind, however, that in the present discussion of the physiology of chloroform, as manifested in these stages, reference is made to the administration as ordinarily given, and not with the utilization of the various factors mentioned.

Four stages of chloroform anesthesia are usually described. It should be noted, however, that the division of chloroform narcosis into these four stages is more or less arbitrary. Administered by modern methods, with proper care, the induction period is so gradually merged into that of surgical anesthesia that only the keenest observer is able to detect the successive steps. On the other hand, when improperly administered, the induction period passes so quickly into the fourth stage, or stage of overdose, that the anesthetist is unable to detect the danger signals until it is too late. For this reason, it is often stated that death from chloroform most frequently occurs during the initial stage.

The First Stage, or Stage of Light Anesthesia.—The first few drops of chloroform may have no appreciable effect upon the subject, except to stimulate respiration and circulation. If a light vapor (two per cent of chloroform in the air inhaled) is administered, practically no subjective phenomena are noted during this stage, which is of longer duration under these circumstances than when a more concentrated vapor is employed. With the heavier vapor, breath-holding, coughing, resistance to the anesthetic, and other disturbances, such as retching, vomiting, or cyanosis, may occur. The pupil may enlarge, all the senses may become slightly more active, and incoherency of ideas and speech may become apparent.

Analgesia appears at this stage, but operation should not be undertaken at this time, as the reflexes are often exaggerated, and death may result from reflex cardiac inhibition. An increase in the heart's action and a rise of blood pressure are invariably present.

The cerebral centers are affected in this stage. Different subjective sensations, such as ringing and roaring sounds, may be present, usually varying with the vapor concentration, but sometimes occurring despite the careful administration of the vapor.

The breathing is usually deep and regular, and the pulse quick and full.

The order of disappearance of reflexes during this stage is: (1) superficial skin; (2) vomiting; (3) swallowing; and (4) coughing.

The Second Stage, or Stage of Excitement.—This stage should never occur when chloroform is properly administered. (See Administration, p. 311.) Carelessly employed, however, chloroform anesthesia may be marked by a definite stage of excitement, during which the respiration becomes irregular, the pulse becomes more rapid, there may be struggling, shouting, disconnected talking, crying, and laughing. The face is flushed, and the pupils continue dilated. Muscular spasms, particularly spasm of the muscles of the jaw and neck, chest, and abdomen may occur, indicating the need of air.

When the chloroform vapor is too dilute the patient, if a child, may pass into a "chloroform sleep"; if an adult, vomiting may be induced. "False anesthesia" is known to be present when a patient consciously or unconsciously begins breathing automatically, when the anesthetist knows that not enough chloroform has been given to induce full surgical anesthesia. It is best to ignore the pupil and corneal reflexes at this time. If respiration is slow, or if it interferes with the quiet induction of full surgical anesthesia, a few drops of ether upon the mask will usually remedy this trouble. The eyes are poor guides at this time. The pupils are usually widely dilated, the eyeballs may move from side to side, or may be stationary. As the anesthetic is increased in strength, the movements of the eyes become less marked, the muscles relax, and the subject passes into the third stage.

Stertor may occur, but is not necessarily indicative of anesthesia. Vomiting will take place if the stage of excitement is unnecessarily prolonged, its imminence being indicated by feeble, small pulse.

The cerebellar centers are now progressively affected. Sensibility to pain is greatly diminished. The patient may answer questions, of which there is no recollection afterwards. There may be unintelligent mutterings.

With alcoholic and athletic patients it is difficult to induce anesthesia without a conspicuous stage of excitement.

By the maintenance of an open airway, by the manipulation of the lower jaw in such a way that the presence of an open airway is always apparent, and by the insistence upon absolute silence in the room, the anesthetist may successfully carry a patient from the induction period into full surgical narcosis without any signs of the stage of excitement.

The Third Stage, or Stage of Surgical Anesthesia.—In this stage the muscles are relaxed, the pupils contract to normal size, the respiration (*this is the principal guide*) becomes *regular and automatic.* Phonation and the conjunctival and corneal reflexes disappear. The pulse rate is lessened, and the face becomes pale. When the pulse rate falls below fifty, and extreme pallor is present, shock is imminent. The pulse should be normal, or a little below normal.

When the stage of surgical anesthesia is established, which usually requires from four to eight minutes, it must be maintained. A lightening of the anesthesia may affect the vomiting center.

The eyes are usually fixed during this stage, with the pupils contracted but responding to light. Hewitt found, by taking measurements with the pupillometer (see illustration, p. 195), that in most cases the pupil, in this stage, measures from two to three millimeters in diameter, usually about two and a half millimeters. Occasionally it remains widely dilated. "A very small pupil (1 to 1½ mm.)," Hewitt says, "in most cases indicates a light anesthesia; while a somewhat dilated pupil (3½ to 4½ mm.) usually means either that the anesthesia is very profound, or more probably that the dilatation is of reflex origin and is associated with a light anesthesia."

The muscular phenomena of the stage of surgical anesthesia are important danger signals. As previously stated, complete muscular relaxation should accompany this stage. Under the caption, Effects upon the Muscular System, attention is directed to the fact that surgical anesthesia may be accompanied by certain clonic muscular movements, as well as by slow, coördinated movements of certain muscles, and by jerky adductor movements of the arms following spasm of the pectoral muscles. The significance of these phenomena is that they may be taken by the anesthetist or by the surgeon to indicate a lightening of the anesthesia; in other words, a return to the second stage. If, under this misapprehension, the anesthetic is pushed with a view to obtaining more perfect relaxation and quietude, the subject may be at once plunged into a condition of apnea, which may eventuate in respiratory paralysis and death.

The third stage is always marked by a lowering of body temperature.

The order of disappearance of reflexes in the third stage is as follows: (1) phonation; (2) conjunctival; (3) corneal; (4) pupil to light; (5) bladder and rectal. The last two disappear with deepening narcosis.

The Fourth Stage, Stage of Deepening Narcosis, or Stage of Overdose.—It has been previously stated that the subject may pass so quickly from the first stage, or the induction-period, into the stage of overdose, that the intervening phenomena, the danger signals, cannot be noted, and that death supervenes, therefore, during the first few minutes of the administration. The present discussion of the stage of overdose, however, refers not to this state of affairs, but to the more gradual sequence of events, with culmination, through misapprehension of conditions, or other exigencies of administration, in what has come to be known as the fourth stage.

The ushering in of this stage is indicated by extreme pallor, abolition of all reflexes, and very great relaxation of the muscles. The breathing becomes more and more shallow; the pulse becomes weaker, irregular, and thready. Blood pressure continues to fall. Vasomotor paralysis, sudden or gradual respiratory failure, and complete cardiac inhibition are the final phenomena of the stage of overdose, which thus culminates in death.

Elimination.—From studies upon the influence of chloroform on intravital staining with methylene-blue it has been found [1] that, although the results in rabbits were not uniform, evidence was obtained of diminished reduction on the part of chloroformed brains. The increased circulation of the dye in the blood is due to the impaired excretory activities of the kidneys and liver. This explains a more abundant passage of the dye into the digestive tract, and the tint of the blood in part accounts for the appearance of the brain. The muscles, however, are less deeply stained than in control animals.

The amount of chloroform in the urine of dogs, subjected for prolonged periods to the anesthetic, has been found [2] to be extremely small, namely, from 6 to 8 mg. per 100 c.c. of urine. The urine after anesthesia, it has been noted, has a high specific gravity, a strongly acid reaction, and, in 70 per cent of the cases examined by Baldwin [3] (40 in number), there was a marked acetone reaction, due to a disturbance of metabolism, probably in the liver cells. Tests made by Vitali [4] with urine of four patients, during and after the administration of chloroform, revealed the fact that chloroform did not pass into the urine, and that the presence in the urine of other organic chlorin compounds could not be detected. This observation is not in harmony with the findings of others,[5] who state that the urine may show traces of chloroform, the drug existing in an unchanged state for as long as twelve days after administration.

[1] Herter and Richards: *Am. J. Physiol.*, *12*, 297.

[2] Nicloux: *J. pharm. chim.*, 1906, *24*, 64.

[3] Baldwin: *J. Biol. Chem.*, *1*, 239.

[4] Vitali: *L'Oroso*, *22*.

[5] Thien and Fischer: *Deutsch. med. Ztg.*, Dec. 2, 1889. See also Demeraux and Minet: *L'Echo méd.*, June, 1904.

Chloroform is largely excreted through the expired air, according to Meyer and Gottlieb.[1] A small part is broken down in the organism, increasing the chlorid content of the urine.

INDICATIONS AND CONTRAINDICATIONS

The indications and contraindications for chloroform may be categorically stated. For further discussion of the subject *see* Chapter VIII, Selection of Anesthetic.

Indications.—(1) *Obstetrical cases,* in which the heart is usually hypertrophied and only primary anesthesia is required; (2) *young children,* particularly as an introduction to ether; (3) *old people,* as a preliminary to ether; (4) persons afflicted with *epilepsy, convulsive seizures of any kind, tetanus;* (5) *affections of the respiratory system*—pulmonary tuberculosis, asthma, emphysema; (6) aneurysm; (7) pleurisy; (8) *operations involving the upper respiratory tract*—excision of tongue, inferior or superior maxillæ, enlarged glands, or tumors that encroach upon the airway; (9) *operations in which the Trendelenburg position is indicated;* (10) *obese* and *flabby* patients, particularly as an introductory anesthetic; (11) *insane patients;* (12) *operations upon the brain;* (13) *operations in which the actual cautery is to be used close to the face.*

Contraindications.—(1) *Weak, anemic children,* with enlarged glands in different parts of the body; (2) *status lymphaticus* (see Chapter VIII, Selection of Anesthetic); (3) *very prolonged operations;* (4) *minor surgery, when a safer anesthetic is available;* (5) *all operations where, for any reason,* the patient is in the *sitting posture,* or when the body must be raised to this position during the operation; (6) *athletes* and *alcoholics* who have had no preliminary medication. (7) patients whose general condition is poor, as indicated by a weak, anemic appearance; (8) *general septic conditions,* especially when due to longstanding tuberculous glands; (9) *diabetic patients;* (10) *very thin persons,* not otherwise diseased;[2] (11) *cyanosis* already present; (12) *low blood pressure* from any cause; (13) the presence of an open flame.

After-Effects.—The after-effects of chloroform narcosis may be considered under two heads, viz.: (1) immediate, and (2) remote.

[1] Meyer and Gottlieb: *Loc. cit.*

[2] "How strong a factor the fat plays is shown by the experiment on hungry animals where the brain takes up much more anesthetic than on well-fed animals in whom the fatty tissues absorb part of such narcotic. From these experiments we can readily imagine the absorption of narcotics by the lipoids of the nervous system during the narcosis and the return of function with their excretion back to the blood and the still further excretion of the anesthetic through the lungs." Meyer and Gottlieb: "Experimentelle Pharmakologie."

Immediate After-Effects.—If chloroform is scientifically administered to a patient carefully prepared, and under proper climatic conditions, the subject passes into a profound sleep, awakening as from natural slumber. Under other circumstances, however, the awakening may be accompanied by nausea, retching, and vomiting, with pallor and almost imperceptible pulse. Hiccough sometimes proves an annoying after-effect. As a rule, with chloroform, bronchial and pulmonary sequelæ are absent. In neurotic and hysterical individuals mental disturbances, sometimes amounting to maniacal seizures, may follow. Delirium of three days' duration has been reported. Aphasia has also been reported as following chloroform.

Remote After-Effects.—Fatty infiltration of all the organs, according to some observers, follows the prolonged or repeated administration of chloroform. Fatty degeneration of the liver, the heart, and the kidneys is particularly apt to occur under these circumstances, this being the outcome of a direct poisoning of these organs by the drug. Even when given in repeated, very small amounts, chloroform will lead to atrophic cirrhosis of the liver.

Albuminuria, acetonuria, urobilinuria, acetonemia, acidosis, which have been noted by various observers as following chloroform anesthesia, are discussed under the special head, Post-Anesthetic Toxemia, in Chapter IX, Treatment Before, During, and After Anesthesia.

Comparison With Other Agents.—It is important for the anesthetist to bear in mind the relative anesthetic value of the agent. The strength of chloroform as an anesthetic, as compared to ether, is calculated by Hewitt as 6 to 1, by Cushny as 8 to 1. Its anesthetic power is greater than that of ethyl chlorid.

ADMINISTRATION OF CHLOROFORM

Drop Method.—When chloroform was first introduced by Simpson, the method employed consisted in putting an unmeasured quantity of chloroform on a handkerchief, placing the handkerchief thus treated over the nose and mouth of the patient, and continuing the administration in a somewhat similar manner. Not many years elapsed before the necessity for a different method suggested itself. Simpson then advised that a single layer, of a towel or a handkerchief, should be placed over the patient's nose and mouth, and that the anesthetic be added, drop by drop. This proved to be so much safer than the first way of administering chloroform that the method has been advocated by every writer since that time. Inasmuch as the drop method will unquestionably continue to be employed, and inasmuch as many will continue to use chloroform alone, it is important that the safest method of administration in this way be considered.

The Patient.[1]—It is more important with chloroform than with any other anesthetic that the head be on a line with the body. If a pillow is placed under the head it should be pushed under the shoulders, in order to prevent asphyxial symptoms during the second stage. This pillow should be removed as the third stage is reached. If in the dorsal position, the head should be turned slightly to one side, the anesthetist holding the symphysis of the jaw with the index finger, the little finger resting upon the carotid artery; the left hand should hold the chloroform dropper. The clothing should be perfectly loose, shoes and stockings being removed; a tight waist or neckband will materially interfere with what might otherwise be a featureless narcosis. If bandages are on the neck or around the waist, these should be cut but not necessarily removed before the operation begins.

Fig. 123.—The Pilling Chloroform Dropper.

The Dropper.—It is even more important that chloroform should be dropped from the original container than ether or other inhalation anesthetics; therefore, containers arranged for dropping should be used. If not so arranged[2] the dropper recommended under ether will serve satisfactorily.

Induction.—As the vast majority of chloroform fatalities reported have occurred in the first few minutes of administration, it is most important that the psychical element be controlled as much as possible, both by preliminary medication and by the conversation of the nurses, physicians, or friends who may be near. In addition the anesthetic will go much more smoothly if some Farina cologne is dropped upon the

[1] For general preparation of patient see Chapter IX, Medication, Preliminary, During, and Post-anesthesia.

[2] Tracings on a smoked drum indicate that the blood pressure is maintained at a much higher level when the anesthetic is induced slowly, as here outlined.

mask. This should be supplemented in one-half minute by one or two drops of aromatic spirits of ammonia, or, preferably, of an alcoholic solution of the oil of bitter orange peel.[1] The first drop of chloroform can now be administered, and in 30 seconds the second drop, that is, two drops the first minute. This can be increased to six drops the second minute. The third minute, two drops may be given every ten seconds; the fourth minute, three to four drops every ten seconds; the fifth minute, five to ten drops every ten seconds. If the patient is not in full surgical anesthesia at this time, the administration may be continued as follows: eight or ten drops every ten seconds for one or two minutes longer. No time is wasted by beginning the administration of chloroform very slowly. The mucous membranes are, in a measure, blunted, and, if conducted methodically in this way, the surgical stage will be ushered in by the automatic respirations of the patient, the first and second stages not being observed ordinarily.

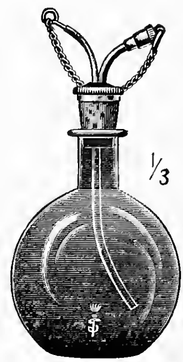


Fig. 124.—A Chloroform Dropper which Should Never be Used.

Maintaining Surgical Anesthesia.—When the surgical stage is reached the amount necessary to continue the anesthesia will be found to be one-half of the amount necessary to induce anesthesia; that is to say, if seven drops every ten seconds induce surgical anesthesia in six minutes, three or four drops every ten seconds will easily maintain an even plane of anesthesia. When the third stage is reached, however, it is well for the anesthetist to continue dropping the maximum amount for one or two minutes and then to go back to three drops every ten seconds for the next minute or so, and then to decrease this amount to two, or increase to three or four drops every ten seconds continuously, after that depending upon the patient's reflexes.

In surgical anesthesia the muscles are relaxed, the pupil contracts to normal, the respirations (and this is the principal guide) become *regular and automatic.* The reflexes disappear; the pulse slows down, and, with chloroform alone, the face is usually pale. "A pulse below 50 and extreme pallor are danger signals for the circulation." [2]

The respiration is slow, regular, and deep; all motor senses except those of respiration and circulation are completely depressed.

It usually requires from four to eight minutes to reach full surgical anesthesia.

When surgical anesthesia is finally obtained the patient must be kept in this stage. A lightening of the anesthesia may touch the vomiting

[1] See Chapter II, General Physiology.

[2] Meyer and Gottlieb: *Loc. cit.*

center and trouble will immediately follow. The pulse should be normal, or a little below normal; if oxygen or ether is given, and the anesthetic warmed, it will be normal, or just a little above. The eyes are usually fixed during this stage, with pupils contracted but responding to light unless morphin has been previously given. When morphin has been given the pupils are contracted throughout. In abdominal operations it is usually necessary to abolish the lid reflex; where muscular relaxation is not required this reflex may be allowed to remain. In either case the reflex should not be consulted oftener than once every two or three minutes. It must be remembered that patients differ in all of these things. It is best, therefore, to be guided by all available signs, *viz.:* respiration, circulation, lid and color reflex, and amount of anesthetic given.

In the third stage the spinal nerves are affected. With the drop method the face is usually pale, but when administered with oxygen the cheeks are usually flushed and the patient presents a very natural appearance. There is usually a reduction of body temperature when given by the drop method, but with warmed oxygen the normal temperature is usually maintained, or slightly raised.

Warmed Chloroform.—The chloroform container should be dipped into a pan of hot water, from time to time, to facilitate the vaporization of the liquid. It is much safer to use the drug in this manner. Occasionally the mask should be entirely removed from the face for one or two respirations. The anesthetist must anticipate stages by careful observation of his patient. Surgical anesthesia may be maintained as follows: If three drops are given for ten seconds the patient will *gradually* come out of the anesthetic stage. As the pulse goes up and becomes full and bounding, the color improves and the reflexes become slightly active; this dosage can be increased to five or seven drops every ten seconds for a minute or so. As the reflexes become blunted again the anesthetist should go back to three drops every ten seconds and continue as before. This method of administration by a watch relieves the anesthetist of a tremendous nerve strain and enables him to produce a continuous and safe narcosis.

In order to determine the comparative value of chloroform as regards life when heated to 100° F., and at normal temperature, a number of experiments were made, using compressed air, and passing this air through chloroform at *room temperature,* and then to a special animal mask, using a Junker inhaler for the chloroform. Gwathmey[1] found that it took 8.92 + minutes on the average to kill (26 animals being used). Employing the same technique, with the addition of another Junker inhaler filled with warm water and placed in a warm receptacle between the chloroform and animal mask, it was found that the average

[1] *J. Am. Med. Assn.,* *47,* 1361-64.

time required to kill (using 17 animals) was 20.35 minutes, thus showing that chloroform at blood temperature is three times as safe as chloroform at room temperature.

Intermittent Narcosis.—Chloroform should never be administered in the manner sometimes employed, unfortunately, with ether, namely, a small quantity, then a pause, and again a small quantity. The objection urged against the drop method outlined above is that the anesthetist is occupied every second of the time the patient is under the anesthetic. This is, in reality, one of the strongest arguments in its favor, as any untoward signs or symptoms are immediately recognized, and avoidable accidents are not encountered.

Color Reflex.—If the anesthesia has been induced as outlined above, the patient's color will vary according to the individual. If, at any time, a sudden pallor appears about the nose and mouth, it indicates shock from some cause, or is a premonitory symptom of vomiting. If the latter, this condition can be immediately rectified by an increased dosage. The anesthetist should touch the forehead or ear of the patient occasionally and note the reflex; i. e., the quickness with which the color returns. This reflex, taken in consideration with other signs to be given below, is a good indication of the heart's action. If the color returns immediately after removing the pressure of the finger, the heart is in good condition. If this reflex is very slow it may not necessarily indicate danger; but it would indicate a weak heart, and possibly dangerous ground.

The Pupil.—If morphin has been given as a preliminary medicament, the pupil will contract as soon as surgical anesthesia is reached, and usually remain so throughout the operation (this, of course, will depend somewhat upon the action of the morphin in that particular subject). It is unnecessary to attempt any observation of the eye as long as the reflexes are active and the patient is in the second stage of anesthesia. If no preliminary medicament has been given the pupil will be contracted a little below normal. If surgical shock intervenes from loss of blood, or handling important nerves and vessels, or if too light an anesthesia is being maintained, the pupil may dilate. If an overdose of the anesthetic has been given the pupil will also dilate, but will remain in this condition. The difference between the dilated pupil of a light anesthesia and one of an overdose must be determined immediately by the anesthetist. This can be done by recalling the amount of anesthetic that has been given within the last two or three minutes.

Conjunctival Reflex.—In order to obtain the conjunctival reflex, place the index finger upon the upper eyelid and gently separate it from the lower lid. Now press down slightly upon the upper lid and bring the ball of the second finger in contact with the conjunctiva of the upper lid thus exposed. All of this should be done quickly. If the lid closes, or if it remains insensitive when considered with the other signs, it will indicate whether or not the necessary plane of anesthesia is being maintained.

Lower Lid Reflex.—This reflex is relied upon by some anesthetists. As the upper lid is separated from the lower, a movement of the lower lid, active, slight, or dulled, would indicate the degree of narcosis.

Eyelash Reflex.—This is obtained by passing the index and second finger quickly over the eyelash of either eye.

Lid Reflex.—Many anesthetists merely open the eye, and only deepen the narcosis when closure ensues. This is not quite so sensitive a sign as the lower lid reflex.

Regardless of the eye reflex used, it should not be resorted to oftener than twice in five minutes, or, better still, once in five minutes. One eye should be held in reserve, for if this sign is resorted to by the anesthetist too often, the reflex becomes either too deadened or too active to be of value.

Pulse.—The pulse is most important in chloroform anesthesia. If cold chloroform is administered, a drop of five beats a minute is easily noted. If given warmed, as suggested in this chapter, the pulse will be maintained at a normal rate (see page 314). If anesthesia is induced as indicated, a rise in the second stage need not necessarily be expected. In full surgical anesthesia the pulse should be full and regular; any change in rhythm or fullness should be a warning to the anesthetist. Color reflex must always be considered in connection with the pulse. If no unusual loss of blood or handling of important nerves has taken place, an increase in the volume and rhythm indicates that the patient is regaining consciousness, and is a call for an increase in the amount of anesthetic. A running pulse would indicate shock from some source; an irregular pulse is always an indication of danger.

Respiration.—The respiration is to be more closely watched than any other sign. The respirations should be maintained as full and regular as possible; shallow respiration indicates vasomotor depression, or it may occur just before vomiting, or as one of the signs of shock. Irregular and shallow breathing may be caused by too small an amount of anesthetic. It should be the anesthetist's aim to keep the respirations full and regular. Even when ether is contraindicated as the anesthetic, one, two, or three drops upon the mask for one or two minutes (at the same time continuing the chloroform administration) is a good procedure. If there is an objection to this, Farina cologne, or an occasional drop of aromatic spirits of ammonia, or an alcoholic solution of the oil of bitter orange peel (as in the beginning) may be tried. The gentle rubbing of the lips with a towel, or piece of gauze, will usually stimulate the respiration. The anesthetist must not rely upon any one of the above signs, but must consider each in its relation to the other, and their relation to the surgical procedure as a whole. In this way only can the proper level of anesthesia be maintained.

From laboratory and clinical experience, the senior author has been fully convinced for a number of years that the dangers from chloroform are reduced to a minimum so long as the respirations are full and regular, and the concentration does not exceed 2 per cent. In the intentional killing of hundreds of animals in the laboratory we have failed to see a death from chloroform in which the respirations did not cease before the heart. The only exception to this rule was when the chloroform was given in a very concentrated vapor. This view is confirmed by Hare,[1] who states that "the dominant action of chloroform is certainly upon the respiratory centers in the medulla, and that this effect is the cause of death in most cases of chloroform accident. Not only does nearly all experimental work teach us this, but in a collective investigation as to the cause of death under chloroform nearly every case reported was found to have suffered primarily from respiratory arrest." These findings were independently confirmed by Randall and Cerna in Texas. The only exception to this would be in cardiac disease of any kind, when it can be easily understood that this organ would be the first affected. When we take into consideration that chloroform affects the respiratory centers and, in addition, has direct action upon the heart itself, and that there is also a lowering of the temperature during the administration, it is easily understood that, in a long operation, all three of these factors acting together would readily produce shock of a serious nature.

Other Methods of Administration.—The best results have been obtained with the Roth-Dräger, or the Gwathmey three-bottle vapor inhaler, or some similar apparatus, in which the percentage of chloroform is approximately known, oxygen being administered conjointly with the chloroform, and the vapors being warmed through rebreathing. The patients come out of this form of anesthesia in as quiet a state as with nitrous oxid and oxygen.

The Roth-Dräger Oxygen and Chloroform Apparatus.—The Roth-Dräger apparatus is designed to supply a mixed anesthetic of chloroform or ether vapor, separately or combined, in an atmosphere of oxygen. The face-piece (which is rigid and is suitable for all faces except the edentulous) forms an additional mixing chamber, as it admits air which dilutes the oxygen and thus presents an atmosphere richly supplied with oxygen and easily respirable. The percentage of anesthetic vapor is always known, as is also the pressure. The patient merely breathes to and fro into the face-piece, which is kept filled with the mixed gases. By gradually increased doses the administrator controls the amount of anesthetic required at different stages of the operation; if he desires only chloroform, he turns that indicator. If ether is to be added he can easily

[1] *Bull. Johns Hopkins Hosp.*, Jan., 1895.

do so, and regulate the amount of each as the patient requires. The average induction period is six to eight minutes for adults. It is seldom marked by excitement or struggling, and respiration seems free and unembarrassed. The narcosis is sufficiently profound for all surgical operations requiring relaxation.

The apparatus is extremely simple to work, in spite of its somewhat formidable appearance. It produces a satisfactory narcosis without any period of struggling or respiratory distress.

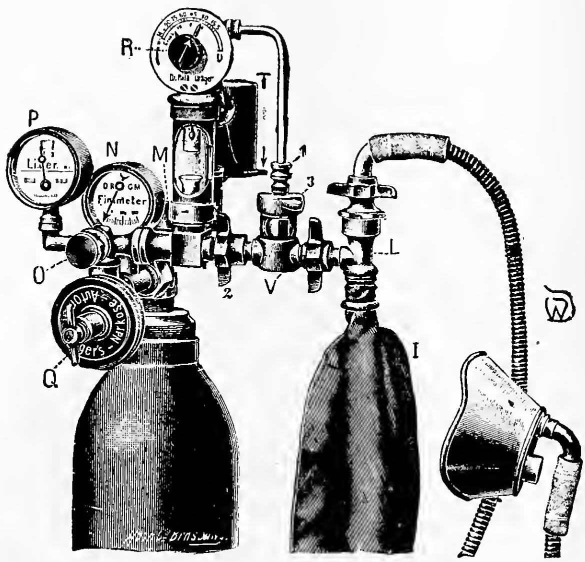


Fig. 125.—The Roth-Dräger Apparatus. Simple hand apparatus.

The after-effects are usually slight, if the anesthetist is careful to limit the amount of anesthetic given. It is clear that the anesthetist is enabled to obtain and maintain an anesthesia which would be either dangerous or impossible without the use of oxygen combined with the anesthetic. Vomiting may occur if too feeble a vapor is given during the induction period.

The apparatus delivers three liters of oxygen mixed with five liters of air, which is the volume of gas necessary for the breathing of an adult, that is, eight liters per minute. The falling of the drops of chloroform or ether is both visible and audible. In this way a constant control of the working of the apparatus is possible. The principal points of advantage claimed for the apparatus are:

(1) The color of the face does not alter; (2) the awakening is infinitely more easy; (3) irritation of the bronchia is reduced to a minimum; (4) the breathing is quiet and regular; (5) depression of

the pulse does not occur; (6) the pupils remain contracted; (7) recovery takes place quickly and completely.

Chemical investigations show that even in a long narcosis a decomposition of the chloroform does not occur. The anesthetist has both hands free at all times.

Statistics of the General Hospital at Lübeck show that the usual amount of chloroform consumed is 39½ grams for a narcosis lasting

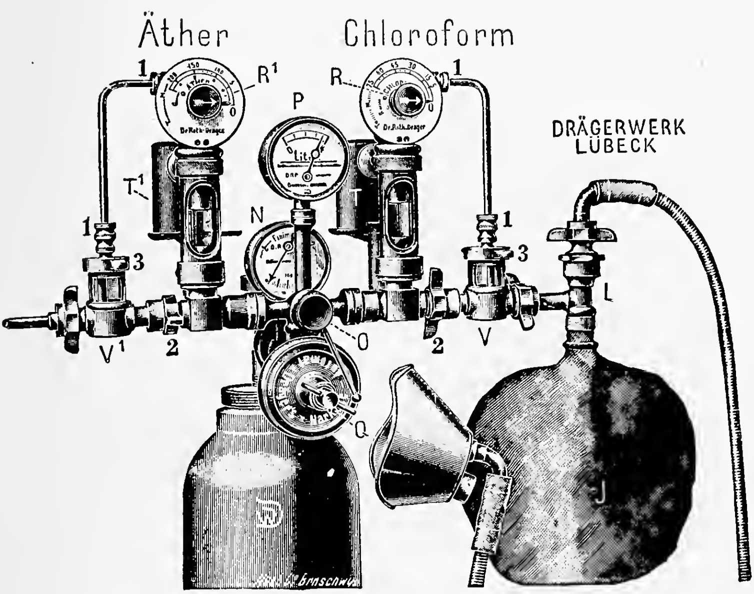


Fig. 126.—The Roth-Dräger Apparatus. Hand double apparatus.

about 40 minutes. The amount of chloroform used with the Roth-Dräger apparatus for the same length of time is 20 grams. The consumption of oxygen for 40 minutes amounts to 129 liters.

In Figures 125, 126, and 127 the parts of the apparatus are lettered as follows: M, the main valve of the oxygen cylinder; N, the finimeter, showing the quantity of oxygen contained in the cylinder at all times, and thus rendering a constant control of its contents possible; O, a small, easily manipulated valve by means of which the stream of oxygen can be quickly turned on and off; P, an instrument which indicates the number of liters of oxygen used per minute; Q, the thumbscrew which is turned to perform the dosing of oxygen (P operates in response to Q); R, the cock which controls the dose of chloroform administered per minute; T, the chloroform in a removable glass which is graduated so as to provide a further means for ascertaining the quantity of chloroform used during each narcosis; V, the gasifier with observation glass; L, the economizing apparatus with bag I. L is connected with the face-mask by a metal hose.

The scale of the chloroform cock R is graduated, the graduations representing drops per minute and grams per minute, so that the strength of the dose being administered can be ascertained by merely looking at the position of the scale. By turning the pointer in another position any change in the strength of the dose can be instantaneously effected. The chloroform reservoir G is kept in position by the arm B. To remove the glass the lever B is pressed downward. The streaming of the oxygen causes suction in the glass S. By this means the chloroform is drawn up through the pipe H and is caused to fall from the drop-former T drop by drop. The drops fall into the stream of oxygen, burst into fragments and vaporize. By turning the chloroform the strength of suction can be adjusted at will, and, if desired, can be stopped altogether.

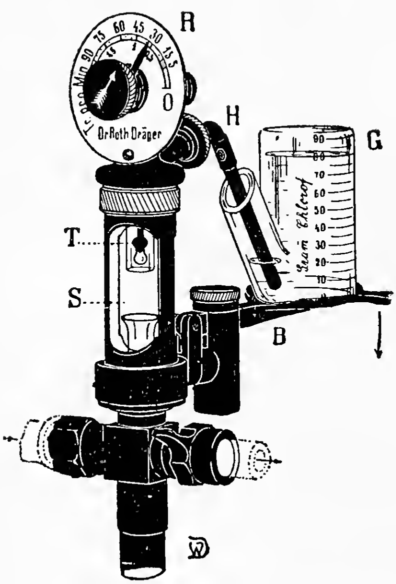


FIG. 127.—THE ROTH-DRÄGER APPARATUS.

Vernon Harcourt's Inhaler.—The improved Harcourt inhaler provides a definite mixture of air or oxygen with chloroform. A maximum two per cent vapor is provided. This is supposed to be the most accurate inhaler ever devised for the administration of chloroform. Two colored glass beads are dropped in the chloroform bottle to indicate the temperature ranges between 13° and 15° C. If the temperature of the chloroform is below 13° C., both the colored beads will float. If it is above 15° C., both will sink. The correct temperature is indicated by the blue bead sinking and the red bead beginning to sink. A two per cent chloroform vapor can be continuously administered, or only air may be inhaled. The valves are of delicate mechanism, and easily moved by the inspiration and expiration of the patient. It has been found that with this apparatus a one per cent vapor, or less, is sufficient to maintain an even narcosis in the average run of cases.

Hewitt's criticism of this inhaler is as follows:[1]

First: That the current through it depends upon the respiratory action of the patient.

[1] Hewitt: "Anæsthetics," 1912, 492.

Second: That the face-piece pressure, which is often necessary in order to obtain proper chloroform percentages, will seriously interfere with the respiration.

Third: That its management becomes irksome to the administrator, particularly in long cases.

Fourth: That it cannot be used for many operations.

Fifth: It cannot be readily sterilized.

Sixth: The disadvantage of making the respiratory pump of the patient act as the pump of the apparatus.

From the fact that several fatalities have been reported while using this apparatus, it would seem that accidents cannot be entirely prevented by accurate chloroform percentages. A comparison of this inhaler with the Roth-Dräger apparatus, taking into consideration the appearance of the patient immediately after the discontinuance of the narcosis, would compel us to prefer the Roth-Dräger apparatus.

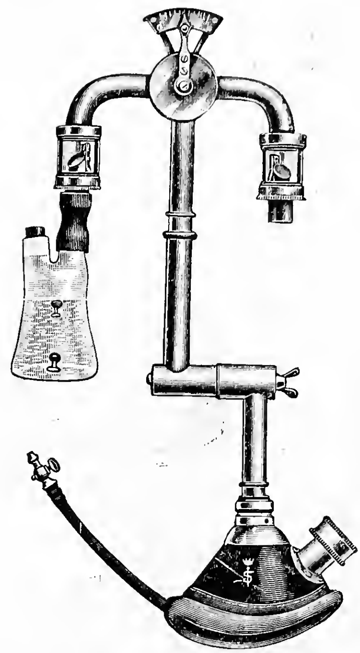


Fig. 128.—Vernon Harcourt's Inhaler, Complete with Face Piece, Bottle and Beads.

There is no provision in the Vernon Harcourt inhaler for rebreathing. In addition, no effort is placed upon the respiratory pump by the Roth-Dräger apparatus, as the oxygen

Fig. 129.—Junker's Apparatus.

or air with chloroform is forced into the bag under certain, definite pressure.

Junker Apparatus.—This was the first vapor [1] apparatus devised, and it is especially applicable for adenoid and tonsil work, or any operations about the head where the anesthetist must constantly change his position. The apparatus is so arranged that an approximate maximum of two per cent is reached. The percentage will vary according to the amount and temperature of ether in the bottle and pressure upon the hand bulb. The great advantage of this and all other similar inhalers is that a continuous narcosis can be maintained with the mouth open. (Fig. 129.) The vapor can also be given through nasal tubes directly into the nares, without interfering with the operator.

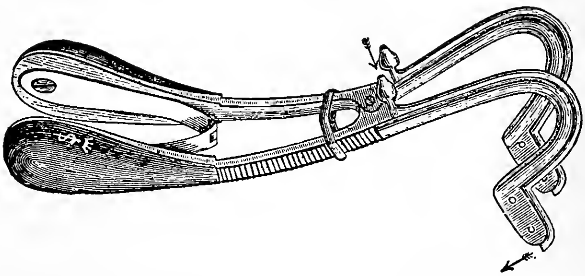


Fig. 130.—Hewitt-Mason's Mouth-Gag with Anesthetic Tubes.

Junker's original inhaler consisted of a bottle holding about two ounces of chloroform; this bottle was suspended from the coat of the anesthetist by a hook. A hand-bellows forced air through a tube running through the top of the bottle to the bottom; air was forced through this tube, and, as it bubbled up through the chloroform, was conveyed to the patient by another tube that merely penetrated the cork; this latter tube was fastened either to a mask or a hollow tube or a nose-piece. It was entirely satisfactory, provided the bottle was not tilted, and that no mistake was made in attaching the rubber tubes from the face-piece and hand-bulb to the tubes entering the top of the bottle. In either event, liquid chloroform would be forced into the upper air passages. Hewitt made a decided improvement upon the Junker inhaler by making it impossible for such an accident to occur. He also devised a metal mouth-tube and mouth-gag, after which other mouth-gags, including one of the author's (J. T. G.), have been modeled. (Fig. 130.)

Oxygen may be passed through the chloroform by merely attaching the tube from the oxygen tank to the afferent tube leading to the bottle.

[1] The vapor method is one in which air, oxygenated air, oxygen, or other gas passes either over or through the drug, thus vaporizing and delivering the anesthetic in predetermined percentages. For a discussion of ether vapor anesthesia, see Chapter V.

Most of the bottles now have compartments for both chloroform and ether, so that the anesthetist can combine the vapors at will. The apparatus was designed especially for operations about the head, neck, and upper air passages, especially operations where the mouth must remain open for some length of time.

Braun's Inhaler.—Braun, of Leipzig, modified Junker's inhaler so that either chloroform or ether alone, or any combination of the two drugs, might be given. A metal mask, without valves, but with a small opening in the top to insure the supply of air, comes with the apparatus. Braun's apparatus originated with the idea of giving a continuous anesthesia with highly attenuated ether vapor to which, from time to time, chloroform is added, according to requirements; he thus secures the advantages of both agents and discards their disadvantages. He adds only small amounts of chloroform when the ether vapor is insufficient to produce the desired effects. The Braun apparatus is simple and easy to operate, and has decided advantages over the Harcourt inhaler.

Gwathmey Three-Bottle Vapor Inhaler.—The apparatus is a modification of Braun's, with the addition of a water bottle, through which all the vapors of chloroform and ether must pass before getting to the patient. In addition, in cold weather, a heater is used to warm the anesthetic to the temperature of the blood. With this apparatus air or oxygen can be increased or decreased without, at the same time, decreasing or increasing the anesthetic vapor. The apparatus consists of three six-ounce bottles. In the ether and water bottles the end of the tube is flattened out so as to get the maximum amount of vaporization; the smaller bottle, containing a little over one ounce, is placed within the large six-ounce bottle marked "chloroform." The tube in the chloroform bottle is perfectly straight. It is estimated that with the mask used a two per cent maximum vapor is obtained. Pure ether, chloroform, or a mixture of these anesthetics, may be given by simply turning one stopcock on the top of the metal holder. (See p. 334.)

CHAPTER VIII

THE SELECTION OF THE ANESTHETIC AND TECHNIQUE FOR SPECIAL OPERATIONS

Conditions Affecting Selection: Inhalation Anesthetics; Safest Anesthetic; Chloroform with Oxygen; Value of Combinations and Sequence in Anesthetics; Safest Sequence.

Rules to Be Observed in Selecting the Anesthetics: Age; Heart Disease; Pulmonary Tuberculosis; Obese Patients; Thin Subjects; Athletes, Alcoholics, and Other Drug Habitués; Diseases of the Lungs; Kidney Diseases; Cancer; Nervous Patients; Epileptics; Insane Patients; Status Lymphaticus.

Special Operations: Short Operations; Nitrous Oxid; Ethyl Chlorid; Chloroform and Ether; The Mastoid; The Upper Respiratory Tract; Excision of the Tongue; Cleft Palate; Submucous Operations; Adenoid and Tonsil Cases; Tracheotomy; Goiter (Angina Ludovici, Exophthalmos—Graves' Disease); Amputations; Operations Upon Fingers and Toes; Circumcision; Rectal Cases; Obstetric Cases; Curettage; Genito-urinary Operations; Laparatomy; Gastro-enterostomy and Similar Operations; Peritonitis or Intestinal Obstruction.

Conclusions.

Bibliography.

CONDITIONS AFFECTING SELECTION

In selecting an anesthetic for a given operation many things must be considered. First of all, the safety to life. Then the applicability of other anesthetics to the patient, whose size, age, habits of life, and condition at the time of operation must all be considered. The surgeon's likes and dislikes also demand attention. If he is accustomed to using chloroform, with its quiet breathing and subdued pulse, he will not be satisfied with ether, with its quick, bounding pulse and rapid respiration. Some surgeons object seriously to a patient moving, although this movement may not interfere with the operation. The very fact of the patient's moving may cause him to become nervous and thus prevent him from doing his best work. Again, other surgeons like a light anesthetic, and those who have adapted themselves to nitrous oxid and oxygen may not be pleased with chloroform with its absolute quiet and relaxation.

Inhalation Anesthetics.—A list of anesthetics, their combinations and sequences, is therefore desirable. The following list, as regards safety to life, is based upon original experiments made, in 1904, by one of the authors (J. T. G.): 1, Nitrous oxid with oxygen; 2, nitrous oxid with air; 3, ethyl chlorid with oxygen; 4, ethyl chlorid with air; 5, anesthol with oxygen; 6, ether with oxygen; 7, chloroform with oxygen; 8, ether with air; 9, C. E. mixture (chloroform two parts, ether three parts, and oxygen); 10, C. E. mixture with air; 11, chloroform with air.

Safest Anesthetic.—Nitrous oxid with oxygen is easily the safest anesthetic known. It is almost impossible to kill normal animals with this combination. If they are asphyxiated, and the mask is removed, the heart will continue to beat for several minutes. This gives sufficient time for the gas to escape as it reaches the lungs, and for breathing to commence again automatically. Such is the case in the laboratory and in the operating room. The only likelihood of a mistake is when the physiological signs of asphyxiation are not known.

Chloroform with Oxygen.—While chloroform is classed as the most dangerous anesthetic, generally speaking, the purity of the chemical, the mode of administration, and the environment may considerably alter its place in the list. If used with oxygen, and in definite percentages, it is safer for certain cases (i. e., patients with abnormally narrowed air passages) than is nitrous oxid with oxygen. Again it is safer in tropical countries and in the summer time than in a colder climate or during the winter. The patient's physique may be such that it would be very difficult, if not impossible, to administer nitrous oxid with oxygen alone.

Value of Combinations and Sequence in Anesthetics.—Again, the relative safety of these anesthetics is enhanced by using them in proper combination and sequence. The following is a list of the usual combinations and sequences:

(1) Nitrous oxid with oxygen, combined with warm ether.
(2) Nitrous oxid with oxygen, combined with ethyl chlorid (either closed or open).
(3) Nitrous oxid-ether sequence.
(4) Nitrous oxid-ether sequence (closed method), followed by ether.
(5) Nitrous oxid-oxygen-ether sequence (vapor or drop).
(6) Nitrous oxid-ether sequence, followed by ether and chloroform.
(7) Nitrous oxid-ethyl chlorid-ether sequence (closed method).
(8) Ethyl chlorid-ether sequence.
(9) Ethyl chlorid, ether-chloroform sequence.

(10) C. E. mixture-ether sequence.
(11) C. E. mixture-ether-chloroform sequence.
(12) Chloroform with ether sequence (vapor or drop).
(13) Chloroform ether-chloroform sequence (vapor or drop).
(14) Chloroform-ether (vapor or drop), followed by ether (closed method).
(15) Ether-chloroform sequence.
(16) Ether-chloroform-ether sequence.

Safest Sequence.—The latest and best development in anesthetics is the use of ether and chloroform in combination with nitrous oxid with oxygen, making nitrous oxid and oxygen the basis of the anesthesia. It has also been found by clinical experience that what is commonly known as the gas-ether sequence,—that is, giving first gas from one to two minutes, and then switching to ether,—is the best method of administering ether in suitable cases. (See page 218.) The gas-ether-chloroform sequence is a still further modification of the above, and for certain cases it is probably the best sequence. No hard-and-fast rules are to be laid down, however, for the selection of the anesthetic, for the method of its administration, or for the time of changing from one anesthetic to another. This must be learned by experience, and the anesthetist must know the physiological effect and the dosage of each drug that he uses.

The fact that these anesthetics are used in combination and sequence by the most expert anesthetists of to-day is good evidence that in many cases no one agent is suitable throughout the anesthesia. It is unwise to suggest or recommend this or that special anesthetic or method, as, for example, ether by the drop method, for this seems like an attempt to fit the anesthetic to the anesthetist rather than to the patient.

RULES TO BE OBSERVED IN SELECTING THE ANESTHETIC

Some definite rules serve to guide us in the selection of a suitable anesthetic.

Age.—Infants.—Children under one year of age should never be kept under the anesthetic longer than one hour. Many children have been successfully anesthetized for one or two hours at a delicate age, but a certain definite risk is incurred when the anesthesia lasts one hour or more for a child under one year old.

Until within recent years it has been the custom to administer chloroform to children. A number of deaths have been reported of children dying two or three days after the administration of chloroform, and post-mortem examination has revealed the fact that these children had what is known as status lymphaticus. (See page 331.) "The clinical evidences of this condition do not allow its certain detection beforehand, but the anesthetist will be wise to be particularly on his guard when the patient is a child or young adult of slight physique, though good height, pale complexion, timorous disposition, or with large tonsils and adenoids. If the spleen is palpable and there are palpably enlarged cervical or abdominal glands, apprehension is still better founded. Lymphoid follicles visible on the epiglottis and much enlarged papillæ at the back of the tongue are also evidences suggestive of the condition."[1] On this account it is now customary to administer ether alone or the C. E. mixture.

If chloroform is given at all to very young children, it should be administered warm, and preferably with oxygen instead of air.

Chloroform should not be entirely abandoned for children or other subjects because it has been misused in the past. It is unquestionably safer and better to induce the anesthesia with chloroform in the majority of instances and to maintain the anesthesia with ether than to shock the child by attempting to commence the anesthesia with ether. It is always best to begin the anesthesia with one or two drops of the essence of bitter orange peel (25 per cent U. S. P.), or any cologne, provided it is not sweet smelling. Any sweet perfume or scent tends to produce vomiting at this time. There are a very few conditions in which the anesthesia should be maintained with chloroform. Some anesthetists have used nitrous oxid from the start by simply allowing it to flow from a tube to the patient's nose and mouth, without any mask, and diminishing the quantity as cyanosis appeared. Crying children are easily and quickly anesthetized, and for this reason should not be given chloroform at all.

Nitrous oxid, unless given by some open method, is a very poor anesthetic for young children, as they do not seem to be equal to the task of breathing through valves.

Ethyl chlorid is preferred by many anesthetists for young children. They usually succumb rapidly and without struggling or cyanosis.

Infants should preferably be anesthetized in the mother's or nurse's arms. The method should be the same as for sleeping children.[2] Care should be taken in anesthetizing children to make the operation as informal as possible. Mental suggestion here plays a great part, as well as gentleness in voice and movement. Questions such as "How old are you?" or "What is your name?" and immediately calling the child by the first name, put them at their ease at once. Avoidance of all appearance of restraint is necessary. Where a child is obstinate or terrified it is best to induce unconsciousness as rapidly as possible. Such children must be firmly restrained until this is accomplished.

[1] Latham A., and English, T. Crisp: "A System of Treatment," *3*, 25.

[2] See article on Alexander's and Gwathmey's "Technique in Adenoid and Tonsil Operations."

Children Five to Eight or Ten Years of Age.—The anesthesia should be commenced with some perfume and continued by the drop method of chloroform or anesthol until the third stage is reached; then the second mask should take the place of the first and the anesthesia should be deepened and maintained by ether. This is the best method to use. English authorities recommend the C. E. mixture. The poisonous effects of chloroform in connection with status lymphaticus need not be feared when chloroform is used in this way. Children under five years of age should not be kept under full surgical anesthesia more than two hours.

Ten to Nineteen Years of Age.—The best anesthetic for young people is a judicious combination of chloroform and ether given by the vapor or drop method. No preliminary medication is usually necessary. In some cases, however, morphin and atropin, in small quantities, can be used to advantage to prevent excessive flow of mucus. One-twentieth to one-twelfth of a grain of sulphate of morphin, with 1/300 of a grain of atropin, is the usual dose.

Nineteen to Fifty Years of Age.—Nitrous oxid and oxygen, the gas-ether, chloroform or anesthol-ether, or ethyl chlorid-ether sequences are probably the best agents for patients from 19 to 50 years of age. Preliminary medication for this class of patients *must* be considered as a *part* of the general anesthetic. It should be varied according to the size and condition of the patient. One-eighth to one-quarter of a grain of morphin, with 1/150 grain of atropin, can usually be given with very great advantage.

Fifty and Over.—Elderly people yield more readily than do younger subjects to the combination of chloroform and ether by the vapor or drop method. The closed method or the gas-ether sequence is usually contraindicated. When atheromatous conditions are present, or cerebral hemorrhage from any cause is feared, ether is contraindicated, as is also nitrous oxid with oxygen. Chloroform with oxygen should be used in these cases. Weak, anemic men and middle-aged women yield better to nitrous oxid with oxygen, either alone or supplemented by small amounts of ether and chloroform.

Many of these patients have some respiratory trouble, as chronic bronchitis or asthma, or arteriosclerosis. There is very little fear of chloroform poisoning in the aged, and yet it is always best to supplement chloroform by ether in sufficient quantity at least to maintain a good type of respiration throughout the anesthesia. Care should be taken to avoid the slightest cyanosis. Elderly patients are, as a rule, good subjects for anesthetization, not only in inducing and maintaining the anesthesia, but also as regards after-effects.

Heart Disease.—Unless some definite signs, such as swollen ankles, pulmonary edema, or dyspnea, are present, it is unnecessary to pay attention to any heart lesion. An open method is usually best in these cases, anesthesia being induced with chloroform, the chloroform-ether mixture or anesthol, and continued with ether and oxygen. If loss of compensation is present, as indicated by any of the above signs, pulmonary anesthesia should be avoided and local or spinal anesthesia used. A preliminary dose of morphin may be used to advantage in these cases. A deep anesthesia is preferable to a light one. For paracentesis of the pericardium, nitrous oxid with oxygen is preferable.

Pulmonary Tuberculosis.—Patients with tuberculosis should have nitrous oxid and oxygen whenever possible. Ether is contraindicated, as it is liable to light up a diseased lung that may have been in a quiescent stage for some time. Warmed chloroform and oxygen is the second choice.

Obese Patients.—As a general rule a healthy obese patient seems to be immune to any poisonous after-effects from chloroform. Obese patients and those with obstructed or narrowed passages are best anesthetized by warm chloroform and oxygen. Any closed method should be avoided with these patients.

Thin Subjects.—With thin, anemic individuals all other anesthetics should be considered before using chloroform, anesthol, or ethyl chlorid.

Athletes, Alcoholics, and Other Drug Habitués.—Athletes and persons addicted to the excessive use of alcoholic stimulants should always receive preliminary medication, regardless of the anesthetic selected. Morphin, with atropin or some other appropriate drugs, may be employed. For alcoholics, especially, if one to two ounces of whiskey in eight ounces of saline solution is administered per rectum, in combination with morphin given hypodermically, the anesthetic acts more satisfactorily than when alcohol is withheld. Persons addicted to the use of drugs, such as morphin, etc., should not be restricted before the anesthetic in the use of the particular drug concerned, but should be given the dose to which they are accustomed. The immediate ill results of withholding drugs at this time are easily recognizable, but the opportunity for its final discontinuance is apparent.

The requisite preliminary medication having been given, the vapor and drop method of anesthesia is preferable to any closed method, as these patients suffer especially from deprivation of oxygen.

According to Mahoney,[1] alcoholic subjects do better with treatment for a week or ten days with bromids, with the gradual withdrawal of alcohol. Treatment for even a few days is better than none.

Diseases of the Lungs.—In *pleurisy, empyema, abscess of the lung,* and in all operations in which one lung is involved, the patient should lie with the diseased lung lower, in order to assist drainage and reduce

[1] Mahoney, Daniel F.: "Some Considerations of Ether Anesthesia." *Boston Med. and Surg. J.*, Oct. 19, 1911.

the chance of infecting the healthy lung, and also to allow the healthy lung perfectly free respiratory action.

If *pneumonia* is present and an operation is absolutely necessary, local, spinal, or rectal should be preferred before pulmonary anesthesia.

In *dyspnea* a local, spinal, or rectal anesthesia is preferable to a pulmonary anesthetic. If, however, a pulmonary anesthetic is used, chloroform with oxygen is the first choice, the patient being allowed to assume the attitude in which it is easiest for him to breathe.

In acute or chronic *bronchitis* or *phthisis, asthma, pneumonia* or any diseases of the *respiratory passages,* ether is, if possible, to be avoided, even with the most improved methods of administration. Oxygen and chloroform or nitrous oxid and oxygen are the anesthetics to be chosen. Morphin or some similar medication should always be used in these cases.

Kidney Diseases.—In all kidney diseases ether and chloroform are usually contraindicated. Nitrous oxid with oxygen is the anesthetic to be preferred.

In cases of *diabetes* in which sugar is either absent from the urine or present only to a slight degree, chloroform with oxygen anesthesia is unattended by risk, but when the quantity is abnormally large there is danger of diabetic coma. Chloroform should be avoided in these cases, and nitrous oxid and oxygen chosen as the anesthetic. These patients should be carefully dieted in order to reduce the amount of sugar to the minimum. Before regaining consciousness they may relapse into a comatose condition and die from acetonemia. (For a discussion of acetonemia, see Chapter IX.)

Cancer.—Wherever the cachectic condition that is usually associated with advanced cancer exists, the patient takes kindly to the anesthetic and requires very little of it to maintain surgical anesthesia. These patients should always be given a preliminary dose of morphin before going to the operating table, as many of them have been accustomed to this medication. For removal of a cancerous breast, nitrous oxid and oxygen for elderly people, and ether and oxygen by the vapor method in younger subjects, are preferable, as the anesthetist is out of the way and shock is less liable to occur than with other procedures. Chloroform may be sparingly used in connection with the ether. It is best to anticipate shock in these cases by giving one pint of saline with one ounce of glucose per rectum two hours before the operation. Fifteen to twenty minutes before any operation is concluded a pint of saline with three or four ounces of glucose should be given per rectum.

Nervous Patients.—Nervous patients should be gotten under the anesthetic as quickly as possible. The gas-ether sequence or nitrous oxid should be used. This prevents hysterical symptoms from appearing.

Epileptics.—A preliminary of morphin is indicated for this special class of patients and the anesthetic induced with chloroform, with a switch to ether in the second stage. The anesthetist must be ready to prop a mouth gag between the teeth if a seizure should occur as the patient is going under the anesthetic. The prop should be inserted between the teeth as the patient is recovering. It is usually well to give a small hypodermic toward the close of the operation, as this will prevent a later seizure occurring.

Insane Patients.—Insane patients should always have a preliminary medication of morphin 1/8 of a grain one hour before the operation, to be repeated, with 1/150 grain of atropin, one-half hour before the anesthetic is commenced. The anesthesia should be induced with chloroform and maintained with ether and oxygen by the vapor method. Mental aberrations have been known to occur after the inhalation of any or all pulmonary anesthetics. This is probably caused by irregular or intermittent narcosis.

Status Lymphaticus.—Definition.—Status lymphaticus or thymicus, or lymphatism, is a condition of infancy and childhood, marked by hyperplasia of the lymphatic structures, spleen and bone marrow, and persistence of the thymus gland (Stedman). It has also been defined as a condition of unstable equilibrium, coma, convulsions, and vomiting accompanying hyperplasia of the persisting thymus (Gould); and as a morbid state due to excessive production or growth of lymphoid tissues, such as the thymus and thyroid glands, resulting in impaired development, lowered vitality, and sometimes death (Dorland).

History.—As early as 1614 attention was called by Felix Plater to the fact that the thymus was enlarged in three cases of sudden death from dyspnea in one family. In 1823, and again in 1829, Kopp mentioned the association of the enlargement of the thymus gland with sudden death. Paltauf, in 1889 and 1890, collected, for the first time, a large number of cases of sudden death in adults, in which there was enlargement of the tonsils, lymphatic gland system, the follicles at the base of the tongue, the spleen, and the thymus gland, with narrowing of the aorta. Kundrat, in 1895, published ten cases of death immediately after anesthesia by chloroform or some mixture containing it, also one case in which ether was the anesthetic. Sudden deaths were noted after this time in many cases in which no anesthetics had been administered. Lymphatic hyperplasia has been found to occur in every chloroform fatality for the past twenty years in the children's clinic at Gratz. The first case recorded in England was reported by Wolff in 1905. Two deaths under local anesthesia have been recorded by Horoszkiewicz.

Anatomy.[1]—"The thymus gland is a temporary organ attaining its full size at the end of the second year, when it ceases to grow and remains practically stationary until puberty, at which period it rapidly

[1] Gray: "Anatomy," 1442.

degenerates. It does not entirely disappear, for the shrunken and degenerate mass even in later life maintains a likeness to the original form and retains within its substance small portions of thymus tissue (Waldeyer). If examined when its growth is most active, it will be found to consist of two lateral lobes placed in close contact along the middle line, situated partly in the superior mediastinum, partly in the neck, and extending from the level of the fourth costal cartilage upward as high as the lower border of the thyroid gland. It is covered by the sternum and by the origins of the sternohyoid and sternothyroid muscles. Below, it rests upon the pericardium, being separated from the arch of the aorta and great vessels by a layer of fascia. In the neck, it lies on the front and sides of the trachea, behind the sternohyoid and sternothyroid muscles. The two lobes generally differ in size; they are usually connected so as to form a single mass but are sometimes separated by an immediate lobe. The thymus is of a pinkish gray color and is lobulated on its surfaces."

Diagnosis.—The majority of writers are agreed that a positive diagnosis of this condition during life is very difficult. The fact is that enlarged tonsils and the conditions termed status lymphaticus by most writers call for the extirpation of the tonsils with the idea of increasing oxygen in the tissues and the blood, and stimulating the growth of the individual. Connor[1] says: "The plainest sign of congenital hyperplasia of the vascular system is the noticeably small size and thin walls of all arteries."

Pasty complexion, a large amount of subcutaneous fat, and, in adults, a scant amount of axillary or pubic hair are usual; also the hair of the head has a peculiar dry, brittle character. Enlargement of the faucial, pharyngeal, and laryngeal tonsils is frequently present. The diagnosis of a tumor running under the sternum would be almost pathognomonic of this condition. Cocks[2] considers the X-ray examination second only to the general condition of the patient in making a diagnosis.

Most patients dying during or immediately after anesthesia have been young people or children, of flabby type, with enlarged adenoids, tonsils, thyroid (usually), and thymus; with narrow, high-arched palate, small mouth and throat, and weak heart sounds. During anesthesia a grayness of complexion or pallor is witnessed, with weak heart action and shallow breathing. Enlargement of the thyroid is said to exist in more than 50 per cent of cases. *Enlargement of the tongue is an important factor in diagnosis.* The spleen has been found to be greatly enlarged in many cases, also the mesenteric, popliteal, axillary, and inguinal glands. Exophthalmic goiter may also be present, in which event heart failure

[1] Connor: *N. Y. State J. Med.*, 1906, 282-284.

[2] Cocks: "A Contribution to the Pathology and Clinical Diagnosis of Status Lymphaticus," read before the Am. Laryn., Rhinol., and Otol. Soc., May, 1912.

under the anesthetic is probable. Congenital defects such as cleft palate and cleft kidney are sometimes associated with status lymphaticus. All patients have a pale, thin skin, pasty complexion, and usually subcutaneous fat. The glands of the neck are also sometimes enlarged. The above complex symptoms are noted when, given chloroform for any length of time, much of the anesthetic is absorbed and less secreted than is usual, with a consequent continual poisoning of the system until death occurs several days after the anesthetic. Sometimes delayed chloroform poisoning is mistaken for status lymphaticus. In status lymphaticus, especially in children, patients seem to dread the anesthetic more than is usually the case. This fear would certainly add to the shock and decrease the normal resisting force of all the organs to the effects of the anesthetic. Two cases of death, noted by Wheelock,[1] at Fort Wayne, were due to cardiac failure and asphyxiation. In cardiac failure no premonitory symptoms are present, but in asphyxiation there is a disturbance of breathing at various times. An enlarged thymus has sometimes produced pressure from which asphyxial symptoms have developed. In some of the reported cases, death occurring during anesthesia always came suddenly, with pallor and dilated pupils. In some there were superficial respiration and intermittent pulse just before the last signs mentioned, together with cyanosis and dyspnea. Ohlmacher[2] states that deaths from status lymphaticus are due to increased intracranial pressure, with sudden edema. Halstead[3] points out the great danger of operating for adenoids and tonsils upon children with status lymphaticus, on account of the great shock which the added fright and violent struggling would bring on—in some cases enough to produce death.

Choice of the Anesthetic for Suspected Cases.—From the study of a large number of statistics, the fact that chloroform is contraindicated cannot be questioned. Roberts[4] concludes that ether is the safest anesthetic for all of these cases. Unquestionably chloroform should be avoided in all suspected cases. Ether by the vapor or drop method should be the anesthetic of choice. No closed method should be used on account of the possibility of pressure symptoms. Children who sink into deep anesthesia quickly from small doses of the drug should at once be considered questionable cases for the anesthetist.

Preparation for Operation.—Great precaution should be taken that the preparation and preliminary medication be complete, so that whatever is given, when the time for operation arrives, the patient will be in a more or less drowsy condition and indifferent to the anes-

[1] *Toledo Med. and Surg. Rep.*, 1909, *35*, 395-399.

[2] *J. Am. Med. Assn.*, Feb., 1904, *42*, No. 7.

[3] *Phila. Med. J.*, Nov. 3, 1900.

[4] *Trans. Am. Laryn., Rhinol. and Otol. Soc.*, St. Louis, 1908, 507-524.

thetic. (See Chapter IX, *Treatment, Preliminary, During, and After Anesthesia,* p. 365; also *Acetonemia.*

Treatment During Anesthesia.—If sudden syncope occurs, massage of the heart, in connection with artificial respiration, should be instituted immediately. Hilliard [1] thinks that the hypodermic injection of morphin and atropin before the administration of the anesthetic is of great value, and that, with this addition, general anesthesia is safer than local anesthesia.

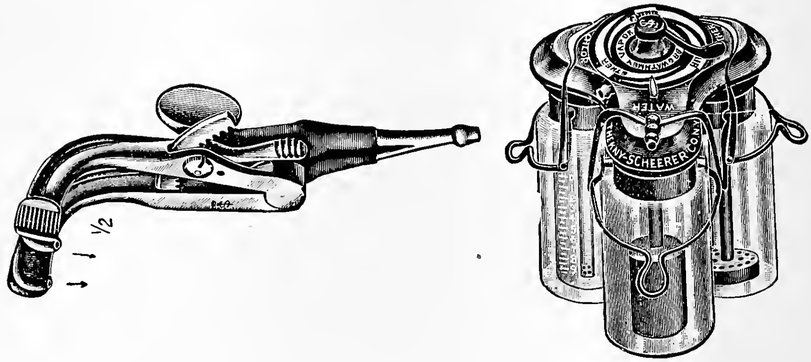


Fig. 131.—The Gwathmey Three-Bottle Vapor Inhaler, Mouth Gag, with Hollow Tubes Attached. (See page 323.)

Mortality.—Harvey Hilliard [2] gives a very complete history of a fatal case of status lymphaticus in a young man aged twenty-one, six feet two inches in height, very thin, and of a highly neurotic temperament. Operation: circumcision.

The patient was a great smoker of cigarettes and subject to attacks of faintness. The patient had the usual preparation, but was allowed to smoke during the morning, the operation being at twelve o'clock. Hilliard found on examination a rapid pulse, poor chest expansion, and considerable enlargement of the thyroid gland. Chloroform-ether mixture was the anesthetic. During the induction period, the heart beat very violently. A light anesthesia was maintained. When the prepuce was severed, the patient turned an ashen color and stopped breathing. Rhythmic tongue traction was employed and amyl nitrite vapor, the administrator pressing the lower ribs to restore respiration. This brought the patient round. The anesthetic was discontinued with the idea of discontinuing the operation, when the patient immediately stopped breathing. The usual restorative methods were resorted to, but proved unavailing. Artificial respiration was kept up for forty-five minutes, but the patient did not again come around.

[1] Hilliard, Harvey: "A Fatal Case of Status Lymphaticus," *Brit. Med. J.*, Jan. 25, 1908, 202.

[2] Idem: *Loc. cit.*

Post-mortem examination showed the thyroid gland enlarged, with degenerated changes. The thymus gland was persistent and weighed 24 grams. The heart was dilated, with thin, flabby walls.

In thirty-five cases reported by McCardie the average age was sixteen years, the youngest patient being six months; seven were under ten years of age, fourteen between the ages of ten and twenty, eight from twenty to thirty, and two from thirty-one to thirty-two, the oldest being fifty-five years. There was no distinction as regards sex.

Cocks [1] reports forty-six cases of status lymphaticus in approximately sixteen hundred autopsies at the Bellevue Hospital Pathological Department.

In thirty cases examined by McCardie for status lymphaticus the deaths during or after anesthesia were: seventeen from chloroform, six from ether, five from a mixture of chloroform and ether, and two doubtful cases, in which the anesthetic was nitrous oxid. There is also recorded the death of an infant, one year old, after an injection of 1/12 of a grain of morphin, in whom post-mortem examination revealed the signs of status lymphaticus. Two deaths are reported under local anesthesia, both patients being women, aged thirty and thirty-one years, respectively.

Death from any cause, and especially during the anesthesia, is always very sudden. In rare instances the enlarged thymus gland may compress the trachea sufficiently to cause death by suffocation. Toxemia induced by the thymus may reduce the subject to such a degree that sudden shock may cause death, toxemia being primarily responsible. Patients have also been known to die from such a trivial shock as bathing.

Post-Mortem Examination.—Autopsy usually showed adenoids and tonsils enlarged, thymus gland very large, and spleen also enlarged; heart and liver healthy. The aorta and small arteries were smaller and thinner than normal, with signs of cardiac dilatation, evidence of recent rickets, and sometimes incomplete development of the sexual organs. In some cases fatty degeneration of liver (principally), kidneys, heart and other muscles was noted. Hyperplasia of the lymphatic glands is usually noted, also evidence of infantilism, such as, for example, scanty pubic or axillary hair. Exophthalmic goiter is frequently associated with status lymphaticus. Cocks reports over fifteen deaths occurring in connection with cerebrospinal meningitis.

Observation Upon Animals.—Offergeld and Müller [2] have made a number of interesting experimental narcoses upon animals with the following results (presumably with chloroform at room temperature in all cases and without oxygen except as stated):

[1] Cocks: *Loc. cit.*

[2] Offergeld and Müller: "Experimenteller Beitrag z. toxischen Wirkung des Chloroforms auf die Nieren," *Arch. f. klin. Chir.*, 1905, *75*, 758.

Animals chloroformed for two hours, after recovery from the immediate effects of the anesthetic. usually died from 48 to 60 hours afterward; post-mortem examination showing parenchymatous degeneration of the heart, liver, and kidneys. When artificial nephritis was produced, extensive injury occurred even with a fifteen-minute anesthesia. When injured by mineral acid, pus, germs, or the injection of diphtheria toxins, it was found that the kidneys were usually affected by chloroform narcosis. When pregnant animals were used, this fact in itself did not favor fatty degeneration unless complicated with kidney lesions. A second chloroformization favored greatly the degenerated changes in the kidneys. Fat seemed to disappear in the tissues and to accumulate in the liver. Offergeld concluded that anemic and cachectic conditions of the patient favored the poisonous action of chloroform, and he warned against the danger of repeated chloroform anesthesias. *He also believed that the prevention of the ill effects of chloroform might be accomplished by a mixture of chloroform and oxygen.*

Müller concluded that the changes in the internal organs always appeared first as fatty changes, depending upon the time and number of the anesthesias; that these changes were in direct proportion to the anesthetic power of the agent used; that they usually disappeared after anesthesia; that a second anesthesia was always very dangerous; that the fatty changes following the second anesthesia were twice as severe as from the first, regardless of the time given; that the second anesthesia should never be given for at least three days after the first; that pneumonias occurred frequently with ether; that chloroform should be the second anesthetic; that mixed anesthesias did not prevent these fatty changes; and that these changes took place in the vessel walls of the brain as well as of the other internal organs.

Bandler's [1] experiments seem to show that ether does not produce the changes in the liver cells caused by chloroform.

Strassmann [2] chloroformed animals previously weakened by loss of blood, with a greater resulting fatty degeneration than upon normal animals.

The senior author (J. T. G.) agrees with Henderson [3] that unskillful anesthesia is more often the cause of death, and especially in adenoid and tonsil cases, than the status lymphaticus or heart disease. Henderson states that "writers assume that status lymphaticus was the cause of death, although there may have been no autopsy. Even in those cases in which an autopsy was performed, the pathologist's report sometimes

[1] "Ueber den Einfluss der Chloroform und Aethernarkose auf die Lieber," *Mittlg. aus den Grenzgebeit. der Med.*, 1896, *1*, 303.

[2] *Virchow's Arch.*, 1899, *115*, 1.

[3] Henderson, Yandell: "Primary Heart Failure in Normal Subjects Under Ether," *Surg. Gyn. and Obstet.*, Aug., 1911.

indicates that if he had not been told what to find he would scarcely have found it.

"On looking up the general subject of status lymphaticus, I find that this mysterious (I might almost say mystical) condition was only a few years ago used in precisely the same way, and with the same confidence, to explain another class of fatalities. It is less than a decade since the time when, if a patient died suddenly after an injection of antitoxic serum, an unsuspected condition of status lymphaticus was invoked as the explanation. In many of the very best text-books of pharmacology (written, by the way, by laboratory men), the practice of occasionally interrupting the administration of ether, and of allowing the patient to come for a few moments pretty well out of anesthesia, is expressly recommended. If anesthetists will only realize that this is a procedure which, above all others, should be shunned, the number of cases of so-called status lymphaticus fatalities, under anesthesia, will, I believe, show a sudden and marked decrease."

Henderson concludes his article by stating that "unsuspected cases of status lymphaticus are often invoked after tonsil operations, which are due entirely to the ether being administered intermittently and the subject rapidly coming part way out of the anesthesia rather than to any connection of the tonsils with the thymus."

SPECIAL OPERATIONS

Short Operations.—*Precautions.*—As many fatalities have been reported from all anesthetics for short operations, it is well to state the means of avoiding them or reducing them to the minimum in the future.

First: With the exception of emergency cases, all patients should be as well prepared for a minor operation as for a major one.

Second: Rules regarding diet, cleansing of the gastro-intestinal tract, and also preliminary medication, if the psychic element is in evidence or much suffering is anticipated after the operation, must not be neglected.

Third: Constrictions around the neck and waist, such as a tight collar band, corsets, or belts, should be removed.

Fourth: The head and trunk should be in one straight line and the anesthetic given as speedily as consistent with safety.

Regardless of the anesthetic used, all *bandages around the abdomen or neck should be cut,* but not necessarily removed. It is impossible to induce a smooth anesthesia with bandages in place. In all operations upon the head, neck, or upper air passages the anesthesia must be considerably lessened before the bandages are reapplied, otherwise cyanosis may appear and the patient will remain under the anesthetic an unnecessarily long time. When the sitting or semi-sitting position is used, chloroform must not be given.

Nitrous Oxid.—For all *short operations* nitrous oxid, first through valves and then with to-and-fro breathing until deep anesthesia ensues, is the best method. Hasbrouck,[1] of New York City, who has given nitrous oxid for the extraction of teeth over 100,000 times, prefers nitrous oxid alone, and administers oxygen only as indicated. From his large experience he declares that while patients suffer little nausea or vomiting from the combination of oxygen with nitrous oxid, a still smaller percentage have any after-effects with the nitrous oxid alone.

No one is justified in giving nitrous oxid without having tanks of oxygen in place and available for immediate use.

Nitrous oxid is the recognized anesthetic for the *extraction of teeth.* It should also be used for *dislocations, opening abscesses, breaking up adhesions, examinations, removing or reapplying painful dressings, etc.*

For *prolonged dental work* the nasal inhaler should be used and a combination of nitrous oxid and oxygen under pressure given.

Nitrous oxid and oxygen may be used for its *analgesic quality,* the patient never reaching the anesthetic stage.

Exceptions to the above rule for selecting nitrous oxid or nitrous oxid and oxygen for short operations is where there is any great *swelling* or *engorgement of the neck.* The administration of gas in this condition may quickly induce dangerous symptoms. The author knows of one case in which a fatality occurred when nitrous oxid and oxygen were given for the extraction of a tooth. An undetected abscess at the base of the tongue burst at the height of anesthesia and immediately filled the patient's lungs with pus, the patient dying within three minutes.

Ethyl Chlorid.—Ethyl chlorid is contraindicated for extraction of teeth unless oxygen is used with it or nitrous oxid is not available, not only on account of the possibility of a fatality, but also because of the nausea and dizziness that so often follow a short application of this anesthetic, the percentage of cases nauseated being much greater than when nitrous oxid or nitrous oxid and oxygen are used.

Chloroform and Ether.—Chloroform is contraindicated, as there is a very great possibility of a fatality unless a deep anesthesia is maintained. There is no contraindication to ether except for the after-effects.

In *ophthalmic* cases, in which quiet is absolutely essential, chloroform by the vapor method, and with oxygen, is preferable to any other combination. This applies especially to such operations as *iridectomies.* Nitrous oxid with air or oxygen is contraindicated in these cases on account of increased congestion of the blood vessels, as is also any closed method. For *enucleations* a preliminary medication is indicated, and

[1] Personal communication.

some closed method preferably should be used to initiate the anesthetic. The narcosis should be continued with some form of vapor anesthesia. Chloroform should be avoided if possible at this time. It is unnecessary now, as formerly, to anesthetize deeply with ether and depend upon the resulting anesthesia for the operation.

Paracentesis of the membrana tympani should only be done under nitrous oxid with oxygen (preferably) or nitrous oxid alone. Ethyl chlorid would be the third choice.

The Mastoid.—Of all serious surgical cases the easiest, from the anesthetic standpoint, is a mastoid operation. A deep anesthesia is required only in the initial stages. The hammering and chiseling seem to have some anesthetic effect, as the vapors can be almost withdrawn and the reflexes allowed to become quite active without the patient evincing any conscious movement. If nausea follows a mastoid operation, the anesthetist has not measured up to his opportunities.

Generally speaking, the best procedure for mastoid cases is to begin the anesthetic by the drop method of chloroform, gradually switching to the drop method of ether and then changing to the oxygen-ether vapor method. This gets the anesthetist completely out of the way and the patient comes out of this anesthetic, as a rule, without any nausea, vomiting, or shock.

The nitrous oxid-ether sequence or any closed method is contraindicated, as the bag and mask are more or less in the surgeon's and assistant's way. Preliminary medication of morphin or something similar is most helpful in these cases.

The Upper Respiratory Tract.—In all operations upon this part of the body a preliminary douching with some antiseptic (in some instances to clear the parts of the blood and pus) is absolutely essential.

As a general rule, any closed method should be avoided with this special class of operations. Chloroform for the induction, and chloroform and oxygen, or ether and air, for the maintenance, is the best procedure.

Excision of the Tongue.—The majority of surgeons seem to prefer the dorsal position for excision of the tongue, with a sandbag under the shoulders, or with the headpiece slightly dropped. In this position, when the head is well flexed and the anesthetist supports the lower jaw with one hand, a clear airway is easily maintained, the blood and other secretions being more easily removed than by any other method, and, consequently, with less discomfort to the patient afterward. Some surgeons prefer the upright position. The anesthesia can be easily maintained by means of this vapor method, with the tube ending in the mouth or nose, or pharyngeal or intratracheal insufflation. Pharyngeal anesthesia (see p. 235) is, as a rule, all-sufficient.

For excision of the glands of the neck or operations upon the lips *and cheeks* some form of vapor anesthesia should be employed. In all of these cases a deep anesthesia is best, unless facilities for removing blood are not adequate when the patient's cough reflex is allowed to remain.

Cleft Palate.—It is well to avoid gas as the initiatory anesthetic for these operations, anesthol or chloroform being the best. The anesthesia can be maintained by ether with oxygen or air and by the vapor method.

In *intranasal* and *antrum of Highmore* operations the anesthesia should be maintained by the vapor method.

Submucous Operations.—While the majority of physicians do these operations in their offices under some local anesthetic, lately it has been urged that these can be better operated upon under a general anesthetic. Closed methods should be avoided, and the anesthetic should usually be induced with chloroform and maintained with chloroform and ether by a tube in the mouth. The patient should always have some preliminary medication.

Adenoid and Tonsil Cases.—In *adenoid* and *tonsil* cases, to-and-fro breathing of nitrous oxid followed immediately by ether, and supplemented later by the vapor of ether passed through a tube placed either in the mouth or nostrils, is the best. In all operations upon adults, where the mouth must be open, as the excision of the tongue, jaw, etc., the vapor method should be used, preceded by the drop method of chloroform and ether, or the nitrous oxid-ether sequence, according to the patient. The exception to this rule will be where the patient has some lung trouble. In that instance, rectal or morphin anesthesia, or spinal analgesia, should be used.

Alexander's and Gwathmey's technique [1] in adenoid and tonsil operations covers the ground for the operations in the recumbent position. We quote voluminously from this paper. The ideals for which one should strive may be divided as follows: 1, preparation of patient; 2, good anesthesia; 3, good technique; and, 4, after-treatment.

Preparation of Patient.—The night previous to the operation the patient is given a cathartic; to adults, some cathartic pill; to children, castor oil or calomel. The next morning, if the result is not satisfactory, a simple enema should be given, at least two hours before the operation. The temperature is then taken. No food is allowed for six hours before the time of operation. If the operation is early in the morning, no food whatever should be given. The last meal should consist of a plate of clear soup or bouillon with two crackers. Cases are on record of children vomiting a bolus of food or a small piece of undigested meat, which, getting into the trachea, caused serious disturbances, even septic pneumonia. Milk is especially prohibited. From nervousness or other

[1] "Technique in Adenoid and Tonsil Operations," *N. Y. Med. J.*, March 11, 1911.

causes this coagulates, and the vomited curds are as much of a menace as particles of any other article of food.

For nervous children over six years of age, chloretone, five grains, given one hour before operation, is valuable. From fifteen years upward, one-eighth or one-sixteenth grain of morphin, and one one-hundredth-and-fiftieth grain of atropin should be given, or ten grains of chloretone one hour before operation.

Immediately before the operation, the upper air passages should be sprayed with some antiseptic solution. Liquid petrolatum with menthol is especially recommended, as it lubricates the passages, facilitating the passing of the catheters. This procedure has quite a psychic effect, in addition to the physical, that is most beneficial.

In addition to the preliminary treatment, mental suggestion is here of the utmost importance, and varies with the characteristics of different patients.

On the table, the patient wears a loose, warm gown or robe, thick woolen socks, and is covered by a blanket, over which is placed a rubber sheet, fitting closely around the neck. Care should be taken to prevent any constriction at the neck or waist. The hair is covered with a sterile towel, as is also the rubber sheet.

Anesthesia.—The ideal anesthetic for this particular operation must be safe; deep enough to abolish all reflexes, including the cough, swallowing, and tongue reflexes; and continuous, so that there will be no necessity for the reapplication of the anesthetic or for the delay caused by the removal of blood from the operative field. Furthermore, the patient should come out of the anesthetic within fifteen minutes, in a natural way, without delirium or nausea. Vomiting is reduced to a minimum if no blood is allowed to enter the stomach during the operation.

For a very nervous child, or one having experienced previous fright from any cause, the time of operation should be in the early morning, say, one hour before the usual time for the child to awaken, or during the noonday nap.

The patient should be anesthetized while asleep. This has been done many hundreds of times, and with children is much safer than any other method. To successfully anesthetize a sleeping child, the mask or gauze should never touch the face. The anesthetic is begun with chloroform, a few drops at a time, and gradually increased until rhythmical and automatic respiration indicates the commencement of surgical anesthesia. A change to ether by the vapor or drop method is then made.

On account of the undeveloped muscles of children under six years of age, these patients should be anesthetized by the vapor or drop method of ether or chloroform. Any closed method puts too severe a strain upon the chest walls. The usual procedure is as follows:

In all cases in which the drop or vapor method is used, a few drops of cologne upon the mask, just before the anesthetic is started, will allay fear, and increase confidence in the anesthetist. From three to six drops of chloroform are then given, followed by as many of ether, then alternating, and changing entirely to ether as surgical anesthesia is reached. This procedure gets the patient under the anesthetic in from three to five minutes, and without any struggling.

One should always bear in mind that many of these little patients have the lymphatic temperament, in which chloroform is absolutely contraindicated. Whenever this is suspected, the drop method of ether, given carefully and slowly at first, and increased rapidly as the stage of surgical anesthesia approaches, will bridge over the disagreeable features which sometimes occur with this method of anesthesia.

From six years of age upward, decidedly the best technique is the gas-ether sequence, followed by the vapor method. The ether or chloroform is passed through a tube attached to the mouth gag.

If a patient has bronchitis or a catarrhal condition of the upper air passages, ether is absolutely contraindicated. Warm chloroform and oxygen is the safest anesthetic for this condition.

.The tube on the suction apparatus in the mouth, as employed in a large number of cases, has been found to be more or less in the way, and, to obviate this, we have adopted the plan of placing the catheters attached to the suction apparatus in the nares, so that the ends are just visible when the tongue is depressed. This compels the patient to breathe through the mouth, and the anesthesia is more easily maintained in this way than by any other method. (Fig. 93.) The patient thus receives all the vapor, and the blood is not in the way of the operator. Surgical anesthesia is as easily maintained in this way with ether as with chloroform.

Hewitt uses the gas-ether-chloroform sequence for this operation, as do also others who make a specialty of anesthetizing for nose and throat operations.

With the bent tube in the ether chamber we are enabled to get a more nearly saturated ether vapor than ever before, thereby rendering the use of the chloroform unnecessary in a large majority of cases. This method seemed to work well in one or two cases, but was not a complete success, so we finally abandoned it and developed the present method.

So far, the nasal tubes have acted perfectly in taking up the blood, and no trouble is experienced in keeping a clear field for the operator. A tube was formerly attached to the tongue depressor, but it was found that the tongue depressor had to be removed occasionally, during which time the patient might regain the lost reflexes and thus cause the surgeon embarrassment. With the vapor apparatus as now perfected, we are able to give a continuous anesthesia after the mouth gag has been placed in position, and the patient is in any posture desired by the surgeon.

If the operator prefers the patient in a dorsal position, it is unnecessary to turn the head to either the right or left, to stop the operation for the reapplication of the anesthetic mask, or to remove the blood from the oral or nasal cavities.

By means of this continuous narcosis, together with the use of the blood suction apparatus, the time of operation is reduced from one-third to one-half. The surgeon is also enabled to do more thorough work, without the feeling of the necessity of hurrying lest the patient come out of the anesthetic, since as even a plane of anesthesia can thus be maintained as for any other surgical procedure.

Deep chloroform narcosis, with great profusion of blood in this position, is more or less dangerous. For this reason the gas-ether sequence to get the patient deeply under the influence, followed by ether vapor anesthesia, is nearly ideal for this particular operation.

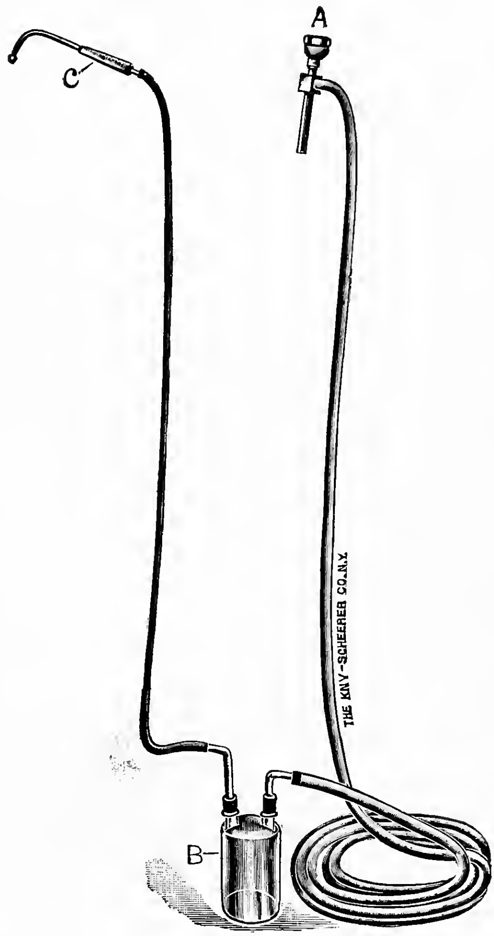


Fig. 132.—The Water Suction Apparatus for Adenoid and Tonsil Operations.

When ether is contraindicated, a tube from the oxygen tank replaces the foot pump. Warm oxygen alone, or oxygen with chloroform, may thus be given as indicated (Fig. 107).

Suction Apparatus.—This consists of a vacuum water pump (Fig. 133), which is attached to any spigot or tap by an adjustable connection (Fig. 133). The rush of water through this brass cylinder creates a diminished pressure which is transmitted to a Wolff bottle by connecting rubber hose. Another rubber hose leads from the Wolff bottle to the patient; to the free end of this hose are attached two rubber catheters, which, when placed in position, utilize the vacuum and complete the apparatus.

Good Technique.—The desiderata in the matter of good technique are: 1, Good light; 2, bloodless field; and, 3, maximum speed.

Good Light.—After experimenting with various forms of reflected light, we find direct illumination of the operative field to be the most

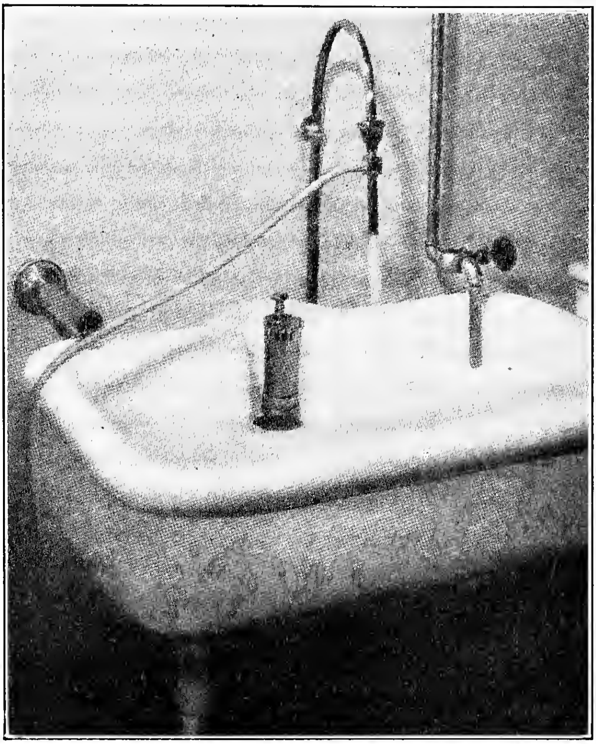


Fig. 133.—Pump Attached to Spigot With Water Turned On.

desirable. This is obtained by using an electric headlight and condenser, supplied by a dry cell battery, or, better, by a current controller. Shielded lights on instrument and anesthetic tables prevent interference with the operator's light.

By means of the brilliantly illuminated field so provided, anomalies of formation are noted, and bleeding vessels may be seen and clamped, thereby avoiding much tissue laceration and bleeding.

Bloodless Field.—Our attempts at reaching this ideal are still in the formative period; so much has already been gained, however, that we feel justified in reporting the method. Our efforts were addressed to, firstly, the reducing of the blood lost; and, secondly, to the removal of that which was lost. We attempted, as detailed under anesthesia, to decrease by sequestration the amount of blood volume in the operative area. Our experiments to date have convinced us that this procedure, when perfected, may be of positive value. Immediately after the enucleation, a pad of gauze, firmly pressed into the bleeding area, helps to reduce the hemorrhage; however, the sum total of blood lost was not much affected, until, after much experimenting, we evolved the present method of blood removal. This consists of a graduated Wolff bottle, suction pump, and attachments.

Rubber catheters, with several additional holes made near their tips, are introduced through the nares as soon as surgical anesthesia is present. They are allowed to lie alongside of each other in the pharynx, their ends about an inch above the epiglottis. The enlarged ends of the catheters are joined by a Y connection with the rest of the apparatus, the tube passing over the patient's head. With the patient's head thrown back, this region becomes a natural reservoir, which is thus readily drained.

As soon as we began using this method, we noticed a marked reduction in the amount of blood and mucus collected. Previous to using the catheters, our average of many cases was four ounces; now it is seldom over two. A study of the blood supply of the tonsillar area throws no light on the reason for the diminished hemorrhage, yet it has occurred in too many cases to be a coincidence.

After complete removal of adenoids and tonsils, the patient is turned on one side, the catheters are withdrawn, and the vault is explored with the finger for shreds.

The vault is now wiped over with alcohol on gauze, and the nares are douched with cold saline solution. This latter procedure washes out all clotted blood, and hastens the patient's return to consciousness.

Maximum Speed.—Maximum speed is obtained by simplicity of method in operating. A skilled anesthetist and an assistant physician or nurse are essential. An occasional swab is employed to remove clotted blood not sucked up by the catheters. The adenoids are then removed in the usual way. The average time of operation is eight minutes.

After-treatment.—The patients are kept in bed for twenty-four hours, and given liquid food. The throat is sprayed every two hours with mild liquid antiseptics and a hydrogen peroxid solution, used alternately. When cervical stiffness is present, massage and hot applications are employed. Complications are met with appropriate remedies.

The Upright Position.—Many operators prefer the upright position for adenoid and tonsil operations. French,[1] of Brooklyn, has devised a chair table, and has worked out a technique that approaches the ideal for operations in this position. "The method consists in placing

[1] French, Thomas R.: *N. Y. Med. J.*, June 1, 1912, 1125.

the patient upon a table for anesthetization in the recumbent position, and, when the stage of excitement has passed, in converting the table into

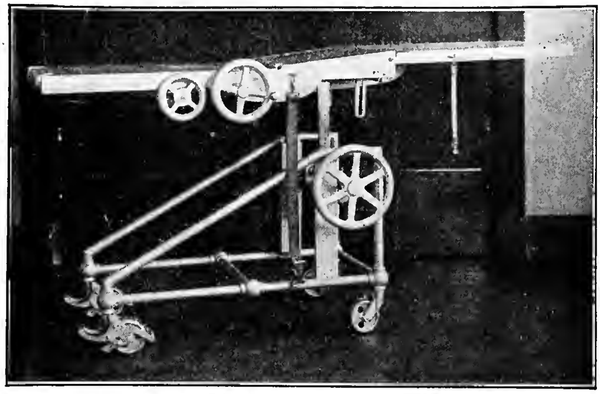


Fig. 134a.—Dr. French's Chair Table.

a chair and bringing the body to the sitting posture; or, for that matter, placing it in almost any position except one with the face downward. (See Figs. 134a to 134j.)

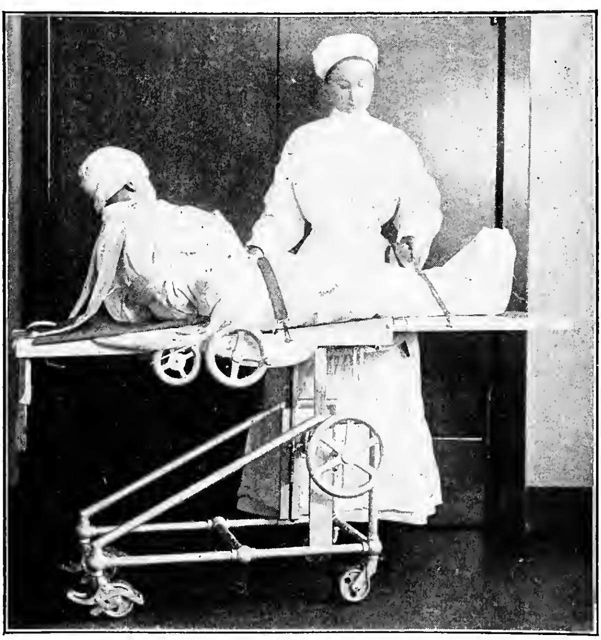


Fig. 134b.—Dr. French's Chair Table.

"Before the patient is wrapped in a blanket, a stout, four-inch bandage is made to encircle the upper part of the back, the ends being drawn up under the axillæ and over the front of the shoulders, and for the moment allowed to hang in the recesses on either side of the head

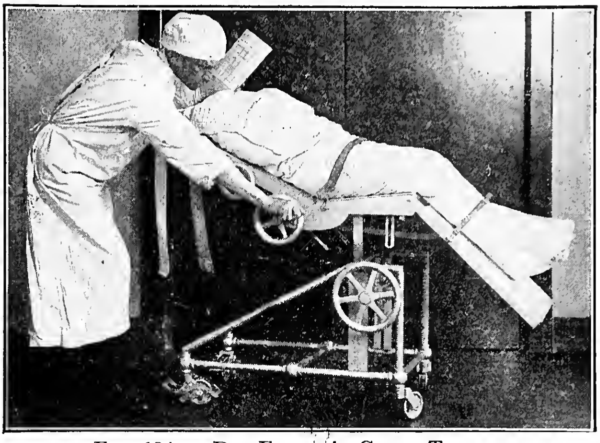


FIG. 134C.—DR. FRENCH'S CHAIR TABLE.

rest (Fig. 134 B). After the patient has been wrapped in a blanket, the leather straps attached to the seat are fastened rather loosely around the hips, and the legs, below the knees, are strapped to the footrest (also shown in Fig. 134 C). When the patient is nearly anesthetized

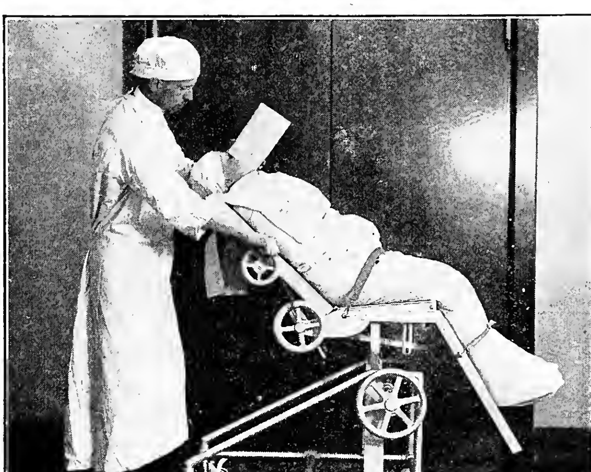


FIG. 134D.—DR. FRENCH'S CHAIR TABLE.

the anesthetist turns the wheel at the junction of the back of the chair with the seat, and the body is thus raised slowly forward (Fig. 134 D) to the upright position, the mechanism being so constructed that as the back ascends the footrest descends. The seat, which is a trifle higher in front than at the back, is covered with a mat of corrugated rubber, which checks largely, if not entirely, the tendency of the body to slide toward the foot of the table or chair. While the upward movement is taking place, the headrest is adjusted to the patient's head by means of

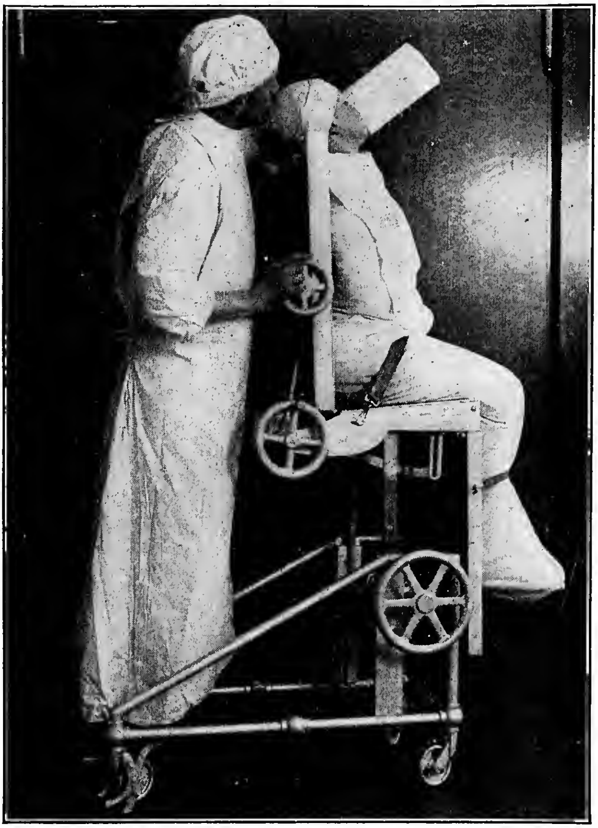


Fig. 134e.—Dr. French's Chair Table.

the smaller wheel on the side of the back section (Fig. 134 E), and this is accomplished with such ease and accuracy that the position of the head for the proper administration of the anesthetic and the desired display of the field of operation can be readily maintained. At the same time the shoulder bandage is adjusted by drawing the ends around the headrest, when they are caught under, and tied to a hook on the back of the chair. The patient has now reached the upright position and is ready for operation. If the surgeon desires to operate while standing, the chair part of the mechanism can be raised (by means of the large wheel in the frame of the base) sufficiently to bring the head of the patient opposite his own (Fig. 134 F). If, however, he desires to operate while sitting, the chair can be lowered, if necessary, as far as the base (Fig. 134 G), and these movements can be made with surprising ease, even if the patient's body is of great weight. Figure 134 G also shows the anesthetist standing inside the rear part of the frame of the base, in

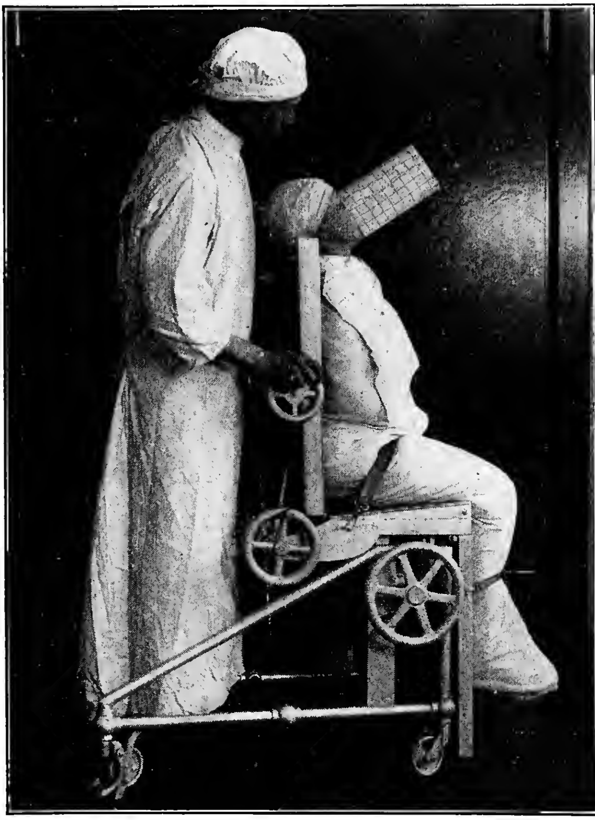


FIG. 134F.—DR. FRENCH'S CHAIR TABLE.

which position he can administer the anesthetic and control the mechanism of the chair. If respiratory troubles arise, and it is desired to lower the patient's head, this can be quickly done by tilting the chair backward (Fig. 134 H), and then by wheel action converting the chair into a table top in the Trendelenburg position (Figs. 134 I and 134 J).

"With an ordinary chair, or even with the special chair as previously constructed, it has been, at times, very difficult to place and keep the head of the patient in the required position for the proper administration of the anesthetic and for easy access to the field of operation. With the new method, the inexperienced interne or newly graduated medical

Fig. 134g.—Dr. French's Chair Table.

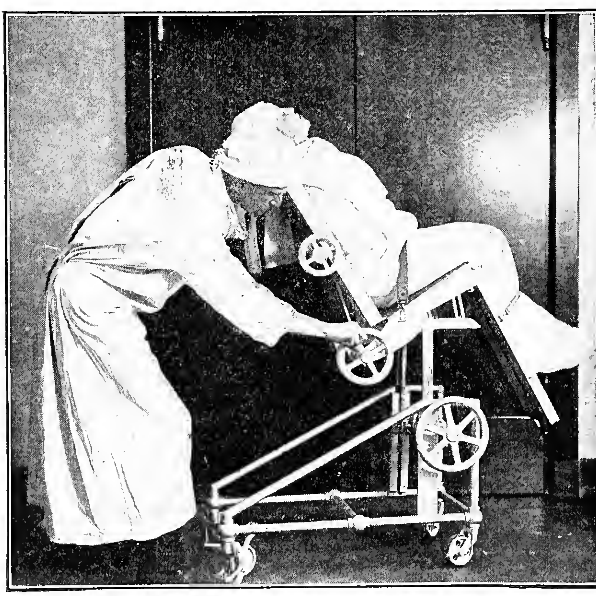


Fig. 134h.—Dr. French's Chair Table.

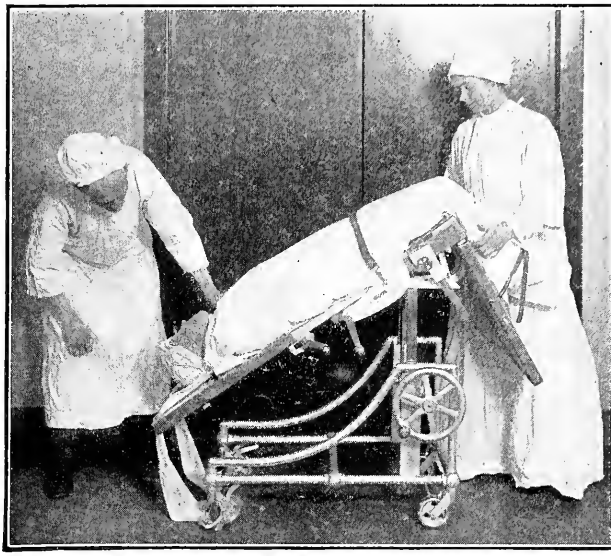


FIG. 134I.—DR. FRENCH'S CHAIR TABLE.

man can, under instruction, bring the patient to, and maintain him in, the upright position, with perfect ease and safety. This is accomplished partly by means of wheel devices, the slightest turn of which either raises or lowers the upper portion or the whole of the body, or elevates or de-

FIG. 134J.—DR. FRENCH'S CHAIR TABLE.

presses the headrest, and that, too, without further need of attention than is required in turning them.

"The secret of a safe and an uninterrupted administration of an anesthetic in the upright position is in keeping the neck somewhat stretched and the head moderately extended over the headrest."

French states that "a sudden change from the horizontal to the upright position, while the patient is under ether narcosis, is apt to occasion a too rapid development of cerebral anemia and a consequent loss of cardiac balance.

"Experience would seem to show that the danger of blood flowing into the trachea is no greater during the routine operations which we are wont to perform in the nose and throat when the body is upright than when in the Rose position.

"The blood thus flowing into the gastro-intestinal tract has never, in our experience, made its presence manifest by untoward disturbances in that canal. Our results, in the considerable number of patients upon whom we have operated in the upright position, have led us to the conviction that the fear of blood flowing into the air passages is based upon theory and not upon fact.

"There is less shock, and less disturbance in other ways, to the patient after operation because less ether is required to maintain narcosis when the sitting posture has been attained. This is, no doubt, due to the diminished blood pressure in the vessels of the head when the body is in the upright position and under the influence of a general anesthetic. The difference between the flushed face in the recumbent position and its relatively pale appearance in the upright position is at times very marked. The difference in the quantity of the anesthetic required is, we believe, due to the difference in the amount of blood in the brain in the two positions, which, in French's opinion, is another reason for this special technique.

"The abstraction of a considerable quantity of blood from an anemic child adds to the cachexia, diminishes its rallying powers, and reduces the body resistance in the event of the onset of any special disorder. Shock is felt more by the child than the adult, and although the child recovers from the shock more rapidly the ultimate recovery will be retarded if a considerable amount of blood has been lost. As a rule, children in a fair state of health before operation sustain the loss of a relatively large quantity of blood in a very remarkable way, and in time recover their usual, if not better, health, but they do not always do so without concurrent disturbances; and how often such disturbances are due directly or indirectly to the loss of blood it may be difficult to say."

For operations upon the tonsils and adenoids under nitrous oxid and oxygen, see page 156.

Tracheotomy.—It is sometimes safer to perform this operation under a local anesthetic on account of the congestion produced or difficulty in breathing if a general anesthetic is used. When there is no obstruction in any part of the air passages, there is no objection to doing a tracheotomy under general anesthesia. After the tracheal tube is inserted, anesthesia is easily maintained by chloroform or ether vapor. If no vapor apparatus is convenient, an ordinary mask is held over the trachea, and the anesthetic carefully given. For thyroidectomies careful preliminary medication is essential, and the anesthetic should be instituted very slowly and carefully. Chloroform and oxygen is probably the best anesthetic to use. Any closed method is contraindicated, as there is always the possibility of the thyroid lessening the diameters of the air passages by pressure.

Goiter (Angina Ludovici, Exophthalmos—Graves' Disease).—If a general anesthetic is determined upon, ether and chloroform with oxygen by a tube is probably the best method of administration. Closed methods should be avoided with these cases, as deaths have been reported under nitrous oxid and ethyl chlorid. Many surgeons prefer a local anesthetic. (See page XIV.)

Crile's method of "stealing upon the thyroid" has been widely adopted. He states:

"In cases of Graves' disease the mere proposal to perform an operation becomes also a pathological excitation; this excitation may so much increase the disease that the patient is even less able than before to bring herself to submit to adequate treatment. On all sides this disease is beset by vicious circles; by pathological interactions. The ideal plan of approach, at least in my experience, is to assure the patient that hers is a curable malady, that it can be treated in a hospital, and that non-operative measures will first be tried; then if they prove inadequate a simple operation will be done; that it will be best to leave this decision to the judgment of her medical adviser, and that, since even the discussion of operation is both unpleasant and injurious, it would be best not to open this subject again. The patient usually gladly consents to leave the whole matter to the judgment of the physician, and the way is then opened for the most effective treatment which in my judgment has ever been proposed—namely, ligation or excision on the new principle of *anoci-association.*"

The technique is as follows: "For about five days before the operation the patient is treated every morning. A hypodermic injection of sterile water and inhalation of fresh air with a little nitrous oxid through the same inhaler that will be used on the day of operation is what constitutes the treatment. The entire treatment lasts five minutes each day. The tachycardia and other nervous symptoms that usually occur with each treatment become less marked as the day of operation approaches. On the morning of the operation, which is performed in one of the favorable phases of the numerous cycles of the disease, the patient receives the treatment as usual. One-eighth to one-sixth of a grain of morphin and scopolamin (atropin should be omitted in these cases) is substituted for the sterile water, and the nitrous oxid is carried to the stage of surgical anesthesia. The patient falls asleep in her bed without realizing that the first step of an operation has already begun. The patient is then transported anesthetized to the operating room, where the operative field is prepared. The anticipation of the operation and excitement usually attendant upon the induction of anesthesia, sometimes producing fatal shock, are by this method eliminated.

"Up to this point the patient's brain, hence the remainder of the body, is in a negative state, and this is half of the innovation of the specialized operation; the other half is this: any injury of any sensitive part of the body, though the patient is under inhalation anesthesia, excites the brain, and hence, through the brain, all of the motor mechanism, especially the thyroid. Inhalation anesthesia is but a thin veneer, and, although the patient is unconscious, the afferent impulses set up by the operation reach the brain apparently as readily as if no anesthetic was given.

"This is the source of the hyperthyroidism, so called, that constitutes the greatest danger of the operation. Operation under inhalation anesthesia on any sensitive part of the body produces precisely the same exacerbation of the disease (hyperthyroidism) as operations upon the thyroid gland itself. How may this be avoided? It may be wholly avoided by the use of complete local anesthesia in addition to general anesthesia, by the use of novocain throughout the entire operation, just as completely as if the patient had received no general anesthesia."

"By this technique," Crile states, "the scope of the operation is greatly increased and the gland can be safely removed from any patient whose condition will endure the metabolic influence of the sudden withdrawal of so much active gland tissue."

With operations upon the *brain,* it is better to use chloroform and oxygen. Nitrous oxid and oxygen are contraindicated, as they raise arterial tension with unnecessary bleeding. For the same reason ether should be avoided as a preliminary, as any struggling will immediately induce congestion with increased bleeding. In an emergency case, or if the patient is unconscious, preliminary medication should be avoided.

Amputations.—For amputations, dislocations, setting fractures, and similar operations, preliminary medication is essential, and a fairly deep anesthesia should be used. Gas and oxygen by some closed method is preferable for work of this character.

Operations Upon Fingers and Toes.—Operations upon fingers and toes require a deep anesthesia in order to avoid reflex movements, on account of the unusually large nerve supply in these parts.

Circumcision.—For circumcision of a child the best plan is to start with one or two drops of the essence of bitter orange peel and supplement this with chloroform drop by drop until the second stage is reached, when a switch to ether by the drop method is instituted. A change to the closed method may then be advantageously made. The anesthesia should be considerably lessened before the final dressings are applied.

Rectal Cases.—All rectal cases should have full physiological doses of morphin with some other drug. The anesthesia can be induced and maintained with nitrous oxid and oxygen or ether by the closed method. Chloroform should be avoided in these cases.

Obstetric Cases.—In obstetrical practice, on account of the enlargement of the heart at that period, and the patient always welcoming the anesthetic, chloroform with oxygen is preferred, and is unattended with the immediate risk that might be inseparable from chloroform at another time. An additional reason for chloroform being safe at this time is the continuous dilatation of the sphincters of the uterus and vagina, compelling the patient to take deep breaths, and thereby get rid of the anesthetic almost as soon as administered. A deep anesthesia is not indicated at any time, both on account of the child and the mother. The anesthesia should be maintained between the second and third stages if possible. The reported fatalities from chloroform in this connection are exceedingly rare, and are usually due to gross carelessness, ignorance, or attempting to maintain too deep an anesthesia. If ether is used it can easily be deodorized by the vapor method. Nitrous oxid and oxygen given to the stage of analgesia is becoming more and more popular.

Anesthesia should be avoided during the menstrual period, as there is a greater possibility of hysterical or maniacal excitement afterward. If, however, an operation is imperative, a warm oxygenated chloroform vapor is indicated.

Curettage.—For *curettage* or similar operations, nitrous oxid and oxygen, or warm chloroform vapor with oxygen or air, if the type of patient permits, is best.

Genito-urinary Operations.—In *genito-urinary* operations, where deep anesthesia is always required, the nitrous oxid-ether sequence is indicated.

Laparotomy.—In laparotomies, where absolute relaxation is required, the nitrous oxid-ether sequence, to be followed by chloroform when the patient is in the Trendelenburg position, is the combination preferred by such men as Hewitt [1] and Boyle.[2] Boyle's routine procedure is to change to chloroform or the chloroform-ether mixture after fifteen or twenty minutes.

Chloroform is administered with less danger when the patient is in

[1] Hewitt: "Anæsthetics."

[2] Boyle: "Practical Anæsthetics," 142.

the Trendelenburg position, on account of the large amount of blood in the brain at that time. Relaxation of the abdominal muscles is assisted by placing a sandbag under the knees and slightly raising the shoulders.

Gastro-enterostomy and Similar Operations.—In addition to the usual preliminary preparation, Crile's method is as follows:

"Starved and Anemic Patients.—A preliminary transfusion of blood brings back the vitality of patients exsanguinated by hemorrhages and makes them good risks; thus the surgeon may reclaim the bad risks in hemorrhage from ulcer of the stomach or duodenum.

"In starvation cases the risk cannot be so successfully reclaimed, though the patient may be much improved by transfusion. The risk in these cases is not shock and depression, but a broken metabolism expressing itself as acidosis.

"Since employing transfusion I have had the opportunity of seeing more clearly the dangers of acidosis, for I have operated on cases all but moribund, and have seen them pass through the operation unchanged, and have seen metabolic death follow. Heretofore such cases would not have been operated, and if operated would not have survived long enough for study. There is a stage of acidosis rather easily recognizable which proves fatal as a metabolic process in spite of complete control of the blood volume, and measurably of the blood pressure. This does not in the least apply to acute or chronic hemorrhage. Here transfusion gives an absolute control."

Crile states, further, that "the combination of nitrous oxid, general anesthesia, and novocain, local anesthesia and quinin, and urea hydrochlorid as a post-operative anesthesia combined with ample incision and gentle handling establishes *anoci-association*—or shockless operation."

Other surgeons get excellent results by starting a hypodermoclysis as soon as the patient is in surgical anesthesia and continuing this throughout the operation. As much as two quarts of normal saline can be taken by a patient in this way with splendid results. With the vapor method of ether anesthesia, the patient's pulse can be easily maintained at normal, provided the surgeon is gentle in his manipulation.

Peritonitis or Intestinal Obstruction.—If morphin has been used to quiet pain the anesthetist should be informed of this fact. Otherwise too deep an anesthesia may be instituted at the commencement of the operation. Surgeons here should not insist upon absolute relaxation, as in many cases it is almost impossible to maintain this condition. If regurgitation of fecal matter is present, the stomach should be well washed out before the induction of the anesthetic and the stomach tube left in place during the operation. The open method of administration should be used, initiated preferably with chloroform and continued with ether. If vomiting occurs, the anesthetist must immediately insert a mouth gag (but must not pull the tongue forward) and with his finger or a sponge on a sponge holder keep the throat absolutely clear. Death by suffocation is always imminent in these cases.

CONCLUSIONS

With these general indications as a guide, it can readily be seen how impossible it is to say that some one anesthetic should be used at a certain age, or for a given disease, or for some specific operation. The conditions blend in such a way that the anesthetic must be selected for each case; the safety of the patient, and the successful termination of the operation, being the results sought. If the surgeon is so situated that he must work without a trained assistant and without the refinements of anesthesia customary in the larger cities, ether should be the anesthetic of choice. Finally, when thus handicapped, the surgeon should always remember that it is possible with morphin and whiskey, plus a very small amount of general anesthetic, to complete successfully nearly any operation. Fatalities have unquestionably occurred from the use of some one anesthetic or method. No hospital or clinic can be considered to rank among the first when a routine procedure is countenanced. When for any reason, after careful choice and deliberation, the anesthetic is taken badly a change should be made immediately.

BIBLIOGRAPHY

Abelin: *Jahrb. f. Kinderkr.*, 1870, *55*, 116.
Adami & Nicholls: "Principles of Pathology," *2*, 697.
Albwot: "System of Medicine."
Bagensky: *Cent. Zeit. f. Kinderh.*
Bartel, J.: "Ueber die hypoplastische Konstitution und ihre Bedeutung," *Wien. klin. Wchnschr.*, 1908, *21*, 783-790.
Barten & Stein: "Ueber abnormale Lymphdrusenbefunde und deren Beziehung zum Status thymicolymphaticus," *Arch. f. Anat. u. Entwicklungsgesch.*, Leipz., 1906, 231-249, 2 pl.
Von Bardeleben: *Arch. f. klin. Chir.*, *46*, 149.
Beneke: *Berl. klin. Woch.*, 1894, *31*, 216.
Biechele, R. A.: "Status Lymphaticus with a Report of Cases," *Arch. Pediat.*, New York, 1904, *21*, 500-508.
Biedert: *Ibidem*, 1896, *33*, 581.
Blake: *Ann. of Surg.*, 1902, *35*.
Blumer: *Johns Hopkins Hosp. Bull.*, Oct., 1903, *14*.
Bonnet: *Gaz. des Hôpitaux*, Dec. 9, 1899.
Bovaird, D., Jr.: *Arch. of Pediat.*, 1906, *23*.
Bradley, E. B.: "Death Under Anesthesia Due to Status Lymphaticus," *Jour. Am. Med. Assn.*, Chicago, 1910, *59*, 1785.

Brickner: Foster's "Therapeutics, Ether."

Carlyll, H. B.: "The Thymus Gland and the Status Lymphaticus," *Guy's Hosp. Rep.*, Lond., 1910, *64*, 1-37, 1 pl.

Clessin: *Münch. med. Woch.*, *55*, 330-1898.

Cocks, G. H.: "Status Thymo-Lymphaticus and Its Relation to Sudden Death," *Man. Eye, Ear & Throat Hosp. Rep.*, N. Y., 1911, *12*, 199-216.

Conner, L. E.: "The Clinical Diagnosis of Status Lymphaticus," *N. Y. Med. J.*, New York, 1906, *6*, 282-284.

Coolidge, E. L.: "Status Lymphaticus, Report of a Case." *Bull. Lying-in Hosp.*, N. Y., 1908, *4*, 149-151.

Daut: *Jahrb. f. Kinderkr.*, 1898, *47*, 14.

Day: "Another Case of Status Lymphaticus," *Pediat.*, N. Y., 1910, *22*, 428-433.

Ehrhardt: *Arch. f. klin. Chir.*, *78*, 598.

Epstein: *Münch. med. Woch.*, 1902, *49*, 1728.

Escherich: *Berl. klin. Woch.*, 1896, *33*, 645.

Ewing: "The Lymphatic Constitution." *N. Y. Med. J.*, July 10, 1897, 37.

Farret: *Thèse de Paris*, 1896. Quoted by Hotz.

Fer: *Corr. f. schwei. Aertze*, 1904, *34*, 2.

Fischl: *Münch. med. Woch.*, 1902, *49*, 1728.

Flügge: *Vrtljschr. f. gerichtl. Med.*, 1899, *17*, 20.

Friedjung: *Centralbl. f. d. Grenzgeb. d. Med. u. Chir.*, 1900, *111*, 465.

Friedlander: *Arch. of Ped.*, 1907, *24*, 490.

Friedleben: *Die Physiologie der Thymusdrüse*, 1858.

Ganghofer: *Münch. med. Woch.*, 1902, *49*, 1728.

Gardner: "Lymphatism," *Proc. Roy. Soc. Med.*, Lond., 1909-10, *111*, Sect. Anæsthesia., 19-44.

Gluck: *Berl. klin. Woch.*, 1894, *31*, 670.

Grawitz: *Deut. med. Woch.*, 1888, *12*, 429.

Griffith: *Trans. Ass. Am. Phys.*, 1903, *18*.

Halsted: *Phila. Med. J.*, 1900, 859.

Harris: "The Laryngoscope," Feb., 1910, 199.

Hart: *Centralbl. f. d. Grenzgeb. d. Med. u. Chir.*, May to August, 1909.

Hedinger: "Ueber die Kombination von Morbus Addisonii mit Status Lymphaticus." *Frankf. Z. f. Path.*, Wiesb., 1907, *1*, 527-543, 1 pl. "Ueber Beziehung zwischen Status Lymphaticus und Morbus Addisonii." *Verhandl. d. deut. path. Gesell.*, 1907; Jena, 1908, *11*, 29-32.

Henderson, Yandell: "Primary Heart Failure in Normal Subjects Under Ether," *Surg. Gynec. & Obstet.*, Aug., 1911, 161-165.

Heussler: *Deut. med. Woch.*, 1894, *38*.

Hinrichs: *Berl. klin. Woch.*, 1908, *45*, 825.

Hotz: *Beit. z. klin. Chir.*, 1907, *55*, 525.

Howland: "The Symptoms of Status Lymphaticus in Infants and Young Children." *Tr. Am. Pediat. Soc.*, Phila., 1907-08, *19*, 51-59; also, *Proc. Path. Soc.*, Phila., 1909, *12*, 267-276.

Humphry: "Clinical and Post-mortem Observations on the Status Lymphaticus with Deductions and a Plea Against the Maligning of Ethyl Chlorid as a General Anesthetic." *Lancet*, Lond., 1908, *11*, 1870-1874; also, *J. Ment. Sc.*, Lond., 1909, *55*, 473-481; "Status Lymphaticus," *Lancet*, Lond., 1909, *11*, 1703-1705.

Jackson: *J. Am. Med. Assn.*, May 25, 1907.

Jessen: *Aerz. sachverstand. Zeit.*, 1898.

Kassowitz: *Münch. med. Woch.*, 1902, *49*, 1728.

Kauffmann: "On Two Cases Suggesting Relationship to Status Lymphaticus." *Rep. Soc. Study Dis. Child.*, Lond., 1907-08, *8*, 435-438; also, *Birmingh. Med. Rev.*, 1908, *64*, 182-184; also, *Brit. J. Child. Dis.*, Lond., 1908, *5*, 430-432.

Kern: "Status Lymphaticus." *J. Indiana Med. Assn.*, Fort Wayne, 1909, *2*, 480-482.

Koch: "Status Lymphaticus mit Persistierendem Thymus." *Deut. med. Woch.*, Leipz. u. Berl., 1911, *37*, 1102. "Mechanische Thymus—Erstickungstod mit Status Lymphaticus."

König: *Central. f. Chir.*, 1897, *24*, 605. *Verhandl. d. deut. Gesell. f. Chir.*, 1898, *35*, 119.

Kopp: *Denkwürdigkeiten*, 1830, *1*.

Krause & Cohen: *Deutsche med. Woch.*, 1890, 450.

Kundrat: *Wien. klin. Woch.*, Jan. 3, 10, 17 and 24, 1895.

Lange: *Jahrb. f. Kinderkr.*, 1898, *48*, 119.

Marfan: *Bull. Soc. Hôpit.*, 1894, *11*, 361.

Mau: "Enlarged Thymus and Sudden Death." *Med. Chron.*, Manchester, 1910-11, *53*, 216-223. 1 pl.

McCardie: "Status Lymphaticus in Relation to General Anæsthesia." *Brit. Med. J.*, Lond., 1908, *202*, 196.

Munro: "The Status Lymphaticus." *Lancet*, Lond., 1909, *2*, 1468.

Musser & Ullom: "A Case of Status Lymphaticus." *Med.*, Detroit, 1904, *10*, 351-359. Also *reprint*.

Nettel: "Ueber einen Fall von Thymustod." *Arch. f. klin. Chir.*, 1904, *73*, 636.

Nordmann: *Correspond. f. schweiz. Aerzte*, 1889, 202.

Norton: *Phila. Med. J.*, 1898, 249.

Oehme: "Lymphfollikel im kindlichen Knochenmarke." *Münch. med. Woch.*, 1909, *56*, 446-449.

Ohlmacher: *J. Am. Med. Assn.*, Feb. 13, 1904.

Paltauf: *Wiener klin. Woch.*, 1889.

Park: "The Status Lymphaticus." *Tr. Am. Surg. Assn.*, Phila, 1905, *23*, 241-250. Also, *Surg. Gynec. & Obstet.*, Chicago, 1905, *1*, 140-145. Also, *St. Louis Med. Rev.*, 1906, *53*, 394.

Penkert: *Deut. med. Woch.*, 1902, *28*, 810.

Plater: "Observatorium in Hominis Affectibus Plurisque, etc." *libri tres*, 1614, *111*, 172.

Purrocker: *Münch. med. Woch.*, 1899, *46*, 943.

Rachford: *Tr. Assn., Am. Phys.*, Phila., 1910, *25*, 570-579; also, *Am. J. Med. Sci.*, Phila. and N. Y., 1910, *140*, 550-557.

Ranke: *Ibidem*, 1902, *49*, 1728.

Rehn: *Verhand. d. deut. Gesell. f. Chir.*, 1906, *35*, 2, 364.

Richter: *Münch. med. Woch.*, 1902, *49*, 1728.

Roberts: "The Status Lymphaticus with Particular Reference to Anæsthesia in Tonsil and Adenoid Operations," *Tr. Am. Laryngol. Rhinol. and Otol. Soc.*, St. Louis, 1908, 507-524.

Rubra & Brown: "Note on a Case of Status Lymphaticus with Reference to the Administration of Anæsthetics." *Lancet*, Lond., 1907, *11*, 1759.

Satterlee: "A Case of Status Lymphaticus." *Arch. pediat.*, N. Y., 1909, *25*, 689-692. Discussion, 702. "Status Lymphaticus." *Brit. Med. J.*, Lond., 1909, *1*, 1042.

Schultz: *Beit. z. klin. Chir.*, 1901, 638.

Schwinn: *J. Am. Med. Assn.*, 1908, 2059.

Siegel: *Berl. klin. Woch.*, 1896, *33*, 887.

Simon & d'Œlsnitz: *Bull. Soc. Pediat.*, 1902, 26.

Söderland & Backman: "Studien öfver Thymusinvolutionen." Upsala Lökareför Forh., 1908, *13*.

Sorgo: *Central. f. Grenzgeb. Med. u. Chir.*, 1898, 6-10.

Starr: *N. Y. Med. News*, 1896, 421.

Targhetta: *Thèse de Paris*, Jan., 1902.

Thremich: *Vrtljschr. f. gerichtl. Med.*, 1901, *21*, 300.

Todd & Emery: "Specimens from a Case of Status Lymphaticus." *Rep. Soc. Study Dis. Child.*, Lond., 1903, 1904, *4*, 293-296.

Vintras: "Status Lymphaticus." *Lancet*, Lond., 1907, *1*, 295.

Von Werdt. "Zur Frage der Beziehung swischen Status Lymphaticus bzw. Thymolymphaticus und Morbus Addisonii." *Berl. klin. Woch.*, 1910, *47*, 2383-2386.

Warthin: "The Pathology of the Status Lymphaticus with Lantern Demonstration." *Am. J. Obst.*, N. Y., 1909, *60*, 348-356.

Weigert: *Berl. klin. Woch.*, 1906, 887.

Wheelock: "Anesthesia in Lymphaticus." *Toledo M. and S. Rep.*, 1909, *35*, 395-399.

Wiesner: "Gefässanomalien bei sog. Status Thymicolymphaticus." *Verhandl. d. deutsch. path. Gesellsch.* Jena, 1909, 217-219.

Witmer: *Beitr. z. klin. Chir.*, *29*, 189.

CHAPTER IX

TREATMENT BEFORE, DURING, AND AFTER ANESTHESIA

Duties of the Anesthetist in Addition to Giving Anesthetic.

The Anesthetist's Kit: Anesthetist's Motto; Mouth Gag; Contents of Kit; Emergency Treatment to Insure Breathing.

The Management of Ordinary Cases: Preliminary Treatment; Treatment During Anesthesia; After-Treatment.

Management of Difficult or Unusual Cases: Respiratory; Muscular; Nervous; Idiosyncratic; Shock; Post-Anesthetic Toxemia.

DUTIES OF THE ANESTHETIST IN ADDITION TO GIVING THE ANESTHETIC

The anesthetist who thinks his duties comprise getting the patient under, maintaining narcosis until the surgeon gives the signal to let up,

Fig. 135.—Supporting Jaw to Maintain Free Airway with Two Fingers on the Carotid Artery.

and seeing to it that the patient is safely removed from the operating table to the bed is doomed to failure. Much more than this devolves upon him. He must be assured that the proper preliminary hygienic, psychic, and medicinal preparation is attended to; he must find out whether the breathing is oral or nasal, and direct his anesthetic vapor accordingly; he must keep a clear airway either by manipulating the lower jaw or by a suction pump or sponging; he must maintain an even narcosis; he must keep the mouth gag (if used) in position; he must protect the patient from too much pressure upon the throat and chest either from artery forceps, or from an assistant or anyone leaning too heavily upon the chest; he must assist the surgeon in any way that may be desirable, according to the exigencies of the case. He must be equipped for the management of all manner of emergencies which may concern his part of the surgical procedure or the after-treatment of the case.

In order to meet the exigencies, whatever their nature, as they arise, the following equipment will be found invaluable:

THE ANESTHETIST'S KIT

Anesthetist's Motto.—The difficulty with all inhalation methods of administration, as before mentioned, is respiratory. While the motto of the anesthetist should be *Anticipation,* yet there sometimes occur cases in which asphyxial symptoms take such a course that interference is necessary in order to retain a clear air passage.

Mouth Gag.—The skilled anesthetist seldom uses a mouth gag and tongue forceps. In thousands of cases it should not be necessary. (This does not apply to cases in which the mouth is to be operated upon.) Nevertheless, the anesthetist should always be prepared to use both.

Contents of Kit.—The following is a list of the apparatus that should be convenient whenever an anesthetic is given, regardless of the method:

(1) A wooden gag or screw with which to open the mouth.

(2) Mouth gag, so patterned that the blades will fall one behind the other when closed, this being the easiest to place between the teeth.

(3) Tongue forceps. The best tongue forceps have a small projection to clasp the tongue directly in the middle. If this is placed in the median line, there will be little or no bleeding, as there are very few blood vessels and nerves in this part of the tongue. The tongue is really composed of two parts joined in the median line. The tongue forceps with two projections will invariably cause a flow of blood.

(4) A tracheotomy set. This should be in a case, every part sterilized, and ready for use. It should not be open unless an emergency calls for its use.

(5) A curved needle threaded with silk, sterilized, and wrapped up.

(6) A hypodermic syringe.

Emergency Treatment to Insure Breathing.—*Whenever the anesthetist anticipates trouble of any kind,* he should examine the mouth of the patient, and, if this is not done before the administration, it requires but a second to open the lips and determine immediately which side of the mouth will be the best in which to place the wooden wedge or screw. Before placing the wedge or gag in the mouth, however, the anesthetist should exhaust every plan to have the patient breathe naturally. If unsuccessful in this, while every second counts in an emergency, it is unnecessary to destroy or injure the patient's teeth. After the mouth has been opened sufficiently with the wooden screw, place the mouth gag in position, insert the tongue forceps in the median line, one-half to one inch from the tip of the tongue, and pull the tongue forward. If an airway is thus secured, and the patient recommences breathing, it is always best to then remove the tongue forceps and gag. Nevertheless it must be borne in mind that, if such a procedure has become necessary once, it is likely to recur at any time. Very little traction is necessary to pull the tongue forward. In addition to moving the jaw and head in different directions, one of the best means of overcoming asphyxial symptoms is by placing a tube from the oxygen tank in the nose or the mouth. If a stream of oxygen has to be kept up in this way during the remainder of the operation, the patient will be no worse for it.

Again, the anesthetist must bear in mind that, if in the midst of an operation asphyxial symptoms continue to assert themselves, it is always possible to considerably diminish the amount of pulmonary anesthetic by administering a hypodermic of morphin.

For excision of the tongue, or any operation in which it is necessary to hold it forward for any length of time, a thread would be less in the way than the tongue forceps. The needle should be inserted in about the same place as the tongue forceps, the thread pulled through and tied in a convenient loop, and the needle cut off. The thread may then be caught with an artery forceps.

It is the purpose of this chapter to give, in condensed form, certain practical suggestions concerning the management of surgical cases, from the anesthetist's point of view. It is now well known that the success of the anesthesia as regards the ultimate recovery of the patient is largely dependent upon the preliminary preparation, the treatment during the course of the narcosis, and the care after the anesthesia is discontinued.

In order to render this part of the present volume as available as possible for practical purposes, the subject is divided into: (1) The management of ordinary cases before, during, and after anesthesia; (2) the management of difficult and exceptional cases before, during, and after anesthesia.

THE MANAGEMENT OF ORDINARY CASES

Under this category come the ordinary run of surgical cases—patients who need, perhaps, a certain amount of suggestive therapy along with the requisite medicinal treatment, regardless of the anesthetic agent to be employed.

Preliminary Treatment

The preliminary preparation of a patient about to be anesthetized may be: (1) Hygienic; (2) psychic; (3) medical. Some patients require one or the other; others require all the preliminary adjuvants that may be brought into requisition.

Hygienic.—Grooming of Patient.—The patient should be as thoroughly prepared (as far as his or her condition permits) as if for an athletic event. A warm bath with thorough cleansing of the skin and a shampoo for the hair, followed by an alcohol rub, should precede *all* other treatment. Removal of hair over and adjoining site of operation with scissors and razor should be done the night previous to a morning operation, or in the morning for an afternoon operation. "One of the most essential points in preparing the patient for operation is to make sure that the preceding night is a restful one. If the patient is in pain, or is particularly nervous, a hypnotic should always be administered."[1]

The Mouth and Nose.—If possible, a dentist should cleanse the teeth thoroughly, removing loose and hopelessly decayed teeth, and then giving the patient a suitable antiseptic mouth wash to be used every four or five hours until time for the operation. This wash should be used to cleanse the nasal passages as well.

"The disinfection of the mouth is a matter of so much importance in the prevention of pneumonia from aspiration during anesthesia that it should never be neglected." Hydrogen dioxid, one part to three of water, or potassium permanganate in a weak solution, may be used for this purpose.

The Bladder.—"Patients should either empty the bladder or be catheterized immediately before the operation.

"If urine is scanty, bicarbonate of potash or citrate of potash in small quantities, not more than 20 or 30 grains within twenty-four hours, added to pure water should be given freely to flush the kidneys.

"Should a more active diuretic be desired, small doses of sweet spirit of niter may be added to the draft, since this simple remedy acts as

[1] "American Practice of Surgery," *4*, 132.

an efficient diuretic, in many cases overcoming any tendency to spasm of the renal vessels and flooding these organs with blood."[1]

INTESTINAL TRACT.—No athlete is ever given a purge on the night immediately preceding a contest, and the time should be past when a patient is thus debilitated before entering the operating room.

All are agreed on the advisability of emptying the intestinal tract, the method and time of doing this varying with different hospitals and surgeons.

"Two days before the operation the patient is given one or two tablespoonfuls of castor oil or a dessertspoonful of natural Carlsbad salts in a glass of warm water, or at noon on the day before the operation a purgative should be given, followed in eight or nine hours by an enema, the amount of purging being increased or diminished according to the patient's strength.

"In intestinal obstruction, with frequent vomiting or regurgitation, a careful insertion of the stomach tube, which may be left in place, is necessary before commencing the anesthesia.

"The bowels should not act more than twice in the twenty-four hours previous to the operation. Many surgeons dispense entirely with purgation, as the worst condition of all is when the patient is suffering from an artificial diarrhea at the time of operation. The number of bacteria increases as the intestinal contents become more liquid, and diminishes with the abatement of the diarrhea.

"The intestinal tract should be cleansed and practically emptied before the time of operation. Two ounces of castor oil are administered 12 to 16 hours before operation, and the large bowel is emptied by a soapsuds enema on the morning of the operation. The cleansing of the entire intestinal tract, together with the withholding of nourishment, renders the canal practically sterile in its upper portions, facilitates intra-abdominal manipulation, and lessens the possibility of gaseous distention after the operation. The administration of sterilized foods is also a good procedure." [2]

DIET.—"While advantageous to have the stomach empty, it is not essential to starve the patient for twelve or eighteen hours. Easily digested gruels of barley or rice can be given in small quantities up to within two or three hours of the operation with distinct advantage. Starchy gruels permit the liver to store up glycogen and thereby place it in a favorable position for maintaining its function. Animal broths throw an undue strain upon the kidneys in the elimination of extractives. Hunter believes that the absence of glycogen from the liver, by diminishing the combustion processes in that organ, diminishes the antitoxic power of the liver cells, so that the starved individual is more

[1] Keen's "Surgery," *5*, 1008.

[2] *Am. J. Surg.*, *4*, 131.

easily affected by poisons than the glycogen-rich person. So, too, an absence of carbohydrate material results in extensive changes in fat metabolism, which results in an increased formation of acid, and so tends to the development of acidosis."[1]

"The patient should be kept in bed and given liquid diet for eighteen hours prior to the operation. Water is freely given by mouth up to within three hours of the time of operation. The practice of withholding water involves unnecessary hardship and discomfort, while its free administration aids materially in the subsequent elimination of ether, and is undoubtedly a factor in preventing the possibility of shock. When inadvisable to give water by mouth, one-half pint of normal saline may be administered per rectum two hours before the patient goes on the table."[2]

Psychic.—Some patients, as we have stated, require one or all forms of preliminary preparation in order to insure a smooth, safe, and altogether satisfactory anesthesia. The expert anesthetist must be able to judge of the particular requirements of the individual case. Over seventy per cent of cases, according to conservative estimates, require both mental and medical treatment in order to insure the best results.

Children and nervous and irritable adults require psychic preparation for the coming ordeal, and the anesthetist who ignores this factor runs the risk of having to deal with more or less serious difficulties during some portion of the time when the patient is under his care. In this connection the Chapter on Hypnotism will be found helpful.

Idiots and insane persons, as a rule, require only medical preparation. In many cases, however, in which the mental defect is of a mild degree of severity, the patient is susceptible to the reassuring influence of a calm and forceful personality. Those who have had occasion to witness operations in homes or hospitals for defectives or the insane have observed this. The senior author (J. T. G.) recalls the case of a feeble-minded boy who, when about to be operated upon for the removal of adenoids and tonsils, flew into an uncontrollable rage at the sight of one anesthetist, who made no pretense of giving the patient the benefit of suggestive therapy, whereas another anesthetist, availing himself of this aid, experienced no difficulty in getting the child to take the anesthetic quietly.

Patients already in a state of coma require no preliminary treatment.

Necessity for Preliminary Mental Preparation.—"There can be little doubt that the mental condition of the patient does not receive enough attention from the average anesthetizer. It is remarkable that patients, whose thoughts are made to run in pleasant channels as the an-

[1] Keen's "Surgery," *5*, 1000.

[2] "American Practice of Surgery," *4*, 131.

esthetic is first given, usually take the drug more quietly than those who inhale it in a condition of mental distress. This is particularly true of nervous women and children. When the fears of a patient who is conscious are developed into the terrors of semiconsciousness, in which the patient imagines the most frightful accidents are taking place, it can be readily understood that profound nervous shock is produced."[1]

"Where but little is required to turn the scales toward the side of death, unquestionably fear may sometimes lead to fatal results through psychical shock, through the lack of coöperation of the patient in declining proper nourishment, through loss of sleep, and finally through impaired resistance, which results from the combination of these factors. Such extreme dread as is referred to here should be carefully considered, so that every effort may be made to soothe the fears of the sufferer, as the successful outcome of an operation sometimes materially depends on the tranquilized state of the patient's mind. It is often not the most formidable and dangerous operations which thus terrify patients, and it is not always the hysterical or simple-minded who are the victims of this dread. Psychical shock, although rarely fatal of itself, may readily prove a determining lethal factor in a patient with unsound organs, who is also subjected to the physical shock and loss of blood of an operation."[2]

Crile states that: "Although there is not convincing proof, still there is strong evidence that the effect of the stimulus of fear upon the body without physical activity is more injurious than the effect of fear with physical activity. It is well known that the soldier lying under fire waiting in vain for orders to charge suffers more than the soldier that flings himself into the fray; that a wild animal in an open chase against capture suffers less than when cowering in captivity."

If this is true, exactly the same state exists when a patient lies in bed awaiting an operation. Crile goes even further, and states: "That the brain is definitely influenced, even damaged, by fear has been proved by the following experiments:

"Rabbits were frightened but not injured, and not chased, by a dog. After various periods of time the animals were killed and their brain cells compared with the normal. Widespread changes were seen. The principal gross phenomena expressed by the rabbit were rapid heart, accelerated respiration, prostration, tremors, and a rise in temperature.

"The dog showed similar phenomena, excepting, instead of muscular relaxation, as in the rabbit, it showed aggressive muscular action. Both the dog and the rabbit were exhausted and, although the dog exerted himself actively and the rabbit remained physically passive, the rabbit was much more exhausted than the dog.

"Other observations were made upon the brains of foxes chased for

[1] Keen's "Surgery," *5*, p. 12.

[2] *Am. J. Surg.*, *4*, 120.

various distances by members of a hunt club, then finally overtaken by the hounds and killed. The brain cells of these foxes as compared with those of a normal fox showed extensive physical changes."

Illustrations Showing Necessity for Mental Treatment.—There is recorded the history of a patient in whom the psychic element predominated to such an extent that the patient suddenly expired during the shaving of the groin, preparatory to an operation for hernia.[1]

There is a record of another patient whose dread of the anesthetic was such that the narcotiser dropped water upon the mask for a few minutes with the idea of assuaging his anxiety and distress of mind, but even this procedure did not prevail, and the patient died before a single drop of chloroform touched the mask.[2]

A patient at Bellevue Hospital, in New York City, cut his throat in anticipation of an operation which was to be performed upon him the following day.

A patient (in private practice), who had been given only a few breaths of nitrous oxid, jumped from the table, fled from the room, and was never afterward located, so far as operation was concerned, by the surgeon.[3]

We see the other extreme in obstetric practice. The patient always welcomes the chloroform, as she is in such a state of mind that she is willing to do anything to relieve her suffering. The vast majority of surgical cases come between these two extremes.

Mental Depression.—It is interesting to note that the majority of fatal cases reported, in which the psychic element predominated to such an extent that a fatality resulted, were men, and these are the patients who have this mental depression. Not only so, but they are men in robust health, requiring possibly but a slight operation.

In the light of these statistics, it is wrong to place an alcoholic or an athlete upon the table without endeavoring to eliminate this psychic element.

Diagnostic Evidences of Fear.—In spite of the fact that most patients claim not to be fearful of the ordeal through which they are to pass, and possibly present no outward manifestation of fear, the anesthetist, listening to the heart of the patient just before the administration, discovers that things are not what they appear to be on the surface. In a great many instances the palpitation of the heart is alarming, and seems to be absolutely out of the control of the patient. In a great many others the heart is beating faster and with more force than normal. This state of affairs means that, when the anesthetic is finally administered, the patient is in an attitude to resist the effects of the anesthetic.

[1] Sir James Y. Simpson's work, *2*, 144.

[2] Kappeler: "Anæsthetics," 118.

[3] This case was reported to the senior author by the surgeon.

On the other hand, even though the patient may say that she is afraid (men never admit it), if this patient has had the proper preliminary medication, the heart will be found normal. In other words, the nervous mechanism has been taken out of the patient's control temporarily; not only so, but the mind is now in a condition where a few suggestions in the proper spirit and manner are readily grasped by the patient. When the patient, thus doubly prepared, has the anesthetic administered, the chances are all in favor of a sleep approaching that of nature. "The transition from partial sleep to complete anesthesia is not so sudden as from complete wakefulness, and is more easily accomplished." (Crile.)

Influence of Omission of All Preliminary Medication in Possible Subsequent Operations.—When this preliminary medication is omitted, even if everything goes on, to all appearances, smoothly, the patient's condition of mind as he approaches the operating table may come back to him at some future time when a second operation is needed, and so act upon his nerves as to make him defer the operation until, possibly, too late for anything but palliative surgery.

Importance of Preliminary Medication.—Not only is a patient in a proper frame of mind to receive suggestions when preliminary medication is used, but the whole nervous system is obtunded, especially the olfactory nerve and the vomiting center. The patient, therefore, takes more kindly to the anesthetic, passing quietly and quickly into full surgical anesthesia. If, during the operation, it is possible to lighten the anesthesia without disturbing the surgeon, the patient can be held between a light and deep narcosis without once disturbing the dangerous vomiting center. The patient comes out, as a usual thing, without either conscious or unconscious vomiting. The kidneys and lungs have also been saved unnecessary irritation by thus reducing the amount of pulmonary anesthetic one-third to one-half.

Even when this element of fear is seemingly entirely absent, the patient, disregarding preliminary treatment of all kinds, incurs a certain definite and needless risk, often out of all proportion to the operation to be performed. A gentle laxative, rest in bed at the place of operation, and a small physiological dose of morphin or some other sedative should be insisted upon for even slight operations.

Two illustrative cases from the writer's and one from a noted surgeon's practice in New York City will suffice.

(1) Adenoid and tonsil case of a young girl twenty-two years of age. She refused to stay in a private sanitarium over night, and consequently did not have any morphin preliminarily. Patient walked in from the street, and, while the surgeon and myself retired to another room, disrobed and laid herself upon the table, and was draped by the nurse for operation. Heart sounds normal and no outward appearance of nervousness. Induction of anesthesia uneventful. About two min-

utes after beginning the operation patient stopped breathing, and after the usual procedure was revived and the operation completed. Patient was compelled to stay in hospital for two days on account of laxity of the sphincter ani, and the surgeon was put to his wits' end to explain the relation of this condition and subsequent diarrhea to the adenoid and tonsil operation.

(2) Patient, male, sixty-five years of age. Carcinomatous gland of neck. Patient walked into hospital on the morning of the operation, and had no preliminary medication before coming to the operating room. Heart slightly hypertrophied and sometimes failed to compensate. After operation had progressed about fifteen minutes, respiration ceased for no apparent reason except lack of preliminary treatment of all kinds. A quick slap on chest wall over precordial region failed to start the respiratory pump. The head of the table was quickly lowered; sphincter ani stretched, traction on tongue and artificial respiration with massage of precordial region were immediately instituted. All of these factors acting together resulted finally in the patient's respiratory center reasserting itself, and the operation was successfully completed.

(3) Patient, male, age thirty-five; vigorous health, slight operation under cocain. No preliminary medication of any kind was attempted beyond cleansing the immediate field of operation. A few drops of cocain were injected into the urethra, when the patient immediately stopped breathing, and all efforts at resuscitation failed.

The above fatal case and the two nearly fatal cases illustrate most forcibly the imperative necessity of safeguarding patients by preliminary medication in so-called minor operations.

In order to completely eliminate the element of fear, Crile has elaborated a method which he calls anoci-association. This consists of blocking off the nerve supply to the field of operation (in external operations) by the local or intraneural infiltration of novocain. The brain is thus completely isolated from operative influence, and, according to Crile, "is not more affected than if the operation were performed on clothing."

This is of importance aside from the comfort of the patient, because, as Crile has shown, the element of fear has a definite effect on the cells of the brain. These changes, to whatever due, are always proportional to the extent of the loss of vital force.

Medical.—The medical treatment consists of:

(1) The treatment necessary to prepare the patient for the operation, which is in part included under hygienic treatment.

(2) The narcotics and hypnotics preliminarily given as a desirable part of the anesthetic.

There is a complete unanimity among surgeons as to the preliminary use of morphin in local, spinal, intravenous, and rectal anesthesia. (See remarks in each of these chapters.) On the other hand, there is a wide diversity of opinion as to prescribing morphin and other narcotics before pulmonary anesthetics, most surgeons believing thoroughly in their use, while others never employ them before an operation, but inconsistently prescribe some of them immediately afterward. As all pulmonary anesthetics are improved by use of these drugs more than are the four special classes of anesthesia mentioned above, there should be a greater unanimity of opinion concerning their value than exists at present.

Rules Governing Preliminary Medical Preparation.—Preliminary medication consists usually of morphin, hyoscin, chloretone, bromids, and whiskey, either alone or in combination. The following rules will assist in determining whether or not preliminary medication, and especially morphin, should be used.[1]

(1) Whenever morphin (or other narcotic) is to be given at all, it should always be given before, instead of after, the operation, in order to obtain the benefits of it in the induction and maintenance of anesthesia.

(2) After taking it, the patient must be kept in bed absolutely quiet, and at the proper time carried to the operating room.

(3) All athletes, alcoholics, neurotic and plethoric patients should have preliminary medication in order to take away, as far as possible, the physical control which might enable them, when the second stage of narcosis is reached, to take a deep breath, hold it, and thus force upon the heart all the anesthetic vapor in the lungs, creating an overdose.

(4) In the extremes of life, the very young, the very old, under seven and over seventy, if morphin is given at all, it should be with very great caution.

(5) Whenever morphin is given a lighter narcosis should be maintained than when this drug is not employed.

(6) Care must be taken in administering the usual doses of morphin when chloroform is the terminal anesthetic. It is best to use some other drug, as both morphin and chloroform have a depressing effect on the respiratory centers. Atropin is the best drug to employ as a preliminary to chloroform (or any combintion of drugs with chloroform), rendering inhibito-respiratory reflexes less liable to occur. If used alone, atropin, 1/100 to 1/150 of a grain, 30 minutes to 1 hour before the operation, is the proper dose. One-eighth of a grain of morphin with 1/150 grain of atropin is a good combination when chloroform is used alone.

Preliminary narcotic medication increases the confidence of nervous patients, lessens the amount of anesthetic required, prevents the excessive accumulation of mucus in the throat, reduces the liability to shock, and eases the immediate post-operative pain, while often giving to the patient a happier exit from the influence of the anesthetic."[2]

[1] Collins, C. U.: *J. Am. Med. Assn.*, Mar. 26, 1911.

[2] *Am. J. Surg.*, *4*, 132.

"Through countless experiments it has been found that narcoses are possible with far smaller amounts if preceded a few hours before by a hypnotic, even though these hypnotics act on entirely different organs." [1]

Time for Giving the Preliminary Medication.—Whenever medication is used, it should be given for its full physiological effect to be apparent just before the time scheduled for the operation. It is just as important not to give the preliminary medication too *long* as too *short* a time before the operation.

For morphin or any of its combinations, at least 30 minutes should be allowed. The physiological effect of morphin and atropin is indicated by dryness of the mouth and slight slowing of the heart and respiration.

Doses of Preliminary Medicaments.—When chloretone is used alone, it is best to start at least 1 hour or an hour and a half ahead of time. Probably the best way to give this drug is 5 grains with ½ glass of water every 15 minutes until 15 grains have been taken. The last dose is to be given at least 30 minutes before the operation. When chloretone and morphin are used in combination, only small doses of both drugs are necessary, in order to have the desired effect. Ten grains of chloretone with ½ glass of water, 1 hour before the time, and ⅛ to 1/6 grain of morphin 30 minutes before, is usually sufficient.

Some experimental laboratories report that ¼ grain of morphin with 15 grains of chloretone would be absolutely safe for an athlete or an alcoholic.

The average dose is 1/8 to 1/6 grain morphin with 1/150 grain atropin, for women; and 1/6 to ¼ grain morphin with 1/100 grain atropin for men. One-eighth to ¼ grain of morphin, with 1/100 grain scopolamin 1½ hours before the operation has been used by some surgeons with very great success.

Collins' [2] perfected technique is probably the best ever published, and for this reason is given in full. His "final choice resulted only after using hyoscin-morphin-cactin combination in 70 cases and morphin and atropin in a few cases. He first used chloroform, but in the majority of his cases ether was the anesthetic used. Lately he has been using nitrous oxid, and finds this acts equally well. This preliminary medication is given to all patients over seven years old.

In exophthalmic goiter cases, on account of the nervous element, it is given the night before and repeated one and a half hours before the operation.

All relatives and friends are excluded from the room, and every necessary manipulation and handling of the patient is now completed.

The hypodermic is administered 1½ hours before the operation, and consists of a solution containing scopolamin, 1/100 grain, and morphin,

[1] Meyer and Gottlieb: "Experimentelle Pharmakologie."
[2] *Loc cit.*, 15.

1/6 grain. The room is now darkened and quiet maintained. In about 30 minutes the patient becomes drowsy and in a tranquil condition of mind.

Twenty minutes before the operation a layer of gauze or cotton is placed over the eyes, and the patient is now carried and placed upon the operating table.

The anesthetic is administered while the final cleansing of the operative field is concluded.

After the operation the patient usually sleeps from two to five hours before becoming completely awake. The smarting pain of a recent operation is thus entirely eliminated.

In over 1,000 cases there were no deaths and only 1 case presented unpleasant symptoms, and there was practically no post-operative vomiting (about 1 in 10).

INDICATIONS AND CONTRAINDICATIONS OF PRELIMINARY MEDICATION.—The contraindications of morphin are the extremes of life; acute or subacute nephritis; a state of coma; where, for any reason, the reflexes are not to be abolished; in those extremely rare cases in which morphin is taken with distress, with accompanying disagreeable after-effects, and especially in cases of idiosyncrasy; also very weak and feeble patients, and those with any respiratory affection.

If for any reason morphin in any of its various combinations is contraindicated, an ounce of whiskey and 7 ounces of saline solution per rectum, ½ hour before the operation, usually has the desired effect of quieting the patient.

When ether is contraindicated and chloroform or ethyl chlorid is the anesthetic of choice, atropin is especially indicated as the preliminary medicament to be used. It maintains the respiration, and with ethyl chlorid prevents profuse salivation with consequent nausea and vomiting.

The experimental and clinical experiences of Herrenschmidt and Beauvy [1] have made them come to the following conclusion:

"That adrenal extracts should be administered to chloroformed subjects, whether the suprarenal capsule shows evidence of weakness or whether it gives evidence of struggle and consequent reaction. The effect of prolonged chloroform administration on the medullary portion of the adrenal is diminution and even disappearance of both chromaffin and adrenalin.

"Delbet has administered adrenalin to more than 1,000 chloroformed patients. The results have been splendid. He believes that adrenalin unquestionably regularizes the narcosis and diminishes (in most cases eliminates) post-operative shock."

[1] P. Delbet, A. Herrenschmidt, and A. Beauvy: *Revue de chirurgie*, Apr. 10, 1912.

Treatment During Anesthesia

The object of treatment during anesthesia is the maintenance of the patient's vitality on as nearly normal a plane as possible.

The anesthetist should at all times anticipate the needs of the surgeon, and also give necessary directions for any treatment the patient's condition demands during the operation, for instance, during a laparotomy, if a Trendelenburg posture is called for and a light anesthesia is being maintained at the time, the anesthesia should be immediately deepened, otherwise the muscles will stiffen up with the changed position and cause trouble.

Again, if there is shock from handling important vessels and nerves or inflamed tissues or breaking up an adhesion, the anesthetic must be lessened and the oxygen increased, and a rectal saline or hypodermoclysis given, thus keeping the pulse and respiration as nearly normal as possible.

Hydrant Water or Saline Enema to Relieve Thirst, Prevent Nausea, and Assist Kidneys.—Furthermore, to mitigate the thirst which may arise from the morphin, to give strength and volume to the pulse and also to assist the kidneys and prevent the formation of gas in the intestine, two pints of normal saline solution, 105° to 115° F., per rectum materially assists in this direction, and brings the patient out in a far better condition than when this has not been included. This should be given as a routine measure, and for the special purposes here mentioned, while the patient is still in *full surgical anesthesia,* a slight Trendelenburg position assisting greatly in the retention of the fluid.

If the saline enema is quickly absorbed or has been given continuously during the operation, it may be discontinued 10 to 15 minutes before the conclusion. Instead of the normal saline, ordinary hydrant water may be used with advantage, according to Trout.[1]

He [2] compared over 400 alternate cases. Actual experiments proved that tap water could be continued over a longer period with less rectal irritation than with any saline solution. He cites the fact that "therapeutists sometimes obtain wonderful results in the treatment of acute and chronic nephritis by substituting a salt-free diet." He also refers to deaths that "showed experimentally that they were due to the sodium chlorid and not to the amount of water or to hemolysis." Reference is also made to experimenters who have "actually produced not only an acute, but a chronic, nephritis in rabbits by the continual administration of this drug." He refers to Vincent, who "was able to control to a large extent a number of cases of hysteria by employing a salt-free diet with-

[1] On the abuse of normal salt solution, see G. H. Evans: *J. Am. Med. Assn.,* Dec. 30, 1911, 2126.

[2] Trout: "Proctoclysis," *J. Am. Med. Assn.,* May 4, 1912, 1352.

out their knowledge, and accentuated the symptoms by a corresponding increase in salt."

Trout mentions specifically one of his own cases, an interval appendix, in which "there followed a transient albuminuria which remained for two days." *Water* was then substituted for the salt solution per rectum, and at the end of twenty-four hours the albumin had disappeared. At the end of the next twenty-four hours, salt solution was again used and albumin appeared within the next twenty-four hours. Salt solution was then discontinued and water started, and the patient did not show any more albumin up to the time of his discharge from the hospital. In this case there was never any edema.

"When a poison is introduced into the system it unites to form new compounds with the cell protoplasm, and this molecular union must be broken up before the poison can be eliminated. Salt solution has no specific action in either bacterial or vegetable poisoning.

"If absorption is a process of osmosis it is certainly reasonable to presume that a solution which is not isotonic with blood will be more readily absorbed from the rectum, and our series of cases tends to confirm this view."

"Conclusions.—(1) All patients show less rectal irritation from proctoclysis if given a soapsuds enema before the operation.

"(2) The patients given water by rectum absorbed nearly 400 c. c. more to the 24 hours than did the patients given salt solution, the average for the water series being 2,444 c. c. per 24 hours and the average for the salt series being 2,041 c. c. per 24 hours.

"(3) The patients given salt solution by rectum required nearly twice as much water by mouth to relieve thirst, or, to give exact figures, in the water cases only 332 c. c. were taken in the first 24 hours; in the salt cases 696 were required in the first 24 hours.

"(4) The amount of urine was practically the same in both cases.

"(5) In 17 cases the patients complained of tasting salt without having any idea that normal salt solution was being given by rectum. None of the water series made any such complaint.

"(6) In drainage cases more fluid may be taken by rectum than in those laparotomies closed without drainage.

"(7) Proctoclysis should be employed more frequently than it has been in the past and in all classes of cases in which it is possible. Care should be exercised to prevent "water logging" of the entire system, and this applies to both salt and water.

"(8) In peritonitis cases with drainage it is possible to have the patients take four or five times as much fluid by rectum as in the cases on which this paper is based."

Lawson [1] corroborated Trout's findings. "Theoretically, at least," he

[1] Lawson, George B.: *J. Am. Med. Assn.*, Apr. 18, 1908, 1267.

says, "it seems better in the toxemias to use plain water in place of normal saline so that the osmotic pressure would increase the absorption; also by increasing the fluids of the body without increasing the sodium chlorid one better facilitates urinary secretion."

Olive Oil to Restore the Opsonic Index.—The administration of five ounces of warm olive oil is strongly recommended by Ferguson.[1] He states that "anesthesia by ether or chloroform lowers the opsonic index, that is to say, reduces the patient's power to resist an infection which was existing at the time of the operation or which may be a post-operative acquirement; second, the bacteria are not materially affected either in respect to number or activity; third, this impaired resistance is brought about through the medium of both phagocytes and serum."

Ferguson cites a number of experiments to prove this theory, upon both animals and human beings: "In the human experiments 5 ounces (150 c. c.) of warm olive oil were passed slowly into the rectum through a tube immediately after the patient had returned from the operating room. This was followed after three to six hours by a restoration of phagocytic power, while, on the contrary, the injection of the same amount of physiologic salt solution had no appreciable effect in shortening the period of phagocytic depression."

It is suggested that a certain amount of the oil is absorbed and enters the blood stream; and, furthermore, "in all probability a certain amount of ether is present in the intestinal tract which may be held by the oil, and thus prevented from becoming reabsorbed."

Where long exposure of intestines is unavoidable, as in gastro-enterostomy and similar operations, hypodermoclysis should be begun as soon as the patient is in surgical anesthesia, thus anticipating and in a great measure preventing surgical shock.

When sudden hemorrhage occurs rectal saline, with the patient in a slight Trendelenburg position, will more quickly restore the volume of blood lost, and in this way reëstablish circulatory equilibrium, than any other procedure. This, of course, is in addition to whatever measures the surgeon may institute for the control of hemorrhage.

As a further preventive of post-operative shock, filling the abdominal cavity with oxygen at the close of the operation is a useful procedure.

Aëration of Lungs.—As the operation is drawing to a close, if the anesthetic has been other than nitrous oxid, a system of aëration of the lungs should be initiated as follows:

Place any mask with rubber bag over the face of a patient and commence pumping in warm air, the bag to be kept slightly distended or overdistended for two or three minutes and then emptied, and this

[1] Ferguson, Robert H.: "The Opsonic Index in Relation to Surgical Anesthesia." E. R. Squibb & Sons.

process is repeated (unless the patient is entirely conscious) until he is ready to be removed from the operating table.

Removal of Patient.—The patient should be moved with as little jolting as possible, and should be well covered over with hot blankets while on the stretcher, special care being taken to protect the head as well as the feet.

Technique of Removal to the Bed.—Unless straps are under the

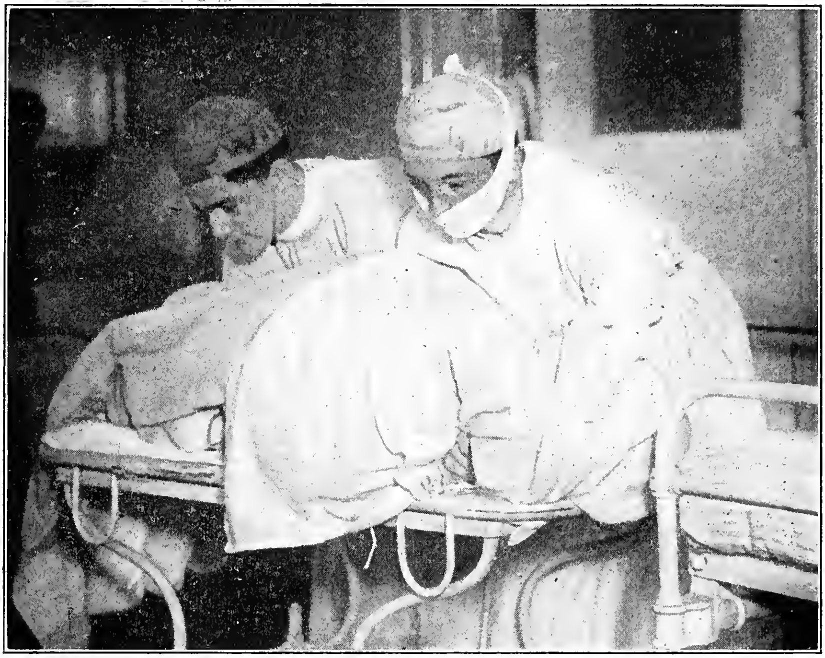


FIG. 136.—PREPARING TO LIFT PATIENT. Head of patient to foot of bed.

patient or there is an abundance of help, instead of lifting the patient directly over the stretcher into the bed, place the head of the patient at the foot of the bed, the stretcher and bed thus forming a right angle, with anesthetist and nurse standing within the angle thus formed. In this position a very heavy patient can be easily lifted by one, or, at most, two, people and placed in bed without jarring or jolting and without straining the backs of those lifting. The patient should always be lifted as high as the head, in order that the principal weight of the body be carried in a vertical position. The strain upon the muscles of the back is thus materially lessened.

If a sedative is indicated after the operation, it is best to use some other drug than morphin, if this has been used as a preliminary, as a repetition of morphin may induce nausea. If, however, it is repeated, the atropin should be omitted, as the dryness of the throat caused by this drug is usually a source of very great discomfort to the patient. The whiskey and saline enema is one of the best medicaments to use after an operation. Chloretone, in 5-grain doses, and hyoscin, either alone or combined with morphin, is also good.

Finally, with proper preliminary medication, the anesthetic may be discontinued much earlier. Patients usually continue to sleep or doze

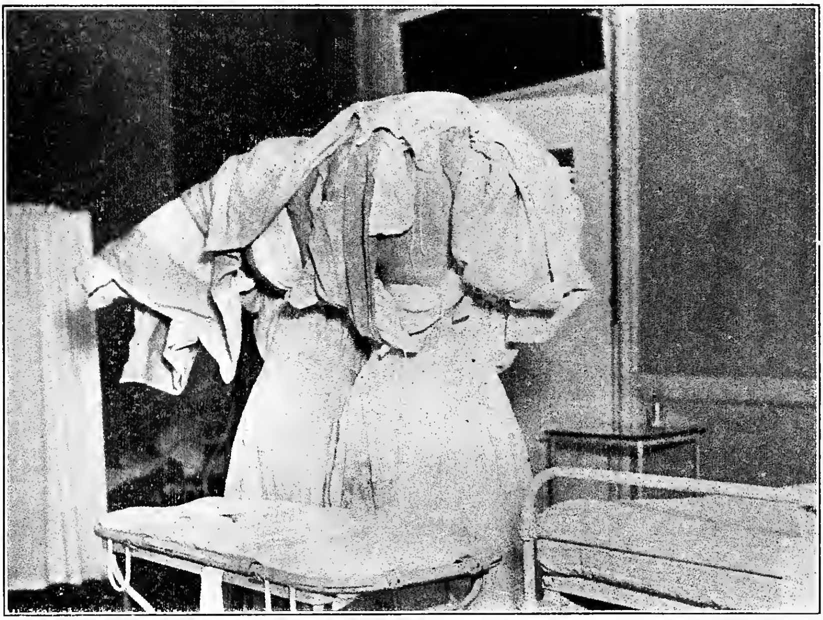


Fig. 137.—Carrying Patient Head High. This patient weighed over two hundred pounds and was easily lifted.

from the morphin given for from ½ to 1 hour after the effects of the pulmonary anesthetic have worn off. The acute pain of the operation is thus minimized and the necessity for any further medication is not so great.

After-treatment

If the anesthetic has been properly administered, all reflexes should be present as the patient is being placed in bed.

Two pillows should be immediately placed under the head and shoulders of the patient, unless indications of shock are evident. A towel should be placed over the eyes to keep out the light, and the room darkened but well ventilated, the patient being protected from draughts by a screen.

The saline or water enema should be repeated every few hours, unless olive oil has been given.

Permit no loud talking or moving around, thus allowing the patient to sleep partly from the preliminary medication and partly from the nerve exhaustion usually accompanying any surgical operation, until he awakens from this twilight slumber in a quiet and natural manner.

Water.—As soon as he is awake, free administration of either cold or hot water will make the patient comfortable. If nausea is present, and vomiting ensues, the stomach is washed out and the nausea will subside much more quickly than if the water had not been taken. This should be "further supplemented by small quantities of salt solution, 200 or 300 c. c., per rectum every 4 hours. The free administration of water not only hastens the elimination of ether, but also supplies fluid for active kidney work and militates against the occurrence of shock. After 36 to 48 hours, a liquid diet may be begun, and buttermilk, fresh milk, or lager beer, albumin water flavored with fruit juice or sherry, or tea or coffee, may be acceptable." [1]

For post-anesthetic vomiting it is a routine custom among many British surgeons to give tincture of iodin, ½ minim (½ minim of U. S. P. tincture) in a teaspoonful of water, every half hour for 3 or 4 doses.[2]

If vomiting occurs in spite of preliminary medication and anesthetization by proper methods, one of the oldest and simplest methods of relief is the inhalation of vinegar fumes.

Sometimes it may be necessary to give a rectal injection of 30 to 40 drops of deodorized tincture of opium with 60 grains of sodium bromid, to quiet the vomiting center.

MANAGEMENT OF DIFFICULT OR UNUSUAL CASES

In the foregoing pages we have considered the adjuvant management of ordinary cases—cases in which the course of anesthesia conforms to what, from experience, one may safely predict; cases in which, in other words, the expected happens.

The anesthetist, however, who settles himself comfortably at the head of the patient, believing that no dangers need be anticipated so long as he has observed the rules for preliminary medication and so long as he is careful in his technique of administration, is apt at any moment to have a rude awakening, for anesthesia is no exception to the general rule of life, and the unexpected must always be anticipated. This is true (1)

[1] *Am. J. Surg.*, *4*, 152.

[2] The post-anesthetic treatment varies, of course, with the nature of the operation.

particularly, because of the fact that individual susceptibility, or insusceptibility, to the given agent or method of administration may upset all calculations; (2) because a slight error in technique may convert minor difficulties into those of major proportions; (3) because the exigencies of the surgical procedure itself may create unexpected emergencies for the anesthetist; because latent or undiscovered pathological conditions may become complicating factors.

The minor difficulties which may be encountered may be grouped under the following heads:

(1) Respiratory; (2) muscular; (3) nervous; (4) idiosyncratic.

Respiratory

Dyspnea, hyperpnea, apnea, and stertor are among the respiratory difficulties most commonly encountered. Some patients, particularly young children and nervous women, persist, despite suggestive therapy, in an irregular or hesitating manner of breathing, while others "hold their breath." If allowed to go under the anesthetic in this way, the manner of breathing may characterize the stage of surgical narcosis. In some cases more serious respiratory disturbances, even temporary respiratory arrest (apnea), may supervene, calling for the more heroic management discussed hereafter (see p. 393).

A too strong vapor (chloroform or ether) may give rise to hesitant breathing after loss of consciousness. As a rule, safe, rhythmical respiration can be induced reflexly by the manipulation of the lips (brisk rubbing with towel or sponge), or fauces (swabbing out with rough gauze), or other form of peripheral stimulation.

The convulsive inspiratory effort (sobbing) with contraction of the diaphragm and spasmodic closure of the glottis, particularly noted in children, may lead to unpleasant complications because of the liability to the sudden inhalation of too large quantities of the anesthetic, with consequent asphyxia, or overdose symptoms, varying according to the anesthetic employed.

If the anesthesia is begun while the patient is still breathing in this manner, the administrator must be on guard and the anesthetic dose regulated accordingly. If the graver respiratory manifestations present themselves, they must be dealt with as hereinafter indicated.

In chloroform narcosis one must always be on guard for so-called *false chloroform anesthesia*—early shallow breathing instead of augmented breathing, which marks the second stage in the uneventful cases. If this be mistaken for a quickly induced surgical narcosis, with complete loss of sensation, etc., and the anesthetic be continued and the operation begun as if this were so, the patient may be plunged into profound shock, calling for the treatment outlined in this chapter, or the error may be recognized and corrected by peripheral stimulation, friction applied to lips, or face, or hypochondriac region, vigorous rubbing, slapping, or pinching.

Sometimes in intranasal surgery, *sneezing,* of reflex origin, may occur and persist, becoming so violent as to cause a distinct complication. This can usually be controlled by spraying the nasal passages with cocain. Sneezing, according to Hewitt, may be so violent as to constitute a distinct difficulty, especially in delicate operations about the face.[1]

In operations upon the intestines, *hiccough,* due to some reflex irritation, may become a disturbing factor. If the anesthesia is initiated properly, and care is taken to prevent an accumulation of mucus in the fauces, and hence the swallowing of an undue quantity thereof, this phenomenon is easily controlled.

The *coughing, retching, and vomiting,* minor difficulties arising early in the administration from improper preparation of the patient or from imperfect technique, may become annoying features in the stage of surgical narcosis. Deepening the narcosis will generally obviate these phenomena.

Muscular

Various muscular phenomena have been noted by different observers, aside from the struggling and other manifestations of muscular reflexes which accompany the stage of excitement as ordinarily observed. Trismus, or jaw spasm, spasm of the abdominal muscles, general persistent muscular rigidity, fine muscular tremors, such as the "piano playing" movements of chloroform anesthesia, the spasmodic contractions of the pectoral muscles indicating slight asphyxia, are all to be met with in exceptional cases. The various clonic muscular phenomena may become a serious menace to life if mistaken for a return to the second stage of anesthesia (particularly with chloroform). If the narcosis is deepened under this misapprehension, the patient may be quickly and unexpectedly plunged into the stage of overdose, which may call for vigorous measures of resuscitation.

Nervous

In exceptional cases, particularly among neurotic subjects, and when preliminary medication has been neglected, the administration of any inhalation anesthetic may be followed by the immediate onset of violent insanity. If operation is imperative in such cases, it is best to delay the further administration until narcotic medication has had time to take full effect. The anesthetic should then be given very gradually,

[1] Hewitt: "Anæsthetics," 1912, 912, 543; see, also, *Lancet,* Dec. 2 and 16, 1893.

beginning with the essence of orange, if an open method is indicated. If a closed method, essence of orange or nitrous oxid.

Idiosyncratic

It is a well-known fact that some individuals cannot be operated upon under local or spinal analgesia. (See case reported by Bainbridge, p. 623.) So, with inhalation anesthetics, very rare cases of insusceptibility, apparent or real, are encountered. Hewitt[1] reports two cases in which there was insusceptibility to nitrous oxid, probably traceable to alcoholism. He directs attention to the point that an acquired susceptibility may be manifested in persons infected with malarial parasites. The same author reports two other cases in which there was marked insusceptibility. In one the induction was begun with nitrous oxid and ether, with a change to chloroform, then to ether, the C. E. mixture finally proving successful. In the other case the anesthetic was begun with ether by the open method, without preliminary medication. After waiting for morphin and atropin to take effect, another effort was made, beginning with chloroform and switching to ether. Loud crowing breathing lasted throughout, but the operation was completed successfully.

Hypersensitiveness, rather than *insusceptibility,* it would seem, is the difficulty to be guarded against.

There are practically no minor difficulties of any unusual character encountered after anesthesia.

Among the *major difficulties* which may be encountered in the course of inhalation anesthesia, or the after-management of the case, and which directly concern the anesthetist, are (1) *shock,* and (2) *post-anesthetic toxemia.*

These difficulties undoubtedly vary with the anesthetic, with the general preliminary and concurrent management of the case, with the method of administration, with the physical peculiarities of the patient, with the technique and skill employed by the surgeon, and with preëxistent pathological conditions.

Whatever the cause or causes, and however these complications may be precipitated, the anesthetist must know how best and most expeditiously to deal with them. They are, therefore, directly concerned with the prognosis and treatment of the individual case, and it behooves the anesthetist to be familiar with them from the theoretical, as well as from the practical, point of view. In the pages which follow, an attempt is made to set forth, as briefly as possible, the theories, and the views with regard to management, of those who, by virtue of their original observations, are best qualified to speak with authority. Whatever per-

[1] Hewitt: "Anæsthetics," 1912, 332, 333; 548, 549.

sonal experience the authors have had is merely corroborative; we therefore take the liberty of drawing freely from those who have concentrated effort in these given directions.

SHOCK

By far the most important complication which may arise in the clinical experience of the anesthetist is *shock*. When, for any reason, the patient emerges from the even plane of a safe and satisfactory anesthesia into that alarming composite condition which is designated as shock, the anesthetist must be able quickly to marshal all his resources toward the restoration of the normal anesthetic condition.

Shock may be considered under the four heads, according to the chief factors which induce it, of: (1) surgical shock, that for which the surgeon is responsible; (2) psychic shock, shock produced in a patient by inability to control the nervous system; (3) dietetic shock; (4) anesthetic shock, that for which the anesthetist is responsible.

Surgical Shock.—Shock has been described [1] as "a condition of general depression produced by various causes." With shock we have: (1) a fall in blood pressure; (2) nerve centers react feebly to afferent stimuli; (3) pulse rapid and feeble; (4) respiration shallow; (5) all cutaneous reflexes lessened; (6) increased perspiration, with skin cold and moist; (7) temperature lowered; (8) mental condition one of quiet depression, patient may be conscious [this, of course, does not apply to shock during anesthesia]; (9) no pain or discomfort, but a feeling of weakness.

Various factors are concerned in the production of shock, and may pertain as much to the shock produced by surgical procedure, during narcosis, as when shock is the result of accident or any cause operative under ordinary circumstances.

Keen [2] gives these factors as follows:

"AGE.—In the new-born, before the physiological connections between the great divisions of the central nervous system have been established, it is quite probable that at least certain operations are very much more nearly shock-free than they will ever be again. (There is a short period of immunity that disappears with the establishment of the through paths of the nervous system). They are not only shock-free, but free from any appreciation of pain: In the new-born extensive operations for cleft palate are endured without anesthesia, pain, or shock, the only immediate risk being hemorrhage. Within a week or more these physiological connections become established, after which the infant becomes even more susceptible to shock than the adult.

[1] "American Practice of Surgery," *1*, 463.
[2] Keen's "Surgery," *1*, 922.

"ADULT LIFE.—This is the period of greatest resistance to shock.

"OLD AGE.—The senile heart has an uncertain and limited range of action. The arteries are hard and the blood pressure is high. The aged only *apparently* endure operations well. The risk is determined not by the age of the patient, but the age of the circulatory apparatus. Toward the completion of life's cycle the resistance to shock is at a minimum.

"TIME OF DAY.—The vital powers are *highest* in the morning, and the psychic factor at a minimum. The most unfavorable time 12 to 2 A. M. Autumn and early winter the *best*. Summer the *worst*.

"OCCUPATION.—Professional and business men are more susceptible than the farmer, laborer, and mechanic. The industrious are better subjects than the idle. The resistance of criminals is remarkable. Soldiers and sailors are good risks; *athletes*, not so good; worst risk, overworked surgeon over 50 years of age. Cachectic patients bear operations poorly. In *pernicious anemia* the operator's risk is great. In *chronic anemia* the risk is better, but still great. In chronic anemia from *loss of blood* the risk is better; in *acute anemia* from hemorrhage the risk is still better."

Psychic Shock.—Psychic shock is *"due to the powerful impulses from the highly specialized centers of the cerebrum acting upon the vital centers of the medulla."*

It is hard to differentiate between prostration by fear and prostration by injury. In most injuries the psychic and mechanical factors are mixed.

"The deep impression left upon the brain by a powerful nervous shock often endures for months and years."

IRRITATING CHEMICALS.—Those which cause marked irritation at the point of contact may produce shock.

(According to Mummery, "Burns of the first and second degree with extreme irritation only are apt to cause more shock than burns of the third and fourth degree causing destruction of tissue." Burns extending over half of the body frequently cause death from shock.)

TOXIC CAUSES.—Abscess breaking into the peritoneal cavity, and pouring out intensely irritating chemical compounds, causes shock by intense local irritation and constitutional disturbance.

MECHANICAL CAUSES.—By mechanical stimulation of nerve centers or trauma afferent impulses are sent toward the centers.

"An abnormally *low blood pressure* is the essential phenomenon of the state commonly designated surgical shock."

"Shock is the problem of the various kinds of stimulation of the nervous system."

Susceptibility of the various tissues depends upon the quality and quantity of their nerve supply.

"A fall in blood pressure usually occurs while incising the skin over the abdomen."

"Asphyxia is always attended by a retarded pulse and slow and powerful respiratory efforts. *A fall in temperature is the result of low blood pressure.*"

CIRCULATION.—The entire arterial system bleeds into the dilated venous system, and the bulk of the blood is not freely circulated.

RESPIRATION.—It is accelerated. Sighing and irregular or increased action may appear. The respiration wave is shortened. Inspiratory and expiratory efforts are quickened, and the pause is lengthened. Later, the gasping type of respiration with tracheal and chin tug indicates impending dissolution.

MUSCULAR SYSTEM.—The voluntary and involuntary muscular systems are relaxed; kidney and digestive tract diminished in function; skin relaxes; pallor with consequent outflow of water or perspiration. Face is shrunken, pinched, and elongated; eyes lusterless and sunken, with lids only half closed; lips parted, thin, and pale, but may be cyanotic; drooping jaw, partly open mouth, falling in of cheeks.

Crile,[1] in his epoch-making experimental researches concerning shock, made the following observations concerning its production and the resultant effects. These observations were made upon animals in the laboratory.

"*Skin.*—Cutting and tearing caused in the greater number of instances a rise of blood pressure, though sometimes no effect was observed.

"NEGATIVE RESULTS.—*Kidney, Spleen, Bladder, Eyes.*—Mechanical injury caused usually no appreciable change in either the circulation or the respiration.

"*Ears.*—As skin usually.

"*Mouth.*—Crushing, tearing, cutting, and puncturing the tongue produced no effect on either the circulation or respiration.

"*Heart.*—The slightest direct contact with the heart caused marked changes in its beat and in the blood pressure,—a fall in blood pressure, with short, irregular strokes.

"*Diaphragm.*—Contact, however slight, with the abdominal side of the diaphragm caused in every instance markedly arhythmic respiration.

"*Abdomen.*—In making the incision through the skin in the abdominal sections there was frequently noted a fall in the blood pressure; this, in fact, was the rule.

"Cutting muscles or fascia produced little or no effect. On opening the peritoneum a fall was noted.

"*Liver.*—Manipulation of the gall-bladder caused a marked temporary fall.

"*Uterus.*—A rise in blood pressure.

"*Testicles.*—A fall in blood pressure.

[1] Crile, George W.: "An Experimental Research into Surgical Shock."

"*Penis.*—A fall in blood pressure.

"*Vagina.*—A rise in blood pressure, and increase in depth and frequency of the respirations.

"*Anus.*—Same.

"*Peritoneum.*—Contact, however slight, with the peritoneum or visceral peritoneum caused marked arhythmic respiratory action. The diaphragmatic peritoneum produced the most marked respiratory changes. Continuation of the manipulation does not secure tolerance unless confined to the same area."

The *duration* of an operation was found to be an important factor in the production of shock. Animals may be killed by the effect of continuous anesthesia alone, though the anesthetic is carefully administered, so that a percentage—calculated upon the ratio between the actual duration of anesthesia and the average length of time a dog may survive continuous anesthesia,—is allowed for the pure anesthetic factor in any given case; that is to say, if ten hours be allowed as the average length of time a dog may live under continuous anesthesia and the given experiment lasted two hours, then twenty per cent of the cause of death was calculated to represent the anesthetic factor. This calculation applies to ether. There is strong evidence tending to show that chloroform, even barring accidents, is a more potent factor in destroying the animal than is ether.

Contact with air is a very great irritant to local tissues, owing to the lowering of local temperature and to the drying. Exposure of the thoracic cavity causes great disturbance of respiration, and the time of exposure should be as short as possible. "The element of time in abdominal operations in every experiment was unmistakable."

Temperature.—The effect on the intestines of cold water and of the intravenous cold saline solution showed more directly the depressing influences of the cold. The direct effect of warm towels applied to the exposed intestines, of warm saline in the abdomen, improved the respiration immediately, and as nearly as could be estimated caused at least a check in the declining blood pressure.

Anesthesia.—The respirations in over-anesthesia became generally more shallow and slower, and if the anesthetic was continued would fail suddenly. The blood pressure *pari passu* gradually fell. Upon removing the ether both would rise, much as they fell. The respiratory indications were usually in advance of any other symptom in foretelling the tendency of the anesthesia. The effect upon respiration was so constantly in advance of other effects, for example, that upon the circulation, that the latter was habitually neglected. Ether in no instance caused sudden cardiac arrest; chloroform, three times, each time early in the inhalation and before surgical anesthesia had been induced. Chloroform proved to be more toxic than ether. Over-anesthesia rendered the animals subject to early collapse and decidedly less capable of withstanding a protracted experiment.

Hemorrhage.—Loss of blood always predisposes to shock. Respirations are always accelerated and deepened in profuse hemorrhage. Hemorrhage from the large venous trunks caused the most profound effect upon the blood pressure, because the quantity of blood supplied to the heart was immediately diminished, while if the hemorrhage was arterial the income of. blood was not so suddenly diminished.[1]

Dietetic Shock.—Chauvin and Œconomos [2] state that disturbances of metabolism are observed regardless of the anesthetic, or method of administration, whether local, spinal, or general. This "dietetic shock" is due to fasting immediately preliminary to and following anesthesia. This shock can be avoided by the use of glucose, 150 gm., tincture of cinnamon, 6 gm., and tincture of nux vomica, 0.59 gm. and water to make 300 gm., or some other easily digested carbohydrate diet. When this mixture was taken the day before and the three days following the operation, the urine showed no pathologic changes such as occurred when this régime was not followed.

Anesthetic Shock.—In the preceding pages we have discussed shock from the surgical and theoretical points of view. We come now to the consideration of shock caused by the anesthetist,[3] independently of the

[1] According to *J. Am. Med. Assn.*, June 14, 1913, in post-partum hemorrhage the patient may survive a loss of about half of the total amount of the blood in the body. Whether or not this conclusion is applicable to other forms of acute loss of blood is not definitely determined, but it is probably not far out of the way.

[2] Chauvin, E., and Œconomos, S. N.: "Necessity for Avoiding Dietetic Shock in Operative Cases," *Revue de Chir.*, Paris, Mar., 33, No. 3.

[3] Shock, hemorrhage, and the anesthetic are closely related, according to French: "In the testing work in anesthesia the writer has had foremost in mind the great need of reducing shock. It is generally conceded that the child is more susceptible to shock than the adult, due, in some way, no doubt, to the fact that the child is anatomically and physiologically different from the adult. The tests have, therefore, been applied especially to children in the controlling of hemorrhage and in the administration of anesthetics. We find no variance from the belief among surgeons who have given careful thought to their work upon infants and children, that the losing of blood is a matter of the greatest import to them and that all means should be used to prevent hemorrhage in operating upon them. And we are now convinced that shock from the loss of blood and from the anesthetic can be materially reduced by the *manner* of administering the anesthetic.

"According to the observations of the writer of this paper there is, irrespective of all other conditions, a well defined and never failing relationship between the degree of skill in which a patient is anesthetized in the upright position and the amount of hemorrhage which occurs during the anesthesia, for there seems to be no question but that hemorrhage is reduced if the anesthetic, from the beginning, is smoothly administered, the second stage omitted, and the patient surgical procedure The subject is partly covered in the discussion of the fourth stage, or the stage of overdose, of each of the inhalation anesthetic agents. Other factors, however, besides overdose, may enter into the production of anesthetic shock. These, together with the treatment of the condition, however it may be produced, are considered in the following pages.

Anesthetic shock may be produced in three ways: (1) By giving an overdose of the anesthetic; (2) by maintaining too light an anesthesia; (3) by failing to keep an open airway. We will discuss these briefly, *seriatim.*

Shock Caused by Giving an Overdose of the Anesthetic.—It has been stated that the liability of shock from an overdose of the anesthetic varies with the subject, with the method of administration, with the agent employed, and with various other factors. The signs of overdose have been given under each inhalation anesthetic, respectively, and need not be reiterated here.

With *nitrous oxid,* if a slight degree of asphyxia, by delimiting the supply of air or oxygen, is maintained throughout a long operation, this, in itself, is apt to produce a state of shock. This is all the more apt to occur if a certain amount of shock has been caused through the manipulation of the surgeon, or through hemorrhage. This combination of circumstances may lead to complete shock, calling for the measures of resuscitation described under Surgical Shock, provided the immediate withdrawal of the anesthetic and the restoration of carbon dioxid balance, in accordance with the theory of Henderson, are not sufficient to restore respiration and circulation to a plane of safety.

With *ether* the chief danger of shock from an overdose is caused by the maintenance of too deep an anesthesia during a long and difficult operation. Such a state of affairs always calls, primarily, for lightening the anesthesia. If this is not sufficient, other methods described elsewhere should be employed.

With *ethyl chlorid* it is to be remembered that shock from overdose is especially liable to occur with a careless or inexperienced administrator, for the reason that anesthesia is so rapidly induced that the

brought into full surgical anesthesia without jarring or body disturbance of any kind. The uniform employment of helpful mental suggestion by every individual in contact with the patient up to the time of the induction of anesthesia, to assist in preventing an excessive discharge of nervous energy through fear—which is one of the elements in the 'anoci-association' of Crile; the administration of morphin to patients who display a marked degree of apprehension; an anesthetizing room free from an atmosphere of excitement and from unnecessary noise; the preliminary use of nitrous oxid or the essence of orange.'' French, Thomas R.: ''Nitrous Oxid, Essence of Orange, Ether and Sequestration in General Anesthesia.'' *N. Y. Med. J.,* May 24, 1913.

border line between safety and danger may be quite easily passed. This is particularly true because of the fall in blood pressure which always accompanies anesthesia by this agent. In the presence of the signs of shock already stated, if immediate withdrawal of the anesthetic does not revive the patient, the more active measures must be quickly instituted.

With *chloroform* it is more dangerous to keep the patient under deep surgical anesthesia than with any other agent, except, perhaps, ethyl chlorid. The shallow respiration, weak, thready pulse, sudden and complete dilatation of the pupil, and extreme pallor of the face are the danger signals which, separately or combined, should put the anesthetist on his guard. At times the anesthetic, in conjunction with the surgical procedure, brings about a condition of shock with startling suddenness. Withdrawal of the anesthetic may answer the purpose, but it is more than probable that more heroic measures will be necessary.

Shock During Light Anesthesia.—This form of shock is especially seen during laparotomies in which the patient has been too hastily or improperly anesthetized and the surgeon begins the operation before full surgical anesthesia is reached.

We will suppose the patient just beyond the second stage, but not in full surgical anesthesia. In this condition, if the operation is a laparotomy, every tug upon the viscera will increase the respiratory effort. If this hyperpnea is kept up during the entire period and the operation is a lengthy one, it will result in acapnia, and thus finally affect the circulation.

If the patient is already in a reduced condition there is a possibility of this condition being a serious one.

If the operation is upon an extremity, where no important vessels or nerves are involved, the chances for a dangerous degree of shock are materially lessened.

Shock from an Obstructed Airway.—The space between the external respiratory orifices and the epiglottis has been very properly called by Meltzer the "death space," inasmuch as this part of the respiratory tract causes more trouble to the anesthetist than everything else combined.

Shock may be caused from allowing a slight degree of cyanosis throughout a long operation, this being caused by allowing a more or less continuous interruption to the breathing. Shock is more often caused in this way than is commonly supposed.

Obstruction by Closure of the Alæ of the Nose.—In elderly people especially, or in very weak or nervous individuals, obstruction of the air passages by closure of the alæ is not an unusual thing. It is easily prevented by placing rubber tubing of convenient size, about an inch and a half long, in each nostril, allowing the ends to project a quarter to half an inch outside. This condition may also be remedied by manipulating the lower jaw in such a way that the patient is compelled to breathe through the mouth instead of the nose.

Shock from Labial Stertor.—A dangerous degree of shock from this source is not apt to occur because this form of stertor is so objectionably apparent to all present that it is usually quickly remedied if the open method is in use. It may cause serious trouble if the closed method is being used and the anesthetist is unable to observe the lips of the patient. This condition is modified by pressing the jaw upward and at the same time slightly forward. Also by placing the end of a towel or a piece of gauze between the lips.

Closure of the Glottis by the Tongue Dropping Back.—This is the most common form of stertor met with, and is fortunately remedied very easily. It is caused by the relaxation of the muscles supporting the tongue as the patient reaches the third stage of anesthesia. The tongue drops back, thus closing or partially closing the glottis. Tongue stertor may be caused in the beginning of the anesthesia by failure of the anesthetist to remove the pillow, or anything that may be under the patient's head, or by allowing the head to remain in a straight line with the body, instead of having it turned either to the right or left side. There are a small number of patients who breathe better when the head is propped up and the chin pressed in, but these are the exceptions. The vast majority of patients breathe much better in full surgical anesthesia with the head on the same horizontal plane with the body, and also turned slightly to one side. This does not apply to obese patients with a short neck. These patients' heads should be supported in such a way that no effort is thrown upon the neck muscles.

Respirations.—If a patient's *respirations* are perceptibly increased or interfered with by a closed method, and it is impossible to maintain an even anesthesia in this way, a change to the open method should immediately be made.

Many anesthetists use an *artificial airway* during surgical anesthesia. Ferguson's description of the original Hewitt's airway and his own follows:

"Hewitt's airway (Fig. 138) consists of a somewhat rigid rubber tube, C, curved so that, when it is in position in the patient's mouth, it will conform to the upper aspect of the base of the tongue. It has its laryngeal end beveled to correspond with the opening into the larynx. At the proximal end a metal funnel-shaped mouthpiece is attached, Figure 138 B. This has a deep groove so as to enable it to be clutched by the teeth in order to hold it in position. The tube is introduced into the pharynx and respiration takes place through it.

"Ferguson's modification of Sir Frederick Hewitt's airway, Figure 139, differs from its predecessor in having the proximal end of the funnel closed (Fig. 139, D) and two openings (one on each side of the truncated cone) for the ingress and egress of air, Figure 139, E. Thus there can be no danger of dropping ether into the top of the funnel, because it is not open, and since the orifices are in the sides which slope toward the lumen of the tube, and therefore away from the source of dropping, it is almost impossible to get any ether into the tube. Should the patient's cheek be resting on the table, any ether that might enter the upper fenestra would pass across the funnel and out of the lower fenestra, so that it is almost impossible for any liquid ether to enter the airway, no matter what the position of the patient may be.

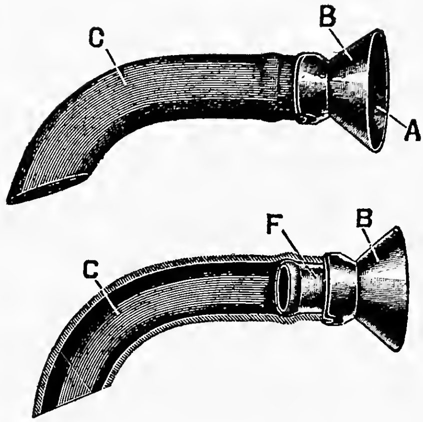


Fig. 138.—Hewitt's Artificial Airway.

"Ferguson lengthened and otherwise changed the metal thimble (Fig. 138, F) so that it extends well into the rubber tube C without enlarging the middle of the tube (Fig. 139, G). Consequently a patient's teeth may clutch the rubber tube C anywhere between G and the groove near E (Fig. 139) and the inside metal tube will resist the pressure and the lumen of the airway remain open.

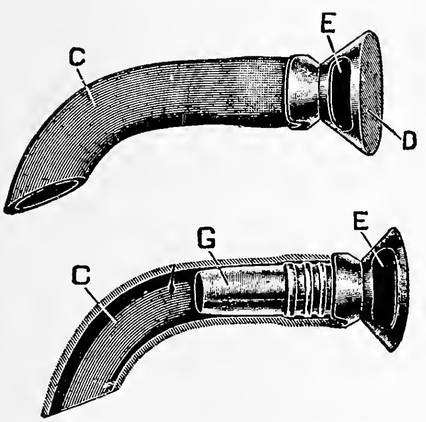


Fig. 139.—Ferguson's Modification of Hewitt's Artificial Airway.

"This airway should be introduced after surgical anesthesia has been reached. If the patient is not well under the anesthetic, the contact of the tube with the pharyngeal wall may incite gagging. To adjust the airway the jaws should be separated, the tongue brought gently forward, and the airway passed back into the pharynx with the convex portion of the curved rubber tube nearest the roof of the mouth. The instrument of itself will then assume a proper position.

The pharyngeal tube is useful to do away with respiratory embarrassment due to any form of occlusion of the extrapharyngeal respiratory tract."[1]

Connell's Breathing Tube.—Connell's breathing tube (Fig. 140) is a flattened copper tube curved to fit the roof of the mouth, easy of introduction. It provides for the minimum displacement of oral structures and abundant free gas channel from the outer world to the lower pharynx. This tube is used in ordinary anesthesia with any face mask. An attachment at the end of this tube permits the placing of a rebreathing bag fitted with a stopcock at the distal end. Rebreathing may be regulated by this stopcock. A rubber dam is placed on this pharyngeal tube and so adjusted between the gums and lips as to make an airtight joint.

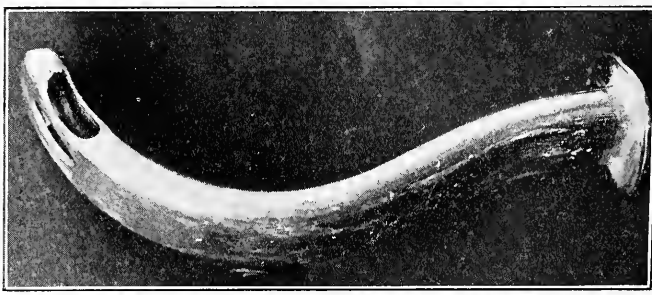


Fig. 140.—Connell's Breathing Tube. A flattened metallic tube curved to fit the palate and pharynx. Provides a free non-collapsible airway without displacement of oral structures.

With the placing of any breathing tubes, or the maintenance of a free airway by other methods, the stertor due to the anesthetic is eliminated.

Treatment of Anesthetic Shock.[2]—When the pulse disappears and the respirations become very shallow or cease, in the absence of cause for suspecting surgical shock, the anesthetist may know that he is to blame for the condition. He must be able to quickly judge the particular error of technique which has brought about the state of shock, and to correct this error accordingly. If withdrawing the anesthetic, deepening the narcosis, or restoring openness of airway fail to revive the patient, certain other measures must be resorted to, according to the severity of the shock. (1) *A quick, vigorous slap on the chest;* (2) *immediate lowering of the head.* If the subject is an infant, it should be suspended by the heels; (3) *dilatation of the sphincter ani;* (4)

[1] *J. Am. Med. Assn.*, June 14, 1913.

[2] For Resuscitation by Electricity, see Chapter XVI.

the application of hot or cold cloths to the face. If these simpler measures do not suffice, one must resort to (5) *artificial respiration.* This is accomplished by various methods, some of which are given below.

Artificial Respiration by Manual Means.—(1) The anesthetist grasps the arms of the patient near the elbows, and presses them firmly against the sides, thus expelling any chloroform vapor that may be in the air passages. The arms should be held tightly against the patient's sides for at least fifteen seconds. (2) They should then be drawn laterally below the head and held in this position for ten or fifteen seconds. This procedure should be repeated fifteen times a minute. Massage of the precordial region by an assistant is most helpful, as is also intermittent dilatation of the sphincter. Hypodermics do little, if any, good at this time. It is the anesthetist's duty to see that an open airway is maintained during this procedure. The mouth gag should be inserted and the tongue forceps applied, and the tongue pulled well forward, if there is any occlusion of the air passages. Traction of the tongue sometimes stimulates the respiration. (3) If none of these efforts is successful and the patient is in a state of collapse, the following method of Lewis[1] should be tried:

FIG. 141.—THE LEWIS PENDULUM SWING.

Lewis "Pendulum Swing."—"The patient should be suspended by the fully flexed knees and swung forcibly from side to side for a period of from one to two minutes. Suspension is best accomplished by the operator's forearms so grasping the patient's knees as to hold the anterior surface of both legs against operator's chest, allowing dependence of thighs, trunk, arms, and head of patient, facing away from operator. Except in children it is necessary for the operator to stand upon a dais, box, or chair of sufficient height to permit full pendulum swing of the patient from side to side without contact of patient's arms or head with the floor. Swinging should be done as vigorously as possible to secure by centrifugation a

[1] Lewis, Eugene Richards: In a private communication.

forcible distention of heart and intracranial vessels. The suffusion of neck and face which is brought on by this swinging is the index by which to judge the effect of centrifugation. Notes on several cases follow.

"September 1, 1899, male, 15 years, brought to Wilkes-Barre City Hospital with dislocation of right femur, 20 hours' standing. Physical examination negative; chloroform was administered; patient resisted considerably and suddenly ceased breathing. Usual measures and artificial respiration continuously for over ten minutes, during which time strychnin and atropin were administered hypodermically, but failed to reestablish respiration. We then attempted to restore the patient by increasing the volume of blood in head, neck, and chest, using forcible centrifugation to accomplish this. Accordingly the patient was grasped by the knees, and was swung to and fro, sideways with all possible force, until there was manifest a deep suffusion upon neck and head. The patient was then placed upon the table, and was found to be breathing spontaneously. Chloroform was continued cautiously, and reduction of the dislocation was effected.

"In July, 1901, at Wills Eye Hospital, Philadelphia, service of Dr. Radcliffe, case for squint operation. Chloroform was given, with early collapse and cessation of respiration. Slapping chest, cold douching, atropin, and strychnin hypodermically and artificial respiration all failed to restore breathing. After about four minutes, patient was swung as above described, until marked suffusion of face and neck occurred; spontaneous respiration was reëstablished.

"Trinity Hospital, Milwaukee, service of H. V. Wurdemann, January 28, 1902, Patterson, medical student, 22 years, for brossage of lids and canthoplasty. Physical examination negative. Chloroform anesthesia, collapse and cessation of respiration before beginning of operation. After three minutes of ineffectual attempts to revive the patient, he was swung vigorously till face and neck were well suffused, resulting in establishing spontaneous respiration. Operation was thereupon completed under chloroform anesthesia without further trouble.

"In 1903 or 1904 chloroform was given in a case of tonsillectomy. Collapse occurred and respiration ceased. Douching, slapping chest, stretching sphincter ani and artificial respiration for four or five minutes failed to revive patient. Swinging for about 45 seconds succeeded in establishing spontaneous respiration without further trouble.

"March 29, 1911, Max L., 8 years, brought to Mercy Hospital from Wisconsin. Hypertrophic tonsils and adenoids. Physical examination negative. Chloroform was given, patient somewhat nervous, but resisted very little. Early in narcosis, before loss of all reflexes, patient's respiration suddenly became superficial and then stopped entirely. Very slight grade of cyanosis followed by a sudden marked pallor with radial and

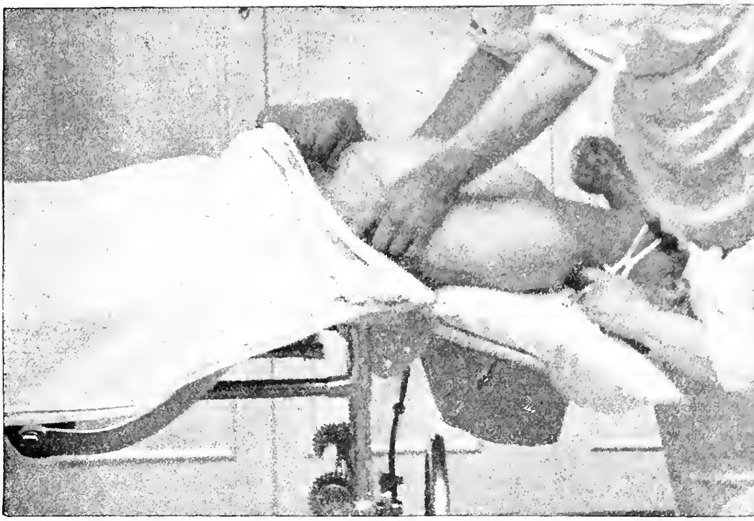


Fig. 142 a.—Artificial Respiration. First Movement.

temporal pulse not palpable; widely dilated pupils. Artifical respiration with lowered head was ineffective. Dilating sphincter gave no re-

Fig. 142 b.—Artificial Respiration. Second Movement.

sponse whatever. Amyl nitrite was useless because patient's respiration had ceased. The patient was now grasped under flexed knees and swung from side to side with considerable force, much the same as one might swing an asphyxia livida at birth. A pale cyanosis soon appeared about the mouth; respiratory movements, at first shallow and irregular, could be made out, and soon spontaneous respiration was established. The force of the heart beats remained irregular for at least an hour, and a circumoral pallor was present for at least two hours. The operation was performed the following day, ether as anesthetic, with no return of symptoms of day before.

"April 19, 1911. Well-built girl of 24 years, weight about 150 pounds. Chloroform as anesthetic. Did not struggle, but refused to breathe anesthetic quietly and regularly. Had reached a deeper stage of narcosis than preceding patient. Failure of respiration came on suddenly, but pulse remained fair. Cyanosis became marked. Artificial respiration, camphorated oil, ammonia hypodermically, with stretching of sphincter ani failed. Resuscitation was now attempted by swinging the 150-pound patient as above described. Since this was primarily and entirely respiratory failure, the reaction following suspension and swinging was all the more marked. The operation was sucessfully completed with ether, after resuscitation."

Apparatus for the Induction of Artificial Respiration.—It cannot be too strongly emphasized that, no matter how efficient may be a given apparatus for the maintenance of artificial respiration, when the exigency arises no time must be lost while the apparatus is being put in place. It is necessary, therefore, to resort to one or more of the measures for the induction of artificial respiration described in the foregoing pages, while the mask is being placed upon the face, or the tubes into the pharynx or trachea, as the case may be. Nor should such measures be discontinued until the apparatus is working—in other words, until air is being forced into the lungs.

Draeger's Pulmotor.—The Draeger pulmotor is being used with great success. It will not overdistend a small lung, and will fully distend the adult lung. It works automatically, adapting itself to the capacity of the lung. The different parts, and the manner of application, are illustrated and explained in the accompanying figures.

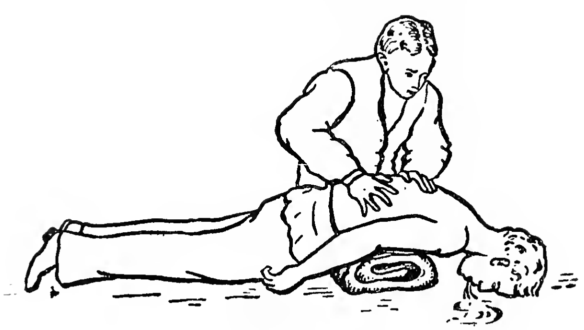


Fig. 143a.

Preliminaries.—

1. Remove the clothing from

the upper part of the patient's body. In cases of drowning, lay the patient face downward, on a support that raises the abdomen, and apply pressure to the back so as to make the water rush out of the lungs and stomach.

FIG. 143B.

2. Free the mouth and throat from mucus, preferably by means of a cloth wrapped round the forefinger.

3. The unconscious patient should be laid on his back, and the shoulders raised by means of a folded garment, leaving the head well thrown back.

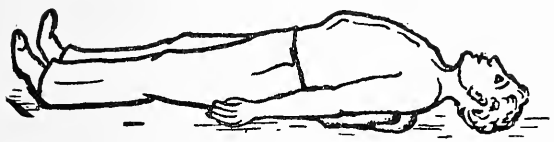


FIG. 143C.

4. To enable the air to gain free access to the lungs, the tongue should be gripped with the forceps provided for that purpose, and then drawn forward as far as it will come, and held in that position.

Placing the Pulmotor in Position.—5. The pulmotor mask must be buckled firmly to the head, leaving the tongue projecting between the lower jaw and the edge of the mask. The flexible tubes should rest on the forehead, not over the mouth. Take care that the mask fits airtight. This can be accomplished by bending the edge of the mask and tightening its two straps.

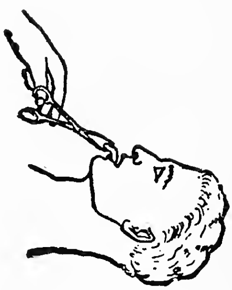


FIG. 143D.

The lower jaw must not be forced back (downward). If necessary, it should be pushed forward, by means of the manipulation illustrated in Figure 143D, to such an extent that the teeth in the lower jaw project beyond those of the upper jaw, not forgetting to keep the tongue firmly drawn out.

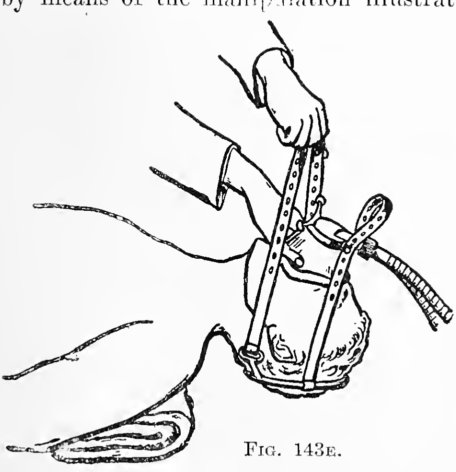


FIG. 143E.

6. The lever U of the apparatus should be moved into the position marked "Pulmotor," and the valve of the oxygen cylinder V opened. If the passage to the lungs is open, and the mask fits airtight, respiration will commence.

Fig. 143f.

If this does not occur, and the apparatus is found to reverse too quickly, and to continue doing so, it is a sign that the passage to the lungs is not free. In such event, remove the mucus, draw the tongue further out and push the lower jaw forward.

If the apparatus does not reverse at all, then the mask is not fitting tight. (See 5.)

If necessary, the pulmotor can be made to pulsate (delivery and suction strokes) by hand. (See 8.)

The Pulmotor in Operation.—7. The air forced in and out of the body by the pulmotor should pass only into

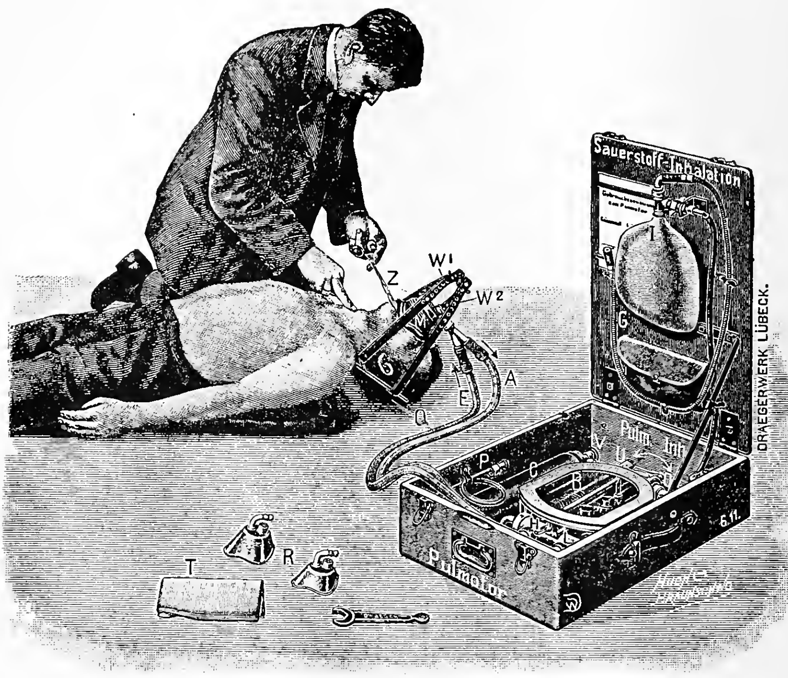


Fig. 143g.

the lungs, and not into the stomach. In order to insure this and to close the esophagus, the manipulation devised by Dr. Roth

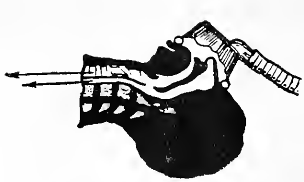


Fig. 143h.

Fig. 143i.

of Lübeck, consisting in the application of finger pressure to the Adam's apple of the throat, is practiced. Two fingers are gently pressed on the middle of the throat against the windpipe, which, being firm, closes the underlying esophagus, and thus completely prevents access to the stomach.

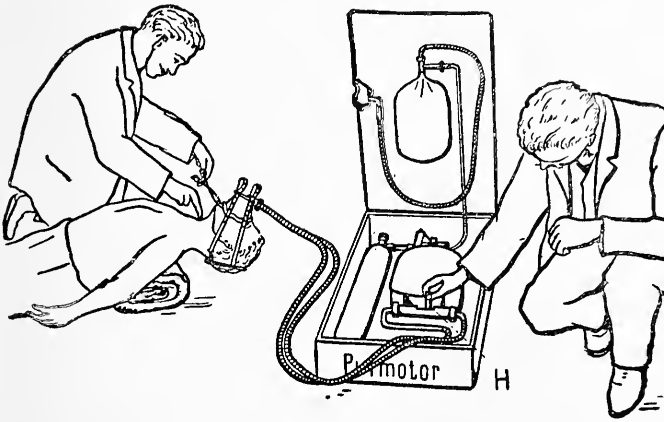


Fig. 143J.

8. If, from any cause, respiration should not go on automatically, the pulmotor may be reversed by hand, by moving the small lever H to and fro, the lever being firmly held all the time.

The Lungmotor.—The lungmotor is a device operated by hand, with notched gradations for different ages, as shown in Fig. 144. It does not depend upon back pressure in the lungs, but exhausts the air upon expiration. The advantages claimed for it are that it requires less physical labor than manual methods, and delivers a positive volume of air with each movement. It is available for persons of all ages and correspondingly varying lung capacities.

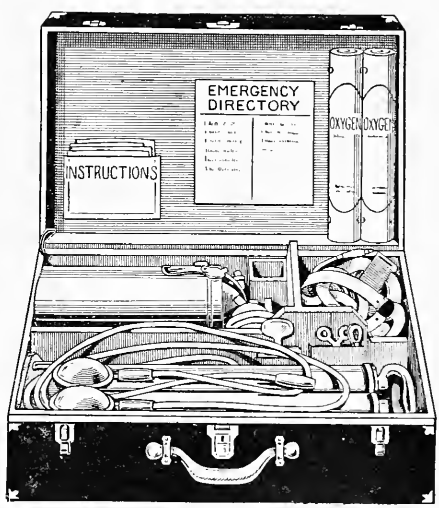


Fig. 144.—The Lungmotor.

Meltzer's Devices for Artificial Respiration.[1] — Meltzer has evolved two methods for the induction of artificial respiration: (1) Pharyngeal tube; (2) mask, as in other devices. In either case the

[1] *J. Am. Med. Assn.*, May 10, 1913, 1407.

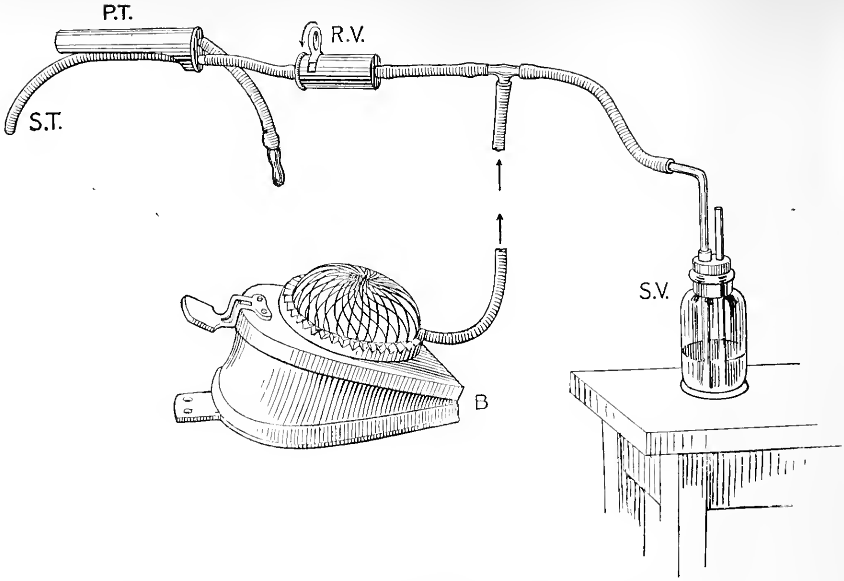


Fig. 145.—Meltzer's Apparatus for Artificial Respiration with Pharyngeal Tube and Foot Bellows. P. T., pharyngeal tube; R. V., respiratory valve. The ring turns the valve; turning to the right (facing the pharyngeal tube) brings an inspiration and to the left brings an expiration. B., foot-bellows; S. V., safety-valve. The bottle of the safety-valve should be shorter and have a wider diameter than the one in the figure; it is less likely to turn over. S. T., stomach-tube introduced through the opening in the pharyngeal tube.

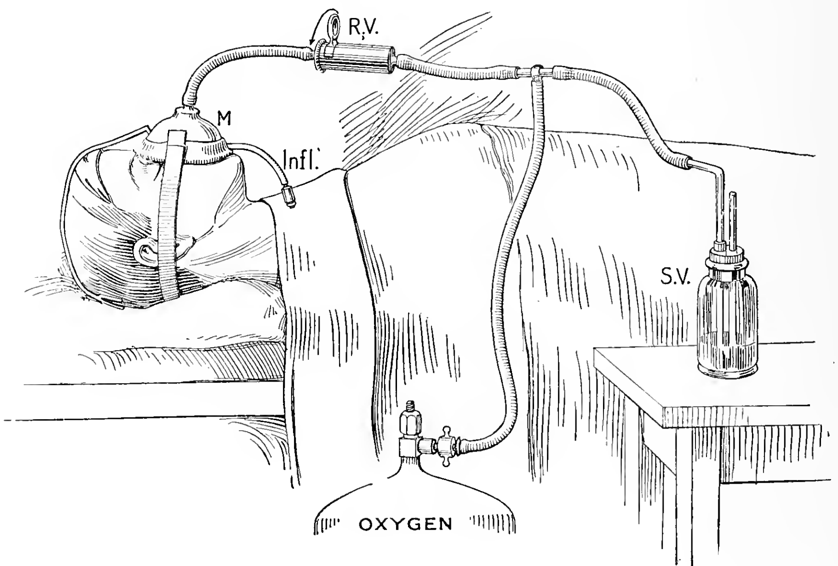


Fig. 146.—Meltzer's Apparatus for Artificial Respiration with Mask Attached to Oxygen Tank. M., mask; Infl., tube for inflating the rubber ring around the rim of the mask; R. V., respiratory valve; S. V., safety-valve. An oxygen cylinder provides here the insufflation pressure. The figure shows also the weight on the abdomen and the belt around it.

apparatus is operated by means of foot bellows, compressed air or oxygen from a tank, or a motor. Figs. 145 and 146 illustrate clearly the mechanism and application of these devices.

Meltzer demonstrated that the blood pressure is considerably raised by placing weights upon the abdomen, thus greatly increasing the probability of a successful termination of the efforts at resuscitation.

"The weight of the abdomen prevents the entrance of air in any considerable quantity into the stomach, and the little which gets there escapes again when the insufflation is cut off; it never gets into the intestines. The pressure on the abdomen has still another significance. In patients with completely abolished respiration usually the blood pressure is also very low, and most of the blood may be accumulated in the abdominal viscera. The heart is then scantily filled, and not enough arterial blood is sent to peripheral organs. Under such circumstances a good pressure on the abdomen may raise the blood pressure by even as much as 30 millimeters of mercury; the heart is filled more efficiently, and sends more blood to the medulla oblongata, arousing there the activities of the respiratory and vasomotor centers."

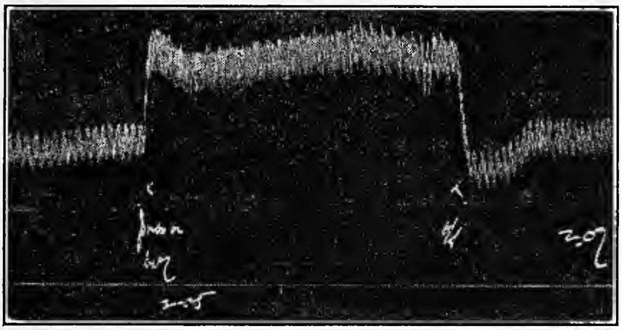


Fig. 147.—Blood-Pressure Tracing from an Etherized Dog Which Received an Intravenous Injection of Sodium Nitrite. Blood-pressure low, 44 millimeters; pressure on the abdomen brings up the blood pressure to 70 millimeters mercury, and the pulse pressure is nearly doubled in size.

Figure 147 shows the effect of abdominal pressure on the blood pressure.

Theories Concerning the Cause of Shock.—The theories concerning the cause of shock, however produced, whether by the anesthetic or by the surgical procedure, have come to be accepted as falling under two heads:

(1) Crile's theory of deoxygenation, or paralysis of the vasomotor centers, with a "manifest transference of the blood from the arteries into the veins."

(2) Henderson's acapnia theory, or the hyperactivity of the vaso-

motor centers through loss of carbon dioxid from the tissues and the circulating blood.

Vasomotor Paralysis (Deoxygenation)—Crile.—The phenomena of shock, according to this theory, are due to the exhaustion of the vasomotor centers in the medulla and spinal cord, with the resultant loss of contròl of the pressure of the blood in the arterial system and the consequent collection of the blood in the great splanchnic reservoir in the abdomen. The fall in blood pressure which follows this loss of control is accompanied by a fall in the general body temperature; the respirations become weak from secondary exhaustion of the respiratory centers, the blood and tissues are not properly oxygenated, and the oxygen starvation described heretofore (see p. 97), if not checked, leads to loss of consciousness and eventual paralysis of all vital functions and death.

This theory of shock is accepted by Mummery, Latham, and English, and a number of others.

Prevention of Shock (*Crile*).—Prevent as far as possible the loss of blood. Atropin, hypodermically administered, was an efficient protection against cardiac inhibition in operations in the "inhibition area" in the larynx, and in such operations as might cause mechanical stimulation of the vagi. Cocain, hypodermically injected, guards the heart against cardiac inhibition almost as efficiently as does atropin. "For morphin and alcohol, our observations were negative." Tearing, manipulating, stretching, forced dissection, all tend to produce shock, more than the use of sharp instruments and gentle manipulation.

"Animals to which, while inducing anesthesia, an overdose had been given did not endure a prolonged experiment, and not only was it more difficult to maintain an even anesthesia afterward, but the animal also showed a marked tendency to recurring respiratory failures."

So far as could be judged, less shock was produced when warm solutions were used than when cold; when the laboratory was warm, than when near the freezing point.

Moist heat[1] protecting the tissues lessened the amount of local irritation, and hence the shock.

Posture.—Posture is of considerable importance. The blood pressure always rose when the head was tilted downward, and fell when the board was tilted in the opposite direction.

Operations upon the extremities, if performed bloodlessly, and if the nerve trunks had been subjected to a cocain "block," produced no shock. Amputation of a leg caused no more effect than did cutting the hair. In rough axillary and chest dissections there was a marked tendency to respiratory failure. In abdominal procedure, if the omentum was made

[1] See Chapter on General Physiology (Warming the Anesthetic; The Utilization of Moisture).

to cover the viscera, thereby preventing direct contact with them, there was very much less shock. Handling the omentum did not produce vasomotor and respiratory disturbance. Dragging in the mesentery was followed by a decline in blood pressure. In operations upon the gall-bladder and liver it was necessary to be cautious as to traction on account of the great fluctuation in blood pressure likely to be caused by mechanical interference with the larger venous trunks. The most dangerous area is in the region of the duodenum, pylorus, and gall-bladder. The least dangerous area is the pelvic peritoneum and its viscera. The uterus, tubes, and ovaries contribute but little to shock, even when they are severely crushed and torn. The severity of shock induced in abdominal operations is in direct ratio to the distance from the pelvis. Injuries of the large intestines produce much less depression of the blood pressure than those of the small intestines; injuries of the stomach about the same as the small intestines.

Intravenous infusion of normal saline solution causes all the blood pressures to rise. Quantities up to twice the amount of blood calculated to be in the animal have been given before the pressure was sustained. The value of these injections is apparently wholly mechanical. The combination of small and frequently repeated hypodermic injections of strychnin, together with saline infusion, produces a sustained effect. Overstimulation was followed later by a greater depression. The application of heat was of benefit.

Treatment of Shock in Accordance with the Vasomotor Paralysis or Deoxygenation Theory.—Naturally, if one accepts the theory of shock proposed by Crile, the treatment must be carried out accordingly. Crile recommends the use of strychnin sulphate and artificial respiration; in other words, an increase in the supply of oxygen.

Latham and English [1] advocate the following measures: "The principal factor in treating shock is to maintain an efficient circulation until such time as the vasomotor centers have recovered, and at the same time to secure rest to the brain during that period. The use of stimulants is therefore contraindicated, especially strychnin. Inject morphin and raise the foot of the bed three feet so as to place the abdomen on a higher level than the head and thorax (chairs are better than blocks for this purpose), this position to be maintained until all symptoms of shock have worn off. Bandaging the abdomen tightly assists in raising the blood pressure. This bandage must not embarrass the movements of the chest; for the same reason heavy bedclothes must be supported on a cradle. Bandaging the extremities is also useful in some cases.

"Increasing the total quantity of fluid in the circulation by infusion of normal saline tends to raise the blood pressure, and aids in recovery of vasomotor centers. Adrenin in suitable quantities added to the

[1] Latham and Crisp English: "A System of Treatment," 93.

saline materially assists. Adrenin, they hold, acts directly upon the peripheral arteries, and causes a great increase in the blood pressure without acting upon the nerve centers. Its action is transitory, and it must be put directly into the vein. It should only be added to solutions which are introduced directly into the veins. It is useless to add to solutions which are introduced per rectum or subcutaneously. Rectal infusion is useful in cases of slight or early shock (or to prevent shock), as is also subcutaneous infusion."

Intravenous Infusion in Serious Cases of Shock.—Infusion, to be effective, must be carried out continuously until the patient is well on the way to recovery and is out of danger.

Transfusion of human blood is far more effective than any form of saline infusion.

Pituitary Extract.—This is similar in action to adrenin, although as used at present the drug is not so powerful. It has the advantage over adrenin that its effects last from a half hour to one hour. It must also be injected into a vein. It can be administered in fairly large doses with safety, but subsequent doses have less effect than the original dose.

Keen [1] recommends the following measures: "(1) The prevention of further shock; (2) the support of the circulation; (3) the securing of physiologic rest."

Support of the Circulation.—Head-down posture increases blood in brain, heart, and lungs. Extremities and abdomen may be bandaged. Use heavy layers of cotton and broad flannel bandages. Crile's pneumatic rubber suit is the best, as the pressure is under control, and the air placed in the suit may be warmed and the pressure increased or diminished without disturbing the patient. The blood pressure may be raised in this way from 15 to 40 mm. mercury. Saline infusions may be given.

Physiologic rest is the most important consideration in the treatment of shock. "When the motor activity takes the form of obvious work performed, such as running, the depletion of the vital force, expressed by various phenomena, is termed *physical exhaustion.* When the expenditure of the vital force is due to stimuli which lead to no obvious work performed, especially if the stimuli are strong and the expenditure of energy rapid, it is designated as *shock.*"

Under nitrous oxid anesthesia the physiologic changes and the brain cell changes, following an equal trauma, were approximately one-third those following ether.

Traumatized animals whose blood pressures were maintained by direct transfusion of blood, thereby eliminating the factor of anemia, still showed physical changes in their brain cells; animals similarly anes-

[1] *Loc. cit.*

thetized and transfused, but not traumatized, showed no change. "Shock is an overstimulation of the whole motor mechanism."

Anoci-association.—"If the patient be kept free from any emotional excitations by special management and by narcotics, or be not permitted to know that the operation is to be performed at a special time, and if such patient be anesthetized in such a manner that no adap-

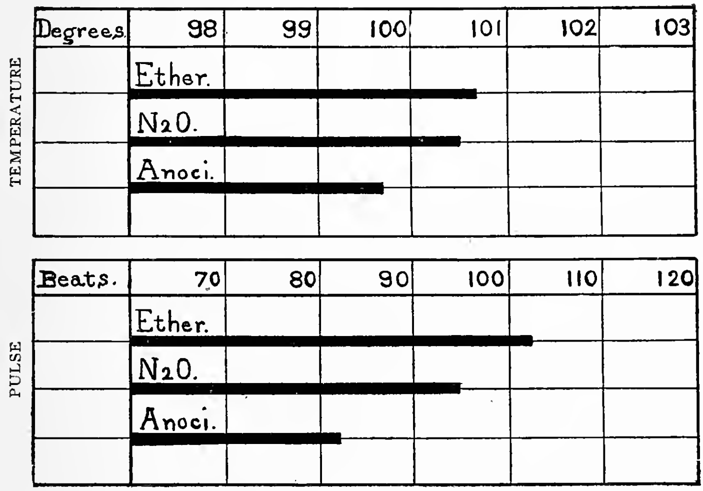


FIG. 148.—CRILE'S ABDOMINAL HYSTERECTOMY CHART. Temperature: each heavy line represents the average 5:00 P. M. temperature of ten patients during the first four days after operation. Pulse: each heavy line represents the average 5:00 P. M. pulse rate of ten patients during the first four days after operation.

tive response is excited by such an anesthetic as the pleasant nitrous oxid, and if the field of operation be so completely blocked by local anesthesia that no traumatic impulse reaches the brain, and if in closing the wound another local anesthetic is employed that will block nerve impulses for, say, twenty-four hours, thus preventing the after-pains, such a patient will then have been operated upon in such a manner that the motor mechanism has received no adequate stimulus." Hence there is no surgical shock, nor interference with digestion, nor nervous impairment afterward, i. e., no change in the circulation, the respiration, the digestive functions, nor the mentality of the patient.

"Although ether anesthesia produces unconsciousness it apparently protects none of the brain cells against exhaustion from the trauma of surgical operations."

Under nitrous oxid anesthesia there is approximately only one-fourth as much exhaustion, after equal trauma, as under ether. "Either nitrous oxid protects or ether predisposes to exhaustion under trauma."

CAUSES AND PREVENTION OF POST-OPERATIVE GAS PAINS.—"The patient is anesthetized as usual, but the entire line of incisions is carefully blocked with novocain, including the peritoneum. If then, at the end of the operation and before the peritoneum is closed, there is applied

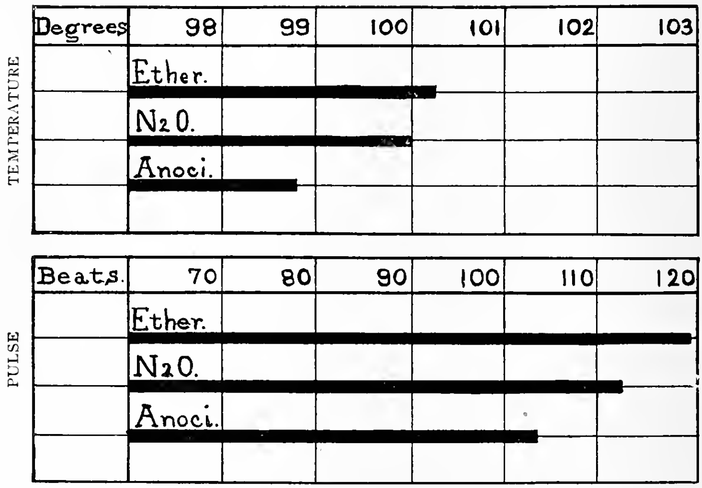


FIG. 149.—CRILE'S THYROIDECTOMY CHART. Temperature: each heavy line represents the average 5:00 P. M. temperature of ten patients during the first four days after operation. Pulse: each heavy line represents the average 5:00 P. M. pulse rate of ten patients during the first four days after operation.

around the entire line of stitches a complete anesthetic block that will last a number of days (as 50 per cent alcohol or quinin and urea hydrochlorid), and if in stitching the peritoneum every stitch is placed within this blocked zone, then the afferent impulses caused by stitch irritation are blocked, and hence cannot excite the protective mechanism of intes-

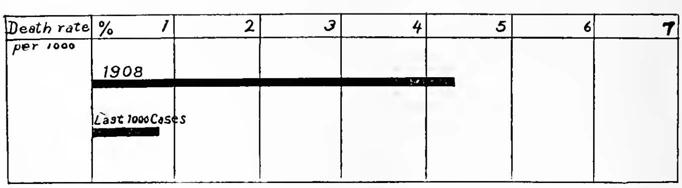


FIG. 150.—CRILE'S CHART OF MORTALITY RATE PER THOUSAND OF OPERATIVE CASES FROM LAKESIDE HOSPITAL. The last thousand were under anoci.

tinal inhibition. It has been found that such blocking does minimize or even prevent post-operative gas pains in all sorts of abdominal operations."

VASOMOTOR HYPERACTIVITY (ACAPNIA)—HENDERSON.—The chief opponent of the vasomotor paralysis or deoxygenation theory of shock is Yandell Henderson, the originator of the theory that shock is due to the hyperactivity of the vasomotor centers, as a consequence of the loss, for some reason, of carbon dioxid, and the effort on the part of the organism to compensate for this loss.

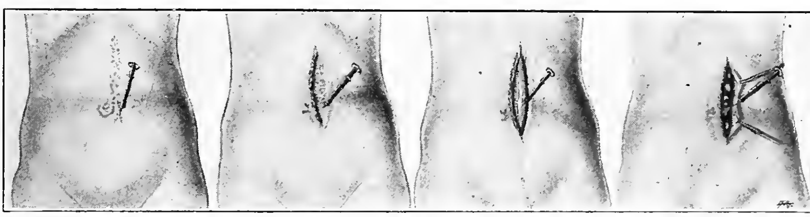
We cannot, perhaps, better explain Henderson's theory than by quoting from one of his papers [1] an illustrative case:

"A man in the prime of life was setting off fireworks when a giant

A. B. C. D.

Fig. 151.—Operations Under Anoci-association. A. Appendectomy. B. Herniotomy. C. Hysterectomy. D. Cholecystotomy. (Crile.)

firecracker exploded in his hand and shattered it. There was no considerable loss of blood. For two hours he suffered intensely, although he received a quarter of a grain of morphin. Then anesthesia with ether was attempted, and his breathing immediately began to fail. The anesthetic was withdrawn, and respiration improved. Three hours after the accident he stopped breathing quite suddenly. Artificial respiration and stimulants were ineffective, and he died. Yet his pulse was fairly



A. B. C.

Fig. 152.—Technique of Abdominal Operation Under Anoci-association. A. Infiltration of skin and subcutaneous tissue with 1-400 novocain. B. Infiltration of fascia and muscle. C. Infiltration of posterior sheath and peritoneum. D. Peritoneum inverted; infiltration with ½ per cent. of quinin and urea hydrochlorid. (Crile.)

good before and even for some minutes after respiration ceased. Why did that man die? In order to make the further discussion of my topic clear, I will present immediately the explanation to which, as it seems to me, all the data point. During the period after the accident his breathing was of the type which insupportable pain always excites. This hyperpnea involved a far greater ventilation of the lungs than normal breathing affords. Consequently the CO_2 content of the blood, and finally also of the body as a whole, was greatly diminished. When the

[1] Henderson, Yandell: "Fatal Apnea and the Shock Problem," *Johns Hopkins Hosp. Bull.*, Aug., 1910, *21*, No. 233.

anesthesia was attempted it was almost inevitable that respiration should show signs of failure. CO_2 is the normal stimulant of respiration; therefore, after this normal chemical stimulant to breathing had been reduced, pain alone maintained the breathing. Anesthesia removed the pain. Finally breathing stopped for the very simple reason that there was not enough CO_2 left in the blood to excite the respiratory center to activity. To this condition of diminished CO_2 content in the blood Mosso has given the name "acapnia," from the Greek "kapnos," smoke. Literally, acapnia means smokelessness. Perhaps I should remind you that the arterial blood normally contains 20 volumes per cent of oxygen, and 40 of CO_2, and that the body as a whole has an enormously greater store of CO_2 than of oxygen."

Henderson instituted a long series of experiments which are now too well known to need repetition here. His observations led him to the conclusion that the condition of low arterial pressure, noted in shock, is not due to fatigue or inhibition or failure of any sort in the vasomotor center. On the contrary, in his opinion, this center does its full duty almost to the last. The failure of circulation appears, in his experience, to be due to diminution in the volume of the blood by transudation of its fluids out of the vessels into the tissues, a process resembling edema. "It is a complex peripheral process," he says, "induced initially by the influence of acapnia upon the veins and capillaries and upon the tissues. Thus when death (or shock) follows intense physical suffering, not complicated by hemorrhage, there are two principal stages. At first the excessive breathing diminishes the CO_2 content of the blood. If, at any time after this condition of acapnia has been induced, the pain is greatly diminished, and the respiratory center is thus allowed to relapse into standstill, fatal apnea vera may occur. If, on the other hand, the pain is sufficiently continuous to keep the respiratory center continually excited, then apnea is prevented, and the condition of acapnia becomes more and more acute and general until the circulation fails, and the subject sinks into surgical shock." Both fatal apnea and the more slowly developing failure of circulation, he holds, are due initially to acapnia induced by the excessive breathing occurring under torture.

He does not agree to the importance of the rôle ascribed by others to oxygen in maintenance of the function of the respiratory center. On the contrary, he considers that Mischer expressed the essential truth regarding the regulation of normal breathing: "Over the oxygen supply of the blood CO_2 spreads its protecting wings."

Henderson considers that death from respiratory failure is explained as due to these "protecting wings."

"Those cases of fatal apnea," according to Henderson, "which more than any other interest the clinician, are, I suppose, the failures of respiration under anesthesia. If the patient ceases to breathe in his bed, it is his own fault, but if he does so on the operating table the anesthetist has to bear the responsibility. For such cases of apnea the acapnia hypothesis affords a simple explanation. Anesthesia diminishes the strength of inflowing afferent irritations. Furthermore profound anesthesia raises the threshold of the respiratory center for CO_2. In other words, the respiratory center of a man or animal in profound anesthesia automatically maintains more than the normal CO_2 content in the blood. Thus, when a man or a woman or a child has suffered prolonged pain, and thereby has been brought into a condition of more or less acapnia, the production of anesthesia by removing the afferent pain stimuli, and also by raising the threshold, that is, by diminishing the sensitiveness, of the respiratory center for CO_2, inevitably leads to apnea."

Prevention of Acapnia.—The prevention of acapnia calls for the prevention of excessive pulmonary ventilation. According to Henderson, the administration of morphin and full anesthesia diminishes the activity of respiration under pain, and thus prevents acapnia. If, however, morphin and chloroform be administered to an animal which has suffered pain for some time, apnea is hastened unless carbon dioxid is also administered.

In moderate degrees of shock, induced by irritation of afferent nerves or by exposure of the viscera, Henderson has found it possible to induce rapid recovery by the infusion into a vein of normal saline or Ringer's solution saturated with carbon dioxid, and then making the subject breathe an atmosphere of oxygen and carbon dioxid or oxygen alone.

In profound shock he has found that these measures fail to effect an ultimate recovery.

Treatment.—Henderson outlines two methods of treating acapneal respiration under anesthesia. One method involves the intratracheal insufflation of a gentle stream of oxygen gas, according to the method devised by Volhard. For man the quantity of oxygen should be not less than 400 c. c. per minute.

The other method of restoration of breathing to which Henderson refers has been found by him to be remarkably successful in restoring dogs during apnea. It consists in the administration of air or oxygen containing 5 or 6 per cent of carbon dioxid, the breathing being started by one or two artificial respirations. As soon as the normal tension of carbon dioxid in the lungs is restored, spontaneous breathing immediately recommences and continues as long as the inspired air contains a sufficient quantity of carbon dioxid to stimulate the respiratory center.

McKeson for the past five years has used an apparatus for measuring the blood pressure in connection with all anesthetics, for the special purpose of anticipating shock. His remarks follow:

THE INTERPRETATION OF PULSE, RESPIRATION, AND BLOOD PRESSURES WITH SPECIAL REFERENCE TO SURGICAL SHOCK

"What is the purpose of taking blood pressures during operations?

"'Feeling the pulse' has proved to be an unreliable method in determining the pressure values of the pulse. And, if the anesthetist is to be acquainted with the condition of his patient, he must be able to determine quite accurately these pressures for comparison as the operation proceeds. To anticipate shock and to apply remedial measures before the process has become well advanced requires an earlier recognition than is possible without the sphygmomanometer.

"Before shock (excluding shock from hemorrhage) becomes so well established that it may be positively diagnosed clinically, the patient passes through certain circulatory disturbances which are indicative of the condition to follow as certainly as certain weather conditions forecast rain.

"What are the important factors in making this interpretation?

"Let us first state briefly a few facts concerning the physiology involved in the maintenance of blood pressure. The heart is the pump; the great arteries are more or less elastic and admit more blood from the heart by distention; the arterioles are the 'shut-off' valves controlling peripheral resistance and determining the volume of blood to pass through a certain group of capillaries; the capillaries and veins act in this connection as return tubes to the heart and lungs, which return the blood through the pressure of various muscles, gravity, and suction by the heart and lungs.

"The pressure in the arteries before systole represents the conditions of resistance and elasticity of the vessels. Other things being equal, an increase in the diastolic pressure means more resistance; a decrease, less resistance in the arterioles. At the next ventricular contraction the heart must produce enough pressure to equal the diastolic pressure before the valves will open; from this point the remaining portion of the contraction will produce the discharge of blood into the aorta, and is called pulse pressure—the discharge power of the heart.

"The pulse pressure is the working pressure in moving the blood, and concerns the heart only. So that it represents the most important single guide to the power of the heart.

"The systolic pressure represents the pressure developed during systole, and is the sum of the diastolic and pulse pressures. It is evident that the systolic pressure will be more variable than the diastolic, for it must accommodate itself to variations in the heart rate and pulse pressures, and is therefore not as valuable a sign as was formerly supposed in determining oncoming shock.

"The heart must maintain a certain pressure in the aorta that its own tissues may be properly bathed in blood through the coronaries. This may be accomplished in falling pressures by increasing the output of the heart and, to some extent, by increased peripheral resistance, although, clinically, after arterioles once dilate, the heart must usually compensate by increasing its output, as they seldom regain their tone during operation.

"Respiration aids the heart in producing blood pressure in the hu-

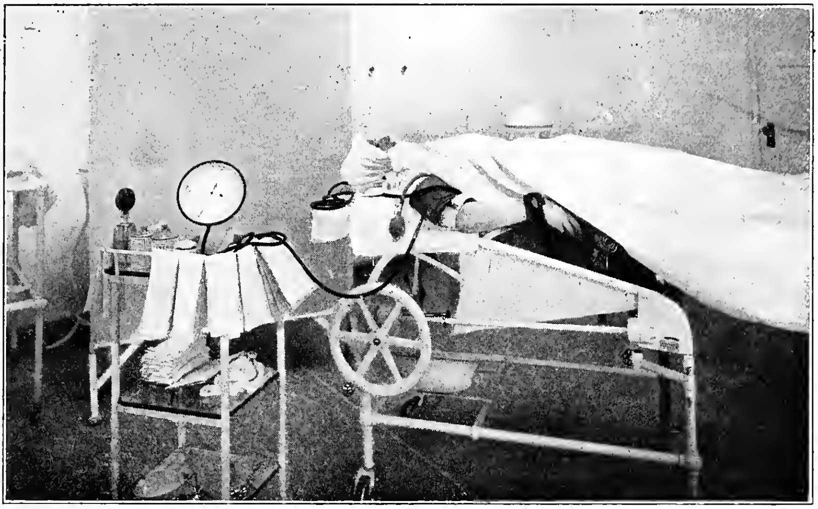


Fig. 153.—Blood Pressure Apparatus as Used by McKeson.

man subject. Intrapulmonary pressure is increased during exhalation, aiding the heart to force the blood out of the chest. This force under anesthesia normally increases the blood pressure from 5 to 10 mm. of mercury above the reading obtained during inhalation. During inhalation the blood is drawn out of the great veins leading into the thorax, so readily seen during extensive neck or breast operations; at the same time the capillary resistance in the lungs is greatly reduced, so the right heart can more easily force a large volume of blood over to the left side. And when exhalation begins again the lungs squeeze out the excess blood into the left heart, increase intrapulmonary pressure, and again blood pressure is elevated.

"It should be remembered that with the abdomen open the diaphragm cannot increase intra-abdominal pressure, and the return of blood from the abdomen at the time of chest aspiration (inhalation) will not be as perfect as usual, which may be an important element in venous stasis here.

"A respiratory rate of more than 30 per minute is too rapid to assist in moving the blood, throwing the whole burden on the heart. Also, a constant intrapulmonary pressure interferes with venous supply to the heart.

"An obstructed airway of any considerable degree, on the other hand, increases the respiratory variation of blood pressure, but if the respirations are too long and powerful it has the same effect as a continued positive pressure—interfering with the venous return and increasing the danger of a dilated right heart.

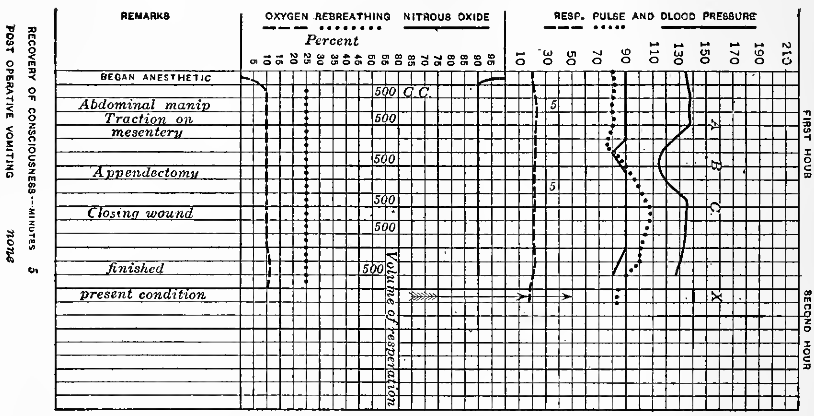


FIG. 154.—McKESON'S BLOOD PRESSURE Chart No. 3908.

"In order to clarify our previous statements and to apply them to a concrete case, let us examine a copy of our chart No. 3908; a woman aged 64, weight 120, in good physical condition, was operated on for obstruction of the colon with adhesions, and the appendix was removed. An H. M. C. tablet containing 1/6 grain morphin was given hypodermically about 1 hour before. The anesthetic was N_2O and O_2 without novocain infiltration in the line of the incision. Just before anesthetization, the (S) systolic pressure was 135, the (D) diastolic pressure 90, making a pulse pressure of 45, pulse 82, respiration 20.

"During the first 15 minutes of the anesthesia nothing happened except a very slight increase in respiration frequency. During the latter portion of this time abdominal manipulations and traction on the intestines was followed by a slight fall at (A) in the pulse rate, a 25 mm. fall of systolic, and a 10 mm. fall of the diastolic pressures. In the beginning we had a pulse pressure of 45 mm., which was probably nearly normal for this patient, while at the end of 25 minutes it was 35 mm. What had happened?

"When the intestines were exposed, handled, and dragged up, and rough gauze pads introduced into the belly to pack certain loops away from the desired field, the arterioles relaxed and the diastolic pressure fell. With an easier outlet for the blood and a comparatively slow pulse, the pulse pressure weakened slightly and the systolic fell markedly.

"This is not shock, but if it should continue as started it would result in shock in about 30 minutes or when the pulse pressure is but 10 to 15 mm. and the diastolic is 70 mm. or less. There was no reason for apprehension in this case, for, between (B) and (C), when less trauma was inflicted while doing the appendectomy, there was a compensatory increase of the heart rate, bringing the pressures to their former positions. Of course, this cost the heart 25 beats more each minute, but the reserve power in a heart not already complicated with disease is usually sufficient to keep up a rapid rate for several hours, provided that pressure is maintained. It shows here that the arterioles are still open, and even in the last 10 minutes, when more O is used in the mixture, as the pulse falls the diastolic falls; but 10 minutes after the anesthesia and operation are completed the pulse, respiration, and blood pressure relations are practically reëstablished as before the anesthesia was begun.

"So it is possible by an intelligent interpretation of the pulse, respiration, and blood pressure to anticipate the occurrence of surgical shock at least 20 minutes and usually much longer.

"Anesthetic overdosage, however, must not be confused with surgical shock, although many of the signs are similar in the relative overdosage cases, and the respiration and heart may be brought to a standstill in a very few minutes."

Post-Anesthetic Toxemia

The second of the major difficulties which may arise as a consequence of the administration of an inhalation anesthetic is post-anesthetic toxemia. Acetonuria, acetonemia, acidosis, acid intoxication are terms applied to delayed chloroform poisoning, concerning which a voluminous literature has been compiled within recent years. Ether also is now believed to give rise to acid intoxication.

It is the opinion of some observers, the senior author among this number, that so-called post-anesthetic toxemia exists only in cases in which there is already a tendency to acidosis, or in which this condition is precipitated by careless technique on the part of the anesthetist.

In every case the presence of acetonuria or other acid conditions should be ascertained beforehand, and treatment instituted to correct the trouble as nearly as is possible before the anesthetic is administered. Elimination, by bowels, kidneys, and skin, should be stimulated for several days previous to the anesthesia, and the tendency to hyperacidity should be counteracted by the administration of suitable alkaline medication. An important part of this preparation is careful attention to the diet.

Four or five days before the operation the patient should be given sodium bicarbonate, fifteen grains daily, until the urine is alkaline in reaction. Meats should be restricted or excluded, and the patient placed upon a strictly vegetable diet for this length of time. Two hours before the operation a saline enema, one pint or more, with one ounce of olive oil and one ounce of glucose, should be given. One hour before the operation small amounts of morphin should be administered, according to the patient's condition. (See Preliminary Medication, p. 70.) If chloroform is used at all, it should be used only in the beginning of the anesthesia, and a change should be made to ether at the second stage. The rule of Mortimer[1] in connection with these cases is a good one: "*Never give chloroform alone except for rare and special reasons.*" Small amounts of chloroform may be used until the second stage is reached; this excludes the element of fear, and is a desirable procedure if the psychic element is very much in evidence. This method is preferable to inducing the anesthetic with ether, which might give rise to very great fright and necessitate holding the patient.

Beven and Favill[2] collected over twenty-nine scattered cases, seemingly identical, in regard to acid intoxication and late poisoning effects from chloroform and ether anesthetics. The first case reported is so typical of the poisonous after-effects of chloroform that all the facts in connection with it are worthy of being recorded.

An unusually long time and a large amount of the anesthetic were required to establish surgical narcosis. The time of narcosis and operation is not stated, but the patient was thoroughly conscious a short while afterward with a pulse of 102 and a temperature of 101°. About two days later the first symptoms of poisoning were marked, the mother of the child noticing that she was not quite natural in her remarks. The physicians were called, and found the child talking incoherently and exhibiting evidences of great fright. This mental condition appeared without warning, as all symptoms had pointed to an uneventful recovery up to this time (44 hours after the operation). There was a rising pulse, with unremitting delirium and a curious shrieking outcry. The delirium was partly controlled by small amounts of morphin. At regular intervals a period of excitement—practically a convulsion—would occur, lasting for one minute or perhaps longer. Death occurred 110 hours after the operation, with a gradually rising temperature, irregular and rapid pulse. Cheyne-Stokes respiration was present. During the last two days before the child's death a sweetish, acetone odor was noted on her breath.

Other Cases.—Several clinicians have noted symptoms appearing from two to six days after chloroform narcosis. Violent and persistent

[1] Mortimer: "Anesthesia and Analgesia," 65.

[2] Bevan, Arthur D., and Favill, Henry B.: *J. Am. Med. Assn.*, Sept. 2, 1905.

vomiting, icterus, sometimes piercing shrieks, profuse sweating, and a picture of terror on the face seemed to be the clinical symptoms, also air hunger, as evidenced by deep breathing and cyanosis. Fatty changes have been noted in liver, heart, or kidneys, or all of these organs, on autopsy; acute yellow atrophy, fatty denegeration, or fatty infiltration of the liver have also been noted. Death usually occurs from exhaustion, the patient sinking into a state of coma from the third to fifth day. The urine contains albumin in all cases, and is usually scanty. Probyn-Williams[1] states that, while deaths have followed the inhalation of chloroform more frequently than any other anesthetic, cases have been reported with both ether and ethyl chlorid. Brewer[2] reports a case following an operation for acute appendicitis.

When death occurs from acidosis,[3] it seems to be due to lack of oxygen, as there is struggling for breath and cyanosis. The symptoms are vomiting, sweetish odor of breath, face flushed, lips dry, weak, rapid pulse, restlessness, unconsciousness. In children the acetone is given off through the lungs. In adults it is excreted by the kidneys. Pathology of acidosis is fatty degeneration of liver, kidneys, and muscles. Conditions under which acidosis may occur: Diabetes, carcinoma, digestive disturbances, starvation, gastric ulcer, excessive fat ingestion, infectious fevers, chronic morphinism, fatty liver, starvation (lack of carbohydrates), and following ether or chloroform anesthesia, in 120 cases etherized by the "cone method," acetonemia developed in 88.5 per cent. Of the same number with the drop method only 26 per cent showed acetonuria.

[1] Probyn-Williams: "A Practical Guide to the Administration of Anesthetics," 166.

[2] Brewer: *Ann. of Surg.* (1902), *36*, 481.

[3] Hamblen: *Univ. of Penn. Med. Bull.*, June, 1909.

CHAPTER X

ANESTHESIA BY INTRATRACHEAL INSUFFLATION

Charles A. Elsberg, M.D.

Definition.

History.

The Apparatus for Intratracheal Anesthesia in the Human Being: Apparatus No. I; Apparatus No. II; The Catheter or Tube to Be Used; The Introduction of the Tube.

The Course of the Anesthesia.

Errors Which May Occur in Technique: Accidents and How They May Be Avoided.

The Indications for Intratracheal Anesthesia.

The Value of Insufflation of Pure Air or Air and Oxygen as a Method of Artificial Respiration.

Bibliography.

Definition.—Intratracheal insufflation is the name given by Meltzer and Auer to a method by means of which a mixture of air and ether is driven deep into the trachea by means of external pressure through a tube which has been introduced into the trachea through the larynx.

History.—Physiological Basis.—*Animal Experiments.*—In 1909 Meltzer and Auer [1] first published an account of their experiments, which culminated in the method of anesthesia to which they gave the name "intratracheal insufflation." Physiologists had long known that animals could be kept alive by blowing air into the lungs, but this method had never been satisfactorily applied to the human being. Fell, O'Dwyer, Kuhn, Volhard, and others attempted to apply methods of this kind to man. Hirsh, Robinson, and others showed that the blood could be well oxygenated by passing a stream of oxygen intermittently through a tube to the bifurcation of the trachea.

It is well known that breathing is kept up by alternating respiratory movements and that the proper ventilation of the lungs depends upon the normal activity of the muscles of respiration and the intact condition of the walls of the thorax. Meltzer and Auer discovered that the proper exchange of the air in the lungs can be accomplished by an

[1] Meltzer and Auer: *J. Exper. Med.*, 1909, *11*, 622.

almost continuous stream of air passing in one direction. They found that if they passed a tube through the larynx of a dog almost to the bifurcation, and blew air through this tube in a continuous stream, the animal could be kept alive for many hours, even after all voluntary respiratory movement had been abolished by curare. By allowing the stream of air to pass over the surface of ether in a bottle, they found that animals could be very satisfactorily anesthetized. In these animals it was possible to open both pleural cavities widely and to have the animals remain alive for many hours.

The apparatus used by Meltzer and Auer [1] was a very simple one.

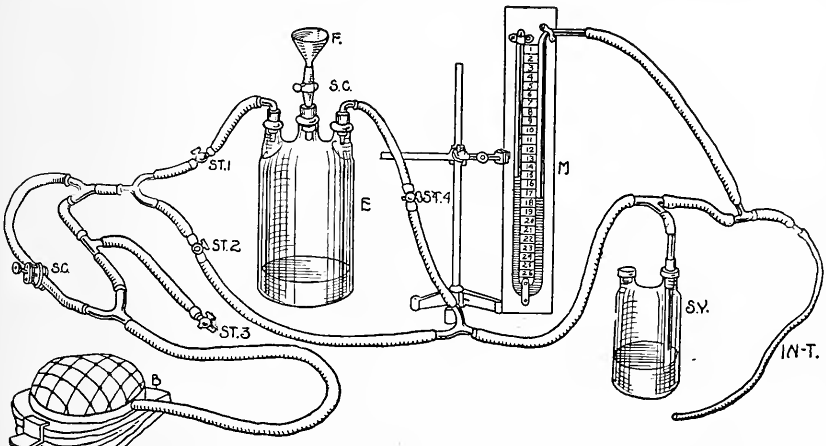


FIG. 155.—MELTZER'S SIMPLE APPARATUS FOR INTRATRACHEAL INSUFFLATION. B, foot-bellows; S. T, stopcocks; E, ether bottle with S. C, stopcock and F, funnel; M, manometer; S. V, mercury safety valve; IN-T, intratracheal tube.

It consisted of a foot bellows connected by tubes with a bottle containing ether and with a mercury manometer. The tubes were so arranged that more or less of the air from the bellows passed over the surface of the ether, and thus became more or less saturated with ether vapor. The air and ether mixture was blown in at a pressure of 15 to 20 mm. of mercury. The only condition essential to success was that the tube be of a size less than one-half of the diameter of the trachea, so that the air and ether which passed up the trachea and out through the larynx and mouth in a continuous stream had free escape. Later it was found of advantage to interrupt the stream three to six times a minute, so as to allow the lungs to partially collapse for a moment at times, and thus to get rid of small quantities of carbon dioxid which are apt to remain in the pulmonary alveoli.

With this simple apparatus, Meltzer and Auer [2] made many investi-

[1] Meltzer and Auer: *J. Exper. Med.*, 1909, *11*, 622.
[2] *Med. Rec.*, 1910, *77*, 487.

gations upon animals, and they recommended the method as an eminently safe one for anesthesia. They pointed out that it might have great value for intrathoracic operations, and that it was an ideal method for artificial respiration. Elsberg [1] made a large number of experiments on animals, and performed numerous operations upon the lungs of dogs, and Carrel [2] used the method with great satisfaction in his operative work upon the heart and thoracic blood vessels of dogs. In all of these experiments one or both pleural cavities were widely opened, the heart action remained good and regular, superficial respiratory movements persisted. In other words, the method of intratracheal insufflation was effective in preventing collapse of the lungs when the thorax was opened. Later, Nordman,[3] Schlesinger,[4] Boothby and Ehrenfried,[5] Fischer,[6] and others investigated upon animals the value and advantages of the method from the standpoint of the anesthesia and with regard to its efficiency in the presence of a single or double pneumothorax. The reports of all these authors have been uniformly in favor of the method.

From an extensive and thorough experimental investigation of anesthesia by intratracheal insufflation of air and ether, Meltzer [7] concludes as follows: "The essentials of the method of intratracheal insufflation consist [8] in the introduction deep into the trachea of a flexible elastic tube, the diameter of which has to be much smaller than the lumen of the trachea, and [9] the driving through this tube of a nearly continuous stream of air which returns through the space between the tube and the walls of the trachea. The distinguishing features of this method consist in the following two new principles: 1. By bringing the pure air directly to the larger bronchi, and by driving out the vitiated air from these bronchi through the force of the returning air stream, that part of the 'death space' is eliminated which is represented by the mouth, pharynx, larynx, and trachea. The chief aim of the complicated nervous and muscular mechanisms of respiration is to establish an efficient ventilation, capable of overcoming the obstacles offered by the mentioned 'death space.' A well-arranged intratracheal insufflation is fully capable of relieving and replacing the normal respiratory mechanism. 2. The practically continuous recurrent air stream prevents the invasion of indifferent or infectious foreign matter from the pharynx into the trachea.

[1] Elsberg: *Med. Rec.*, 1910, *77*, 493.

[2] Carrel: *Med. Rec.*, 1910, *77*, 491; *J. Am. Med. Assn.*, 1910, *54*, 28.

[3] Nordman: *Archiv f. klin. Chir.*, 1910, *92*.

[4] Schlesinger: *Archiv f. klin. Chir.*, 1911, *95*.

[5] Ehrenfried: *Boston Med. and Surg. J.*, *164*, 532

[6] Fischer: *Surg. Gyn. and Obstet.*, 1911, *13*, 566.

[7] Meltzer: *J. Am. Med. Assn.*, Aug. 12, 1911.

[8] Meltzer and Auer: *J. Exper. Med.*, 1909, *11*, 622.

[9] Meltzer: *J. Am. Med. Assn.*, Aug. 12, 1911.

"The usefulness of the method is at least threefold. 1. It is capable of keeping up an efficient respiration in cases in which the normal mechanism of external respiration fails. 2. It overcomes efficiently and conveniently the difficulties presented by double pneumothorax. 3. It offers a safe and reliable method for anesthesia, especially for the administration of ether."

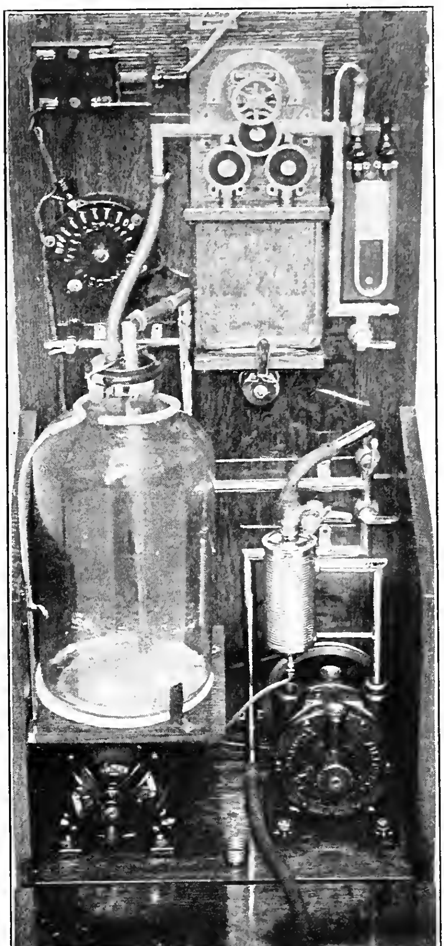


Fig. 156.—Elsberg's Apparatus, for Hospital Use.

Meltzer and Auer and the investigators who took up their work thus demonstrated that in animals the method of intratracheal insufflation is very efficient both for anesthesia in general and for thoracic operations in particular. Its first applications in the human being were made by Elsberg,[1] who was soon followed by other surgeons in the United States and elsewhere.

The Apparatus for Intratracheal Anesthesia in the Human Being.—A very simple apparatus constructed upon the plan of the one used in the laboratory can easily be put together by anyone. Such an apparatus would suffice in an emergency. The construction and working of the one suggested by Meltzer can be easily understood from the diagram (see Fig. 155). For general use in the human being, a more complete apparatus is necessary, one that cannot get out of order, and which is surrounded by every possible safeguard in case of trouble with any of its parts.

The essentials for such an apparatus are: (1) A source of air (electric blower, foot bellows, hand pump); (2) a system of tubes connected with an ether reservoir and a mercury manometer; (3) a regulator or automatic blow-off that should prevent too great pressure in the tubes;

[1] Elsberg: *Am. Surg.*, Feb., 1911; June, 1911; Dec., 1911.

(4) a warm water tank, by means of which the air stream can be warmed and moistened.

For hospital use, it is advisable to have an apparatus which works automatically, and to reserve the foot bellows as an addition which can be used if the motor and blower are out of order, or if there is no electric current. Elsberg devised two forms of apparatus, *viz.:* (1) an apparatus meant for hospital use; (2) a smaller and more easily portable apparatus. A description of these follows.

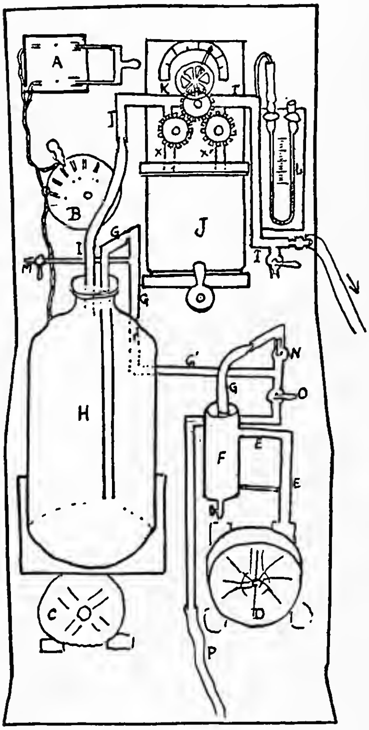


Fig. 157.—Diagram to Explain the Parts of Elsberg's Apparatus No. 1. The letters refer to the letters in the text.

Apparatus No. 1 (see Figs. 156 and 157).—The entire apparatus is contained in a wooden box 38½ inches long, 11 inches deep, and 18 inches wide. It is easily transportable. The box is placed on the floor near the head end of the operating table, and the front is turned down[1] in order to expose the interior, which contains the following (Fig. 157). By means of the switch A and the rheostat B the electric current is carried to the 1/6 horsepower motor C, which drives the blower D. The air passes through the tube E and the oil filter F and the tube G into the bottle H. This bottle contains hot water, so that the air, as it bubbles through the water, is warmed, washed, and moistened. The current of air then passes through the tube I to the rubber tube, which is connected to the intratracheal catheter. To this tube, No. 1, is connected the ether reservoir J.

The ether reservoir consists of a glass jar, which is held air-tight against its cover by a spring clamp below. The cover contains the openings of two tubes (X, X′), which are connected with the main tube I. The hand wheel K, which moves an indicator on a scale above it, is arranged to control the air passing through the tube I. When the indicator stands at zero at the scale, pure air is passing through the tube I. As the indicator is turned, more and more of the air is diverted into the one tube (X), which leads into the ether reservoir. When full ether is turned on, all of the air has to pass into the ether reservoir and over the

[1] The box is now arranged so that the front can be entirely removed.

surface of the ether, so that it becomes saturated with ether vapor. When the indicator shows that pure air is passing through the tube I, the tubes which lead into the ether reservoir are closed, and the ether reservoir can be removed if necessary and refilled.

The manometer L is connected with the tube I, and records the pressure of the air current which is flowing through it. The ends of the

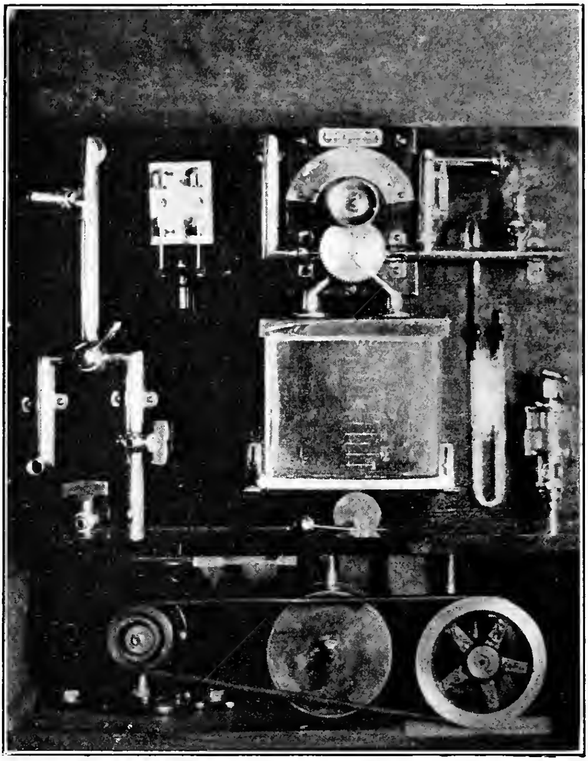


FIG. 158.—ELSBERG'S SIMPLIFIED PORTABLE APPARATUS FOR INTRATRACHEAL INSUFFLATION. To show the motor and blower.

manometer tube have hard rubber stopcocks, which can be closed when the apparatus is to be transported—a possible spilling of the mercury in the manometer being thus prevented.

The tube M leads into the main tube G and has also a stopcock, and to its tip the tube from an oxygen tank can be connected so that oxygen can be added to the air if desired. The tube P leads to a foot bellows, which has been added to the apparatus as a safety device if anything should happen to the motor or blower, or to be used where no electric current is available. When the stopcock N is closed and O is opened, and the foot bellows used, the air passes into the tube G′ and into the water bottle. When the stopcock N is open and O is closed, no air can enter the main tube from the bellows, and air passes to the water bottle from the blower. It takes only a moment to turn the two stopcocks so that one can instantly switch from air from the blower to air from the foot bellows and vice versa.

The water bottle H is held firmly in place by a clamp. The tubes from it are connected to the main tube by bayonet points, so that the

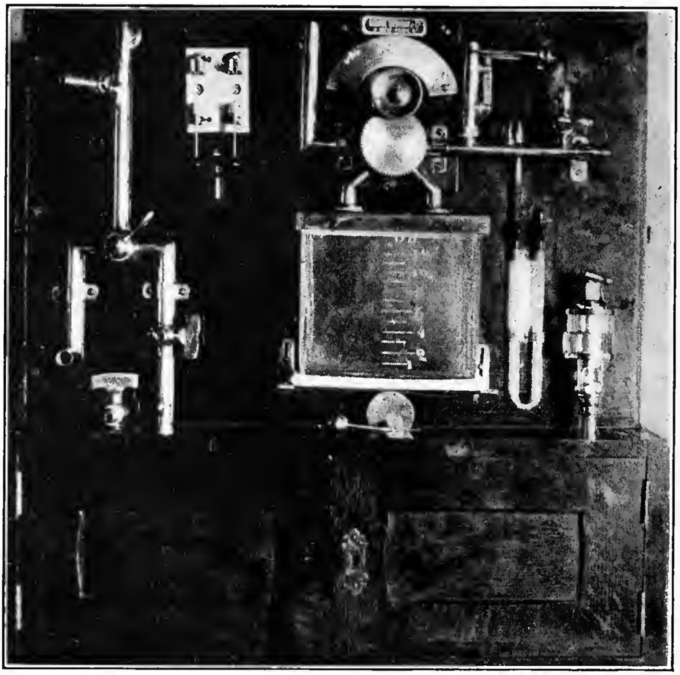


FIG. 159.—ELSBERG'S APPARATUS. Lower compartment closed.

bottle can be easily removed when it is to be filled or emptied. The perforated cork is held firmly and air-tight by a clamp.

The apparatus and its handling are simple. When it is to be used, the water bottle is first one-third filled with hot water, the stopcocks on the manometer opened, the stopcock N opened and O closed, the switch turned on, the rheostat turned on full, and the motor and blower thus set in motion. The stopcock M is left wide open. As soon as the apparatus has been connected with the intratracheal tube the stopcock M is slowly turned until the manometer shows that the pressure of the air is 20 mm.

The percentage of ether is regulated according to the depth of the anesthesia; usually the indicator has to be turned until it shows that half or full ether is being used.

By means of the stopcock at I (below the manometer), the air and ether current can be diverted from the intratracheal tube so that no air enters the intratracheal tube, but all of it escapes through the open stopcock.

The management of this apparatus is extremely easy. From the moment the power is turned on and the pressure regulated, the anesthetist's principal duties consist in watching the pressure gauge and occasionally interrupting the current of air so as to momentarily collapse the lungs. He can be seated near the table so as to observe the pulse of the patient.

Apparatus No. 2.—This apparatus is much smaller than No. 1. It can be easily carried around like a handbag. It is 21 inches high, 20 inches broad, and 9½ inches wide (Figs. 158 and 159). The apparatus is similar to No. 1, but is much lighter and much more compact. The motor and blower are underneath in a closed compartment. At A the foot bellows, which lies in a compartment above, is to be attached. B is the stopcock for regulating the pressure, C is a simple lever by which the anesthetizer can switch from air from blower to air from bellows. The tube D leads into the metal water tank in the inside of the box. E is the ether reservoir held by the eccentric below. Above this is the ether regulator. F is the manometer, G the safety valve allowing regulation of pressure. H is the stopcock for making interruptions of the current.[1]

The apparatus of Janeway is very complete, but very complicated (Figs. 160A and B). The following description will serve to explain the various parts of the machine. No. 1 is a motor which turns the wing blower 2. From the blower the air passes through the air filter and muffler 3. By the valve 4 the current of air may be divided into two reciprocally varying quantities; one portion passes directly over the heated water (heated by electricity) in jar 5, while the other portion passes through jar 5, after first passing over the surface of ether in jar 6. Thus the whole current of air or any desired proportion may be mixed with ether, and in this manner varying quantities of ether supplied to the patient. Provision is also afforded for still further saturating the air with ether by valve 7, which is so arranged that a small quantity of the air passing through jar 6 may be made to bubble through only the top layers of the ether irrespective of the level of the ether in the jar. The blow-off valve 8 prevents any injurious excess of pressure, and valve 9, operated by worm wheel 10, mechanically interrupts the current of air passing to the patient at any desired intervals.

In Fischer's apparatus (Fig. 161) the air pressure is obtained by means of a hand pump. Fischer published a complete description of his apparatus,[2] but a study of Figure 161 will allow the reader to gain a fair idea of it.

[1] A full description of this apparatus will be found in the *Ann. Surg.*, 1912.
[2] *Surg. Gynec. and Obstet.*, Nov., 1911.

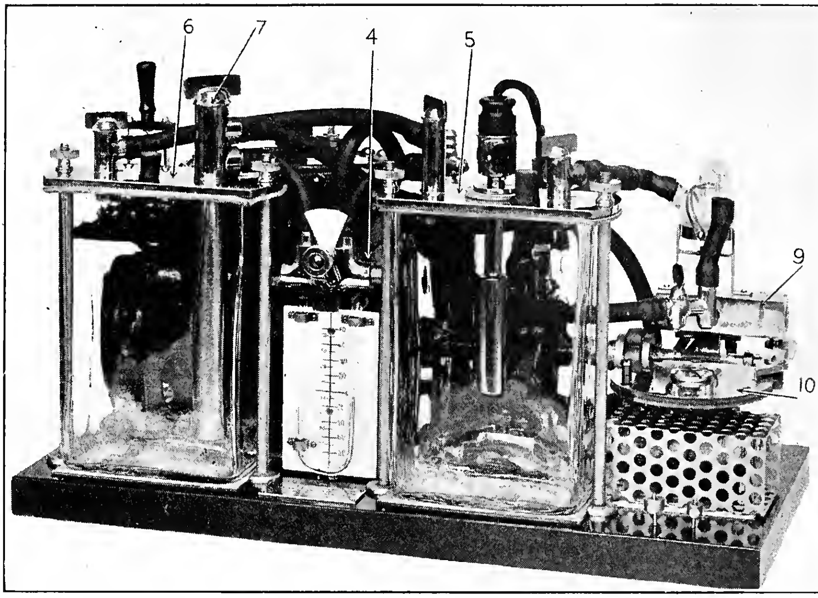


FIG. 160A.

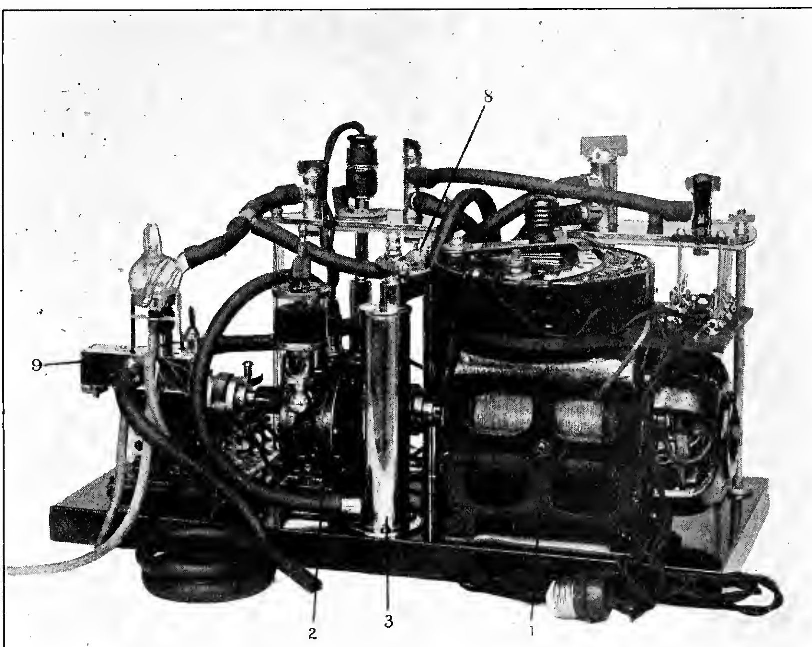


FIG. 160B.

FIG. 160A and B.—JANEWAY'S APPARATUS.

Ehrenfried's apparatus (Fig. 162) has the merits of simplicity, but, like Fischer's apparatus, has no safety device by means of which the method can be continued if any part of the main apparatus is broken or out of order.

The Catheter or Tube to Be Used.—The tube which is to be introduced into the trachea must be fairly rigid, so that it cannot be coughed out of the trachea when it is once in place. A soft rubber tube should never be used. Not only is the introduction of a soft rubber tube more difficult, but it is not rigid enough, as it might be compressed if a spasm of the larynx should occur. The ordinary silk-woven urethral catheter with a side opening near its end fulfills all requirements. It has

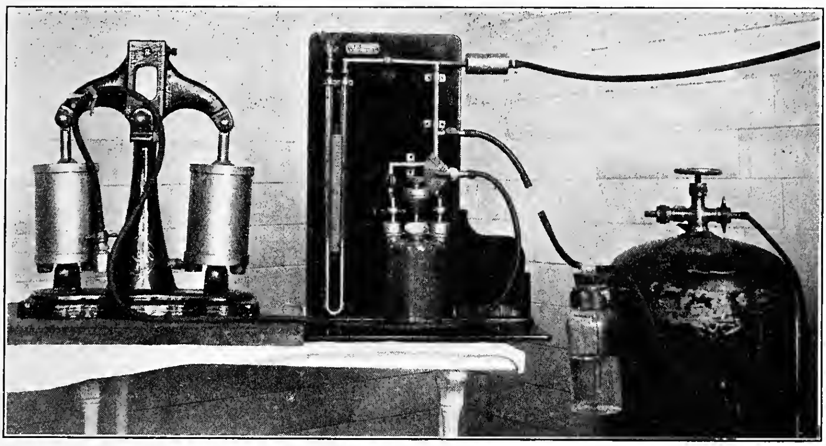


Fig. 161.—Fischer's Apparatus. The handle of the hand pump is not shown in the photograph.

the additional advantage that it can be obtained everywhere. The catheter should have two marks upon it—one 13 centimeters and a second 26 centimeters from the tip. The average length of the adult trachea is 12 to 13 centimeters; of the thyroid cartilage, 5 centimeters; of the distance from the incisor teeth to the glottis, 14 centimeters. Therefore, if the tip of the intratracheal tube is 26 to 27 centimeters from the incisor teeth, it will lie about 5 centimeters or less above the bifurcation of the trachea.

The size of the catheter must, of course, vary with the diameter of the trachea and the size of the larynx. For the adult, it is advisable to use a tube of the size 24 of the French scale. The diameter of this size of tube corresponds to about one-half of the length of the glottis, as seen through the direct laryngoscope. Sometimes a somewhat larger catheter must be used, but it is always better to use a tube that is too small than one that is too large.

In children the catheter must be correspondingly smaller. The length of the catheter in the trachea will vary with the size of the child, but it has been found that in general the length of the catheter that should be below the glottis measures about the same as the length of the tube from the glottis to the incisor teeth. In other words, if the

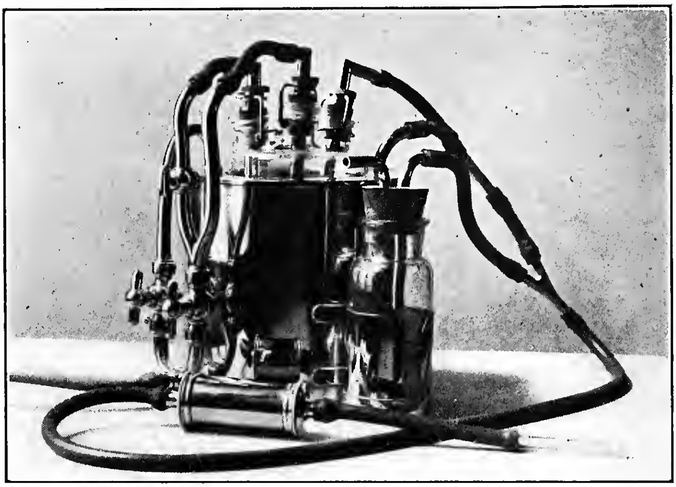


Fig. 162.—Ehrenfried's Apparatus for Intratracheal Etherization. (Driven by foot pump which is not shown in the photograph.) It consists essentially of a copper hot-water jacket, holding a Wolffe bottle containing ether. There are cocks by which the air from the bellows may be sent in any proportion through a coil in the hot water, over the surface of the ether, or made to bubble through ether. Attached to the outside of the jacket is a mercury bottle safety-valve. On the delivery tube is a contrivance to filter the air and to prevent droplets of condensed ether from being carried over into the lungs.

catheter has been introduced as far as the glottis, it will have to be pushed again as far downward as to have the tip in the proper part of the trachea.

The Introduction of the Tube.—In many patients it is possible to

Fig. 163.—Cotton-Boothby Introducing Cannula, Ehrenfried's Modification, for Soft-Rubber Tubes.

introduce the catheter after the epiglottis has been pulled forward by means of the index finger, which acts also as a guide. In children the intubation is always easy by this means. In many adults the epiglottis cannot be reached by the finger; in these patients the intubation is impossible by touch alone, and a special instrument must be used. Various guides with a laryngeal curve and variously shaped laryngeal forceps have been tried. None of these has been uniformly satisfactory, but Boothby and Cotton recommend their introducer (see Fig. 163), and Ehrenfried has one of his own (Fig. 164). I have found that the tube can always be quickly and easily introduced when the larynx is in plain view, which can be easily accomplished by means of the Jackson direct laryngoscope (see Figs. 92 and 165). With a very little practice, one can learn to use this instrument and obtain an admirable view of the glottis, so that the catheter can be readily introduced between the vocal cords. Anyone who is to use the method of intratracheal anesthesia

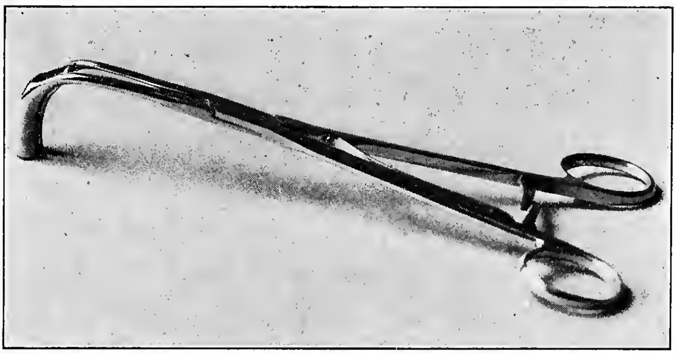


FIG. 164.—EHRENFRIED'S INTRODUCING FORCEPS FOR STIFF OR SOFT-RUBBER TUBES.

should practice the method of the exposure of the larynx with the Jackson instrument.

If the larynx is well cocainized it is possible to introduce the catheter and anesthetize the patient by means of intratracheal insufflation of the anesthetic. The introduction of the tube is unpleasant, however, and the beginning of the insufflation may cause the patient much discomfort because of the reflexes at the bifurcation of the trachea. In the cases where a preliminary anesthesia by inhalation is inadvisable (where there is danger of collapse of the trachea, etc.), the best plan to follow is to introduce the catheter after the larynx has been well cocainized; then to anesthetize the patient by means of ether given through a mask or cone held over the end of the catheter and the mouth.

In general, it is best to give the patient a dose of morphin and atropin and then to anesthetize him in the usual manner with ether. When the patient is well under anesthesia, he is brought into the operating room and placed upon the operating table, with the head hanging well downward over the end of the table and the mouth held open with an ordinary mouth gag.[1] The direct laryngoscope is then introduced and

[1] Preliminary cocainization of the larynx is unnecessary.

pushed along the posterior wall of the pharynx until the epiglottis is in plain view. The epiglottis is pulled well forward by the beak of the instrument and the glottis well exposed. One usually obtains a fine view of the larynx, can clearly see the opening between the cords, and can

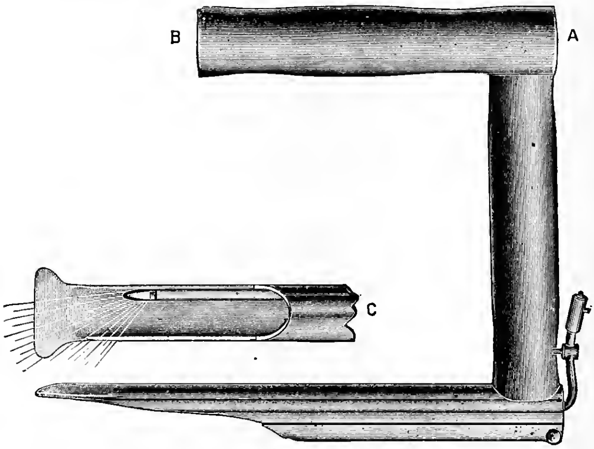


FIG. 165.—JACKSON'S DIRECT LARYNGOSCOPE. (See p. 226.)

estimate its size and length. If there is any difficulty in exposing the vocal cords, the head and neck are pulled forward as a whole, the head being kept bent backward as before. A catheter whose outside diameter measures about one-half of the length of the glottis (in general No.

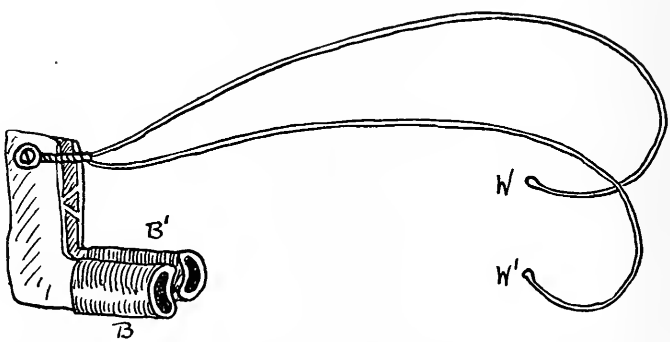


FIG. 166.—ELSBERG'S CLIP TO HOLD THE INTRATRACHEAL TUBE IN PLACE. The rubber covered arms B B′ lie between the teeth and hold the tube between them. The wires W W′ fit over the ears like the wires of spectacles.

24 F can be used) is then selected. This is introduced through the laryngoscope and into and through the larynx. The tube is then pushed forward until the second mark on it shows that the tip is 3 to 5 centimeters above the bifurcation of the trachea. Air will now be heard rushing in and out through the catheter. The patient is very apt at this time to

have an attack of spasmodic coughing and to hold his breath. This need not cause concern, as respiration will soon begin again. One must be sure that the tube is in the trachea and not in the esophagus. If one is in doubt, the catheter must be withdrawn and reinserted. One soon learns, however, to recognize the sound of the air rushing in and out through the tube.

The tube is now held in place and the laryngoscope withdrawn, the entire manipulations thus far having occupied only a minute or two. The patient is then pulled back upon the operating table.

A small clip serves to hold the catheter in place (see Fig. 166). It consists of a clip bent at right angles, the branches covered by rubber tubing. This fits between the teeth so that the patient cannot bite the catheter, which is held firmly in place. The clip is held in position by elastic wires, which fit over the ears like a pair of spectacles. After the clip is in place the mouth gag is removed, the catheter is connected with the connecting tip of the tube which leads from the insufflation apparatus, and from which the mixture of air and ether is flowing, and the insufflation is begun.

The Course of the Anesthesia.—Ether is the safest anesthetic to use for intratracheal insufflation. The dosage of chloroform has not yet been sufficiently well worked out. Nitrous oxid and air or oxygen can also be given by insufflation. The ether anesthesia is usually very satisfactory. The patients are quiet, their musculature is relaxed, they breathe quietly and superficially. Some respiratory movements should always persist, and the anesthetizer should never keep the pressure, as shown by the manometer, so high that active breathing ceases altogether.

If the catheter that has been introduced into the trachea is of correct size and in the proper position, the face of the anesthetized patient will be of a pink, rosy color, with the veins of the forehead slightly prominent. The pulse is full, bounding, and regular. If the patient is cyanosed, it means that the tube is not deep enough in the trachea or that too large a tube has been used.

When the insufflation is begun, the patient may have a short attack of spasmodic coughing. This need cause no concern, and the insufflation can be continued. The cough will sometimes persist if the end of the intratracheal tube is too near the bifurcation; it must then be withdrawn one or two centimeters.

There is a complete absence of mucus rattling in the throat during the entire period of the insufflation.

It is advisable to insufflate pure air for a few minutes at the end of the anesthesia in order to blow out the anesthetic from the lungs and trachea. Then the patients will awaken very quickly; they will often answer questions before the dressings have been applied. When the intratracheal tube is withdrawn, there is often a short period of apnea, then regular deep breathing again begins.

Cough and expectoration do not occur after anesthesia by intratracheal insufflation unless the patient had a pulmonary lesion before the operation, or an operation was performed upon the lungs. No pulmonary complications, of even the mildest kind, have been observed in more than 500 anesthesias. As soon as the patients are awake, they speak freely, are not hoarse, and do not complain of pain or discomfort in the throat. The larynx and trachea have a remarkable tolerance for the tube, which can remain in place for hours without danger.

Post-operative vomiting is certainly quite unusual after intratracheal insufflation. This is probably due to the fact that no ether vapor can be swallowed.

The patients seem to be less apt to show symptoms of shock than those anesthetized for long operations by ether inhalation. They are never too deeply under the anesthetic; in no instance has dilatation of the pupils as an evidence of too deep an anesthesia been observed.

Occasionally, with patients upon whom an abdominal operation is to be performed, complete relaxation of the abdominal muscles is not obtained. These patients will also be found to be refractory to ether anesthesia by inhalation.

Errors Which May Occur in Technique.—When the technique of intratracheal insufflation is once learned and the apparatus used by the anesthetizer is understood, errors or accidents should never occur. Special attention must be paid to the following features of the method.

The catheter that is used should be too small rather than too large, so that there is never an interference with the free escape of the air and ether by the side of the tube and out through the larynx and mouth. If the proper size of intratracheal tube is used, there should be no danger of the overdistention of the lungs. The Elsberg apparatus is arranged so that no excess of pressure in the lungs can occur. Every apparatus should have an automatic safety valve or blow-off, to act as a safeguard against a temporary or prolonged over-pressure, which might be injurious to the lung tissue.

Accidents, and How They May Be Avoided.—The accidents that have occurred so far have been due to errors in technique. In the case of Fischer,[1] one of the tubes which led into the ether reservoir was under the surface of the ether, and, by turning the wrong stopcock, pure ether was blown into the lungs. The tubes which lead into the ether bottle should never be below the surface of the ether; in fact it is only necessary that they reach into the cover of the ether reservoir.

In three other cases, two of which resulted fatally, the pressure was too high, so that injury to the lung tissue and emphysema in the sub-

[1] *Loc. cit.*

cutaneous tissue resulted. This could not have occurred if the apparatus had been provided with a safety valve for the prevention of excess of pressure. In one of the cases an intratracheal soft rubber tube was pushed down until it completely filled one of the branches of a bronchus, allowing no air to escape. With a proper apparatus and the proper technique, all these accidents could have been avoided. In Mt. Sinai Hospital almost 500 patients have been anesthetized without accident.

Another advantage of the method of intubation, in which the vocal cords are brought into view, is that the catheter can be introduced when the glottis is open, no force being necessary in pushing it down into the trachea.

It need hardly be mentioned that one must be sure that the tube is in the trachea and not in the esophagus, otherwise overdistention of the stomach could easily occur. It is probable, however, that in such a case the air would be regurgitated as fast as it entered the stomach.

The anesthetizer should never give an anesthetic by insufflation unless he thoroughly understands the working of the apparatus he is using, nor should he forget to interrupt the entering stream of air and ether 2 to 4 times a minute.

To sum up particular points to which attention must be paid, the anesthetizer must be certain: (1) That the catheter is in the trachea; (2) that it is not too far down—too near to or beyond the bifurcation; (3) that there is a safety valve on his apparatus; (4) that the interruptions in the air stream are made; (5) that respiratory movements persist.

The Indications for Intratracheal Anesthesia.—Anesthesia by intratracheal insufflation is of value:

(1) In thoracic surgery (whenever the thoracic cavity has to be invaded, to prevent the collapse of the lungs).

(2) In operations upon the head and neck, where the anesthetizer can be out of the way or where the giving of the anesthetic is ordinarily difficult, as in bilateral suboccipital craniotomy or laminectomy, where the patient has to lie flat on the abdomen.

(3) It is almost indispensable in those operations in the mouth where the pharynx and larynx must be kept free of fluid or blood. The stream of air and ether which is continually escaping from the larynx and mouth blows out any blood that might run down the throat, so that the operator need have no fear of any passing into the trachea. In such operations as complete removal of the tongue, removal of the upper or lower jaw, excision of malignant disease of the tonsil, the intranasal or intrabuccal approach to the hypophysis, etc., packing the pharynx is unnecessary. These operations are made much easier when the patient is anesthetized by the intratracheal method. The tube is kept in one cor-

ner of the mouth, and is never in the way of the operator. In the operation of laryngectomy, intratracheal anesthesia is advisable.

(4) Operations around the trachea, especially removal of the thyroid gland, can be made much easier when the patient is anesthetized by intratracheal insufflation. The interferenec with the smoothness of the anesthesia when the trachea is pressed or pulled upon is avoided, and there is no danger of collapse of the trachea.

(5) In operations in which there is danger of vomiting and aspiration of vomited material. Thus in operations for intestinal obstruction done under intratracheal anesthesia, the danger of the patients "drowning" in their own vomitus is avoided.

(6) In prolonged operations, and with cachectic individuals. Shock seems particularly rare in patients anesthetized by this method.

The future may show that intratracheal anesthesia will have a still larger field of usefulness than that here outlined.

The Value of Insufflation of Pure Air or Air and Oxygen as a Method of Artificial Respiration.—This is a feature upon which too little stress has thus far been laid. Whenever there is need for prolonged artificial respiration, such as in opium poisoning, drowning, etc., the method will surely be very useful. In several instances we have kept patients alive in good condition for three, four, six, or seven hours although during that time not a single respiratory movement was made. The color of the patient remained pink, and the blood was well aërated. It is a valuable characteristic of this method that the patients need not breathe in order to have oxygenation of the blood occur, the apparatus doing the breathing for them. In this respect the method differs from all others for this purpose. It may be added that it has the same advantage over both the positive and negative pressure methods for thoracic surgery. In the latter the respiratory movements of the patient are absolutely necessary, aëration of the blood being impossible without them. With intratracheal insufflation oxygenation of the blood will occur just as well whether or not the patient makes respiratory movements.

BIBLIOGRAPHY

Boothby and Cotton: *Surg. Gynec. and Obstet.*, 1911, *13*.
Elsberg: *Langenbeck's Archiv*, 1911.
Unger: *Berl. klin. Woch.*, 1910, 1748.
Woolsey: *N. Y. State J. Med.*, Apr., 1912, *12*, No. 4, 167.

CHAPTER XI

ANESTHESIA BY COLONIC ABSORPTION OF ETHER AND OIL-ETHER COLONIC ANESTHESIA

PART I

ANESTHESIA BY COLONIC ABSORPTION OF ETHER

Walter S. Sutton, A.B., A.M., M.D., F.A.C.S.

History.
The Physiology of Colonic Anesthesia.
Development of the Method.
Sutton's Apparatus: The Generator.
The Afferent and Efferent Tube Systems.
Technique of Method: Preparation of the Patient; The Administration; After-treatment.
Discussion of Cases.
Conclusions: Indications; Contra-indications; Advantages; Disadvantage.

History.—The high efficiency of the intestinal mucous membrane of vertebrates in general as a transmitter of gases to and from the blood stream has long been recognized. As early as 1808 Erman [1] opened the abdomen of *cobitus fossilis,* and observed that when air was swallowed the liver and the intestinal veins of the fish became bright red; while when hydrogen or nitrogen was substituted the color of the organs changed to dark purple. Baumert,[2] in 1855, analyzed the gas passed per rectum by the same kind of fish, and found a marked decrease in the oxygen content and corresponding increase in nitrogen when swallowing of air had been prevented for several hours. Jobert,[3] in 1877, discovered that in *callichthys asper,* a Brazilian fish, air-swallowing is essential to life, the fish dying in about two hours if prevented from the exercise of this form of accessory respiration. In mammals, also, similar

[1] Erman: *Ann. d. Phys. und Chem.,* 1808, *30,* 113.
[2] Baumert: "Chemische Untersuchungen u. d. Respiration d. Schlemmpeitgers," Breslau, 1885, 24.
[3] Jobert: *Ann. d. Soc. Nat.,* 1877, *5,* No. 8.

phenomena have long been known. Thus, Paul Bert,[1] in 1870 found that if the trachea of a kitten be clamped the animal will die of asphyxia in about 13 minutes, but, if the intestine be inflated with air, life may be prolonged for 21 minutes. A similar absorption of oxygen by the intestinal circulation in man is indicated by the results of Tappeiner,[2] who, in 1886, on analysis of gases from various portions of the alimentary canal of an executed criminal, found in the stomach 9.19 per cent of oxygen, in the ileum only a trace, and in the colon and rectum none at all, while the percentage of carbon dioxid showed a regular increase from stomach to colon.

Recognizing this activity of the intestinal mucosa, the early experimenters with ether as an anesthetic attempted its administration by this route. The method is first mentioned in Pirogoff's [3] work on etherization, published in 1847. The original idea of Pirogoff was the introduction of liquid ether into the rectum. Being warned by Magendie that this could not be done with impunity, he devised the method of vaporizing the ether by means of heat and administering the drug in this form. He reported 81 cases with two deaths, but unfortunately failed to give a detailed report of the latter. In the same year, Roux,[4] y'Yhedo,[5] and Duprey [6] employed injections of liquid ether, pure or in aqueous mixture, with the result of producing complete anesthesia. Pirogoff, in particular, wrote enthusiastically of the advantage of the rectal method, even expressing the belief that it might supplant the inhalation procedure. The method, however, disappeared from current literature, not to reappear until 1884. In this year Mollière [7] revived interest in the subject, introducing a new technique, in which he employed a Richardson hand bellows for forcing the ether vapor into the intestine. This method he later abandoned in favor of the earlier process of placing the ether container in a water bath (for which he recommended a temperature of 120° F.) and employing the pressure incident to the generation of vapor to force the latter into the gut.

Before the close of the year 1884 Yversen, Hunter, Bull,[8] Weir,[9] Wancher,[10] and Post [11] had recorded their experience with the method.

1 Bert: *Physiol. compt. de la respir.*, Paris, 1870, 173.

2 Tappeiner: *Arbeiten a. d. path. Institut zu München*, 1886.

3 Pirogoff: "Recherches pratiques et physiologiques sur l'etherization," St. Petersburg, 1847.

4 Roux: *J. d. l'académie d. Sciences*, 1847, *18*.

5 Y'Yhedo: *Gazette méd. d. Paris*, 1847.

6 Duprey: *Académie royale de médecine*, March 16, 1847.

7 Molliere: *Lyon médical*, *45*, 1884.

8 Bull: *N. Y. Med. J.*, March 3, 1884.

9 Weir: *Med. Rec.*, 1884.

10 Wancher: *Cong. internat. d. sciences méd.*, 1884.

11 Post: *Boston Med. and Surg. J.*, 1884.

Among these cases a number showed more or less marked diarrhea and melena and one death was directly traceable to the procedure.

The method again fell into disuse, not to be revived until 1903, when Cunningham added to the technique of administration a new feature in the employment of air as a vehicle for carrying the ether vapor into the intestine. The first publication of Cunningham (written jointly with Leahy [1]) appeared in 1905, being preceded by articles by Dumont,[2] and Krugeline,[3] the latter reporting 43 cases without untoward symptoms.

Stimulated by the records of improved results following the use of the Cunningham technique, many surgeons and anesthetists hastened to give the method a new trial, with the result that the subject has now acquired a considerable literature.

In 1906 Stucky [4] reported 4 cases with favorable comment on the utility of the method. In the same year, Lumbard [5] reported four laparotomies done under this method of anesthesia.

Buxton,[6] in the 1907 edition of his "Anæsthetics," in speaking of "rectal etherization," says: "I have now used the method pretty extensively, and find it to answer admirably for operations about the mouth, nose, and post-buccal cavities, for intra- and extralaryngeal operations, for staphylorrhaphy, and for operations for the relief of empyema. For the removal of the tongue, for excision of the jaw, or jaws, and for plastic operations about the face, the method gives greater facilities and freedom to the operator than any other plan I have tried. Mr. Appleby recommends the method also for prolonged dental operations."

Buxton gives no figures on number of cases or number of disadvantageous results. Of the latter he says: "I have met with grave complications, which, although in part due to the physical condition of the patients, were undoubtedly not wholly independent of irritation caused in the intestines by the entrance of ether vapor." In a paragraph on after-effects he says: "Colicky pains in the intestines, urgent tenesmus, diarrhea sometimes dysenteric in character, painful distention of the intestinal tract with more or less severe collapse, are complications which have been recorded. Deaths have occurred." Unfortunately he does not state which of these have occurred in his own skillful hands. His method is practically identical with that advocated by Pirogoff, i. e., the generation of ether vapor by heat and its direct conveyance under its own power to the intestines.

[1] Cunningham and Leahy: *Boston Med. and Surg. J.*, April 20, 1905.
[2] Dumont: *Correspond.-Bl. f. schweitzer Aertze*, 1903; *ibid.*, 1904; *ibid.*, 1908.
[3] Krugeline: *Wiener klin. Woch.*, Dec., 1904.
[4] Stucky: *J. Am. Med. Assn.*, July 28, 1906.
[5] Lumbard: *Med. Rec.*, Dec. 1, 1906.
[6] Buxton: "Anæsthetics," London, 1907.

An intercepter is used to prevent passage of liquid ether into the gut, and a temperature of not higher than 120° F. is recommended for the water bath in which the ether container is immersed.

Leggett,[1] in 1907, reported a series of animal experiments and 13 personally conducted cases, which in the main gave satisfactory results. Leggett added to the Cunningham apparatus an outlet communicating with the vapor-carrying tube by a branched connection. This facilitated the relief at any time of intra-intestinal pressure.

Dumont,[2] in 1908, reported 4 cases, in all of which a smooth and satisfactory narcosis was maintained, practically without undesirable after-effects. The apparatus was a modification of that described by Dudley Buxton. Though commending it highly for suitable cases, Dumont justly warns his readers that it is a method for exceptional cases; that it should be used only on properly prepared patients without intestinal lesions, and only by a skillful administrator.

In the same year Anna Morosow [3] reported from the clinic of Professor A. Kadhan at St. Petersburg a series of 68 head and neck cases. Of these, 61 slept smoothly; in 5 narcosis was incomplete; in 2 surgical anesthesia could not be attained. The duration of anesthesia varied from 10 minutes to 2 hours and 45 minutes. Anesthesia was first induced by inhalation, and then maintained by the rectal method. The average consumption of ether for the induction and maintenance of anesthesia together was 1.2 grams per minute; that for the period during which the rectal method was used 0.6 gram.

Morosow observed that awakening was very prompt. Bloody diarrhea occurred in 1 case, blood-streaked stool in 5, abdominal pain in 3 cases, vomiting during narcosis in 3 cases.

The apparatus used was essentially that of Pirogoff and Buxton, a temperature of 50° C. being recommended for the water bath.

In 1909 Denny and Robinson [4] recorded a series of 10 cases with gratifying results. In this year also Baum [5] reported 8 cases anesthetized with the apparatus of Pirogoff. Three cases showed ideal anesthesia, 2 cases were restless, in 1 (an operation for epigastric hernia) distention greatly hindered the operator, and the patient became anesthetized to a dangerous degree. In 2 other cases unfortunate after-results were observed. Both complained of abdominal pain during the induction of anesthesia, which lasted unusually long, and both showed marked abdominal distention. The first suffered after operation from profuse hemorrhage from the bowels (680 c. c. in 48 hours), while the

[1] Leggett: *Ann. Surg.*, Oct., 1907.
[2] Dumont: *Ibid.*, 1908.
[3] Morosow: *Russ. Archiv f. Chir.*, 1908.
[4] Denny and Robinson: *J. of Minn. Med. Assn.*, Feb. 1, 1909.
[5] Baum: *Zeit. f. Chir.*, 1909, No. II.

second died the morning after the operation and revealed at autopsy a gangrenous and perforated cecum and general peritonitis.

Carson,[1] in 1909, reported a series of 18 cases, 2 of which were unsuccessful because of incomplete preparation. One of the remaining 16 cases, a large and muscular man who was delirious at the time, could not be anesthetized without the aid of a mask, which was used throughout the operation. One case had slight bleeding from the rectum. There were 2 deaths (an extensive face carcinoma, and a case of extreme hyperthyroidism). The author's apparatus was used.

In July, 1909, Legueu, Morel and Verliac [2] reported a series of experimental cases, and expressed the belief that proper administration by this method is no more dangerous than that by inhalation. Oxygen was used as a vehicle for the ether-vapor, which was allowed to form at room temperature.

In 1910 Sutton [3] published the results of a series of about 140 personally conducted cases together with a description of the apparatus developed in the course of the work and the technique used in the application of the method at Roosevelt Hospital.

About the same time, J. H. Cunningham, Jr.,[4] published his third article on the subject, giving the best review of the literature that had appeared up to this time.

Shortly after this Thomas [5] published a description of an apparatus for rectal and pharyngeal anesthesia, which corresponds in principle almost detail for detail with that described by Sutton (10 *op. cit.*). This author, however, provides for a continuous, or almost continuous, return flow of the ether-laden vehicle, somewhat after the manner described by Vidal [6] in 1906. The article deals exclusively with a description of the apparatus and direction for its use, making no reference to specific cases or to after-results. There are no citations to the literature.

In August, 1910, Churchill [7] reported 47 cases anesthetized with the apparatus of Leggett. The range of age was from 6 months to 73 years. The time of anesthesia varied from 10 minutes to 2 hours, and narcosis was satisfactory to the operator in all but 7 cases. Two of these were herniotomies, in which anesthesia was complete, but in which the operator was embarrassed by abdominal distention. Five could not be fully anesthetized—four because of insufficient preparation, one because of a leak in the apparatus. Alcoholic patients seemed to be more easily narcotized by this than by the inhalation method. Disturbance in the colon

[1] Carson: *Interstate Med. J.*, Nov. 5, 1909, *16*.
[2] Legueu, Morel and Verliac: *Compt. rendu Soc. biol.*, June-July, 1909.
[3] Sutton: *Ann. Surg.*, April, 1910.
[4] Cunningham: *N. Y. Med. J.*, April 30, 1910.
[5] Thomas: *Yale Med. J.*, May, 1910.
[6] Vidal: *Presse médicale, 14*, 1906.
[7] Churchill: *Surg. Gynec. and Obstet.*, 1910, *11*, 2.

was observed in but one case, and only in the form of slight pain and blood in the stool 18 hours after operation on a patient who suffered be-

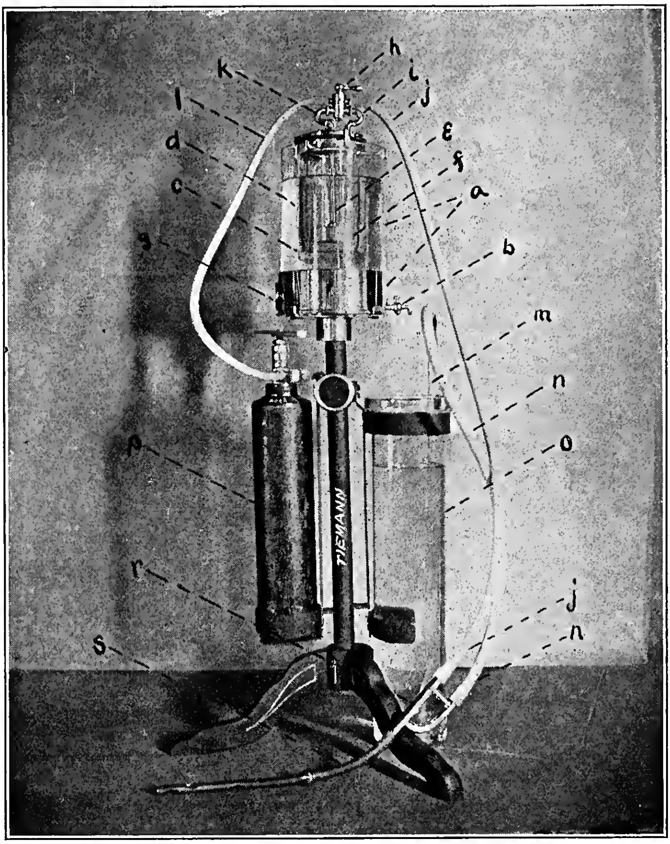


FIG. 167.—LATEST FORM OF COLONIC ANESTHESIA APPARATUS. a, Water jacket for vaporizing chamber; b, Drip cock for water jacket; c, Vaporizing chamber; d, Thermometer suspended in water jacket by metal clip; e, Metal tube carrying oxygen to spiral wier; f, Spiral wier; g, Chamber in water jacket for tubular heating-bulb; h, 4-way cock permitting administration of pure oxygen or oxygen-ether mixture; i, Outlet tube for ether-oxygen mixture; j, Afferent tube to colon; k, Tube connecting 4-way cock with spiral wier; l, Tube from oxygen tank to 4-way cock; m, Glass tube forming terminus of efferent tube from colon; this tube is sealed only by immersion in water of cylinder "o"; n, Efferent tube from colon; o, Water manometer cylinder; the amount of pressure in the colon is determined by the depth to which the tube "m" is immersed; p, Oxygen tank; q, Carrying stand; r, Y-tube connecting rectal tube with afferent and efferent tubes; s, Short rectal tube with sphincter-bulb and multiple fenestræ.

fore with hemorrhoids. Post-anesthetic nausea and vomiting were greatly reduced.

Sanders,[1] in August, 1910, reported 11 cases. In 1, inefficiently prepared, the rectal tube became plugged after a half hour of satisfactory

[1] Sanders: *Homeopath. Eye, Ear and Throat J.*, Aug. 1910.

anesthesia, necessitating resort to inhalation. In 1 staphylorrhaphy, chloroform was required by mouth during part of the operation. In several others momentary whiffs of chloroform were needed, and to supply this need Sanders added to Sutton's simple form of apparatus a Junker vial immersed in the same water with the ether container and receiving its supply of air from the same bulb as the latter.

The Physiology of Colonic Anesthesia.—Theoretically the administration of any anesthetic should presuppose a full knowledge on the part of the anesthetist of the physiological action of the drug. Practically, however, in case of pulmonary anesthesia, this knowledge may be, and, in the vast majority of cases, is dispensed with in favor of an accurate knowledge of the symptoms of incomplete and of excessive narcosis, and of the practical means of correcting each. This knowledge, gained by extensive observation and supervised experience in the pulmonary method of administration, is not sufficient basis for the undertaking of administration by the colonic method.

In the pulmonary method the drug is taken in by the automatic respiratory efforts of the patient, and is eliminated in the same way if pure air be substituted for the anesthetic mixture. No anesthetic-containing reservoir remains to continue imparting the drug to the blood plasma. Further, as the only means of elimination of the anesthetic is the same as the means of absorbing it, only so great an amount of the drug need be absorbed as is necessary to produce in the general circulation the required 1/4 of 1 per cent for the narcotization of the central nervous system (cf. Overton [1]). The absorbing surface of the lungs is so great and so well adapted to the purpose that a comparatively low concentration of anesthetic vapor in the respired air is sufficient to produce the required percentage in the circulating blood.

In the colonic method of administration all these conditions are changed. The drug cannot be taken in by the muscular action of the patient, nor can any unabsorbed excess be directly eliminated in that way. In the case of over-deep narcosis the unabsorbed residue of the drug must be evacuated by the active intervention of the operator. There must be considered in the use of this method the fact that the blood, after leaving the intestine with its load of ether, is obliged to pass through the lungs before reaching its goal in the central nervous system, and that in so doing a considerable portion of the contained ether will be eliminated into the air. The concentration of the drug at the point of absorption, therefore, may not be 1/4 of 1 per cent of the pulmonary method, but 1/4 per cent plus the percentage necessarily lost by exhalation. Again, the absorbing surface of the colon is much smaller than that of the lungs, and the arrangement of the vessels perhaps less favorable to gaseous interchange, so that a higher concentration is required.

[1] Overton: *Studien u. d. Narkose,* 1901, 185.

Each of these differences requires the intelligent attention of the anesthetist. Since the anesthetic mixture must be forced into the intestine, one is immediately confronted with the question of the proper degree of pressure to be used in the process. A sufficient degree must be employed to obtain moderate distention of the entire colon, else the available absorbing surface will be too small. Too much pressure must not be exerted lest by overdistention the vessels of the gut be flattened out, circulation impeded or abolished, and absorption minimized, and the ischemic mucosa be left unprotected by its normal circulation to resist the irritant effects of the ether vapor. The contention may be raised that experiments in which narcosis has been produced by the use of high pressure are sufficient to disprove this statement. The error in this contention arises from the fact that excessive pressure breaks down the resistance of the ileocecal valve, as observed by Leggett on dogs, and by Lumbard [1] in the human subject, and that the narcosis is obtained by absorption under diminished pressure from the coils of the small intestine.[2]

The writer's attention was first directed to the necessity for the use of a moderate pressure by the repeated observation that reduction of pressure often resulted in deepening of the narcosis.

The optimum pressure to be maintained in the colon has been determined experimentally to be about 20 mm. of mercury, which is approximately equal to the sum of the positive pressure in the intestinal capillaries, and the negative pressure in the portal vein. This would be varied according to the blood pressure of the patient, i. e., should be reduced to 10 or 12 mm. in young children and may be increased in individuals with abnormally high blood pressure.[3]

On account of the inevitable loss of ether from the blood in its passage through the lungs, it is sometimes necessary to adopt means, to be mentioned later, for keeping the respired air more or less laden with ether. For the same reason, because of the smaller and less efficient absorbing area of the colon as compared with that of the lung, a relatively high concentration of the anesthetic mixture may be used. To meet this

[1] Lumbard: *Med. Rec.*, Dec. 1, 1906.

[2] In connection with this point it is important for those who make use of the colonic method of etherization to watch for symptoms of the so-called "delayed ether poisoning" since from the foregoing it is plain that the liver—the great sufferer in this condition—is treated to a higher concentration of ether than in the same grade of narcosis from pulmonary administration. No case of this kind has come to the writer's attention, however, unless the peculiar death mentioned on page 455 has some affiliation with this class of cases.

[3] In connection with this question it is well to have in mind the experiments of Quirin, in one of which a normal healthy cat having a blood pressure of 85 mm. died after 5 minutes of an intra-abdominal pressure of 10 mm. *Deutsch. Arch. f. klin. Med.*, 1901, *21*, 79.

last requirement, a number of early investigators and, unfortunately, some recent ones adopted the expedient of passing pure ether vapor into the gut under the pressure incident to its generation. This doubly dangerous procedure has resulted in a number of deaths, in one of which (reported by Professor Baum) autopsy showed a gangrenous and perforated cecum and general suppurative peritonitis.

The danger of too great concentration of ether is obviated in the method used by Sutton, by employing oxygen (or air) as a vehicle and by keeping the ether from which the vapor is derived well below its boiling point. By maintaining a uniform temperature in the ether, with a fairly constant flow of oxygen and a definite period of association of the oxygen stream with the liquid ether, a fairly constant degree may be attained.

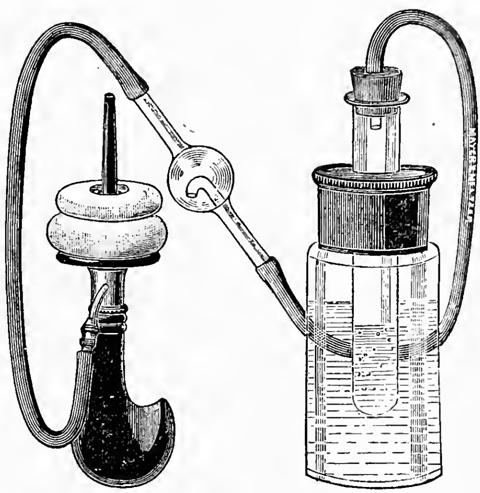


Fig. 168.—Apparatus for Administering Ether per Rectum. (Buxton.)

Development of the Method.—From the considerations just reviewed it is apparent that the history of the development of this method of ether administration is intimately associated with that of the development of the apparatus employed. Pirogoff used an ether container immersed in a water bath at a temperature of 120° F., with a rubber tube to lead the pure ether vapor into the rectum. An almost exactly similar apparatus was used by Buxton, Baum, Dumont, Kadjan, and Morosow (Fig. 168), as well as in the cases reported by Bull, Weir, and Post.

Cunningham, of Boston, made the first great advance by using a water bath of a temperature below the boiling point of ether, and by carrying the vapor of the latter into the intestine in a vehicle of air. (Mollière had previously used a hand bellows to force the ether vapor into the intestine, but without admixture of the air.) In the Cunningham apparatus no provision was made for emptying the distended intestine, this being accomplished when necessary by inserting the finger of the anesthetist through the sphincter ani alongside the rectal tube.

Vidal added to the apparatus a provision for a continuous return flow of gas from the rectum, and a year later Leggett added to the Cunningham apparatus an exhaust tube which could be opened when it was desired to empty the intestine, but which remained closed in the interval.

In July, 1909, Ligueu, Morel, and Verliac (Fig. 169) first reported the use of oxygen as a vehicle for ether vapor[1] in rectal anesthesia. The work of these writers was confined to animal experimentations.

The apparatus (Fig. 170) of Leggett represented the "state of the art" at the beginning of Sutton's series of cases, and, with the exception

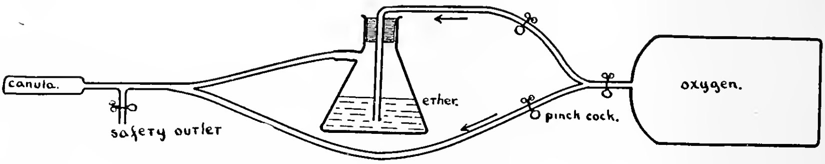


Fig. 169.—Apparatus of Ligueu, Morel and Verliac.

of the U tubes, was essentially the apparatus used in the earlier work. In a number of these cases it gave entirely satisfactory results; in others, obstacles were encountered which made difficult, or even prevented entirely, the attainment of satisfactory surgical narcosis. The study of

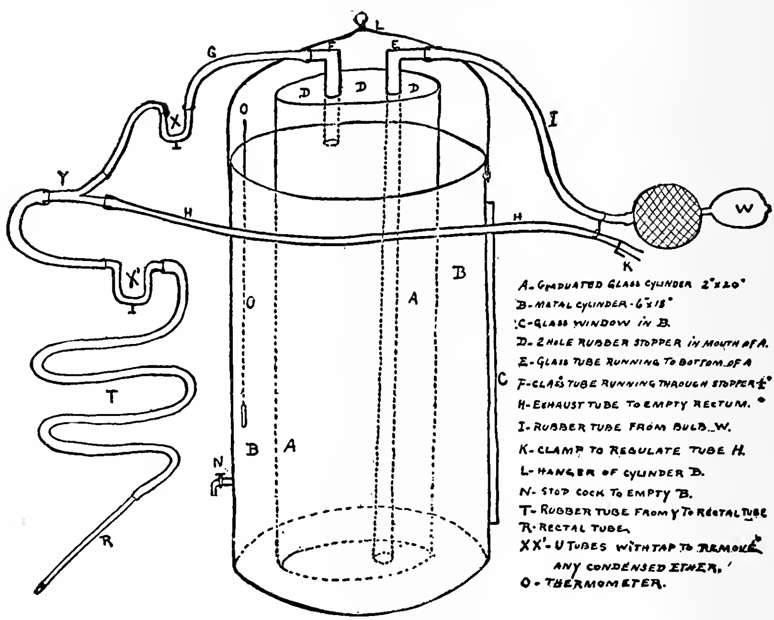


Fig. 170.—Leggett's Apparatus.

each of these difficulties has resulted in some modification of, or addition to, the apparatus.

Thus it frequently happened that semi-solid fecal matter, escaping

[1] Sutton had independently used oxygen in this capacity in etherization of a human subject as early as Nov., 1907.

with the gas on opening the exhaust tube, became lodged in the tubing, and prevented the free passage of gas in either direction. To prevent this, a special form of tube was made and arranged to stand between the patient's thighs close to the anus in such a position that any fluid or semi-solid matter passing in either direction would drop down into the branch of the tube leading to the exhaust. The caliber of the entire exhaust tube was made considerably greater than that used for carrying the ether vapor to the intestine. To meet the changed condition brought about by the new position of the branch tube, the rectal tube was shortened to about 8 inches in length; and, since the one or two eyes of the ordinary rectal tube frequently became closed by prolapse of rectal mucosa, or by the lodgment of fecal matter, tubes having from 5 to 7 eyes have been adopted. On account of the frequency of leakage around the rectal tube, preventing the maintenance of sufficient pressure to inflate the gut, a bulb from ¾ to 1 inch in diameter has been made on the tube at a point which in use lies just inside the sphincter. Another accident which at times prevented the free passage of gases was the weight of the patient's thigh on the flexible afferent and efferent tubes.[1] This difficulty was met by winding the exposed portion of the tubing with steel wire, or by the substitution of tubing having a very heavy wall.

The observation that in some cases a diminution of gas pressure in the gut resulted in a deepening of the narcosis led to recognition of the fact that too great pressure produces ischemia of the gut and consequent interruption of absorption. To guard against this incident a mercury manometer was added to the apparatus, so that the pressure of the gas in the gut might always be kept below that of the blood in the intestinal capillaries. For the more easy recognition of the escape of gas on opening the exhaust, the distal end of the latter was immersed in a bottle of water placed under the operating table; and, to prevent confusion as to whether the gas there seen or heard to escape is coming from the gut or from the generator, a combination clip was devised which necessitates the closure of the afferent tube before the efferent tube can be opened.

Inasmuch as it has sometimes been necessary, as will be explained later, to administer a certain amount of anesthetic by mouth as a supplement to the quantity absorbed by the intestine, a tube has been provided, by means of which ether vapor can be diverted from the main afferent tube and allowed to escape into the mouth or nose of the patient. Finally, on account of the instability of the cylinder form of ether generator and of the more and more frequent use of oxygen as a vehicle for the ether vapor, a compact metal generator has been devised,

[1] These terms are not used in the sense in which they are employed by Cunningham as afferent and efferent to the vapor generator, but as afferent and efferent to the patient.

which, though no more efficient in maintaining narcosis than the cylinder form, presents a number of advantages which will be detailed later.

Sanders has since modified the simpler form of this apparatus by adding a chloroform vapor generator which, when immersed in the same water bath as the ether container, serves to meet the occasional requirement for accessory inhalation anesthesia. Thomas has also produced an apparatus, which, though differing from it in detail, meets the same requirements as that of Sutton. In it he uses as a matter of routine the safety-valve water manometer recommended by Sutton for use in mouth and throat cases.

Sutton's Apparatus.—The original apparatus in use at Roosevelt Hospital was that of Cunningham—the simplest possible means of forcing air through warmed ether and carrying the mixture into the intestines—plus a branch tube used for exhausting the contents of the gut when occasion required. The latter feature, introduced by Leggett, is one of the valuable points in the apparatus with which this section is concerned.

The complete apparatus may be regarded as consisting of three parts: (1) A generator in which the mixture of oxygen and ether is produced; (2) an afferent tube system which carries this product into the intestine; and (3) an efferent tube system for the purpose of exhausting the contents of the gut.

The Generator.—This portion of the apparatus consists of a small generating chamber surrounded by a water jacket and connected with an ether storage chamber, which automatically maintains a given level of ether in the generating chamber. The arrangement and working of the various parts will be most readily understood by a glance at the photograph of the dissected apparatus (Fig. 171) and the schematic sagittal section shown in Fig. 172.

Only one feature will require special description. This is the spiral wire 1, which determines the prolonged intimate contact of the oxygen (or air) with the fluid ether. This device consists of a spirally wound strip of thin brass ¾ of an inch wide and about 14 inches in length, soldered to the bottom of the circular disk *k*, with which the oxygen inlet tube *a* connects.

The level of the ether in the generating chamber is automatically maintained at such a height as just to cover this wire and disk. The oxygen (or air) is admitted to the apparatus through the tube *a*, emerges below the level of the ether under the plate *k*, and finds its way to the surface only after traversing all the windings of the spiral. This necessitates intimate association of oxygen with ether for a distance of 14 inches, and has been shown experimentally to bring about a complete saturation of the former with the latter.

The ether-saturated oxygen rises into the upper part of the generat-

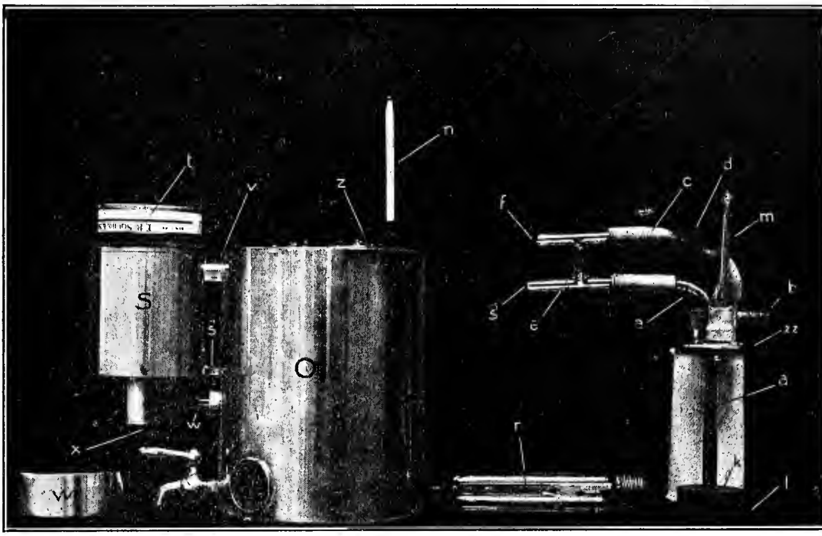


FIG. 171.—PARTS OF VAPOR GENERATOR. a, Oxygen (or air) inlet; b, connection to afferent tube system; c, by-pass for inflating intestine with pure oxygen (or air); d, clip for closing by-pass; e, H-tube connecting oxygen tank and air bulb with generator and by-pass; f, connection of H-tube with air bulb; g, connection of H-tube with oxygen tank; k, disc forming top of spiral wier; l, spiral wier; m, manometer; n, thermometer projecting out of water-jacket; r, tubular incandescent bulb for heating water-jacket; s, ether reservoir; t, ether can inverted in reservoir; with upper part of generating chamber; w, glass tube connecting ether reservoir with generating chamber below level of ether; x, flattened spike for perforating seal of ether can; g′, metal brace between reservoir and generating chamber; z, cover over hole for filling water-jacket; zz, cover of generating chamber.

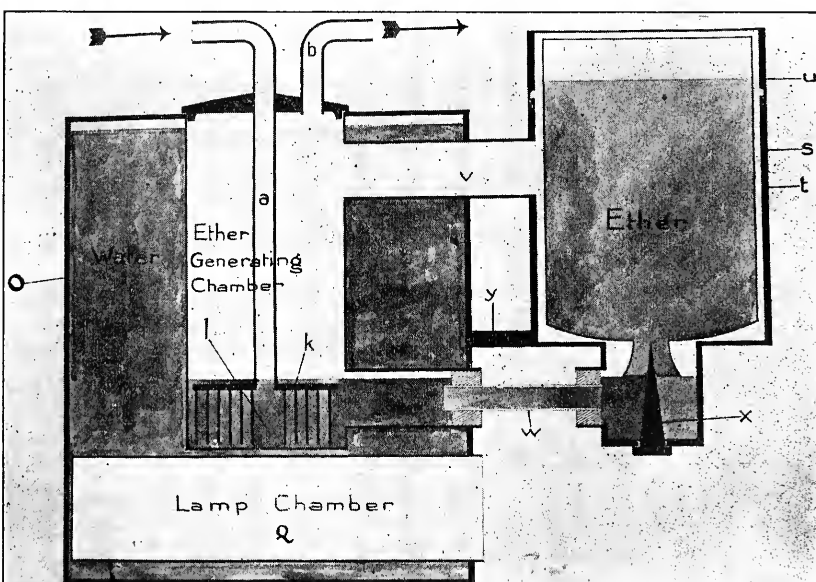


FIG. 172.—SCHEMATIC SECTION OF VAPOR GENERATOR.

ing chamber, and is carried by the tube *b* into the afferent tube leading to the intestine. The main body of the ether remains in the original package *t*, which is inverted in the ether reservoir *s*. To charge the generator, a *sealed* ether can (this apparatus is designed to take a Squibb's 259-gram can) is inverted in the reservoir, the seal being penetrated in the act by a flattened spike *x*, which projects from the bottom of the reservoir. A twist of the can serves to ream out a fair-sized opening. Ether then flows out into the lower part of the reservoir and into the generating chamber until it has reached a level above the perforation in the seal, when, the entrance of air being interrupted, the outflow of ether ceases until the level of the fluid has been again reduced, to allow more air to bubble up into the dome of the ether can. Before any pressure is put on the generating chamber, the cover *u* of the ether reservoir must be screwed on air tight.

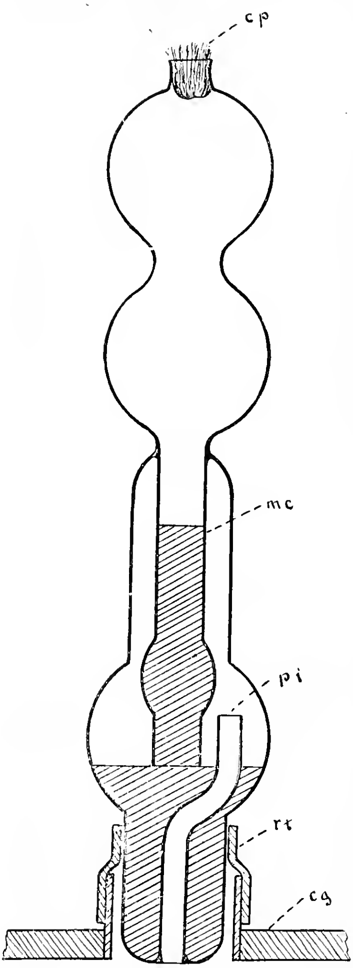


Fig. 173.—Sectional View of Manometer. mc, mercury column; pi, pressure inlet; cp, cotton plug in pressure vent; cg, cover of generating chamber; rt, short piece of rubber tube connecting manometer with cover.

Surrounding the generating chamber is the water jacket *o*, which is maintained at a temperature of 88° to 90° F. (not higher) by the 10 candle power tubular incandescent electric lamp *r* inserted into the blind tube *q*. A thermometer, *n*, projecting from the top of the water jacket, readily shows the temperature of the contained water. A manometer *m* projects from the cover *zz* of the generating chamber, and hence determines the pressure in the intestine of the patient. This manometer, of which a sectional drawing is shown in Fig. 173, also serves the purpose of a safety valve, being so constructed that, when the pressure reaches a point a few millimeters above the maximum, the oxygen-ether mixture of the generating chamber is permitted to bubble up through the mercury and to escape into the air. This point is of importance, since the needle valve of the oxygen tank may be accidentally opened too wide, which, in the absence of such a safety valve, would put a dangerous pressure on the gut. When such excessive pressure has subsided, the mercury falls back from the upper chamber of the manometer, and the safety valve is closed.

The H-tube *c* makes it possible to have, at the same time, means of passing either oxygen or air through the generator and also of inflating the intestine with pure oxygen or air without appreciable admixture of ether. This latter procedure is accomplished by simply opening the pressure clip *d*, which allows the oxygen or air to pass into the afferent tube and on into the intestine without making its way through the generator itself. The generator may be hung by a bracket from the oxygen tank, as shown in Figure 176, or set upon a small table.

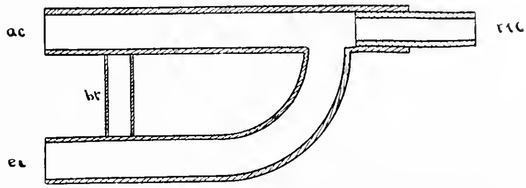


FIG. 174.—SECTIONAL VIEW OF H-TUBE. ac, afferent connection; ec, efferent connection; rtc, rectal tube connection; br, brace.

For those who wish to make their own apparatus, a simpler form of

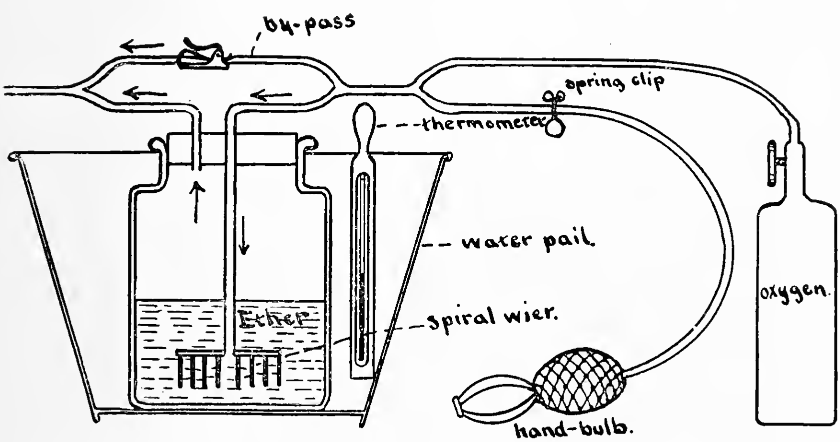


FIG. 175.—SIMPLE FORM OF SUTTON'S APPARATUS. Manometer not shown.

generator will be found quite satisfactory. This may be made by the use of the spiral wire in any wide-mouthed bottle capable of containing 250 to 400 grams of ether and 4 or 5 inches of free space between the fluid and the cork. The manometer is inserted through the cork and the proper afferent connections provided. In the place of the water jacket, a pail of warm water is provided, and the bottle partly immersed in it. The temperature is registered by a floating thermometer, and is kept

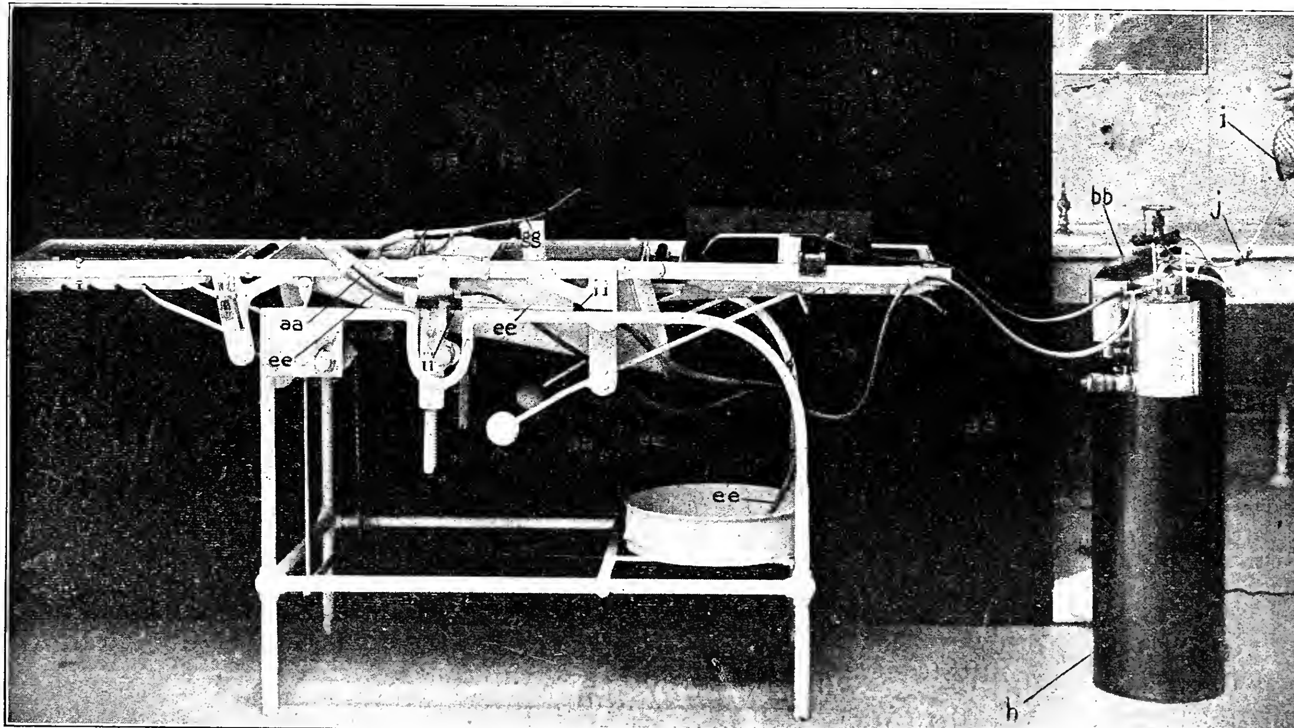


Fig. 176.—Complete Apparatus With Oxygen Tank. aa, afferent tube system; bb, T-tube for connecting accessory mouth tube; dd, clip for same; ee, efferent tube system; ff, Y-tube; gg, rectal tube; hh, combination clip on afferent and efferent tube system; i, air bulb; j, clip on air connection which is closed when oxygen is being used, to prevent leakage through air bulb; ii, sliding clips for holding tube systems on table; h, oxygen tank. Tell-tale bottle not shown, should sit in drip pan of operating table and receive distal end of efferent tube.

up to the proper point by occasional additions of very hot water. (Fig. 175).

The Afferent and Efferent Tube Systems.—These, as will appear from a glance at Figs. 176 and 179, run a parallel course for the greater part of their length—the efferent or exhaust tube being led to the head of the table in order that it may be controlled by the anesthetist sitting there. The afferent tube is of small caliber, since it conveys only gas, while the efferent tube, which is frequently called upon to conduct water and semi-fluid feces, must have greater inside diameter. Both tubes have very thick walls in the portion which passes over the edge of the table and under the patient's thigh. This is to obviate the danger of compression in this situation. The rectal tube is a short single tube having a bulb about 3 inches from its outer end supplied with 5 to 7 fenestræ. This bulb in use aids in the prevention of leakage in case of a lax sphincter, while the multiple fenestræ are a safeguard against closure of the tube due to prolapsed mucosa or to fecal particles when the exhaust tube is opened. Communication between the rectal tube on the one hand, and the afferent and efferent tube system on the other, is established by the use of a Y-shaped tube (Fig. 174) of glass or metal, which stands horizontally between the patient's thighs, close to the anus. The upper straight arm connects with the afferent tube while the lower curved branch leads to the efferent connection. By reason of its position and construction, this Y-shaped tube acts as a trap to catch either condensed ether from the afferent tube or semi-fluid matter coming from the rectal tube when the exhaust is opened.

A strong glass tube is introduced into the efferent system, as shown at *ee*, Fig. 176. This serves the double purpose of preventing a sag in the exhaust tube at this point and of furnishing a rigid support for the sliding hooks *ii*, which form the principal means of attaching the apparatus to the table. The ends of the efferent or exhaust tube are immersed in a few inches of water in the bottom of a wide-mouthed bottle, which sits on the floor under the head of the table, or in the drip pan connected with the latter. This bottle serves both as a collector of any fluid return from the intestine and as a "tell-tale," since the amount of gaseous return following the opening of the exhaust is readily appreciated when it is seen or heard bubbling through the water. Continuous leakage from the exhaust is prevented by a spring clip *hh*, which is modified, as shown in Fig. 177, so that the afferent tube is held in relation with one of the finger rests of the clip. This relation of clip and afferent tube insures the closure of the latter by the same finger pressure which opens the former. Gas is thus prevented from entering the intestines as long as the exhaust is open. For the sake of keeping it in a definite position, this combination clip is attached to the table by a long wire hook. Since, in some cases, it is necessary temporarily to supplement the colonic administration by the addition of ether by mouth, a T-tube, *bb,* Fig. 176, is placed in the afferent system close to the generator, and a small rubber tube is led off and closed by a spring clip.

In mouth and throat cases, where it is desirable for the patient to retain an active coughing reflex, it has proved of advantage to introduce a small mica-plate check valve beyond the origin of the accessory mouth

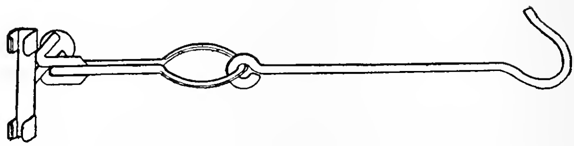


FIG. 177.—COMBINATION CLIP WITH HOOK.

tube. Coughing produces a very marked increase in intra-abdominal pressure, and in some cases before the introduction of this valve a paroxysm of coughing has resulted in the driving of fecal-stained fluid back into the generating chamber. With the check valve, as shown in Fig. 178, this cannot occur. When violent coughing is permitted, it is necessary to open the exhaust during each paroxysm, lest the rectal tube be extruded by the effort; or an automatic safety valve may be arranged by leaving off the spring clip and immersing the distal end of the exhaust tube in about 18 inches of water. (Fig. 179.) This height of water will be sufficient to prevent escape of gas at 20 mm. pressure, but readily permits escape at the higher pressure incident to coughing. When this device is used the intestine may be emptied of gas by simply raising the end of the exhaust tube to the surface of the water.

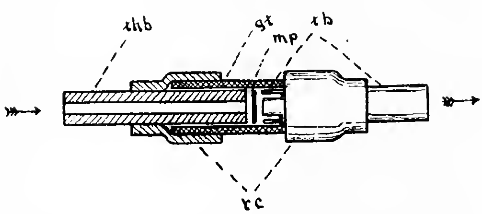


FIG. 178.—CHECK VALVE USED ON AFFERENT TUBE WHEN COUGHING IS TO BE PERMITTED. (Partial sectional view.) thb, thick walled brass tube connecting with generator; tb, thin-walled brass tube —notched on end toward valve—connecting with main afferent tube; gt, glass tube surrounding valve chamber; mp, mica-plate valve; rc, cuffs of rubber tubing connecting glass and brass tubes.

Technique of Method.—PREPARATION OF THE PATIENT.—One of the most important considerations, as observed by all workers with intestinal anesthesia, is the thorough cleansing of the colon. This is accomplished by a cathartic (castor oil) given the night preceding the operation and followed in the morning by high soapsuds enemata repeated until the return is clear. In Sutton's cases three enemata, 1½ to 2 hours apart, were regarded as the minimum number. In alcoholic and very muscular subjects, and in operations on the mouth or upper respiratory tract, it has been found useful to give 1/6 to ¼ grain of morphin and 1/120 to 1/100 grain of scopolamin hypodermically 1 hour before operation.

The Administration.—Before the patient is brought to the etherizing room, the anesthetist affixes the apparatus to the table, as shown in Fig. 179, except that the rectal tube is not attached and the Y-tube and its connections are allowed to hang down at the side of the table, while the accessory mouth tube is permitted to hang from the side of the generator. The ether reservoir is charged, the water jacket is filled with

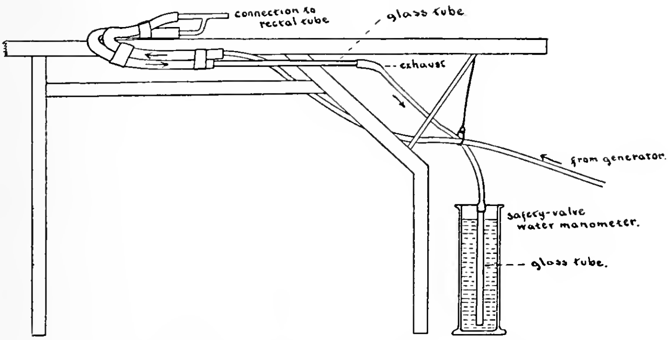


Fig. 179.—Sketch of Pipe-Line System with Safety Valve Water Manometer Attached. Note that combination clip is not used with this arrangement.

water at about 90° F., and the electric lamp is connected with a plug in the wall, *but not lighted at this time.* The end of the exhaust tube is placed in the "tell-tale" bottle under the table.

The anesthesia is then started by the pulmonary method, and carried to a stage of partial relaxation, when the patient is brought to the operating room and placed on the table. The rectal tube, well greased, is then quickly inserted until the bulb lies just inside the sphincter, the anesthetist before starting the initial anesthetic having protected his left hand with a rubber glove. The patient's left thigh is then raised, and the branch tube brought under it to its proper position and connected with the rectal tube. For this brief period the cone has been held over the patient's face by a nurse. The anesthetist then removes his rubber glove, takes his place at the patient's head, and slowly turns on the oxygen. As soon as this is done the cone may be removed from the patient's face. If the operation does not involve the patient's mouth, it is best to cover this, and, if possible, the nose as well, with three or four large sterile towels which, by causing a certain amount of rebreathing, impede the elimination of ether from the lungs. If, during the change from the pulmonary to the colonic method, the patient has "come out" and begun to make troublesome voluntary movements, he can be quickly "put under" by admitting ether vapor to the space under the towels through the accessory mouth tube.

As soon as pressure in the colon has been raised to the required 20 mm., the exhaust should be opened and the gut allowed to empty itself. This process of filling and emptying the intestine should be repeated three or four times in order to eliminate as thoroughly as possible the natural gases of the bowel. The needle valve of the oxygen tank is then set at a point which just maintains the required 20 mm. pressure, and usually demands little or no further adjustment during the rest of the operation. If the patient tends to come out from the influence of the anesthetic, the bowel may be emptied from time to time to carry out any intestinal gases which tend to dilute the anesthetic mixture. If, on the other hand, the anesthesia continues sufficiently deep, no further use of the exhaust need be made until the end of the operation. This is because the oxygen is absorbed by the bowel with the same ease as the ether vapor, in fact, more rapidly, so that no residue of the anesthetic remains.

When air is used as a vehicle, the bowel must usually be emptied every 5 or 10 minutes, as in this case a nitrogen residue tends to accumulate and to act as a diluent of the freshly added anesthetic mixture. Whenever possible, oxygen should be used instead of air as a vehicle. The reasons for this are: (1) It reduces the dangers of anesthesia; (2) it greatly diminishes the rapidity and depth of respiration, in some cases even causing the phenomenon of apnea or hyperoxygenation, thus greatly reducing the loss of ether through the lungs; and (3) it obviates the necessity of the frequent use of the exhaust, and hence contributes to the smoothness of the anesthesia and the comfort of the anesthetist.

In the ordinary case, a smooth anesthesia continues from this point with little further active intervention on the part of the anesthetist. The thermometer must be watched to see that the temperature of the water bath does not become too high. When the temperature tends to rise above 90° F., the incandescent lamp may be partly withdrawn from the water bath, or it may be turned off for a few minutes, being lighted when the temperature has fallen to 88 or 89° F. If, with a lighted 10 candle power lamp inserted the full length of the water jacket, a temperature of 90° F. cannot be maintained, it is certain that there is a leak in the apparatus or from the patient's sphincter, necessitating an excessive flow of the mixture of oxygen and ether vapor to maintain the required pressure.

Too shallow narcosis is met by adjusting the face towels so as to cause increased rebreathing of the exhaled ether (this does not cause cyanosis on account of the constant absorption of oxygen from the bowel), and, if this is not sufficient, by introducing the anesthetic mixture under the towel from the accessory tube.

Too deep narcosis is met by temporarily shutting off the stream of oxygen and allowing the exhaust to remain open for a short time, or by markedly reducing the pressure without opening the exhaust.

The depth of narcosis is determined by the pupils, which are usually at maximum contraction in complete anesthesia by this method (unless morphin and scopolamin have been administered, when they have little value); by the degree of muscular relaxation, and by the color which may be noted from the lips and face, but better from the color of the blood in the wound. The character of the respiration is of less value, as the patient may have excellent color, though breathing very infrequently. Short, shallow, jerky respiration, especially when associated with a dusky color, is a danger sign, just as it is in the pulmonary method.

The writer rarely takes the pulse except in cases which are manifestly doing badly or where cardiac complications are known or suspected. Muscular tone is best determined from the tension of the jaw muscles and from the presence of voluntary movement of the tongue. It is the writer's habit to keep one finger in the patient's mouth in order to detect the first active tightening of the jaw or voluntary movement of the tongue. Sufficient ether need not be given to make the lower jaw entirely relax, but merely enough to prevent actual biting of the finger. Difficulty in breathing is readily overcome by extending the head on the neck by simply pulling with the finger upon the upper incisors. This has always been sufficient, so that in the entire series of cases here reported neither mouth gag nor tongue forceps have been used to improve the respiration of the patient.

At the end of the operation the bowel is filled with oxygen to a pressure of 20 mm. and emptied several times, these "oxygen enemata" serving to carry off the greater part of the unabsorbed ether. Occasionally it seems advisable to massage the abdomen in the direction of the colon before removing the rectal tube, but this is not usually necessary. The rectal tube is then withdrawn and disconnected from the Y-tube.

After-treatment.—As soon as the patient is returned to bed a high soapsuds enema is given, being siphoned off after a few minutes if necessary. This treatment is repeated a half hour later. Vomiting is usually absent; when present it is very rarely severe, the patients, curiously enough, disclaiming any feeling of nausea. Recovery is rapid.

The possibility of the transmission of typhoid, amebic colitis, or other intestinal infection from one patient to another is prevented by keeping the rectal tube and the Y-tube in a 1 per cent solution of formalin between operations. The glass tip of the accessory mouth tube, when not in use, is kept in the same solution.

Discussion of Cases.—Up to the present time the writer has administered ether by this method to about 140 cases on the surgical service of Roosevelt Hospital. Of this number careful records were taken of the first 100 cases. Of the remaining 40, mostly private cases, no detailed records have been made. It may be said, however, that all were satisfactory and that untoward results occurred in none. In only one case—the second of the series—was an attempt made to administer the anesthetic per rectum from the beginning. This proved so slow, and was so uncomfortable and distasteful to the patient, that after about 20 minutes a cone was used to complete the initial establishment of the anesthesia. Inasmuch as there is no real indication for beginning the administration by rectum, the writer has never made a second attempt to do so.

Of the 100 cases in the recorded series, 91 were ward patients and 9, private patients. The age range was 2 to 77 years. The operations were as follows:

Tumors, glands, etc., of neck	31
Amputations of breast	9
Goiters and thyroglossal cysts	8
Craniotomies	6
Corrections of old fractures of limb	5
Resections, sutures and osteotomies of inferior maxilla	5
Partial excision of the tongue	4
Staphylorrhaphy	4
Tracheotomy	3
Mastoid	3
Inguinal hernia	2
Removal of parotid tumors	2
Resection and osteotomies of superior maxilla	2
Removal of Gasserian ganglion	2
Skin grafting	2
Orchidopexy	1
Hydrocele	1
Appendectomy	1
Nephrotomy	1
Ludwig's angina	1
Enucleation of eye	1
Resection of knee	1
Cervical laminectomy	1
Axillary adenitis	1
Excision of sternomastoid	1
Plastic for strictures of esophagus	1
Laryngectomy	1
Neuorrhaphy	1

The longest operation of the series consumed 2 hours and 20 minutes; the shortest, 5 minutes; the average time being 53 minutes.

The average consumption of ether was 87 grams per hour in the 64 consecutive cases in which record of this point was kept.

Twelve of the 100 patients had preliminary injection of morphin and scopolamin.

In 25 cases, oxygen was used as a vehicle for the ether vapor.

Forty-three patients had at some time during the operation a supplementary administration by mouth of ether or chloroform.

In 12 cases, there was eructation of gas, probably indicating the passage of the gas into the stomach from the distended small intestine. Of these only 4 occurred in the 71 cases following the adoption of a 20 mm. maximum pressure in the bowel.

In only 18 cases was there any perspiration, and in none of these was it profuse.

Forty-three patients vomited or regurgitated stomach contents after operation; of these, several disclaimed any sensation of nausea.

Twelve had abdominal pain.

Five had bloody stools or blood-streaked return from the post-anesthetic enemata. All cleared up in from a few hours to 3 days, and in none was the loss of blood accompanied by noticeable weakness or abdominal pain. The most severe of the cases continued to pass small quantities of blood for 3 days, during which the patient also vomited persistently. This patient, Case XXVI of the series, was the last save one in which any hemorrhage (beyond the negligible amount occasionally caused mechanically by the rectal tube) has occurred.

Case XCVII, as an incident to the introduction of a new form of ether evaporator, was treated to an excessively concentrated vapor, so that great care was necessary to prevent narcosis from becoming too deep. In the first 3 days following the operation this patient had 5 bloody stools. He felt no discomfort, however, and was discharged on the fifth day in perfect general condition.

In the series of cases to date there have been 5 deaths from all causes. In none of these, in the judgment of the operating surgeon, was the method of administering the anesthetic a contributing factor. A brief statement of the conditions in each of these cases follows:

Case I.—Large, heavy man, moderately alcoholic. Operation, partial excision of the tongue for epithelioma. Patient somewhat blue; pulse small and rapid throughout operation. Died, apparently of operative shock, about two hours after return to ward.

Case II.—Large, heavy man. Age 35. Moderately alcoholic. Operation, tracheotomy and removal of cervical glands as a preliminary to laryngectomy for carcinoma of larynx. Anesthesia was "shallow" throughout, patient coughing and groaning frequently. Made prompt ether recovery, but died 2 days after of pneumonia.

Case XXV.—Fairly well-nourished man; age 53; moderately alcoholic. Operation, hemi-excision of the tongue and removal of right cervical glands for epithelioma. Patient took initial anesthetic slowly, and was markedly cyanotic. Color and general condition improved after beginning of the administration per rectum. Anesthesia was shallow throughout, patient swallowing frequently. Late in the operation there was a marked hemorrhage, and shortly afterward—1 hour and 35 minutes after the beginning of the operation—the patient died.

Case XLIV.—Muscular man, age 24; brought to hospital almost moribund with compound depressed fracture of skull. After operation lasting 35 minutes, the patient left the table improved, but never regained consciousness and died 2 days later.

Autopsy showed extensive fractures of vault and base, extensive laceration of brain, and marked subdural and epidural hemorrhage. The colon was normal, showing no injurious effects from the ether.

Case XLVII.—Slender negro, age 31; brought to hospital in ambulance with extreme dyspnea of sudden onset. Operation, low tracheotomy, with patient in sitting posture on account of orthopnea. On account of this position the rectum was compressed by the weight of the upper bowel, and introduction of ether vapor and oxygen into the colon was almost impossible. The operation gave little relief, but ether recovery was satisfactory. Dyspnea and cardiac weakness progressively increased, and two days later the patient died.

Autopsy showed a large false aneurysm of the descending arch of the aorta. Colon normal.

One other death has occurred in Roosevelt Hospital from the administration of ether by this method. Another member of the interne staff administered the anesthetic in this instance, but the case came under the writer's observation both during and after the operation.

The patient was a well-nourished child, five years of age, who had been anesthetized on two previous occasions for the correction of harelip and the removal of adenoids. The operation in question was a staphylorrhaphy lasting about 50 minutes. Throughout the operation there was noticeable difficulty in maintaining a smooth narcosis, the latter being too deep and too shallow by turns. In the course of the shallow intervals a little chloroform was given several times on a "sponge stick." There was no excessive loss of blood. Toward the close of the operation the patient's color became very bad, and the pulse small and rapid. She was hurried to the ward, stimulated, and given external heat. In the course of a half hour she became restless and talkative, calling for water and asking to be taken home, but apparently recognizing no one about her. She did not vomit. The pulse continued rapid and small, and an intravenous infusion was given with slight temporary benefit. After this she gradually relapsed again into unconsciousness, and about two hours after operation she died. Unfortunately an autopsy was not permitted.

It is the writer's belief that this method, safeguarded by such improved apparatus as that described, and by the use of oxygen as a vehicle for the ether vapor, is one of extreme safety in the absence of definite intestinal lesions.

Conclusions.—The colonic method of administration of ether is more complex than the pulmonary method in general, and requires from the anesthetist a broader appreciation of the physiological factors involved. For these reasons alone its field of usefulness is limited to cases in which it presents distinct advantage over the pulmonary method. It is, therefore, not a method adapted to the experimental use of the tyro, but rather a valuable addition to the armamentarium of the trained anesthetist. We may summarize the indications and contra-indications as follows:

Indications.—(1) Operations upon the respiratory tract (head, neck, and chest), especially such as lay open the mouth, larynx, pharynx, and trachea. (2) Operations upon patients in whom absorption must be minimized on account of lung, heart, or kidney lesions. (3) Operations upon patients already suffering from respiratory embarrassment.

Contra-indications.—(1) Operations upon patients presenting lesions of the alimentary tract, especially such as might cause weakness of the wall of the colon. (2) Laparotomies in general, except such as do not open the general peritoneal cavity, e. g., suprapubic cystotomy. This is because of the interference of the inflated colon with the work of the surgeon. (3) Operations upon patients with markedly incompetent sphincter ani or with large fistula in ano. A patient with an open appendicostomy would offer the same difficulty of leakage. (4) Operations upon patients suffering with orthopnea. In these cases it may be impossible to inflate the colon because of the obstruction caused by the weight of the other viscera resting upon it. (5) Emergency cases in general, because of the lack of preparation of the colon.

Advantages.—The points in favor of the method in cases in which its use is indicated may be summed up as follows: (1) Freedom of operative field from contamination by the anesthetist. (2) Ability to maintain a smooth and continuous anesthesia in operations involving the respiratory tract, thus shortening the time and reducing the shock of operation. (3) Uniform depth of anesthesia, causing light narcosis and marked saving in ether. This saving is much greater when oxygen is used as the vehicle. (4) Lessening of pharyngeal and bronchial secretion, and of tonic contraction or troublesome relaxation of jaw muscles. (5) Ability to administer oxygen without interruption of anesthesia. (6) Minimized loss of heat during operation because of diminished sweating and ether refrigeration. (7) Reduction of post-operative vomiting and nausea.

Disadvantage.—The only point against the method in cases where its employment is indicated is the occasional difficulty in maintaining profound anesthesia without the use of the supplementary mouth tube.

PART II

OIL-ETHER COLONIC ANESTHESIA

History.
Animal Experiments.
Remarks on the Method.
Preparation of the Patient: Preliminary Medication.
Administration.
Control of the Anesthesia.
Physiology.
Illustrative Cases.

History.—The original work of Cunningham and Sutton's careful record of cases were prominent factors in the development of oil-ether colonic anesthesia. (See Part I of this Chapter for a history of rectal anesthesia.)

In 1913 at the Seventeenth International Medical Congress in London, the senior author read a paper on Oil-ether Anesthesia. The experimental animal work was completed just previous to this date. The practical clinical work with oil-ether was begun at the People's Hospital, and the first successful administration was in September of 1913 to a patient of Dr. I. M. Rothenberg, his brother operating. The work was completed at Columbus Hospital and was successfully demonstrated at other hospitals in New York City, then in neighboring cities.

Animal Experiments.—All of the experimental laboratory work was conducted under the immediate supervision of Professor Wallace, of the pharmacological department of the University and Bellevue Hospital Medical College. In studying the anesthetic value of ether introduced in solution into the rectum, about twenty-four experiments on dogs were performed. The method generally employed was as follows: Several hours before the administration of the ether a saline cathartic was given by a stomach tube; half an hour before, a subcutaneous injection of morphin sulphate (from 0.001 to 0.03 gm.), and immediately before, a cleansing enema of soap and water. The animal was then placed on its back on a holder, and a fairly stiff rubber catheter was inserted into the rectum and pushed up the colon for a distance of about ten inches. The ether solution was placed in a bottle with an outflow tube at the bottom attached with rubber tubing to the catheter. The bottle was then raised to any desired height, from one to six feet, and the flow regulated by a screw clamp on this tubing.

In the first experiment performed, a five per cent ether solution in normal saline was used. About 500 c. c. of this solution was slowly injected into the colon. A very mild excitement stage ensued, and complete anesthesia continued for thirty minutes, gradual recovery then taking place. There was a watery discharge from the rectum during the recovery stage, but no diarrhea on the following day. This experiment was repeated on a second dog under the same conditions, but complete anesthesia was not obtained. I next suggested oil-ether, with the idea of reducing the bulk. Ether is miscible in all proportions in oil. The oil also prevents irritation, and its great affinity for ether prevents a too rapid absorption of the latter; furthermore, when the oil-ether mixture is in the colon, as the ether leaves the oil in gaseous form, heat is extracted from surrounding parts, including the oil-ether mixture and the colon. This cooling checks both evaporation and absorption, and regulates the doses at all times. The difference between the slow absorption from the colon and the rapid elimination from the lungs is the third factor that assists in automatically regulating the anesthesia.

Experiments under the supervision of the junior author were then made to discover if there was any difference in time in the ether separating from the oils. The oils used were olive, cotton-seed, cod liver, neatsfoot, paraffin oils, and Russian mineral oil; also milk and cream. The same quantity of ether and of the oils was placed in separate test tubes and put in a water bath kept at a temperature of approximately body heat. No difference in time was found in the separation of the ether from the different oils.

The experimental procedure with animals was then changed in that the ether was given dissolved in oils and in greater concentration; in one experiment in which 100 c. c. of ether in 250 c. c. of olive oil (i. e., forty per cent) was inserted into a dog of 10 kg., the animal became completely narcotized in one hour, when the whole solution had been inserted. The anesthesia persisted, with a good pulse and regular, deep breathing for forty-five minutes, when the breathing became short and irregular. The respiration gradually became weaker and stopped fifteen minutes later. No effort was made to save the animal. This dog had received a large amount of morphin preliminary to the ether. In two other experiments in which no morphin was given, one dog (weight 6 kg.) received 150 c. c. of a 40 per cent ether solution, and one (weight 6 kg.) 190 c. c. of 40 per cent solution. In neither was complete anesthesia obtained. In the remaining experiments the ether was given in solution in oil from 55 to 75 per cent the amount of ether injected being from 50 to 75 c. c. Ten successful experiments were carried out, with complete anesthesia and no alarming symptoms.

The shortest time required for surgical anesthesia was five minutes, the longest fifty. The duration of anesthesia after the ether insertion was stopped averaged about an hour, except in cases in which the colon was washed out, when recovery set in more promptly. In no case has there been any evidence of more than a mild irritation of the gut following the ether introduction, and this, when present, has disappeared within twenty-four hours. A flushing of the colon with a large amount of fluid has shortened the duration of anesthesia, and the subsequent injection of oil prevented or lessened rectal irritation. The following is the record of an experiment:

Dog, weight 12 kg., given 10 gm. magnesium sulphate in 100 c. c. water by stomach at 10:30 A. M. Morphin sulphate, 0.02 gm. at 3:20 P. M. Rectum washed out at 3:30 P. M. At 3:45, 125 c. c. ether solution (75 per cent in cottonseed oil) injected into colon at a pressure of 20 mm. Hg. At 4:01, complete anesthesia, with no preliminary excitement stage. At 4:05, rectum washed with water. At 4:10, recovery beginning. At 5, animal able to run about. Slight diarrhea during night and following day.

Remarks on the Method.—One of the underlying thoughts in evolving oil-ether anesthesia is to avoid certain dangers that pertain to intravenous anesthesia. The only apparatus needed are a small catheter, a funnel to hold the mixture, and a measuring cylinder. On account of the gradual and equal absorption of the ether from the colon, and of its rapid evaporation from the lungs, it is a comparatively safe anesthesia, provided the same care and attention are given to details as with any inhalation anesthetic. Mucus and saliva are absent, and the patient's lungs and stomach are spared. As yet only ether has been experimented with. The preparation of the patient should be the same as that for ether-vapor anesthesia by rectum. This is most important and is as follows:

Preparation of the Patient.—A cathartic of castor oil should be given the night preceding the operation, followed in the morning by warm water enemas one hour apart until the return is clear. The patient should then be allowed to rest for two to three hours.

Preliminary Medication.—One hour before the introduction of the mixture, 5 to 20 grains of chloretone in a suppository or dissolved in 4 drams of ether and mixed with an equal amount of olive oil are given per rectum with the patient in the Sims position. Both the preliminary and the mixture should be administered very slowly through a funnel which is attached to the end of the catheter which has been well lubricated and inserted 4 inches into the rectum.

As paraldehyd mixes with oil and ether in all proportions, it may be found that two to four drams of paraldehyd with an equal amount of olive oil and given alone is preferable as a preliminary. As isopral, like chloretone, has a slight local analgesic as well as general hypnotic effect, this drug may possibly prove to be superior as a preliminary to the others mentioned. Thirty minutes after the chloretone or paraldehyd has been given, one-twelfth to one-quarter of a grain of morphin with 1/200 to 1/100 grain of atropin is given hypodermatically. For alcoholics and athletes the following is suggested: Two hours before operation give 1/100 grain of hyoscin hydrobromid hypodermatically and one hour be-

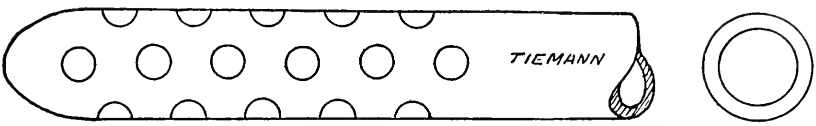


Fig. 180.—Gwathmey Rectal Irrigation Tube.

fore the operation repeat the hyoscin with one-quarter grain of morphin.

Administration.—Twenty minutes after the hypodermic injection, the oil-ether mixture should be given slowly, allowing one minute for each ounce, with the patient in the Sims position in his own bed. If the patient is in a ward the bed should be screened.

It may be administered without exposure of the patient, the rectal tube being introduced between two suitably adjusted sheets. The patient lies

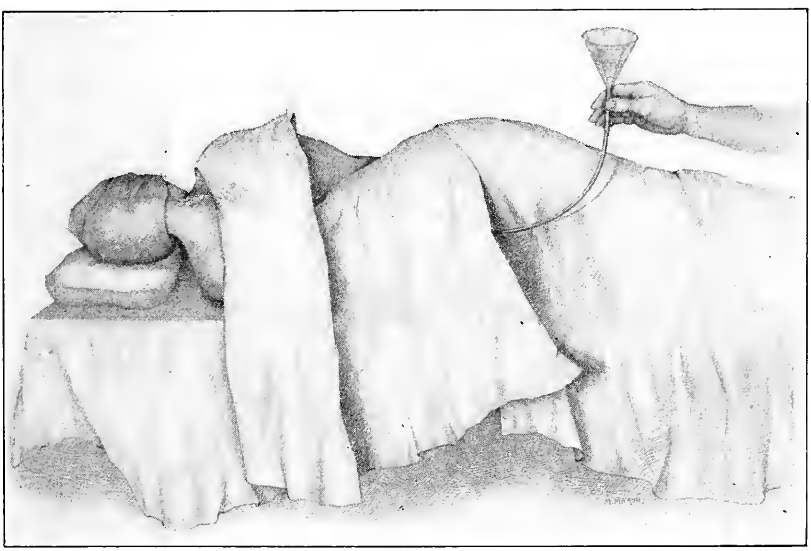


Fig. 181a.—Showing Patient in Position for Oil-ether Administration.

on the left side in perfect comfort, in marked contrast to the disagreeable supine position required for inhalation anesthesia. The preliminary medication, the percentage, and amount of the mixture (roughly, one ounce to every twenty pounds of body weight) vary with the age, size and general condition of the patient. A 50 to 65 per cent solution is sufficient for children and weak, anemic adults, while a 75 per cent solution is usual with normal adults, but this should never be exceeded. The patient should be kept perfectly quiet, not being permitted to talk, and ten to twenty minutes should be allowed for the anesthetic to take effect before the patient is moved. Eight ounces of the 75 per cent mixture will cause the anesthesia to last from two and a half to three hours. No more than eight ounces should ever be given, regardless of the patient's weight.

Control of the Anesthesia.—The anesthetist has good control of the ether at all times. If the patient approaches the danger zone, as indicated by loss of lid reflex, slight cyanosis or stertor, withdrawal of the mixture remaining in the colon will usually immediately remedy the trouble. If this is insufficient, a Connell breathing-tube will usually lighten the anesthesia. If, however, this does not suffice, the patient may be restored to safety by opening a vein and introducing 1,000 to 2,000 c. c. of normal saline solution. If respiratory arrest occurs, a bag filled one-third full of carbon dioxid gas is placed over the face, and with artificial respiration this condition is remedied. If the patient is too lightly narcotized, a towel placed over the face and slightly puckered just above the nose and mouth, but held securely to the face around the edges, will prevent the escape of the ether vapor and induce a certain amount of rebreathing, thus preventing the dilution of the anesthetic with the outside air. In this way the anesthesia is deepened. If this is insufficient, a few drops of chloroform or ether upon the towel will satisfactorily complete the narcosis.

Note: No preliminary medication is needed for children under nine years of age.

Physiology.—When the oil-ether mixture is introduced into the rectum, it requires a very short time to heat the mixture from room to body temperature. When this occurs some of the ether leaves the oil in the form of a gas. It is then absorbed by the blood circulating in the small capillaries surrounding the colon. From this on the physiology is the same as with ether when introduced by the vapor method.

The odor of ether is perceptible on the patient's breath within three to four minutes. The breathing is normal. If stertor commences it indicates unnecessary deepening of the anesthesia. If cyanosis is present, it is evidence of an overdose or an imperfect airway. While the lid reflex is quite active, a very great degree of relaxation exists throughout the whole muscular system. When preliminary medication is given as directed, the pulse remains nearer normal during anesthesia.

Four factors tend to automatically maintain the depth of anesthesia:

(1) The rate of evaporation of the ether from the oil, which is always constant in normal individuals. (2) The distention of the colon. Sutton discovered that when the colon was fully distended not so much ether was absorbed as when it was only partially distended. (3) As the ether

leaves the oil, both the mixture and the gut all cooled off by the process. This retards both elimination and absorption. This process, however, does not noticeably affect the temperature of the patient, which remains constant. (4) The fourth factor is the difference between the absorptive power of the colon and the eliminative capacity of the lungs.

That these four factors, acting harmoniously, produce as even a plane of anesthesia as can possibly be maintained by any other method, is demonstrated by the sphygmographic tracing of a dog under the oil-ether anesthesia for one hour. The pulse and respiratory tracing did not vary during the entire time.

In many hundreds of cases surgically anesthetized by this method in which no supplementary anesthetic was used, the pulse, respiration, reflexes, and blood pressure all remained constant.

When the operation is completed, the rectal tubes already mentioned should be placed in position, as high up the colon as convenient without traumatism, and cold water soapsuds introduced through one tube and drawn off through the other; two to four ounces of olive oil should then be introduced into the rectum and the tubes withdrawn. The patient should be gently returned to bed, with as little jolting or handling as possible; the room should be darkened, and free ventilation secured.

In some of the cases mentioned novocain was injected locally at the site of the operation after the patient came on the operating table. In other cases no local anesthetic was used. Where a local anesthetic is used at the site of the operation, and the ether is administered by the oil-ether rectal method, every principle of anoci-association, as enunciated by Crile, will be fulfilled. The patient awakes quietly, without nausea, vomiting, or pain, the analgesia continuing for some time after consciousness is restored.

Illustrative Cases.—Before the dosage was accurately determined, the following case was given over twice the amount of chloretone necessary as a preliminary, and three ounces too much of the oil-ether mixture; the correct dosage for a patient weighing 100 pounds being chloretone grs. 5, and oil-ether mixture (75 per cent) five ounces.

Case I.—A woman weighing less than one hundred pounds, about thirty years of age, was operated upon for pelvic cellulitis. She was given one-quarter grain of morphin and one one-hundred and fiftieth grain of atropin hypodermatically, and a suppository containing 20 grains of chloretone, as preliminary medication. Eight ounces of a 75 per cent solution of ether in oil was given as the anesthetic. This patient evidently received an overdose of preliminary medication, also of the anesthetic. Respiratory arrest occurred a few minutes after she was placed upon the operating table. Artificial respiration, stretching of the sphincter, and the intravenous introduction of 1,000 c. c. of normal saline were employed. A bag containing a small amount of carbon dioxid was then placed over her face, whereupon respiration recommenced immediately. During the time of respiratory arrest, which lasted eight minutes, the pulse was full, regular, and approximately normal. The color of the lips and tongue was good. The operation was satisfactorily performed, and the patient was returned to bed. An uneventful recovery is recorded, with no nausea, vomiting, or other ill effects.

Case II.—Operation for abdominal hernia. The patient, a woman, aged thirty-seven years, weight about 150 pounds, was given one-quarter grain of morphin and one one-hundred and fiftieth grain of atropin thirty minutes before the operation. At the same time, a solution containing 10 grains of chloretone and 4 drams of ether with an equal amount of olive oil was introduced into the rectum. Just before operation a 75 per cent solution was given to the patient in bed. She sank into deep surgical narcosis before the full amount (8 ounces) was introduced. A slight cyanosis indicated an overdose, therefore three and a half ounces of the mixture was drawn off, as the patient was placed upon the operating table. The relaxation in this instance was perfect; pulse and respiration were about normal. The patient slept for six hours after the operation and awoke without nausea or vomiting.

This six-hour sleep was prior to our discovery that practically the entire unused amount could be syphoned off by massaging directly over the colon from right to left as the lower bowel is irrigated.

Case III.—Private patient; excision of the tongue, floor of the mouth and glands of the neck. On account of adhesions and abnormalities resulting from a cancerous growth, this operation lasted nearly three hours. The patient was a man of about forty-seven years, weighing about 160 pounds. He was given one-quarter grain of morphin with one one-hundred and fiftieth grain of atropin hypodermatically, half an hour before the operation, and ten grains of chloretone in a suppository at the same time. Eight ounces of a 75 per cent mixture of oil and ether were administered. The patient dropped to sleep almost immediately. At the end of one hour the pulse was full and regular, but there was stertor, which perceptibly increased until respiration ceased for three minutes. At the commencement of stertor, the cut-off in the rectal tube should have been removed and the residual mixture allowed to drain off. This would have effectually prevented the respiratory arrest. The rectum was washed out with cold water and as much as possible of the mixture was withdrawn. Respiration recommenced without anything else being done, and the operation was continued and completed without further interruption. When the patient was returned to bed the pulse was 72; respiration, normal. Recovery was uneventful, with no nausea or diarrhea following.

Case IV.—Boy, aged ten years; operation for hydrocele and circumcision. One-twelfth grain sulphate of morphin was given hypodermatically thirty minutes before the operation, and a five-grain chloretone suppository at the same time; between 75 and 100 c. c. of a 75 per cent mixture was introduced very slowly, the patient falling asleep before the full amount was introduced, sleeping quietly through the operation, and making an uneventful recovery.

In children from two to eight years of age, a fifty or fifty-five per cent solution of ether in olive oil has been easily retained, without any preliminary medication, and has been followed by satisfactory anesthesia in ten to twenty minutes. The low percentage absorbed by children is contrary to our laboratory experiments, as the oil does not part with the ether in fifty per cent solutions in a test tube placed in a water bath at the temperature of the body. The difference in the power of absorption from the lower bowel in children and adults would satisfactorily explain this. In adults, eight ounces of ether, with an equal amount of oil, was placed in the rectum with no anesthetic effect whatever.

Case V.—In a girl, nine years of age, 100 c. c. of a 75 per cent solution was given with no preliminary medication. The child complained slightly as the mixture was administered. The operation was for adenoids and enlarged tonsils, and the relaxation was perfect. The child was able to leave the hospital five hours later.

The Sims Position.—*Case VI.*—At the commencement of the series, two patients were anesthetized at Roosevelt Hospital. In each instance, unpleasant symptoms occurred on the introduction of the anesthetic, and in each a supplementary anesthetic was required. These patients received the anesthetic in the dorsal position, which has since been abandoned for the Sims posture.

Regulation of Dosage.—*Case VII.*—A woman, aged thirty-eight, weighing 125 pounds, was operated upon for carcinoma of the breast. The patient was given one-sixth of a grain of morphin, and one one-hundredth of a grain of atropin hypodermatically. Five grains of chloretone, dissolved in two drams of ether and mixed with two drams of olive oil, were introduced into the rectum thirty minutes before the operation. Eight ounces of a 75 per cent mixture were introduced into the rectum in six minutes' time. The patient was in surgical anesthesia four minutes after the total mixture had been introduced. Three ounces were drawn off during the operation, as the patient seemed to be too deeply narcotized. The resultant anesthesia was perfect in every respect, the patient breathing quietly as in natural sleep during the entire time of the operation. An uneventful recovery with no nausea or vomiting followed. Blood and urine analyses proved negative.

Case VIII.—In this instance the patient received one-quarter grain of morphin with one one-hundredth grain of atropin hypodermatically thirty minutes before the operation. No suppository was used, and the patient complained slightly of discomfort in the rectum as the mixture was introduced. The resultant anesthesia was perfect in every particular; pulse and respiration were normal, and prompt recovery without any unpleasant after-effects followed. This patient who had been operated upon twice previously under inhalation methods, and who was able to make an intelligent comparison, stated that, if compelled to undergo another operation, the oil-ether would be the choice of methods.

Comparison with Other Methods.—In Part I of this chapter, Sutton compares ether-vapor colonic anesthesia with other methods. It only remains to compare oil-ether colonic and ether-vapor colonic anesthesia. We can do this effectively owing to the very careful records kept by Sutton and full records of over 500 oil-ether anesthesias administered in New York City by the senior author and others.

(1) One of the greatest advantages of the method is that the anesthetic can be administered to the patients in bed without their knowledge, thus fulfilling many principles of anoci-association as enunciated by Crile. (2) In over 95 per cent of cases there have been no eructations of gas during anesthesia. This is probably due to the pressure in the intestine never being as high as 20 mm. (3) When the patient has been in fair condition, there has been not a single instance of colitis, bloody stools, or blood-streaked returns. (4) The oil-ether narcosis is evenly maintained automatically. (5) Postoperative vomiting, nausea, and gas pains are reduced to a negligible quantity. (6) The patient recovers consciousness in an analgesic state.

Adverse criticisms upon the method have been made by Luke and Coburn, but evidently their technique differed from that outlined by the senior author, and followed by him and others with satisfaction.

Contra-indications.—(a) Whenever ether is contra-indicated *except* when the patient has been ill from a previous etherization. Here it can be given with impunity. In bronchitis and asthma. (b) Colitis, hemorrhoids, fistulæ, and other pathological conditions of the lower bowel. (c) When the patient complains of considerable rectal pain upon the introduction of the solution.

Indications.—(a) Where the element of fear is in evidence, as in goiter and similar cases. (b) Obese individuals with narrowed air passages. (c) For bronchoscopy, gastroscopy, and all operations upon the respiratory tract, head, neck, and chest.

BIBLIOGRAPHY

Gwathmey: 17th Int. Cong. of Medicine, London, 1913 (sub-section VII (b), 163); *N. Y. Med. Jour.*, Dec. 6, 1913, Jan. 31, 1914, and March 28, 1914; *Am. Gen. Surg.*, July, 1914, 268.

Luke, H. C.: *Med. Rec.*, May 9, 1914.

Coburn, R. C.: *Jour. Am. Med. Assn.*, Jan. 31, 1914, 364.

Pate, J. C.: *Ga. Med. Assn. Jour.*, Feb., 1914.

CHAPTER XII

SEQUESTRATION METHOD OF ANESTHESIA

HISTORY.
TECHNIQUE.
INDICATIONS: Brain Surgery; Goiter.
CONTRAINDICATIONS.
MODIFICATIONS IN THE METHOD: Advantages; Disadvantages; Sequestration with the Upright Position.

History.—The ancient Assyrians are supposed to have been the first to attempt anesthesia by limiting the blood supply to the brain when circumcising their children. The procedure was revived by Valverdi in Italy early in the seventeenth century; he attempted to obtain unconsciousness by the compression of the blood vessels of the neck.

This method of inducing the anesthetic state has been used for so long a time and so frequently that it is impossible to say who was the originator. Corning,[1] in 1880, attempted to confine the blood saturated with an anesthetic for a long period in contact with the cerebral ganglia by pressure applied to the carotid arteries, his object being to intensify the effects of the anesthetic. In 1887 he reversed this procedure[2] by cording the thighs of a stout, healthy individual, so as to interrupt both the arterial and venous circulation, thereby cutting off absolutely this amount of blood from the anesthetic. He reports a case of a strong, vigorous patient operated on at the Manhattan Eye and Ear Hospital in New York City, whom it took six to seven minutes to anesthetize with ether on a previous occasion. With this method, by cutting off "one-third of the man" and saturating the remaining two-thirds of the blood mass, the patient was anesthetized in three minutes. Webster then did an iridectomy; the ligatures were removed, and the patient recovered from the effects of the ether instantly. The rapid recovery was witnessed by over half a dozen physicians. Corning states that if he had occasion to test this method again he would ligate the arms as well as the lower limbs.

[1] Corning: "Carotid Compression," 1882.
[2] *Idem.*: *N. Y. Med. J.*, Oct. 22, 1887.

The idea of Corning in employing this procedure was to get the patient under the anesthetic quickly, to maintain surgical anesthesia with a minimum amount of the anesthetic, and to insure rapid recovery from the anesthetic. Corning [1] was acquainted with the procedure of Parry, of Bath, who, in 1792, used compression of the carotids for the alleviation of convulsive disorders, and also that of Blaud, who, in 1819, used compression of the carotids for cerebral engorgements of various kinds. Stroehlin [2] also suggested that tying the carotids on the opposite side to which a convulsion appeared would be of benefit.

Webster [3] further elaborated this idea by suggesting that a certain amount of blood should always be cut off from the body, with the idea of throwing it into the system instantly if alarming symptoms such as cyanosis should suddenly occur.

In May, 1903, Dawbarn [4] applied this method to brain and skull surgery. This method is now known as "sequestration anesthesia." Dawbarn was first led to think of this method from the fact that, in an operation upon an extremity, care is always taken to elevate that extremity and, by gravity and bandaging, to squeeze out all the blood and retain it in the body while the necessary surgical work, such as amputations, is carried on. This method is used by surgeons the world over, but no one attempted to avoid hemorrhage in operating upon the upper trunk or upper extremities. Dawbarn suggested saving blood by reversing this procedure and retaining blood in the extremities, and thereby avoiding hemorrhage at the seat of operation. The method has not received the attention it deserves, and its merits have been tested by comparatively few up to this time.

Technique.—Dawbarn's technique is as follows: "The patient is first thoroughly anesthetized by any pulmonary anesthetic. A towel is then folded lengthwise and wrapped about each thigh very close to the trunk, and upon this the rubber tube is tightened. The towel serves in a measure to prevent subsequent discomfort by spreading the pressure over a wide area. The degree of tightness is quickly learned by practice. It must nearly stop the venous, but not the arterial, current. The limb grows dusky in color, and there is also an obvious swelling. In from five to ten minutes the softened pulse will indicate that you are ready to proceed with the operation. The patient is now placed in the sitting posture, and the operation is begun. The anesthetic given in this way may last from fifteen to thirty minutes. In about fifteen minutes after the commencement of the anesthesia the cords are gradually loosened, and the

[1] Corning: "Carotid Compression of the Brain Arteries," 1882.
[2] Stroehlin: *Thèse de Paris,* 1840, No. 271.
[3] Webster: *N. Y. Med. J.,* Oct. 29, 1887.
[4] Dawbarn: "Sequestration Anemia in Brain and Skull Surgery," *Ann. of Surg.,* May, 1903.

operation is continued, depending upon the anesthetic effects produced from the anemia of the brain. This procedure seems to be perfectly safe, for if any untoward symptoms arise they can be immediately rectified by placing the patient in a horizontal or Trendelenburg position and loosening the cords, when the brain will immediately become filled with blood. The pulse is tested before the tourniquets are applied, so that the softening and lessening of tension will be noticed. Every cut vessel spurts less blood than would otherwise be the case. The limbs corded are warmly wrapped or hot-water bags are placed about them."

Dawbarn states that enough blood can be retained in the limbs to make a striking difference in loss of blood from the operative field, and to constitute, in many cases, the difference between life and death, or shock and absence of shock, in a gravely severe case. The effect is to increase and deepen respiration, the same as if the patient were bleeding from a wound instead of into his own limbs. The cording may be done with a conscious patient before the anesthetic is started, in order to form a reserve guard of pure blood. Dawbarn advises against going to extreme limits, and states that should a tendency toward cardiac weakness be observed, a release of the cordage should be immediate, which will produce a distinct improvement in both the force and number of heart beats. There is no case on record, he says, where absolute stagnation of healthy blood in a healthy limb for half an hour has been followed by gangrene. He prefers, however, to limit the time of cordage to fifteen minutes. His technique for long operations is to tighten the cord in such a way that a small amount of blood is continually entering and some blood escaping into the trunk. If, at any time, the limb grows excessively swollen, or if the patient's pulse demands a change, the tension is lessened. Dawbarn has constricted all four extremities in plethoric individuals, but states that constricting the lower limbs at the groin is sufficient. The blood must be released gradually. He gives several illustrative cases, among which is the following:

Case I.—Excision of cerebellar tumor. Male, age 60. Ether was the initial anesthetic chosen. A glioma was removed. Operation lasted three-quarters of an hour, during which patient took no more anesthetic after being placed in the sitting posture. Slept quietly and without stertor. Recovery was without incident.

Indications.—Brain Surgery.—When the sequestration method is employed, a striking lowering of intracranial pressure occurs. Where a brain tumor is to be operated upon, the safety is greatly increased by thus reducing the pressure.

Goiter.—In thyroidectomy Wyeth also recommends it.

Contraindications.—Dawbarn states that unhealthy blood or blood vessels are contraindications, as the damming of the current of blood by the cording would then become an exciting cause and make sequestration dangerous from venous thrombosis and possible subsequent pulmonary embolism.

Recent typhoid fever, any septic condition of the blood, puerperal sepsis, chlorosis, or severe anemia of any kind, the presence of lime salts in excess, atheroma of the blood vessels, hypertension, arteriosclerosis, and leukemia are all contraindications to its use.

Modifications in the Method.—Where it is necessary, for obvious reasons, to use a minimum amount of the anesthetic, a modification of the sequestration method without cording may be tried. It is a well-known fact that patients are very susceptible to changes in body position while under an anesthetic. Toward the close of any operation, as the surgeon is sewing up the wound, the anesthetic may be discontinued, provided the head of the table is raised in order to keep the patient's head well elevated. It will be found that the anesthesia will be continued for quite a while longer than if this procedure were not adopted. It is also good practice to keep the head elevated by placing pillows under it as soon as the patient is returned to bed. This not only facilitates the continuance of sleep, but it allows mucus or saliva to drain away from the upper respiratory passages, including the olfactory nerve endings, whereas if it remained, it would be apt to cause nausea and vomiting. In recommending this modification, it is taken for granted that the anesthesia has been considerably lightened and that most of the reflexes are present at this time.

The sequestration method is especially valuable in connection with Rose's chair table for the bloodless removal of adenoids and tonsils.

One of the authors gave the anesthetic for Professor Dawbarn in one case in which this method was employed. After inducing anesthesia, the thighs were corded, and the patient was placed in the sitting position upon the operating table. Anesthesia, induced in this way, lasted from ten to fifteen minutes, when a second application of the anesthetic was needed, and the patient was again placed in position for operation. An improvement upon this procedure, of course, would be a continuation of the anesthetic by the vapor method in small amounts, as the operation could then be continued without moving the patient.

Advantages.—Dawbarn sums up the advantages of this method as follows: (1) The diminution in amount of the anesthetic needed; (2) ease of control of hemorrhage; (3) shortening of the operation, because of a dry field; (4) lessened danger of sudden death from pressure upon the respiratory centers; (5) increased depth and frequency of breathing; (6) in brain operations more space between brain and brain case, enabling the operator to work between them in removing old clots requiring curettage or the separation of adhesions, etc., without risk of laceration of the brain surface.

Zoeppritz[1] reports 112 operations, commenting favorably upon its effect upon narcosis, and states there were no ill effects and especially no post-operative vomiting.

Wyeth[2] states: "It has been demonstrated that prolonged and satisfactory narcosis can be induced and maintained by the combination with ether and morphia hypodermically, and nitrous oxid and oxygen, together with the mechanical induction of cerebral anemia by Professor Dawbarn's method of temporarily confining a good portion of the volume of the blood in the extremities. In expert hands, after the anesthetic has been once removed, operations lasting one hour or more have been performed with the anesthetic discontinued, the patient seemingly in natural sleep." Wyeth prefers this method to rectal anesthesia, also for penetrating wounds of the skin and air passages, for the removal of the carotid gland, and for formidable operations about the mouth and ulcers of the tongue. In operations upon the thyroid body, he states that it diminishes the blood pressure in the operative field.

The technique recommended by Klapp,[3] who uses ether by preference, is as follows: The two thighs, not all four extremities (as in the method of Delagenière), are tied near their insertions at the trunk, beginning with the application of a strong compression bandage on each leg, so as to collect a certain amount of blood in the limb. At the end of a few minutes a complete constriction, of the same degree as an Esmarch ischemia bandage, is applied above the congestion bandage. The narcosis is then begun.

Klapp prefers not to begin with ether-drop narcosis, but with a sort of ether-intoxication (*aether rausch*). (See p. 209.) This, or a brief narcosis with ether, is sufficient for small interventions. In prolonged narcosis it is recommended that the lesser circulation be promptly saturated with the ether, the administration being then continued with ether-drop narcosis.

The influence of the diminished circulation, according to Klapp, is much more evident when chloroform is employed. The constriction is preferably made by means of a wide Martin rubber bandage, which is stronger and more elastic than the woven Esmarch ischemia bandage.

Klapp refers to the animal experimentation of Ziegner, which confirmed the accuracy of Corning's idea. He also mentions the work of Hörmann, in Döderlein's clinic, who established the figures of the quantitative requirement of anesthetics, with the diminished as well as the undiminished circulation.

[1] Zoeppritz: *Mitteil. a. d. Grenzgeb.*, 1911, *3*.

[2] Wyeth: "Surgery," 16.

[3] Klapp, R.: "Ueber die Narkose bei künstlich verkleinertem Kreislauf." *Therapeutische Monat.*, Jan., 1910, 14.

Delagenière[1] accomplished this exclusion by means of elastic bandages applied to the bases of the limbs, in such manner as to arrest both the arterial and the venous circulation. Not only the blood contained in the limbs, but the tissues of the limbs as well are excluded, so that they do not become charged with the anesthetic during the narcosis. When the bandages are removed the sequestrated blood and tissues help to bring about, automatically, a rapid dilution of the toxic impregnation of the medulla and the mass of blood. This dilution of the blood impregnated with the anesthetic is accomplished by the excluded blood, which contains no anesthetic, and by the absorption of a portion of the anesthetic contained in the non-excluded blood, through the muscles and other tissues which have been excluded.

General narcosis, with reduced circulation, was carried out in Delagenière's clinical service and in the hospital, 1,144 times with chloroform and 35 times with ether. The results, advantages, and disadvantages noted are summarized as follows:

Advantages.—*The narcosis is more rapid.* The average time required to obtain sleep is only five minutes. The sleep is better, and, as the patient breathes more rapidly, the respiration is more easily watched.

Less chloroform is needed to produce sleep, and especially to maintain it, so that there is a saving of about fifty per cent.

Awakening is more rapid. On an average, the patient awakes at the end of ten minutes, instead of thirty, as in ordinary narcosis. Frequently awakening is instantaneous upon removal of the bands.

Post-operative organic disturbances are diminished. This is perhaps the greatest advantage of the method. The alterative action of the anesthetic is actually diminished, as the toxic agent is taken in smaller quantities and is much more rapidly eliminated. It is therefore a foregone conclusion that all the viscera must be benefited by the method, according to Delagenière. As a matter of fact, vomiting is less common and less abundant. Post-operative icterus and subicterus are much less frequent and less serious.

Post-chloroformic albuminuria practically ceases to exist, so that the sequestration method to a certain extent prevents the danger of post-operative anemia.

Respiratory failure is efficiently controlled through removal of one or several bandages. The excluded blood returns into the circulation, and, as it is at the zero point of chloroform concentration, it accomplishes a favorable dilution, relieving the bulb. Moreover, having become loaded with carbon dioxid during the period of exclusion, it acts upon the respiratory center, stimulating it.

[1] Delagenière: "De l'anesthésie générale avec circulation, reduite ou exclusion des quatre membres dans l'anesthésie générale." *Bull. de l'Acad. de Méd.*, July 25, 1911, 88.

Disadvantages.—The disadvantages are inconsiderable. They consist in tingling sensations in the excluded limbs, lasting a few hours; or small cutaneous ecchymoses, sometimes slight stiffness, or even mild paresis. Phlebitic complications in the lower extremities are perhaps more apt to supervene with this method than with the ordinary method. Among his 1,179 cases, Delagenière observed four cases of post-operative phlebitis of the lower limbs. Three of these four cases concerned gynecological affections, so that the trouble may have been referable to pressure from leg holders, or the border of the inclined plane, upon the veins in which the circulation is more than retarded by the application of the bandages.

As *contraindications,* Delagenière admits only certain cases of myocarditis, or valvular lesions, and certain general infections.

As *absolute indications,* he considers all diseases of the kidneys and of the liver, particularly alcoholism.

Sequestration with the Upright Position.—French [1] is probably the first surgeon to use the sequestration method with the upright position systematically. We quote voluminously from his article:

"The method consists in anesthetizing the patient and at the same time producing congestive hyperemia of the limbs by means of inflated blood pressure cuffs about the thighs and arms (Fig. 180) or thighs alone, to still further reduce the amount of blood in the heart. After beginning with a light pressure of the cuffs upon the thighs alone, which was afterward in other cases gradually increased, we attained at the end of the first operating clinic, in which these tests were made, as high a degree of pressure as we are using now; but it was not until a later occasion that we felt justified in employing the inflated rings upon all four of the limbs at the same time. In the first case in which the trial was made it was found that there was a marked diminution in the amount of blood lost and also that the anesthesia was prolonged after removing the inhaler at the beginning of the operation, to a much greater extent than we had ever known it to be by any other method. And with very few exceptions—in which the conditions were unfavorable —the same experience has been repeated in every case in which the method has been used.

"The sequestration method, in association with the upright position which has been carried out in fifty-eight cases, reduces still further the amount of anesthetic required, and still further the loss of blood. That the amount of the anesthetic is reduced is proved by the fact that full anesthesia has often been maintained for fifteen or twenty minutes after the body was brought to the upright position and the inhaler removed. Indeed, after beginning the operation, in most cases in which this method

[1] French, Thomas R.: "Nitrous Oxid, Essence of Orange, Ether and Sequestration in General Anesthesia." *N. Y. Med. J.,* May 24, 1913.

of anesthesia has been used, except for his assistance in other ways, we have been able to dispense with the services of the anesthetist, which is only another way of saying that during relatively short operations the further administration of the anesthetic has not been needed.

"In quite a number of cases the quantity of blood lost during the removal of adenoid growths and the faucial tonsils (and we use these operations in illustration because the amount of blood usually lost in them is so well known), while sequestration was being applied, was be-

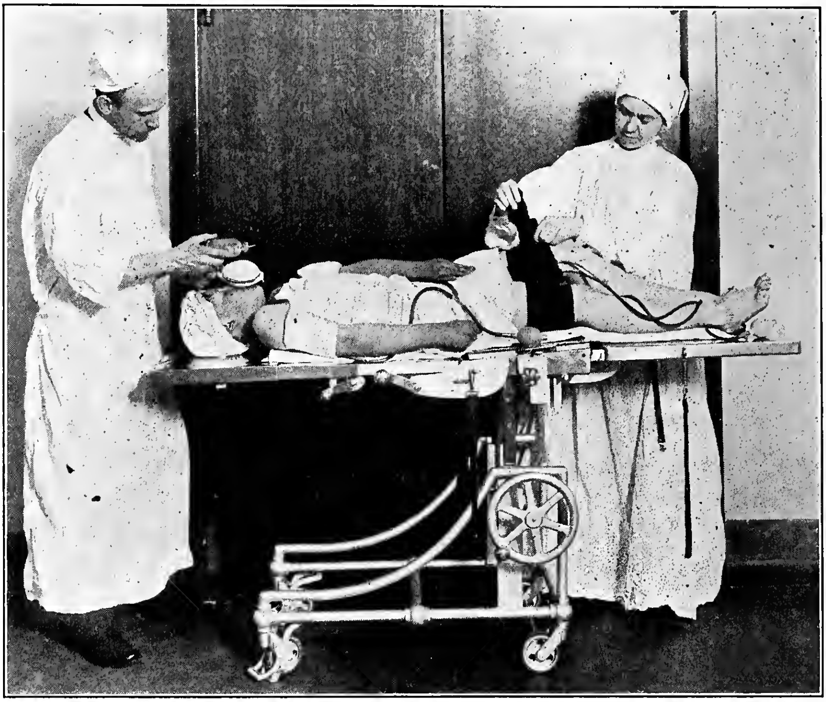


Fig. 181.—Sequestration Method as Used in French's Clinic. White cuffs in place on arms; cuffs being placed on thighs by nurse.

lieved to be less than a drachm. In many of the cases the blood loss, in operations in either the nose or throat, could only be measured by the appearance of the sponges; in most cases it was but slightly in excess of that, and in none was the bleeding as free as in the average case, of similar operative character, under the older methods of anesthesia. It may, therefore, be said that the average blood loss with the sequestration method, whether applied to arms and legs or legs alone, is far below that which occurs without sequestration, and that certain operations, which with the ordinary methods are usually attended with a large loss of blood, may be rendered practically bloodless by the use of the sequestration upright position.

"We had thought of the possibility of secondary hemorrhage being occasioned by the sudden release of the locked-up quantity of blood at practically the same moment that the body was returned to the horizontal position, but, happily, there does not seem to be reason for apprehension on that score, for, after the operations were finished and the bleeding arrested, there was no further hemorrhage in this series of cases.

"The amount of pressure made with the cuffs varied from that needed to effect a slight diminution in, to that needed to produce a complete obliteration of, the pulse in the anterior tibial and the radial arteries, and we feared that the firm pressure required to cause an obliteration of the pulse might produce injury to nervous structures; but in none of the cases could any history of untoward after-effects be elicited. It is quite possible, perhaps even probable, that this can be explained by the comparatively wide distribution of the pressure and the fact that it was made with a flexible air bag. The pressure was maintained in all but the earliest cases, from the end of the induction stage of anesthesia to the time of completing the operation.

"The only patient operated upon since the series of the tests of sequestration was begun, who presented symptoms after operation which suggested a previous injury to the legs, was a very delicate child of five years, about whose thighs the cuffs were applied, but which were not inflated. As the patient was an extremely delicate piece of human mechanism, and the test was in its earliest stage, we regarded it as unwise to expose it to what might seem to be something of a risk. It would, therefore, appear that we just escaped the reputation of having had one harmful effect from this method of anesthesia.

"To be able to administer a smaller quantity of an anesthetic and obtain a full anesthesia; to see the patient enter the anesthetized state without the stage of excitement; to be able to stop the administration of the anesthetic when the body is brought to the upright position and yet have the anesthesia prolonged enough to permit relatively long operations to be performed; to secure a greatly lessened loss of blood; and to insure a reduction in, and in many cases an almost complete abolition of, the disagreeable after-effects is, to say the least, something of a gain, and in a large proportion of cases, with the coöperation of a skillful anesthetist, all of these results are obtainable."

CHAPTER XIII

LOCAL ANESTHESIA AND INTRAVENOUS ANESTHESIA

PART I

LOCAL ANESTHESIA

JAMES F. MITCHELL, M.D.

HISTORY: Adrenalin; Cocain Substitutes; Arterial Injection; Explanation of Poisonous Action of Cocain; Preparation of Solutions; Sterilizing the Solutions; Novocain; Urea and Quinin Hydrochlorid; Syringes; Indications and Scope of Local Anesthesia; Local Versus General Anesthesia; Mortality; General Preparation and Technique; Details as to Comfort of Patient; After-treatment; Healing; Combination of Local and General Anesthesia.

METHODS: Surface Application; Infiltration; The Regional Method; Venous Anesthesia; Arterial Anesthesia.

SPECIAL APPLICATION: Skin; Head and Neck; Face; Ear; Nose and Accessory Sinuses, Tonsils; Eye; Neck; Tracheotomy; Larynx; Thyroid; Thorax and Breast; The Extremities; Genito-urinary System; Circumcision; Rectum; Gynecology; Abdomen; Inguinal Hernia.

HISTORY

The desire to alleviate pain is as old as man; its fulfillment has had to wait long (Braun). Previous to the introduction of cocain but little had been accomplished in attempting to produce local anesthesia for surgical operations. The Egyptians were said to have possessed certain applications for this purpose, but investigation has shown them to have been more superstition than actual fact.

Compression of nerve trunks was probably the earliest method to be of any real service. Originating in antiquity, it was practiced by the Arabs, revived by Paré in the seventeenth century, and throughout succeeding ages one sees it cropping out anew in some special tourniquet or pressure pad, only to be again abandoned. It survives now in the form of the Esmarch elastic bandage, which, it is true, will produce anesthesia of the distal part of a limb. The uncertainty of the anesthesia and the length of time necessary to produce it, the actual pain of the pressure itself, and the danger of gangrene and motor paralysis render it unsafe and impracticable. In slight operations on the fingers and toes, it is often bearable and quite satisfactory, and, in lessening the pain of the first introduction of a hypodermic needle, firm digital compression of the skin is of material assistance.

An Italian surgeon, Severino, through his pupil, Thomas Bartholinus, in the sixteenth century, first called attention to the application of *cold* locally as a means of reducing sensibility. Three centuries later it was again brought into practice by the animal experiments of John Hunter, and in 1807 Larrey, Napoleon's surgeon, reported that in amputations done on the field of battle at very low temperatures (—19° C.) the sensibility of the extremities was completely abolished. In 1886 Sir Benjamin Ward Richardson, an enthusiastic worker for the attainment of local anesthesia, placed this method on a practical basis by the invention of the ether spray. This survives to-day as the *ethyl chlorid spray,* which is more or less widely used for the performance of many minor procedures. Ethyl chlorid, as a freezing agent, was described by Rothenstein in 1867 and reintroduced by Redard in 1891 as a local anesthetic. It is an inflammable gas, but is dispensed commercially compressed into a colorless fluid contained in a cylinder, the nozzle of which is provided with a stopcock. Boiling at 13° C., it evaporates at once at ordinary room temperature. The stopcock is opened and the tube held at a distance of several inches, allowing the spray to play upon the part to be anesthetized until it is white and frozen. The freezing process acts as a terminal anesthetic, and is complete in a few seconds. Applied to nerve trunks, freezing will completely block their conduction of sensation; but this is accomplished only at the expense of great pain. Prolonged or extensive freezing is apt to cause sloughing, and even in limited areas the return of tissues to their normal state is very painful. Its field of usefulness is therefore narrow, and in nearly all cases the injection of some anesthetizing drug is much to be preferred. Both pressure and cold, however, act as aids in intensifying and prolonging the action of injected drugs.

Besides these physical means—pressure and cold—ancient medical literature is replete with instances of *drugs* claimed to produce local loss of sensation. Mandragora, aconite, and a host of others have been exploited as applications to mucous membrane or unbroken skin. All have been discarded as practically worthless.

Electricity came in for its trial as a local anesthetic, and as a means of carrying in drugs was at one time extensively employed. The effect was probably more that of suggestion than of actual medication.

Local anesthesia through the physiological action of special drugs was made possible in 1853 by Alexander Wood, who introduced the *hypodermic syringe,* and thus offered a new means of applying solutions to sensitive parts. Wood began at once with the injection of morphin in the neighborhood of nerve trunks for the relief of neuralgia. Many cases were reported in which local anesthesia was thus produced. The results obtained were due to the general rather than to the local action of the morphin. Many other substances were tried, but none was found satisfactory until *cocain* was introduced in 1884 by Koller. With it begins the development of modern local anesthesia. The earliest clinical demonstrations of the value of cocain were made by Halsted (1884) and Corning (1885). Even at this early stage, Halsted pointed out many of the essential points, and emphasized the importance of intradermal injection and the efficacy of very dilute solutions. Hall and Halsted also demonstrated the fact that injection of a nerve trunk in any part of its course is followed by a sensory paralysis in its entire peripheral distribution, thus paving the way for the neuroregional method, which later was developed by Crile, Cushing, and Matas. To Reclus and Schleich is due the credit of lessening the danger of poisoning by reducing the strength of solutions.

Adrenalin.—The demonstration of the value of *adrenalin* as an addition to solutions of cocain and other anesthetics, as brought out by Elsberg, Barker, and Braun, was an enormous step forward. Adrenalin was first prepared in 1901 in pure form. It is a powerful vasoconstrictor, and in a dilution of 1 : 1,000,000 will produce local ischemia. It takes the place of the physical aids, cold and pressure, and by hindering absorption acts as a valuable safeguard against poisoning. It can be added to solutions drop by drop in the commercial strength (1 : 1,000), or may be prepared with the anesthetizing drug in tablet form.

Cocain Substitutes.—Many substitutes for cocain have been introduced in recent years, chiefly because of their lesser toxicity. Few of these have become popular, *eucain* and *novocain* being the chief survivors. Solutions of *quinin* have been quite extensively used in some quarters, it being claimed for them that their toxicity is almost nothing and the anesthesia produced by them of long duration.

Arterial Injection.—In 1908 Bier suggested a new method of producing local anesthesia in the limbs by the *injection of novocain into a vein,* and in 1909 Goyanes modified this method by making the injection directly into an exposed *artery* instead of a vein. These procedures represent the newest departures in local anesthesia, and will undoubtedly prove to be of great value and wide application.

Explanation of Poisonous Action of Cocain.—*Cocain,* the first drug to make local anesthesia a practical possibility, has been unduly criticized as to the danger of poisoning. This was due at first to the strong solution used and later to faulty technique, too rapid injection, or imperfect control of the circulation. Cocain is a protoplasmic poison, forming with protoplasm an unstable combination which breaks down slowly, after which the tissues return to their normal condition and resume their normal function. That part which has entered into this combination and has exerted its anesthetizing power cannot be absorbed; therefore poisoning can be due only to absorption of the excess, which the tissues are unable to take up. The toxic dose varies with the concentration of the solution and its method of application. Subcutaneously it is stated to be 50 mg., intravenously 2 mg., and intra-arterially ten times this amount. In weak solutions slowly injected, much larger amounts can be used than in concentrated solutions, or with rapid injection. The brain and central nervous system are most susceptible to cocain. Sensory nerves are more rapidly affected than motor. The mildest symptom of poisoning is slight dizziness, and from this there are all grades leading to collapse, convulsions, and death. The inhalation of amyl nitrite is the best antidote for the early symptoms. In considering the question of toxicity of cocain, I can truly state that in a very large experience I have never seen any symptoms which could be certainly attributed to it, nor have I ever seen a real instance of so-called idiosyncrasy. I believe with Bodine that epigastric discomfort, transient pallor, and sweating, often seen at the beginning of an operation, are purely psychic and not toxic, and I have found that these disappear quickly with the administration of a few whiffs of aromatic spirits of ammonia or lowering of the head. I have used cocain almost exclusively, and, except when large amounts are necessary, I see no great advantages in its less toxic substitutes.

Preparation of Solutions.—*Solutions of cocain* are more or less unstable chemically, and do not stand repeated or prolonged boiling. It is better to have freshly prepared solutions in order to insure constant and definite results. They may be boiled once immediately before using without injury. In the preparation of any solution for the production of local anesthesia, certain facts should be borne in mind. Water, forcibly injected into the skin, will produce a transient anesthesia of the edematized area. It is accomplished at the expense of pain, hence the term "anesthesia dolorosa," applied by Liebreich. Chemically indifferent fluids of the same specific gravity and the same freezing point as the tissue fluids, when injected slowly, do not cause pain or anesthesia. Such fluids are called isotonic. Normal physiologic salt solution is an example. Fluids of greater or less osmotic tension cause pain by drawing water from the tissues or by causing them to swell. By the use of isotonic physiologic salt solution as a vehicle for analgesic drugs, the tissues are not injured and recover promptly. The salt solution has no physical effect itself, but allows the drug to act alone. Schleich believed that the edematization of the tissues was the essential factor, and laid little stress on the analgesic drug. This idea has been rather disproved in the development of the method, and more and more dependence has been placed on the analgesic action of the drug. A satisfactory solution should therefore be isotonic with the tissue fluid, and should be capable of control as to absorption. The first condition is attained by the addition of sodium chlorid and the second by adrenalin. Except in special work where application is to be made to mucous membranes, only two strengths will be necessary—one per cent and one-tenth of one per cent cocain. The formulas, as given by Braun, are:

A	Cocain hydrochlorid	0.1	gm.
	Physiologic salt solution (0.9 per cent)	100	c.c.
	0.1% Adrenalin (1:1000)	5	drops.
B	Cocain hydrochlorid	0.05	gm.
	Physiologic salt solution (0.9 per cent)	5.	c.c.
	1% Adrenalin (1:1000)	10	drops.

The one per cent solution is used for the direct injection of nerve trunks, or for local application to mucous membranes. Strong solutions act much more quickly than weak ones; so that, where immediate action is required and the amount to be used is small, as in the removal of warts, moles, or small tumors, this solution may be used to advantage. In more extensive operations, for skin injection and general infiltration, the one-tenth of one per cent solution is used. The adrenalin content not only controls absorption, but prolongs anesthesia, so that the skin is found blanched and anesthetic at the end of two or three hours. The whole amount of either of these formulas may be safely used in a single operation, and I have often used the whole of both. Although such an amount might be considered toxic, the adrenalin control may be relied upon, and a great part of the injected fluid escapes during the course of the operation, or is removed with the tissues which may be taken away. In operations where large amounts are to be used or where extensive edematization is desirable, as in thyroidectomy, solution *A* may be diluted three or four times with salt solution, thus obtaining a strength of from 1: 1,000 to 1: 5,000.

Sterilizing the Solutions.[1]—These solutions, minus the adrenalin, may be boiled just before use and the adrenalin added drop by drop. Cocain solutions stand sterilization in the autoclave very well (20 minutes at 115°—120° C.), and if corked immediately afterward will retain their activity for a long time. A convenient method of preparation is to place the solution in small bottles of one to four-ounce capacity. The bottle is fitted with an ordinary wooden cork, over which is placed a loose hold of cotton covered with gauze, secured by a rubber band around the neck of the bottle. Before placing in the autoclave the cork is

[1] See Chapter XV for Bainbridge's Method.

loosened, without lifting the hood, and as soon as the sterilization is completed the cork is driven in in the same manner. When about to be used the cork and hood are removed together, leaving a sterile surface over which to pour out the solution. A much better method, however, is to have the desired amount of cocain and adrenalin in tablet form. The tablet, prepared according to the formula of Braun, contains cocain hydrochlorid 0.05 gm. (3/4 gr.) and adrenalin 0.00016 gm. (1/400 gr.). Two tablets are placed in a small vial between layers of cotton, for the

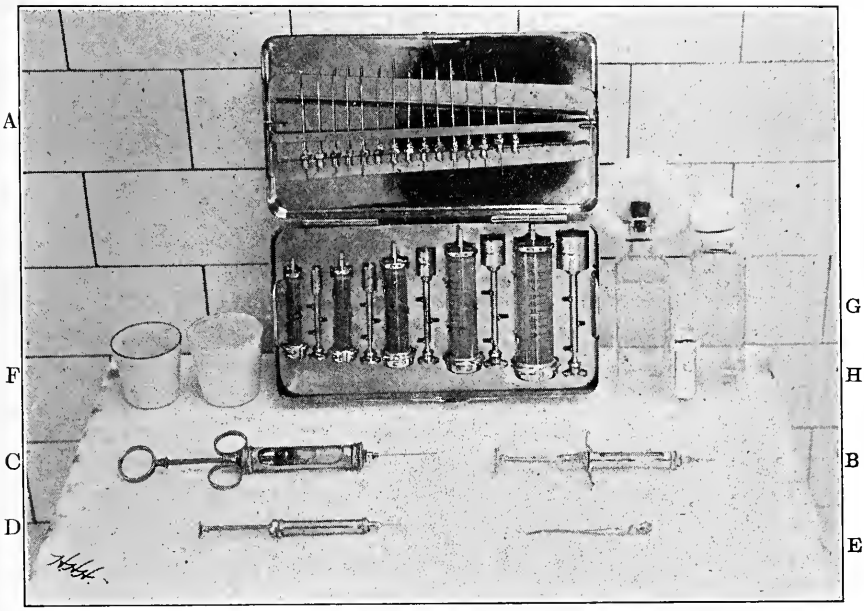


Fig. 182.—Syringes and Solution Bottles for Local Anesthesia.
A, Set of glass syringes of assorted sizes; B, Ordinary hypodermic syringe-glass with asbestos packing; C, Larger syringe of same type; D, All metal syringe; E, Cannula for intravenous anesthesia; F, Porcelain cups for holding sterilized solutions; G, Bottles of sterilized salt solution; H, Vial containing tablets of cocain and adrenalin.

preparation of the two solutions. The vials are plugged with cotton held in place with a gauze hood, and are sterilized by dry heat at 80° C. for an hour on three successive days. Immediately before operation the tablets are dissolved in sterile physiologic salt solution, thus yielding fresh isotonic solutions. One tablet dissolved in 5 c. c. of salt solution makes a strength of one per cent, and in 50 c. c. one-tenth of one per cent. The adrenalin content in the weak solution is about 1:300,000. The salt solution is most conveniently prepared in small bottles sterilized in the autoclave, according to the method given above for the preparation of cocain solutions. Tablets prepared in this way have been kept for many months and both the cocain and adrenalin have been found quite active. This method will be found a great convenience when operations are to be done away from hospital surroundings. Bodine's tubes are also very convenient, and can be obtained already sterilized. Each tube contains cocain hydrochlorid 0.06 gm. and sodium chlorid 0.18 gm. The contents of one tube dissolved in an ounce of sterile water will yield a solution which can be diluted with salt solution to obtain weaker strengths for infiltration. The older solutions of Schleich containing morphin in addition to cocain are no longer used. The morphin is much better given as a hypodermic before operation.

Eucain B has in its favor the facts that its solutions stand boiling well, that it is 3.75 times less toxic than cocain, and that it is mildly antiseptic. Matas states that as much as 8 to 10 gr. remaining in the tissues is well tolerated. It is not as effective as cocain, anesthesia being produced more slowly and wearing off more quickly. For small operations where quick anesthesia is desired cocain is much to be preferred, though when large amounts of solution are to be used eucain may offer an advantage through its lesser toxicity. It is used in the same strength as cocain and may be combined with adrenalin.

Novocain.—Novocain, discovered by Einhorn, was first clinically tested by Braun in 1905. It has been extolled by him in several papers,[1] and has been quite generally adopted. It is now recognized as the best and safest substance for the production of local anesthesia. It is from seven to ten times less toxic than cocain. Its solutions stand boiling and keep for a long time without deteriorating. Its action is increased and prolonged by the addition of adrenalin. It is conveniently supplied in tablet form. The ordinary strength for infiltration purposes is 0.5 per cent, and for the injection of nerve trunks or for rapid results in a small field 1, 2, or 4 per cent. Braun states that as much as 250 c. c. of a 0.5 per cent solution, or 125 c. c. of a 1 per cent solution, can be injected without fear of intoxication, but cautions that in spite of this we should ever bear in mind that novocain is a poison. In the preparation of solutions the same general principles apply as have been described for those of cocain. They should be isotonic, fresh, and absolutely sterile. For ordinary purposes a 4 per cent stock solution of novocain in distilled water may be sterilized, sealed, and kept on hand. This is diluted just before using with sterile normal salt solution and adrenalin added in the proportion of 0.001 gm. to 25 c. c. of the stock solution. The most convenient method is to make up fresh solutions from novocain-suprarenin tablets. The best of these prepared according to Braun's directions contains novocain hydrochlorid (0.125 gm.) and synthetic suprarenin (0.000125 gm.). These tablets are supposed to be sterile; but it is safer to insure sterilization by boiling, which does not destroy the activity of the synthetic suprarenin. One tablet dissolved in 25 c. c. of normal salt

[1] Braun: *Deutsch. med. Woch.*, 1905, *31*, 1667; *Deutsche Ztschr. f. Chir.*, 1911, *3*, 321; *Lokalanæsthesie*, Ed. 3, 1913.

solution gives a 0.5 per cent solution, and two tablets in the same amount a 1 per cent solution. The tablets for the required amount of solution are best dissolved in a small amount of normal salt solution and boiled in a porcelain dish over a flame, and then the necessary amount of normal salt solution is added. It should be borne in mind that one can use with safety a much larger amount of novocain injected slowly in weak solution than in a strong solution rapidly injected, for the same reasons as have been stated for cocain. Novocain is somewhat slower than cocain in its action, and it is therefore wise to wait a few minutes after injecting it before beginning an operation.

Urea and Quinin Hydrochlorid.—This was suggested in 1907 by Thibault as a substitute for cocain. It can be obtained as powdered crystals in tablet form or in solution in sealed tubes. It is claimed for it that after its injection anesthesia appears quickly and lasts for several hours or days, thus eliminating post-operative pain; that its toxicity is practically nothing; and that it causes a deposition of fibrin which serves to prevent post-operative hemorrhage. It has therefore been especially recommended in the removal of tonsils and in operations about the anus and rectum, and as an injection in operations under local or general anesthesia for the prevention of post-operative pain. For application to mucous membranes 10 to 20 per cent solutions are used, while for injection purposes the ordinary strength is 0.5 to 1 per cent. Where prolonged action is desired it is advised to wait from 5 to 30 minutes or longer before beginning the operation. This anesthetic has been tried by many surgeons, and seems to have gained in favor. It has, moreover, some strong advocates, notably Hertzler.[1]

Numerous other drugs have for one reason or another been exploited; but, with the exception of novocain, none is very popular at the present time. It would seem that with cocain, novocain, and quinin all the requirements of local anesthesia of to-day can be fulfilled.

Syringes.—Syringes for injection purposes may be of any type which can be boiled. For ordinary work the usual hypodermic syringes are satisfactory, and for minor operations the all-metal one has proved most economical, and will last for years without need of repair. In more extensive operations and for the intravenous method larger glass syringes are suitable. Sets of them can be obtained with needles of assorted sizes; the syringe barrels being graduated in order to note the amount of anesthetic used. The syringes should be boiled in plain water, and after operation should be carefully dried and a drop of castor oil run into them. This keeps the packing from drying out, and in the case of all-metal or all-glass syringes prevents sticking of the piston. Steel needles are quite satisfactory, and a variety of sizes should be kept on

[1] Hertzler: *J. Am. Med. Assn.*, 1909, *53*, 1393; also "Surgical Operations with Local Anesthesia," 1912.

hand, varying from the short hypodermic needles to those 8 or 10 cm. in length, for deep injections. These should be thoroughly dried after use and a wire inserted in each to preserve the patency of its lumen. Needles of platinum or nickel possess the very distinct advantage of freedom from occlusion by rust, and though expensive are probably more economical because of their longer life. There is no necessity of a syringe larger than one of 20 c. c. capacity. In the days when Schleich's method prevailed and edematization of tissues rather than drug action was depended upon there was more need of such an apparatus as that of Matas. This consists of a graduated bottle containing the anesthetizing fluid under compressed air. The tube to which the injecting needle is attached is controlled by a stopcock, and the fluid can be forced into the tissues in any amount and under any desired pressure. Where several cases are to be done in succession, it would save time and avoid the necessity of repeated punctures.

Indications and Scope of Local Anesthesia.—The last few years have shown a steadily increasing interest in the whole subject of anesthesia. New methods of administering general anesthetics have been developed and the dangers of general anesthesia lessened. The administration of anesthetics has been taken from the hands of the green interne in hospitals, and specialists in this particular branch have developed. Conditions have greatly improved in this respect. Nevertheless there still remains a large field of usefulness for local anesthesia, and in many instances an absolute necessity exists. America, the birthplace of local anesthesia, has left its development to European surgeons, and only lately has shown a revival of interest. One still sees a great deal of skepticism and distrust, which can mostly be attributed to ignorance of the technique and its possibilities. I have seen men attempting operations under local anesthesia who showed from the first needle prick their absolute unfamiliarity with its general principles, and have heard them later express their opinions as to the unsatisfactoriness of the method. American hurry, too, is in a large part responsible. In spite of skill, these operations usually require more time. From the patient's standpoint, the question is different. One rarely hears a patient who has been through an operation in skilled hands condemn the method or select a general anesthetic for a second experience. In our clinic there is a distinctly growing class of patients who demand a local anesthetic. This applies especially to hernia cases, where a general anesthetic is never given. Again, there are those patients of greatly lowered vitality, in whom general anesthesia of itself might be enough to turn the scale downward, who may be safely carried through a serious surgical procedure under local anesthesia. Haste is unnecessary; operations may be much more thoroughly and carefully done than where every effort is bent on shortening the period of anesthesia. Thus in strangulated hernias, especially where the strangulation has lasted some time, I believe local anesthesia imperative, an opinion shared by Lund[1] and Bodine.[2] An important and large class includes a host of minor procedures often considered too trivial for general anesthesia and usually done without any anesthetic—exploratory punctures, opening of furuncles, etc. These can be treated more thoroughly and with vastly more comfort to the patient with the aid of a little cocain. Many persons who would rather bear such ills as disfiguring scars, benign tumors, small anal fissures or hemorrhoids than submit to a general anesthetic will gladly welcome their removal under local anesthesia. When hospital conveniences are wanting or assistants not at hand, as in country practice, a knowledge of the principles of the various local methods will make the apparently impossible an easy possibility. A recent report from an Australian physician,[3] located 115 miles from the nearest medical man, gives an account of such extensive work as hernia operations, external urethrotomy, and complete excision of the glands of the groin repeatedly and successfully accomplished under local anesthesia with cocain and adrenalin.

Local versus General Anesthesia.—Where general narcosis is absolutely contraindicated, as by extensive pulmonary involvement, many operations may be performed by local means without any change in the patient's general condition. In many instances where there are no contraindications whatever to a general anesthetic, the comfort of the patient after operation, the absence of nausea and vomiting, and the additional element of safety are enough to decide in favor of the local procedure. There is no doubt that the blocking of the transmission of nerve impulses from the field of operation is a valuable factor in the prevention of shock. This has been thoroughly demonstrated by Kocher and Crile, who in bad operative risks, when operating under general anesthesia, at the same time shut off the field of operation from the brain by a thorough infiltration with cocain or novocain. Crile[4] states that, "if one combines a complete local anesthesia with a general anesthesia and avoids fear, then it matters not how poor the risk, nor how extensive the operation, the nervous system is wholly protected and the immediate operative risk wholly eliminated." There is no absolute rule; but it is safe to say that, when the field of operation can be made painless and the operative procedure as well carried out under local anesthesia as with general narcosis, local anesthesia may be the method of choice. The question of time may figure largely in this choice, and one of the greatest factors against the local method is the amount of time consumed and

[1] Lund: *Ann. of Surg.*, 1911, *54*, 420.
[2] Bodine: *Ann. of Surg.*, 1907, *45*, 871.
[3] Triado: *Australian Med. Gaz.*, 1911, *30*, 359.
[4] Crile: *Surg., Gyn. and Obstet.*, 1911, *13*, 170.

the greater strain on the surgeon himself. In children and very nervous individuals it is often unsatisfactory. I believe, though, that the very nervous individual is rare who cannot be brought to a neutral state by establishing a condition of mutual confidence which should exist between surgeon and patient, and by a preliminary dose of morphin. I have been able to circumcise a boy of five and operate for hernia on another of ten years with local anesthesia.

Mortality.—Neuber[1] in 1909 collected the statistics of 112 surgeons in Germany, and stated that local anesthesia or the first whiffs of ether were utilized in fully a quarter of all cases that would have required general anesthesia twenty years ago, and that no fatality was reported. Certainly the danger of post-operative pulmonary and renal disturbances is greatly lessened—a most desirable fact in the aged.

General Preparation and Technique.—The general preparation of the patient is the same as for general narcosis; except that, unless especially contraindicated by the nature of the operation, a cup of coffee or a very light breakfast may be taken. It is really better when possible to have something in the stomach. An hour before operation a hypodermic injection of morphin sulphate (gr. 1/6) is given, and to this may be added a small dose of scopolamin (gr. 1/200–1/150). Crile[2] says that "under the influence of morphin and scopolamin no one is a coward, no one is brave, everyone is in a neutral state." The patient should be reassured as to the nature of the operation and its probable outcome, and the surgeon should have the confidence of the patient. When brought into the operating room, instruments and preparations should as far as possible be kept out of sight, and a quiet though cheerful atmosphere should prevail. The recumbent position is the unbroken rule even for the most trivial procedure. The table should be made comfortable by means of a rubber-covered soft mattress and a pad to support the spine. Too much stress cannot be laid on the importance of this pad under the spine, whether the anesthesia be general or local. There is no doubt that nearly all the backache following operations can be avoided by attention to this slight detail.

Details as to Comfort of Patient.—*Sensibility to pain* undoubtedly differs in individuals, and varies with race, age, culture, intelligence, and mental condition. The importance of psychic pain should not be underestimated, and the "moral anesthetist" is a most useful factor. His duty is to record the pulse and to talk with the patient, to divert his attention from the operation or to encourage him as to its progress. An occasional sip of water, a whiff of aromatic ammonia, or a reassuring remark may tide over an important step in the operation or may ward off impending nausea and other psychic phenomena. I frequently allow

[1] Neuber: *Archiv f. klin. Chir.*, 1909, *89*, 1113.
[2] Crile: *Surg., Gynec. and Obstet.*, 1911, *13*, 170.

patients to smoke, and often the anticipation of a promised drink of whiskey will keep their thoughts far from the field of operation. On the part of the surgeon himself, there are certain essentials to success, first of which is plenty of time. He should be able to converse without interfering with his work, an accomplishment readily attained with practice. He must often change his whole style of operating, avoiding the desire for rapid and brilliant work and cultivating tact, patience, self-control,

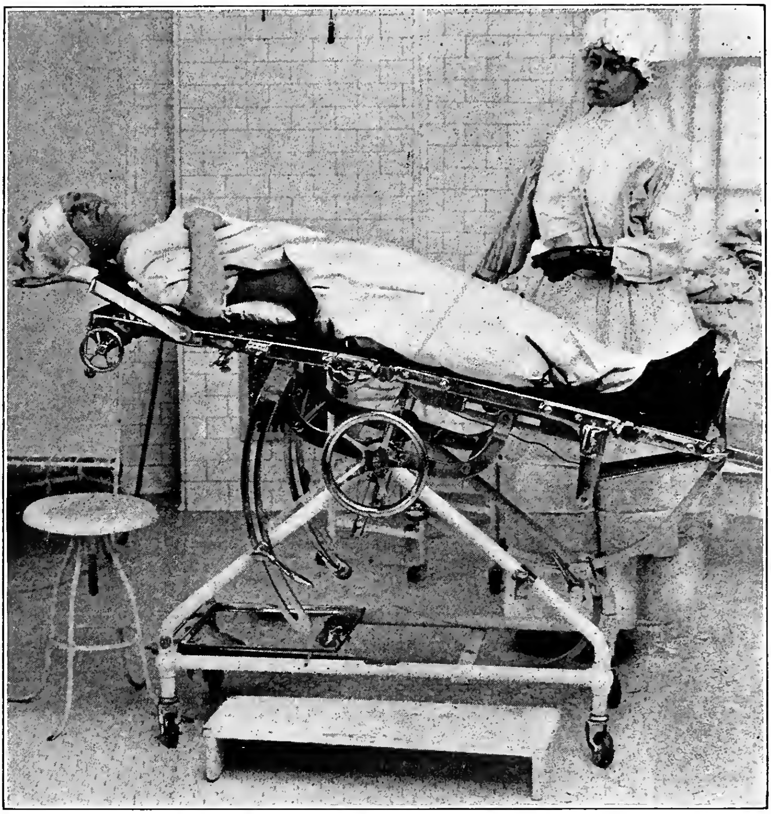


Fig. 183.—Showing Triangular Pad Supporting Back and Sandbag as Support for Feet.

and attention to details. Care must be taken in sponging and in the placing of retractors and their handling by assistants. Haste is always to be avoided, and gentle handling of the tissues is imperative. The accidental clamping of a nerve trunk or traction on some sensitive area in the early stages of an operation is apt to shake the patient's confidence and interfere materially with success. There is demanded then of the surgeon not only familiarity with the course and distribution of sensory nerve trunks, but an accurate knowledge of the sensibility of the various tissues and organs to pain. Much of our knowledge in this respect we owe to the painstaking observations of Lennander.[1] The skin is everywhere sensitive, but varies somewhat in different locations. Once through, the skin, fat, muscle, tendon, and fascia are insensitive, if nerve trunks and large vessels are avoided; likewise bone and cartilage, while periosteum and synovial membranes are exquisitely sensitive. Abdominal organs are not sensitive to pain, but the parietal peritoneum, on the other hand, is acutely so. Bearing these facts in mind, having proper solutions and instruments, the surgeon will find little difficulty in accomplishing extensive operative procedures under local anesthesia, and his success will increase steadily with experience.

After-treatment.—The after-treatment does not differ greatly from that after general narcosis, except that liquid nourishment may be begun immediately, as nausea does not interfere. After abdominal operations it is better during the first twenty-four hours to limit the diet to liquids to prevent distention.

Healing.—Healing is in no way hindered. I have never seen sloughing from the anesthetic except once, when a nurse made up the cocain solution with saturated instead of normal physiologic salt solution. A similar experience is reported by Strobe.[2] If anything, healing is better as a rule than with general anesthesia, a fact which can be attributed to the gentler handling of tissues enforced by the use of local methods.

Combination of Local and General Anesthesia.—While any one of the methods about to be described may suffice for the successful anesthetization of the operative field in individual cases, it often happens that it is necessary to use a combination of methods. It should be remembered also that there are useful combinations of local and general anesthesia. An operation may be started under local anesthesia, and when a procedure is reached which must of necessity be painful some general anesthetic is administered. Under such conditions a few whiffs will often suffice to tide over the painful step, or if it be desired to obtain narcosis this can be done with less anesthetic than would be required ordinarily.

METHODS

The methods practiced in local anesthesia will be considered under the following heads: (1) surface anesthesia; (2) infiltration; (3) the regional method; (4) venous anesthesia; (5) arterial anesthesia.

Surface Application.—Cocain, or other analgesic drug, applied to

[1] Lennander: *Centralbl. f. Chir.*, 1901, *8*; *Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1902, *10*, 38; 1906, *15*, 465; *16*, 19; *16*, 24; also "Tr. Sect. on Surg.," *Am. Med. Assn.*, 1907, 211.

[2] Strobe: *Deut. Ztsch. f. Chir.*, 1909, *99*, 201.

mucous membranes by means of the spray or swab will produce loss of sensibility. Its use in this way is confined for the most part to special work, as laryngology or ophthalmology. Very strong solutions were formerly used (10 per cent cocain), but the tendency now is to reduce the strength. As a matter of fact, 0.5 per cent to 1 per cent is quite sufficient. With these weaker solutions anesthesia appears more slowly, but in time is just as thorough. Here, as elsewhere in local work, one must not hurry, but should wait for 10 to 30 minutes before beginning any step likely to cause pain. Cocain may be applied in this way to produce far-reaching effects, as when anesthesia of the teeth is brought about by the placing of a cocain tampon in the nose.

Infiltration.—By this we mean an artificial edema produced by injecting fluid into the tissues. Anesthesia may be thus brought about physically with plain water or salt solution. The older method of Schleich [1] depended upon the pressure rather than the drug action for its effect, an error which was corrected by the later work of Reclus [2] and others, in which the tissues are injected layer by layer as encountered. Braun [3] accomplishes the same thing by a circumscribing injection through one or more punctures, and aims to anesthetize the nerves before they reach the skin or the field of operation, thus making it unnecessary to separately anesthetize the skin. This naturally requires waiting for from 15 to 30 minutes before beginning the operation. In my experience, it is much more satisfactory to produce a skin wheal in all cases so that the operation may be started almost immediately after the injection, and while the skin is being reflected the deeper injection is taking effect. Bier [4] regards Braun's method as the preferred technique of to-day and novocain (0.5 per cent + adrenalin) as the best drug. He adds that the secret of success in extensive operations lies not only in using the anesthetizing solution freely, but in waiting long enough for it to take effect, i. e., the operation should not be started for at least 15 minutes after the injection. For a circumscribed tumor, for instance, this method is ideal. The line of incision is marked by one or more skin wheals, and through them the whole region about the tumor is freely injected. Then, after waiting a sufficient time, the extirpation can be painlessly done. In many instances, though, the procedure of Reclus—injecting layer by layer as the tissues are encountered—will be satisfactory. Here the sensitive tissues only are injected, and special attention is paid to blood vessels and regions likely to carry sensory nerves. Weak solutions (0.1 per cent cocain or 0.5 per cent novocain) are used for all such infiltrations.

[1] Schleich: "Schmerzlose Operationen," Berlin, 1894.
[2] Reclus: "L'Anesthésie localisée, etc.," Paris, 1903.
[3] Braun: "Lokalanæsthesie," Leipzig, 1913.
[4] Bier: *Archiv f. klin. Chir.*, 1909, *90*, 349.

The Regional Method.—This aims to reach the nerves which supply the field of operation, often at a distance. The anesthetizing fluid is distributed about a nerve trunk so that it is bathed in it (perineural) or is injected directly into its substance (endoneural). This method was first demonstrated by Halsted[1] on the inferior dental nerve for the painless extraction of teeth. It is capable of very wide application, and has been extensively employed by Braun, Crile,[2] Matas,[3] Cushing,[4] and others, who by its use have been able to perform such extensive operations as shoulder amputation or excision of the upper jaw. In *perineural* injection the time required to produce anesthesia, and the thoroughness of the anesthesia, naturally depend upon the size of the nerve trunk and the strength of the solution. Strong solutions (0.5 to 1 per cent cocain) are used about larger trunks, as the ulnar at the elbow. In blocking off a large number of smaller fibers, as the ascending branches in the scalp or the radial nerve about the wrist, the ordinary infiltration solution will suffice (0.1 per cent cocain or 0.5 per cent novocain). In *endoneural* injection the needle is thrust directly into the nerve and the fluid injected until the nerve appears edematous and swollen. The needle should point centrally, as this prevents traction and causes less pain. There is ordinarily no complaint of pain when the needle is introduced. The conductivity of the nerve to all impulses is immediately blocked. Usually the nerve must first be exposed by dissection, but occasionally a superficial nerve, as the ulnar, may be reached through the skin. Here also the strong solutions (0.5 to 1 per cent cocain) give the most rapid anesthesia. Endoneural and perineural injection have had their greatest field of application in the surgery of the extremities for resections, amputations, etc. It seems that they may here in large part be superseded by the intravenous or intra-arterial methods. One of the most useful applications is in the operation for hernia, as first described by Cushing.

Venous Anesthesia.—In April, 1908, Bier[5] presented this new method of local anesthesia for the limbs by injecting novocain into the superficial veins. It is applicable to all operations on the extremities, such as tendon transplantations, joint resections, or amputations. It is contraindicated in cases of diabetic or senile gangrene. The most important point is the production of complete ischemia by means of rubber bandages. The limb is elevated, and a thin rubber bandage tightly applied from the fingers or toes up to a point a short distance above which the vein is exposed. Immediately above this a second Esmarch bandage

[1] Halsted: *N. Y. Med. J.*, Dec. 6, 1884.

[2] Crile: *J. Am. Med. Assn.*, 1902, *38*, No. 8.

[3] Matas: *Trans. Louisiana State Med. Soc.*, 1900, 329; see also, *Phil. Med. J.*, 1900, *6*.

[4] Cushing: *Johns Hopkins Hosp. Bull.*, 1900.

[5] Bier: *Archiv f. klin. Chir.*, 1908, *86*, 1007.

is applied as tightly as possible, being sure to cover a broad surface, as a narrow bandage soon becomes painful. Beginning centrally, the first bandage is removed to a point distal to the field of operation, where a third bandage is tightly placed. The field of operation is then shut off on either side from the circulation. The space between the two bandages should not be less than 10 cm. nor more than 25 cm. In the case of peripheral operations a single central bandage only is applied, but this should not be placed higher than the middle of the forearm or lower leg, except for amputations. The next step is to fill the segment between the two bandages with novocain solution, bringing all the nerve terminals in contact with this solution by means of a reversed venous supply, thus producing a direct anesthesia of the parts lying deeper and beyond the distal bandage. A large superficial vein should be selected, and may be conveniently marked out before applying the bandages—the internal saphenous in the leg or the basilic or cephalic in the arm. A small transverse incision is made under infiltration with cocain or novocain, and the vein dissected free and ligated as high as possible. Using this ligature as a retractor, the vein is lifted up and an oblique incision made into it with scissors. An ordinary cannula is introduced, pointing peripherally into its lumen, and

Fig. 184.—Method of Applying Rubber Bandages for Bier's Venous Anesthesia. (Progressive Medicine, Dec., 1909.)

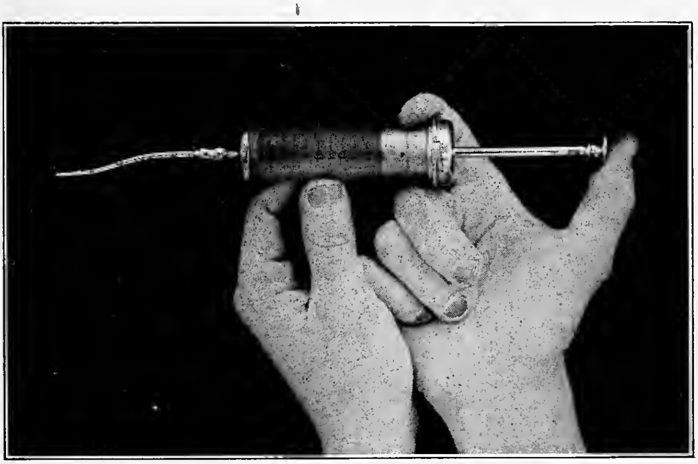


Fig. 185.—Syringe and Cannula for Bier's Venous Anesthesia.

tied tightly in place. The novocain is slowly injected through the cannula, sometimes under considerable force. The cannula may be connected to the syringe by a piece of heavy rubber tubing; but it is easier, as a rule, to fit the syringe directly to the cannula. The superficial veins between the bandages fill out and later collapse, showing that the fluid has passed on. Sometimes a valve offers opposition, but readily yields to the pressure of the syringe. As much as 40 to 50 c. c. of 0.5 per cent novocain without adrenalin may be used in the arm and 70 to 80 or 100 c. c. in the leg. The fluid is prevented from escaping by clamping the connecting tube or the vein itself. In small limbs the segment between the bandages is almost immediately completely anesthetized—direct anesthesia; in larger ones the operation should not be started for a few minutes. In from 5 to 10 minutes there is complete sensory and motor paralysis of the limb peripheral to the distal bandage—indirect anesthesia. Sensory paralysis appears a minute or so earlier than motor. The muscles are flaccid and relaxed. The anesthesia persists as long as the proximal Esmarch bandage is left in place, and disappears soon after its removal. It is necessary therefore to complete the operation before removing this bandage. The bandage in time becomes painful. Bier's longest operation was one and three-quarter hours. The bandage being removed, the cannula is taken out, the vein ligated, and the wound closed. It is unnecessary to attempt to wash out the novocain; for it enters into combination with the tissues, and is returned to the circulation in an altered form. No cases of poisoning have been reported. Adrenalin is, according to Bier, not only unnecessary, but may interfere with the distribution of the anesthetic. Intravenous anesthesia has now been given a fairly extensive trial, and has proven most satisfactory for all operations on the extremities. In traumatic surgery it should find a most useful field. Hayward[1] reports from Bier, 375 operations including amputations and fixation of fractures. Anesthesia was complete in 93 per cent. Kaerger[2] from the same clinic reports another group of 150 cases, and describes the application of this method to minor operations on the hands and feet, a most useful procedure in office or dispensary work.

Arterial Anesthesia.—Goyanes[3] in 1908 first obtained anesthesia of a limb by the injection of an anesthetic into an artery. He later reported a series of operations. The technique is quite similar to that of venous anesthesia, except that, instead of a superficial vein, an important artery is exposed between the two bandages. The artery is not opened, but through a very fine needle thrust into its lumen one injects 50 to 100 c. c. of a 0.5 per cent novocain solution. Anesthesia is complete in from 5 to 15 minutes, and lasts as long as the proximal bandage is in place, with partial anesthesia continuing several hours, thus minimizing post-opera-

[1] Hayward: *Arch. f. klin. Chir.*, 1912, *99*, 993.
[2] Kaerger: *Arch. f. klin. Chir.*, 1912, *99*, 983.
[3] Goyanes: *Centralbl. f. Chir.*, 1909, *36*, 791; *Rev. clin. de Madrid*, 1909, *1*, 12.

tive pain. The novocain enters into combination with the tissues, and is not returned into the general circulation as such. As has been shown experimentally by Oppel,[1] the toxic dose of cocain is much larger intra-arterially than intravenously, so this method should really be safer than the intravenous. There is no apparent effect on the wall of the artery itself. Ransohoff[2] has reported a somewhat similar method, injecting 1 c. c. of 2 per cent cocain into an artery without exsanguinating the limb. This technique would not seem as satisfactory as the injecting of a larger amount of a weaker solution into an empty vessel. The intra-arterial method seems to show no advantages over the intravenous, and has the disadvantage that arteries are more difficult of access than superficial veins.

SPECIAL APPLICATION

As to the application of one or the other of these various procedures to individual operations the discretion of the operator must decide. In certain instances experience has shown the fitness of some particular method, as in Cushing's operation for inguinal hernia; in others, where there is no particular choice, suggestions only can be given. The first thought should be given to the nerve supply of the field of operation and how it can best be reached by the anesthetizing solution. To give the details of the technique in each individual operative procedure would require space far beyond the scope of this work. For the minute working details of special operations references will be given from time to time, while for the more extensive applications one may consult the works of Crile, Matas, Schleich, Bier, Braun, and others.

Skin.—As has been stated in a previous section, the skin may be anesthetized for small incisions by freezing, by pressure, or by infiltration. By far the most satisfactory method is the production of a wheal by the injection of any of the weak solutions which have been discussed. The line of incision should be accurately determined and the injection begun at one end. The skin is picked up between the thumb and finger and firmly compressed. The needle is then quickly thrust in obliquely just beneath the surface, and the fluid slowly injected until the skin turns white. The needle is then pushed along, injecting as it goes, until a wheal has been raised the full length of the needle. The needle is withdrawn and reinserted within the forward edge of the wheal, and this procedure repeated until the whole line of incision is marked by a continuous wheal. In this way the first needle prick is the only painful one. This line is immediately anesthetized, and the incision may be made at once. Careful anesthetization of the skin is very necessary; for if there

[1] Oppel: *Münch. med. Woch.*, Aug. 31, 1909.

[2] Ransohoff: *Ann. of Surg.*, 1910, *51*, 453; *Lancet Clinic*, Aug. 7, 1909.

is pain at the first incision the patient loses confidence. Anesthesia thus produced with 1: 1000 cocain plus adrenalin will last for two or three

Fig. 186.—Beginning of Skin Wheal.

hours. If the method of Braun is used and the incision not made for some minutes, a separate injection of the skin is not necessary. One or

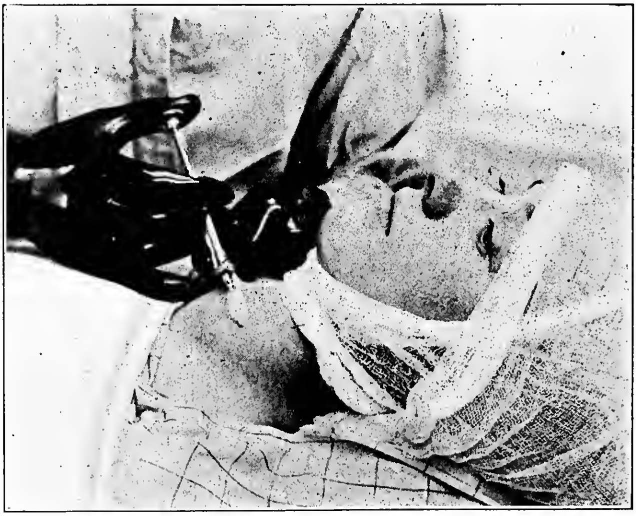


Fig. 187.—Continuation of Wheal.

more small wheals are raised, and through these anesthetic areas the subcutaneous and deeper tissues are injected, thus affecting the nerves before they reach the skin. All injections should be made slowly, as rapid distention of sensitive tissue is always painful.

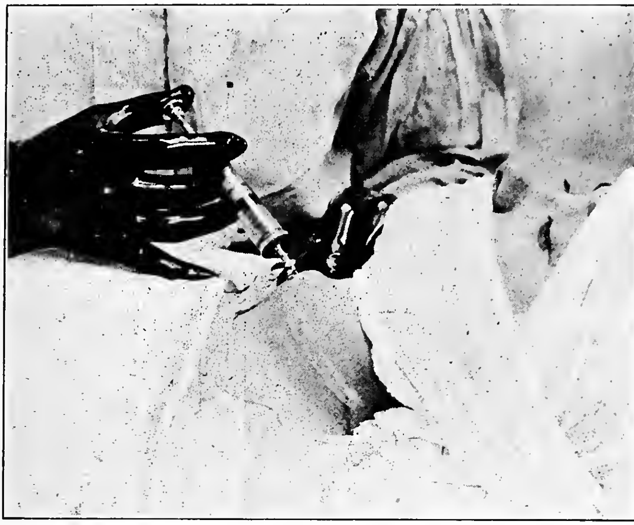


Fig. 188.—Congestion of Wheal and Beginning of Deep Injection.

The *subcutaneous fat* is sensitive only in the vessels and nerve trunks which traverse it. Therefore, after the skin incision is made, these structures may be separately injected and divided. Before a clamp is applied to any such vessel or nerve an injection should be made about it, for pinching is more painful than cutting. With this technique absolutely painless removal of such benign skin lesions as sebaceous cysts, warts, moles, scars, lipomata, etc., can be accomplished. With Braun's circumscribing method it is necessary to wait for some time, while the layer method permits immediate incision, an advantage in minor work. Where a tumor is to be shelled out by blunt dissection, and retraction of the surrounding tissues is required, Braun's

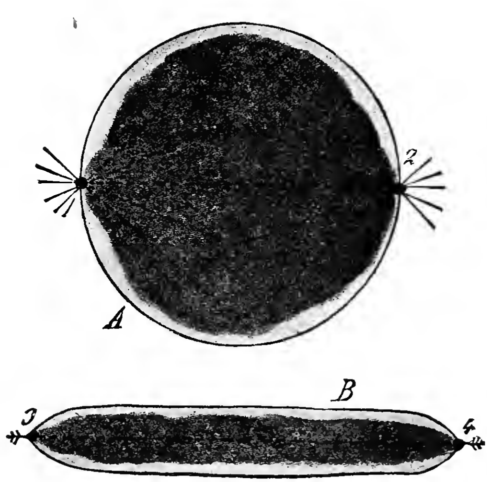


Fig. 189.—Anesthetization of Skin by Subcutaneous Injection, Showing the Wide Area of Distribution Through Two Injection Points. ("The American Practice of Surgery," Vol. IV.)

method is most useful. Here again it must be urged that the essentials for painless work are abundance of the anesthetizing solution and a sufficient interval between its injection and the commencement of the operation. Immediate injection into inflamed skin is extremely painful. In anesthetizing such areas it is important to make the first injection at some distance in normal skin and slowly approach the tender region, or to completely surround the inflamed part with the injection without touching it, thus blocking the nerves at a distance. In this way localized infections may be completely excised, or abscesses opened and drained.

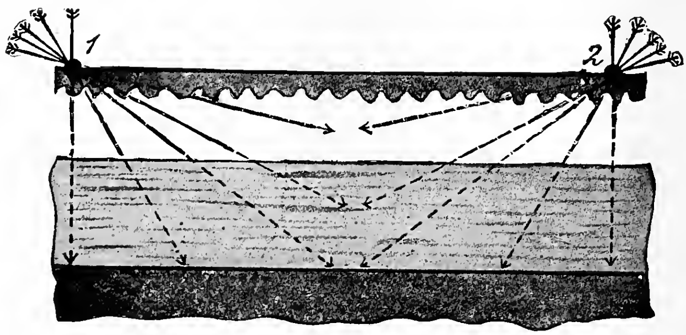


FIG. 190.—INJECTION OF THE DEEPER STRUCTURES THROUGH THE SAME POINTS AS IN FIGURE 189. The arrows represent the needle passing in various directions through skin, subcutaneous tissue, and muscle, to the periosteum. (After Braun. "The American Practice of Surgery," Vol. IV.)

Head and Neck.—In the surgery of the head, face, and neck, with special applications in the throat, nose, eye, ear, and teeth, local anesthesia has a very wide field of usefulness. Attention to the nerve supply will make possible the performance of many extensive operations in which general narcosis is ordinarily required.

The *scalp* with its underlying fascia and periosteum receives its whole nerve supply from below, hence it is possible to render insensitive considerable areas by injecting subcutaneous cross strips below the proposed seat of operation. Ordinary scalp wounds may be repaired by infiltrating about them; and sebaceous cysts and other benign growths removed by infiltration or circumscribing injection. If the periosteum is separately injected and reflected, the skull may be painlessly opened and the surface of the brain examined or even its depths explored. The jarring of the chisel and mallet is unpleasant, but not painful, as I have demonstrated many times in removing osteophytes; but the bone-drill, Gigli saw, or rongeur forceps do not cause any complaint. The brain substance and the dura show no evidence of sensibility to operative manipulation. The treatment of the ordinary compound, depressed fracture, without loss of consciousness, is easy and satisfactory by anesthetizing simply the scalp and periosteum. Cushing[1] has reported the painless removal of a large subcortical cyst without any anesthetic, the bone flap having been freed at a previous sitting. Extensive use of cocain in the scalp was formerly feared because of the danger of absorption, but with the modern pneumatic tourniquet or with adrenalin added to the solution there is practically no risk in using large amounts of cocain or novocain. In cases of delirium or great irritability, head injuries had best be treated with a general anesthetic.

FIG. 191.—NERVE SUPPLY OF FACE AND SCALP FROM THE CERVICAL PLEXUS AND TRIGEMINAL NERVE. 1, N. frontalis; 2, n. supraorbitalis; 3, n. zygomatico-temporalis (trigeminus II); 4, n. auriculotemporalis (trigeminus III); 5, n. auricularis magnus; 6, n. occipitalis minor; 7, n. occipitalis major; 8, n. supra- and intratrochlearis; 9, n. infraorbitalis; 10, ramus nasalis ext. nervi ethmoidalis; 11, n. metalis. (After Braun. "The American Practice of Surgery," Vol. IV.)

Face.—The face offers many possibilities for the local methods. The definite supply of the fifth nerve, with access to its branches at their exit, makes the anesthetization of its distribution an attractive field for nerve blocking. The supra-orbital, infraorbital, and inferior dental are readily attacked at their respective foramina. Plastic operations about the outer ear, the mouth, nose, and eyelids are easily executed with the aid of simple infiltration, and we now do in office practice the majority of operations formerly requiring general narcosis. Postoperative pain is delayed long enough to enable the patient to return to his home and get comfortably settled. A knowledge of anatomy and nerve supply will make possible most extensive procedures, as has been so ably demonstrated by Matas in the painless partial excision of both superior maxillæ by blocking the nerves. Partial removal of the tongue, the cheeks, or gums can be done under infiltration or by blocking the lingual and inferior dental nerves. The technique of blocking the individual branches of the fifth nerve will be found in the works of Offerhaus,[2]

[1] Cushing: *J. Am. Med. Assn.*, 1908, *50*, 847.
[2] Offerhaus: *Arch. f. klin. Chir.*, 1910, *92*, 1.

Braun,[1] and Haertel,[2] who describes the anatomic approach to the Gasserian ganglion by needle puncture. The ganglion is reached through the foramen ovale, and injected with 1 c. c. of 2 per cent novocain-suprarenin solution, obtaining almost immediately anesthesia which lasts about an hour and a half. Haertel reports 16 operations by this method, including six resections of the upper jaw, three of the lower jaw, and two of the tongue. Braun states that under local anesthesia resection of the upper jaw has quite lost its danger. Of ten patients he has lost none, and had no pulmonary complications. Haertel reports nine with equal success. The application in dentistry is given in detail in another section. The lower jaw can be reached, for wiring of fractures, by infiltration with a separate injection of the periosteum, and great assistance may be had from the blocking of the inferior dental nerve. Perineural injection at the mental foramina with submental infiltration will enable one to remove a growth on the lower lip with its area of lymphatic drainage. In elderly persons it is a distinct advantage to carry out this procedure without a general anesthetic. The cervical lymph nodes can thus always be removed. The best routine technique is to first distribute in the submental and submaxillary regions a liberal infiltration of 0.5 per cent novocain-suprarenin solution, and then proceed with the excision of the lip. By the time this is completed and the gloves are changed, anesthesia in the neck is so well established that the dissection can be carried out at will.

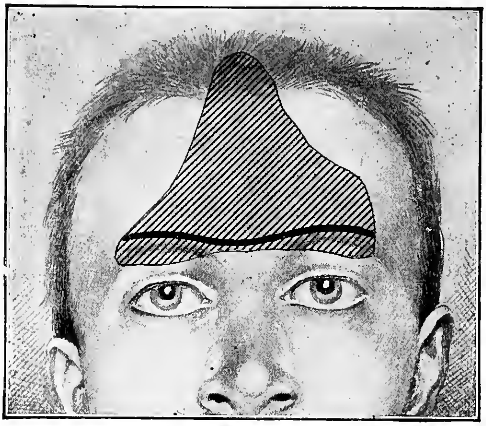


Fig. 192.—Showing the Area of Anesthesia Produced by a Cross Strip of Subcutaneous Injection Above the Supra-Orbital Ridge, Blocking the Nerve Supply from Below. (After Braun. "The American Practice of Surgery," Vol. IV.)

Ear.—The ear, as far as its external part is concerned, can be anesthetized by injections through two points, one close to the superior attachment of the auricle and one below the lobule in the furrow between the mastoid process and the articulation. From these two points the fluid is injected subcutaneously and along the wall of the external auditory canal. This often produces anesthesia of the drumhead as well. A

[1] Braun: "Lokalanæsthesie," 3rd edition, Leipzig, 1913.

[2] Haertel: *Verhandl. d. deutsch. Gesellsch. f. Chir.*, 1911, *1*, 243; also *Arch. f. klin. Chir.*, 1912, *100*, 193.

solution of cocain (1 per cent) and adrenalin applied on a piece of cotton to the drumhead for ten or fifteen minutes will give a sufficient anesthesia for paracentesis.

The mastoid process can be operated upon by periosteal injection,

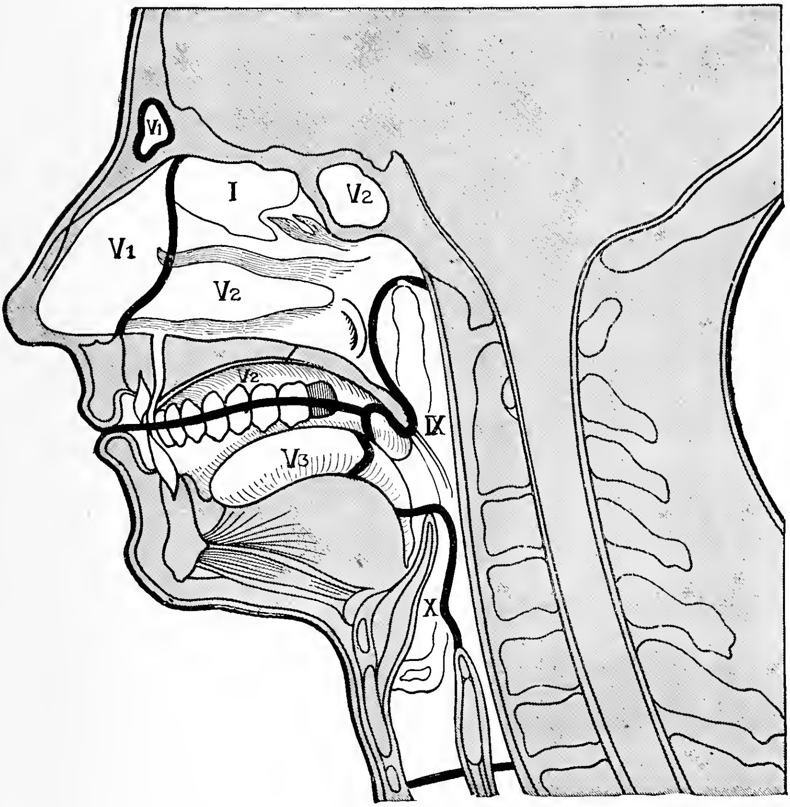


Fig. 193.—Sensory Innervation of the Mucous Membranes of the Head. The areas supplied by the various cranial nerves are indicated by the numbers of the nerves. (After Hasse. Haertel in *Arch. f. klin. Chir.*, 1912.)

and in 1908 forty cases were reported from Politzer's clinic, in which the radical operation was thus done.[1] Unless there is some contraindication, operations upon the mastoid should be left to general anesthesia.

Nose and Accessory Sinuses, Tonsils.—In the treatment of affections of the nose and accessory sinuses cocain occupies a unique position, producing not only satisfactory anesthesia, but, by contracting the mucous membranes, permitting thorough examination and local treatment. It is applied on cotton soaked with the solution and left in place for

[1] Haymann: *Zentralbl. f. Ohrenheilk.*, 1908, 6, 203.

from five to fifteen minutes. The solution ordinarily used is 5 per cent cocain plus adrenalin; but rhinologists are tending now to weaker

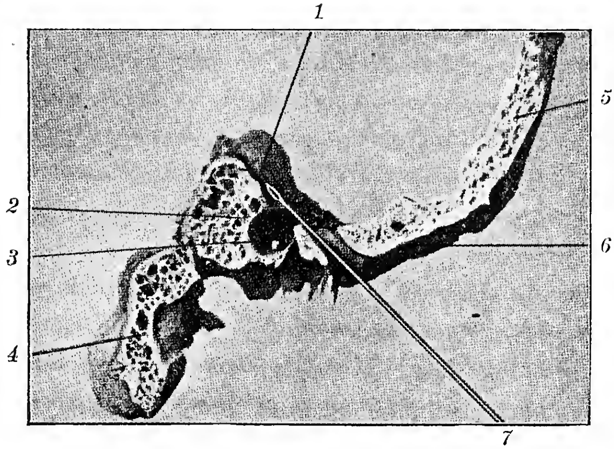


Fig. 194.—Sagittal Section through the Foramen Ovale. The section represents a somewhat obliquely placed vertical plane corresponding to the cannula inserted in the Gasserian ganglion. (1) Gasserian ganglion fossa; (2) Porous portion of temporal bone; (3) Carotid canal; (4) Occipital bone; (5) Anal wing of sphenoid; (6) Infratemporal plane; (7) Cannula in foramen ovale. (Haertel in *Arch. f. klin. Chir.*, 1912.)

solutions, for the same results can be obtained with 1 per cent cocain, except that a longer period of waiting is required. Enucleation of the *tonsils* is in most cases readily accomplished by a thorough infiltration of the peritonsillar area. It has been claimed that there is greater tendency to bleeding after tonsillectomy with cocain and adrenalin, and the method has therefore met with some opposition. Hertzler[1] makes a strong plea for the use of quinin and urea hydrochlorid, claiming that it lessens the danger of post-operative hemorrhage.

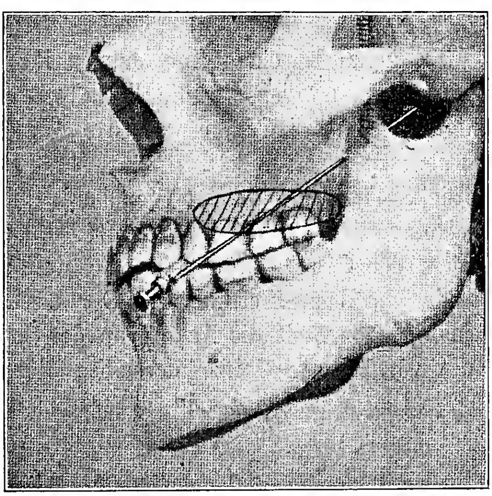


Fig. 195.—Position and Size of Skin Wheal for Puncture of Gasserian Ganglion. (Haertel in *Arch. f. klin. Chir.*, 1912.)

Eye.—The eye was the site of the first practical use of cocain. In many operations upon this organ narcosis has distinct

[1] Hertzler: *Am. J. of Surg.*, 1911, *24*, 351.

disadvantages, and must be very deep in order to destroy sensation. Again the active coöperation of the patient is often desirable. The greater number of all operations are therefore done under local anes-

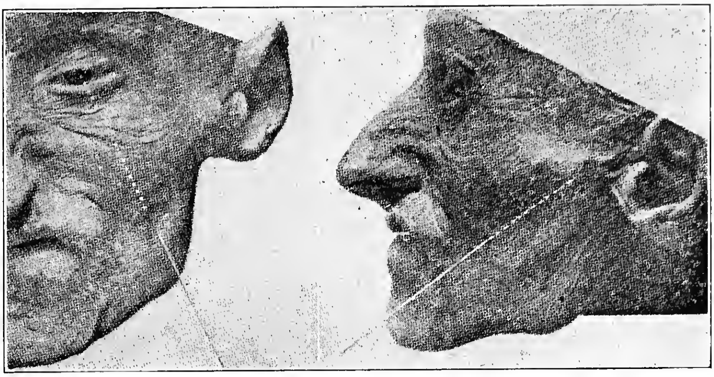


FIG. 196.—FRONT AND SIDE VIEWS SHOWING THE DIRECTION OF THE CANNULA TO REACH THE GASSERIAN GANGLION ACCORDING TO HAERTEL'S METHOD. From the front the cannula points toward the eye; from the side toward the auricular process of the malar bone. (Haertel in *Arch. f. klin. Chir.*, 1912.)

thesia. Two to five per cent solutions of cocain are used, and are applied by dropping into the eye—instillation. Adrenalin increases and prolongs the action of the cocain. Subconjunctival injections are used in extensive operations, and enucleation of the eye can be painlessly done.[1]

Neck.—The greater part of the sensation of the skin and subcutaneous tissue, the fascia and muscles of the anterior part of the neck, is supplied by the branches of the cervical plexus, which can readily be reached along the posterior border of the sternomastoid muscle. The infiltration method, however, finds here a most extensive field of usefulness. Ligation of any of the great vessels can be done with the greatest ease. Benign tumors can be removed and individual glands or groups of glands excised. Complete excision of all the glands is difficult but possible. I have done this several times by blocking of the cervical plexus aided by layer infiltration, the dissection being carried along the

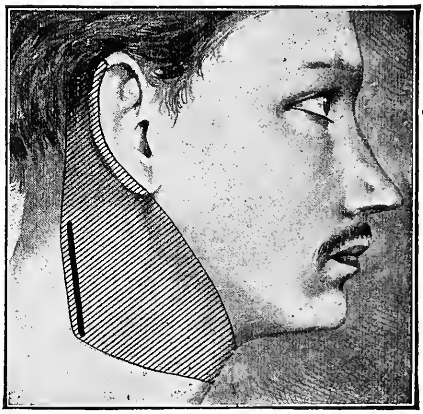


FIG. 197.—AREA OF ANESTHESIA PRODUCED BY BLOCKING THE CERVICAL PLEXUS AT THE POSTERIOR BORDER OF THE STERNOMASTOID MUSCLE. (After Braun. "The American Practice of Surgery.")

[1] Vail: *J. of Ophthal. and Oto-Laryngol.*, Aug., 1911.

jugular vein from the clavicle to the skull. Such dissections, however, are tedious, and unless there is some absolute contraindication, general narcosis is much to be preferred. In extensive malignant disease, as for Crile's block dissection, local anesthesia should not be considered.

Tracheotomy.—In adults *tracheotomy* is by choice an operation for local anesthesia by infiltration. The trachea being opened and its mucous membrane sprayed with cocain, it is possible to explore its lower portion and even the bronchi. The coöperation of the patient may in this way be of great assistance in the expulsion of foreign bodies, so that they may be removed through the tracheal incision.

Larynx.—In operative procedures upon the *larynx* general narcosis has particular disadvantages which may be avoided by the use of cocain. Crile[1] has demonstrated that the reflex-carrying power of the superior laryngeal nerve may be abolished by spraying the mucous membrane with cocain; or the nerve may be reached by infiltration about the tip of the posterior cornu of the hyoid bone. The larynx is readily exposed by infiltration, and may be partially or totally extirpated.

Thyroid.—Kocher, Roux, Bier, and others complete the majority of operations upon the thyroid gland under local anesthesia, and Kocher assigns his low mortality in great part to this fact. Mayo, on the other hand, with his wonderful results, rarely uses local methods. With the recent improvement in the administration of general anesthetics the choice is not so important as it was a few years ago, when deaths under general anesthesia in goiter operations were not uncommon. If one will have the patience to work out the details of operations under the local methods in a few of these cases, he will be impressed with the ease with which seemingly difficult ones can be handled, and many a poor operative risk may thus be brought within the lines of safety. In hyperthyroidism this is especially applicable. These very nervous patients seem to be particularly amenable to the application of the local methods, and it is surprising to see how well they stand even extensive operations when aided by a preliminary dose of morphin or scopolamin.

The ligation of the thyroid arteries in such cases should always be done under local anesthesia. Crile often performs these operations without removing the patients from bed. For the ligation of the *superior thyroid arteries,* or, rather, of the superior poles, on both sides, a single transverse line of skin incision about two and a half inches in length crossing the central part of the thyroid cartilage is infiltrated. Through this a deep injection is made on either side. The incision is carried through skin and platysma muscle. The inner border of the sternomastoid is retracted outward, the omohyoid inward and upward, thus exposing the superior pole of the gland. A linen thread is passed around the pole, including all its vessels. Before this is tied it is well

[1] Crile, Geo. W.: The Laryngoscope (St. Louis), Dec., 1912.

to inject a few drops of 1 per cent cocain about the pole, as the tightening of the ligature is often painful. The *inferior arteries* can best be approached at the posterior border of the sternomastoid muscle just above the clavicle, as recommended by Rogers, the artery thus being secured before it passes behind the carotid. This method will be found much more satisfactory than exposing the artery anterior to the carotid, which necessitates greater retraction and more or less delivery of the thyroid gland. A separate transverse incision is made for each artery, and the ligation is done with practically no pain.

In operations upon the gland itself for the partial or complete re-

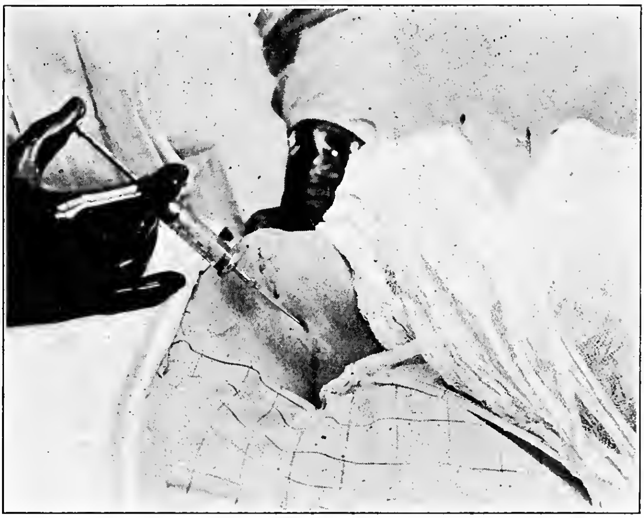


FIG. 198.—BLOCKING THE CERVICAL PLEXUS AT POSTERIOR BORDER OF STERNOMASTOID MUSCLE.

section of a lobe or for the removal of cysts or other tumors, the transverse collar incision is ordinarily used. In this operation one may either anesthetize by Braun's method or by layer infiltration. Bier[1] describes his procedure as follows: "Through anesthetic skin-wheals a subcutaneous injection of the field of operation is made in the form of a quadrant. Then the needle is carried obliquely under the fascia along the border of the sternomastoid, constantly injecting in the direction of the great vessels without reaching them. The needle is introduced upward and downward under the fascia, and in deeply situated goiters the injection is carried behind the sternum. Finally the isthmus is injected. Naturally the needle cannot be passed all the way behind the goiter, but with sufficiently generous use of the fluid (60 to 80 c. c. of 0.5 per cent novocain plus adrenalin) it diffuses everywhere.

[1] Bier: *Archiv f. klin. Chir.*, 1909, *40*, 349.

At times even the recurrent laryngeal may be paralyzed by the novocain. The important point now is to wait a sufficient time before beginning the operation, when the goiter can usually be removed without any complaint of pain."

Another method which has proven quite satisfactory is the following. The line of incision is infiltrated with cocain (1:1000 + adrenalin). Through this a subcutaneous injection of a weaker solution (1:2000 + adrenalin) is carried well above and below, into and under the platysma.[1] An injection of 1 per cent cocain is now made along the posterior border of the sternomastoid to surround the branches

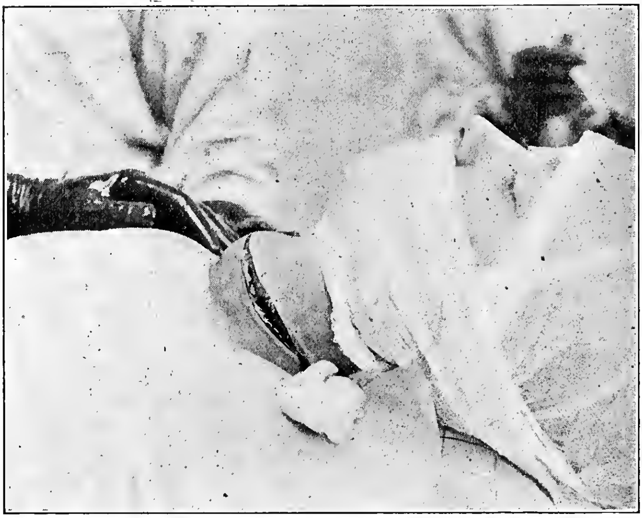


FIG. 199.—INCISION THROUGH SKIN AND PLATYSMA MUSCLE SHOWING ALMOST BLOODLESS FIELD.

of the cervical plexus. This greatly lessens the dragging discomfort so often described when retraction is made or the gland delivered. The incision through the skin and platysma is made, a separate injection being done about each vessel of any size before clamping. The muscles are then retracted or divided and the goiter exposed. An injection of the weaker solution is now made all about the gland, especially about its upper pole. As a rule, no further application of the anesthetic is required. It must be borne in mind that the chief sensitive areas encountered in the actual cutting part of the operation are the skin and the vessels, and that the procedure most likely to cause pain is retraction. The gland itself is not sensitive, and, once exposed, tumors may be painlessly enucleated from it or portions of it excised at will. Braun reports

[1] See Figures 186, 187, and 188.

that from 1908 to 1911 his 150 thyroidectomies have without exception been done under local anesthesia.

The possibilities of extensive operative work in the neck have been greatly increased by the introduction of the novocain-suprarenin solution, because of the enormous amount of the solution which can be used with safety. The special importance of the combination of local and general anesthesia in surgery of the neck has been emphasized by Crile.[1]

Thorax and Breast.—There are two operations in the region of the thorax which in our clinic are always done under local anesthesia, except in very young children: wiring of a fractured clavicle and resection

Fig. 200.—Operation Completed; Wound Closed.

of a rib for empyema or the drainage of abscess of the lung. Other minor procedures, as tapping the pericardium or aspiration of the pleura, so often accomplished at the expense of great pain, may be rendered perfectly painless by the judicious injection of a local anesthetic. Where an aspirating needle is introduced in an intercostal space through a frozen point on the skin there may be intense pain if it happens to strike the periosteum or an intercostal nerve or vessel, and there is always pain when the parietal pleura is reached. The course of the needle may be completely anesthetized by first injecting the skin and then distributing a liberal amount of a weak solution in the intercostal space and about the ribs or in the periosteum and finally in the pleura. A fairly long needle is used and the injection kept up continuously as the needle is pushed in until the pleura is reached. It does not matter if the pleura is penetrated by the needle.

In the *excision of a rib* the injection may be made in the same way

[1] Crile: *Jour. Am. Med. Assn.*, 1912, *59*, 114.

or the tissues may be injected layer by layer as encountered. When the periosteum is reached, it is given a separate thorough injection, then incised and reflected. The division of the rib denuded of periosteum is absolutely painless. The parietal pleura is quite sensitive, and requires a separate injection, but the lung and visceral pleura are not sensitive and may be painlessly incised or punctured.

A *fractured clavicle* may be exposed for wiring in just the same way. Its periosteum being thoroughly anesthetized, no pain is caused by the adjustment, drilling, and fixation of the fragments. As immediate anesthetization is desirable and the amount used is small, 1 per cent cocain is advised, or a liberal injection of the whole neighborhood of the fracture with 0.5 per cent novocain-suprarenin after a few minutes will yield a painless operative field. In complicated fractures with several fragments, perfect reduction can be obtained, and a much simpler and more comfortable dressing may be applied. As there is no need of forced restraint to overcome displacement, the forearm may be left free and the period of disability is materially lessened. The results of this procedure have been most gratifying, and its ease and simplicity are strong recommendations. With careful suturing of skin and subcutaneous tissue the resulting scar is almost unnoticeable.

The *breast* is a poor field for local anesthesia. Its nerve supply is diffuse and abundant. Small benign tumors can be removed by a diffuse circumscribing injection, and exploratory incisions may be made or abscesses opened in the same way. The whole breast can be excised by an extensive infiltration beneath and around it; but large amounts of fluid are necessary, and absorption is rapid. Malignant growths should always be operated under general anesthesia.

In the *axilla,* individual glands and small tumors or abscesses may be treated as in the other parts of the body; but in extensive dissections, because of the rich and diffuse nerve supply and the necessarily painful traction on unanesthetized tissues, general anesthesia is indicated.

The Extremities.—Until the introduction of the intravenous and intra-arterial methods the extremities were fruitful fields for the application of neuro-regional anesthesia. Both perineural and endoneural injections found suitable regions, and by a combination of these with infiltration almost any operation upon the extremities was made possible. The intravenous and arterial methods are so simple and safe that to a large extent they will probably supplant the more complicated procedures, and the anesthesia obtained by them is so satisfactory that many operations are made easy which previously offered serious technical difficulties. The technique has already been given. In many cases the older methods may be simpler and more suitable.

The brachial plexus may be exposed at the scalini and blocked by direct injection, thus making possible amputations or other operations in any part of the arm. Crile[1] has thus done a shoulder-girdle amputation. Kulenkampff[2] has described a method by which he reaches the plexus above the clavicle without incising the skin. He gives anatomic details, and reports 25 cases, in only three of which was a little ether necessary. In the arm the large nerve trunks may be exposed and injected, obtaining anesthesia in the areas of their distribution. This can be done most readily at the elbow. The nerves of the arm are accessible also for perineural injection at various points. The *median nerve* may be reached at the wrist by introducing the needle on the ulnar side of the tendon of the palmaris longus and passing obliquely beneath this

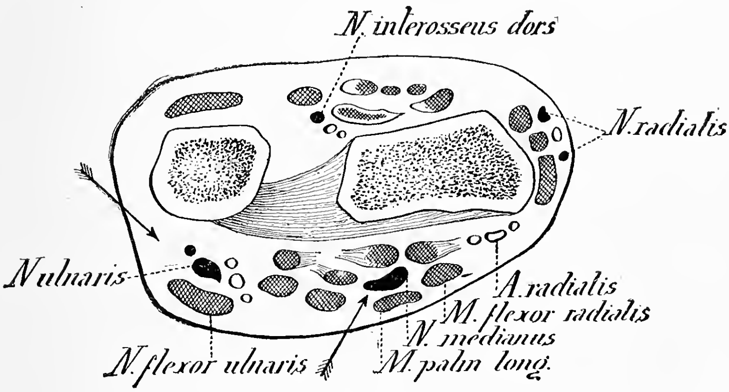


FIG. 201.—CROSS-SECTION OF FOREARM, 5 CM. ABOVE THE WRIST. The arrows indicate the direction of the needle in reaching the median and ulnar nerves for perineural injection. (After Braun. "The American Practice of Surgery," Vol. IV.)

tendon toward the radius, a distance of 1 or 2 cm. The *radial nerve* may be blocked by subcutaneous injection. The *ulnar nerve* may be approached a couple of inches above the wrist by the needle passing between the ulna and the tendon of the flexor carpi ulnaris. Minute details of the anesthesia obtained by injection at various points are given by Braun.[3]

One of the most common applications of the perineural method is in the anesthetization of an individual *finger* or *toe.* Each finger is supplied by four sensory nerves, two anterior and two posterior. These can be surrounded by the solution through two punctures at the base of the finger on the dorsal aspect, the needle being carried close to the bone. The strong solution (1 per cent) is used, and in a few minutes the whole finger can be rendered insensitive. Injections betwen the metacarpals will produce anesthesia of the fingers and metacarpal region as well.

[1] Crile: *J. Am. Med. Assn.,* 1902, *38,* 491.
[2] Kulenkampff: *Zentralbl. f. Chir.,* 1911, *38,* 1337.
[3] Braun: "Die Lokalanæsthesie," Leipzig, 1913.

Many operations on the extremities can be done by infiltration alone. Lerda [1] reports a method for the painless reduction of *fractures* by injecting the region of the fracture freely with a weak solution of cocain and adrenalin by means of a long needle. Anesthesia is complete in 8 to 10 minutes, and in 30 cases there was no pain during the reduction

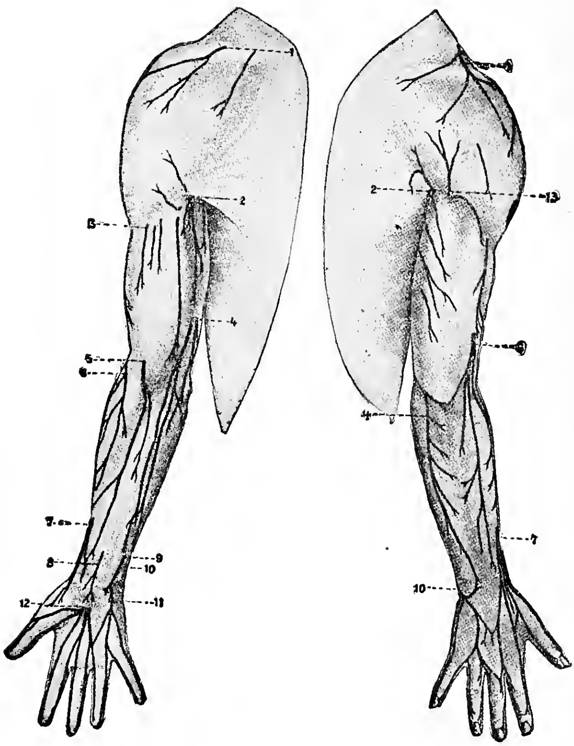


Fig. 202.—Distribution of the Nerves of the Upper Extremity to the Skin Anteriorly and Posteriorly. 1, Supraclaviculares; 2, cutaneus brachii medialis; 3, cutaneus brachii anterior; 4, cutaneus antebr. med.; 5, cutaneus antebr. lateralis; 6, cutaneus antebr. dorsalis; 7, radialis superficialis; 8, ramus palmaris n. mediani; 9, ramus palmaris n. ulnaris; 10, ramus dorsalis n. ulnaris; 11, n. ulnaris; 12, n. medianus; 13, cutaneus brachii lateralis. (After Braun. "The American Practice of Surgery," Vol. IV.)

of the fragments. Where wiring or plating is indicated the bone may in many instances be exposed by infiltration and the periosteum freely injected, when reduction can be painlessly done. This is especially true of the olecranon and patella, which we attack as a matter of routine under local anesthesia. The tibia also lends itself readily to such treatment, and the radius and ulna often without much difficulty. With the addition of nitrous oxid at the moment of reducing the fragments, very extensive fractures may be fixed. In an old lady of 85 years with an

[1] Lerda: *Zentralb. f. Chir.*, 1908, *34*, 1417.

oblique fracture of the shaft of the femur, I was able to expose the seat of fracture painlessly by infiltration. She was then given a few whiffs of nitrous oxid while the greatly displaced fragments were brought into line and secured with a clamp. During the drilling and application of a Lane plate and screws she was conscious and talking, but felt no pain. She was gotten up in a chair on the following day, and left the hospital in six weeks, walking without crutches or cane.

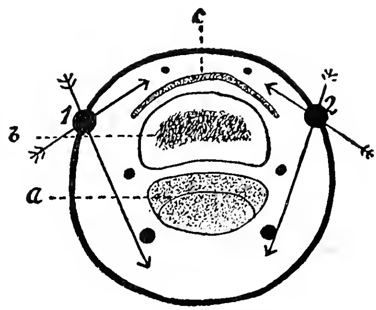


Fig. 203.—Cross-section through Base of Finger. Showing the direction of the needle in anesthetizing the whole finger. a, Flexor tendons; b, bone; c, extensor tendons. The nerves are indicated by black dots according to the size of the individual trunks. (After Braun. "The American Practice of Surgery," Vol. IV.)

Small osteomyelitic cavities can be painlessly gouged out after thorough injection of the periosteum. While the bone substance is insensitive, the medullary cavity of the long bones is sometimes quite the opposite. By means of the intravenous method the great majority of fractures of the extremities

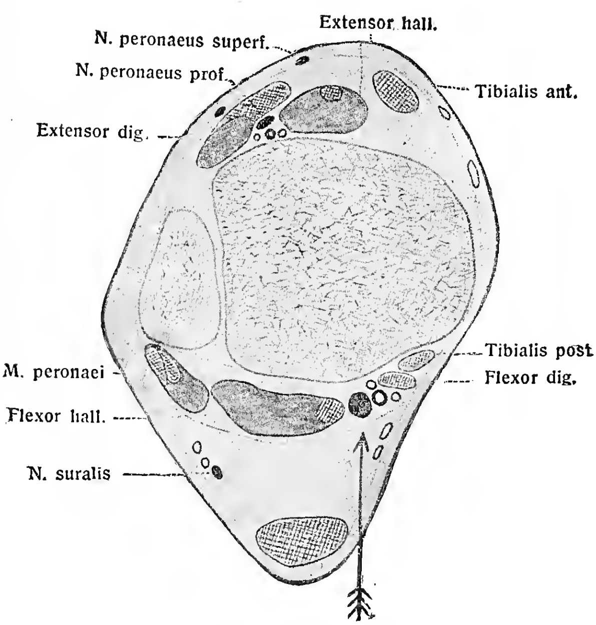


Fig. 204.—Cross-section through Leg Just Above Ankle, Showing Direction of Needle for Perineural Injection of Posterior Tibial Nerve. (After Braun. "The American System of Surgery," Vol. IV.)

can be brought under the domain of local anesthesia for either closed or open treatment.

Fig. 205.—Injection of Skin Incision for Hallux Valgus.

In the *buttocks* and upper part of the *thigh,* local methods are unsatisfactory because of the diffuse nerve supply. The groin, however, is

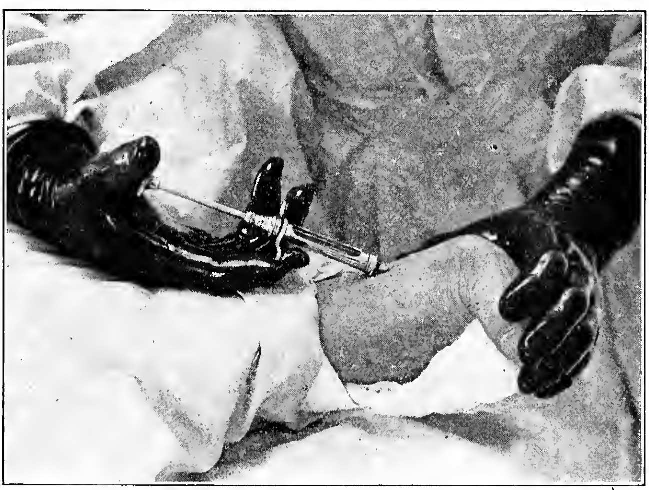


Fig. 206.—Deep Injection Between Metatarsals.

readily invaded by means of diffuse infiltration, and a complete dissection of the glands of this region is not difficult. The sciatic and other nerves of the leg can be utilized for blocking when exposed by dissection. Skin grafts may be cut from the antero-lateral surface of the thigh by blocking the external cutaneous nerves. The posterior tibial nerve can be reached for perineural injection at the internal malleolus by inserting the needle 1 cm. from the median border of the tendo Achillis, passing it directly forward to the posterior surface of the tibia and then withdrawing it slightly and injecting the solution. The various operations

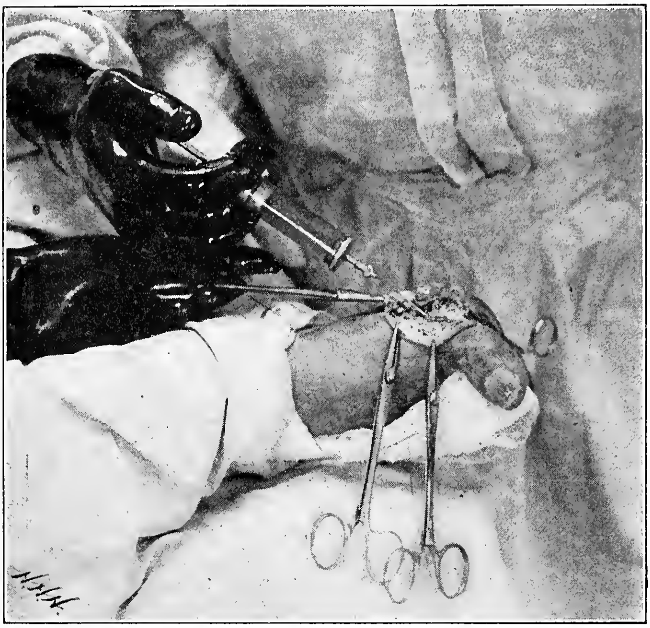


Fig. 207.—Injection of Periosteum.

for ingrowing toe nails can always be done by anesthetizing the toe, as already described. The operation for hallux valgus can be painlessly accomplished by an injection between the metatarsals. Small varices can be excised by infiltration, and by the intravenous method one can do a complete excision of varicose veins of the legs by the open method or by Mayo's stripping procedure. By this method also all *resections of joints* and *tendon transplantation* are possible. It must be remembered when approaching a joint by layer infiltration that synovial membranes are exquisitely sensitive, and a separate anesthetization is necessary. The joint is emptied of what fluid it contains by aspiration, and is refilled through the same needle with 1: 1000 cocain and adrenalin, or 0.5 per cent novocain. In a few minutes it is quite insensitive for exploration or removal of foreign bodies, etc. Laewen[1] in 1911 presented the technique of

[1] Laewen: *Deutsch. Ztschr. f. Chir.*, 1911, *3*, 252.

reaching by puncture the various nerves of the leg. Keppler [1] in 1912 gave further details with the report of cases. Babitzki [2] recently described a method of reaching the sciatic nerve at its foramen, controlling the course of the needle by a finger in the rectum.

Genito-urinary System.—In this field of surgery, as in other specialties, it has been the custom in the past to use unnecessarily strong solutions.

FIG. 208.—RESECTION OF BONE.

The urethra can be anesthetized by applying 1 per cent cocain plus adrenalin and the bladder by running into it 1:1000 cocain and adrenalin, or 0.5 per cent novocain-suprarenin. It is necessary to wait a few minutes to obtain anesthesia. The introduction of instruments for exploration or treatment is then free from pain. Internal urethrotomy is much more painful than gradual dilatation. External urethrotomy by infiltration is quite satisfactory. In suprapubic cystotomy the bladder

[1] Keppler: *Arch. f. Chir.*, 1912, *100*, 501.
[2] Babitzki: *Zentralbl. f. Chir.*, 1913, *40*, 227.

should first be anesthetized and the suprapubic opening made by means of infiltration. Tinker [1] has been able to accomplish perineal prostatectomy by means of infiltration and blocking of the perineal nerves, and Lanz [2] reports similar work. Franke and Posner [3] present a study of the sensory nerves of the pelvis and perineum with the technique of reaching them by puncture. They report ten prostatectomies by their method, all accomplished under absolute anesthesia. The scrotal con-

Fig. 209.—Insertion of Fascial Flag.

tents can be satisfactorily anesthetized by a thorough injection of the cord at or below the external ring. All operations for hydrocele or varicocele thus belong to the routine local anesthesia group.

Circumcision.—Circumcision in adults, likewise, belongs to the same class, and may be considered an office operation. In children it is more difficult, the youngest in my experience being a boy 5 years of age. The mucous membrane may be partially anesthetized by filling the prepuce with 1 per cent cocain and adrenalin and waiting a few minutes. The line of skin incision is then injected with the weak solution, the incision

[1] Tinker: *Jour. Am. Med. Assn.*, 1905, *44*, 471.
[2] Lanz: *Deut. med. Woch.*, 1905, *34*, 953.
[3] Franke and Posner: *Arch. f. klin. Chir.*, 1912, *49*, 139.

made, and the skin reflected. The mucous membrane is now injected with the same solution, the needle being introduced from the skin side. The mucous membrane is slit up the dorsum to the corona and the foreskin rolled back. The circular line of incision in the mucous membrane

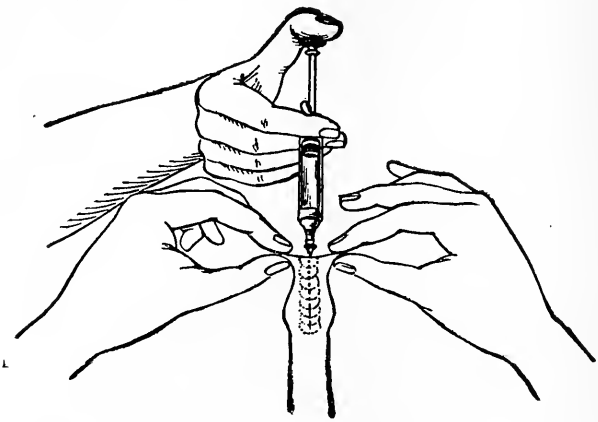


Fig. 210.—Anesthetization of Prepuce in Circumcision. (After Reclus. "The American Practice of Surgery," Vol. IV.)

is now infiltrated, and when the frenum is reached it is given a special injection of a few drops of the strong solution. The mucous membrane is cut away and the sutures inserted. This method is most satisfactory and absolutely painless. Krogius applies the blocking method by inject-

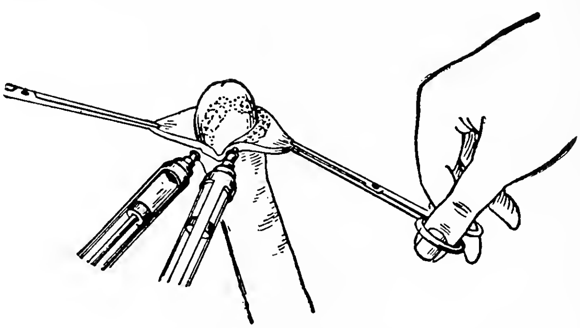


Fig. 211.—Anesthetization of Base of Prepuce in Circumcision. (After Reclus. "The American Practice of Surgery," Vol. IV.)

ing subcutaneously a ring about the base of the penis, while Braun injects 0.5 per cent novocain about the coronary sulcus.

Rectum.—All operations about the anus which do not require dilatation of the sphincter fall readily within the domain of local anesthesia, and with proper technique those requiring dilatation may nearly all be included. As to the anesthetic, many specialists in this line recommend nothing more than sterile water or salt solution, while Hertzler[1] and others are enthusiastic in their claims for quinin and urea hydrochlorid on account of the abolition of post-operative pain, the anesthesia lasting sometimes for several days. I have had no experience with quinin in this region, but have found the ordinary cocain solutions very satisfactory. The anal margin is particularly sensitive, and it is well in attacking it for any operative procedure to begin the skin injection at some little distance in less sensitive skin and gradually work up to the anus by injecting ahead of the needle. In this way external hemorrhoids and superficial fistulæ may be painlessly excised, and even the extensive operation of Ball for pruritus offers no difficulty.

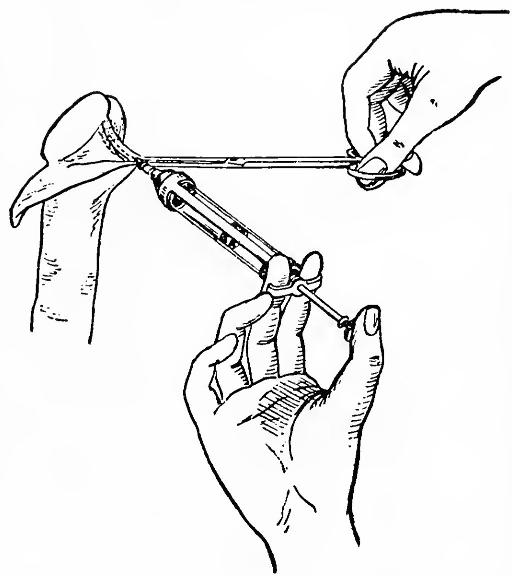


Fig. 212.—Showing Separate Injection of Frænum in Circumcision. (After Reclus. "The American Practice of Surgery," Vol. IV.)

The whole anal region and lower part of the rectum can be anesthetized by a circumscribing injection, so that the sphincter may be painlessly and thoroughly dilated for the excision or cauterization of hemorrhoids, the excision of fissures, etc. The skin is anesthetized about the anus, and through it at four cardinal points one or two centimeters from the anus a long needle is introduced and the weak solution injected. With a finger in the rectum as a guide, the needle is thrust into the substance of the sphincter and along the bowel close to the mucous membrane, injecting always ahead of it. In this way the sphincter is thoroughly infiltrated and the lower part of the bowel encircled by a wall of anesthetizing fluid. In a few minutes dilatation may be slowly proceeded with. I have several times in very poor subjects been able to complete such an extensive procedure as the modified Whitehead operation for the complete excision of the hemorrhoidal area. The rectum is sensitive only in its lower few inches, so that for the treatment of the valves or high ulcers and polyps no further anesthetization is required. For extensive dissection in the ischio-rectal region and in malignant conditions the local methods are not advised.

[1] Hertzler: *Am. J. of Surg.*, 1911, *24*, 351.

Gynecology.—Local anesthesia has not been popular in gynecologic work, nevertheless its possibilities are great, and reports of extensive operations have been made. Most of the classical perineal operations might be done under infiltration. Henrich[1] reports favorable experiences in dilating and operating upon the cervix after thoroughly injecting its substance. Sellheim[2] describes a considerable experience in blocking the pudic nerve for the suture of perineal tears, application of forceps, and various gynecologic operations. Ruge[3] cites numerous vaginal operations and two complete vaginal hysterectomies accomplished painlessly under a simple infiltration with novocain. Kraatz[4] gives an account of 13 cases in which he did the Alexander-Adams operation under local anesthesia. Sampson,[5] and Broese[6] have also reported major gynecologic work under local methods, and Smith and Schwarz[7] describe two cases of Cæsarean section painlessly and successfully accomplished under infiltration with novocain. All of these surgeons support Lennander's views as to the lack of sensation in the pelvic viscera themselves and emphasize the importance of avoiding traction.

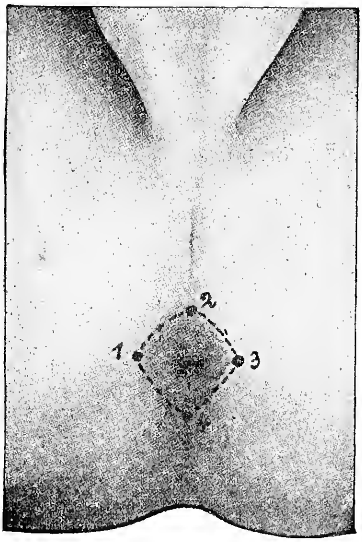


Fig. 213.—Anesthetization of Anal and Rectal Regions. The four dots represent the injection points. (After Braun. "The American Practice of Surgery," Vol. IV.)

Abdomen.—In operations involving only the abdominal parietes without invasion of the peritoneal cavity, little need be said, as the ordinary technique of the infiltration method applies. All the usual incisions for intraperitoneal work are conducted in this way until the peritoneum is reached, when new principles enter, *viz.:* the difference in the sensitiveness of the parietal and visceral peritoneum and the sensibility of the abdominal viscera themselves.[8]

[1] Henrich: *Zentralb. f. Gyn.*, 1909, *33*, 505.
[2] Sellheim: *Zentralb. f. Gyn.*, 1910, *34*, 897.
[3] Ruge: *Zentralb. f. Gyn.*, 1912, *36*, 561.
[4] Kraatz: *Zentralb. f. Gyn.*, 1910, *34*, 1129.
[5] Sampson: *Ann. of Surg.*, 1905, *41*, 216.
[6] Broese: *Zentralb. f. Gyn.*, 1910, *34*, 1523.
[7] Smith and Schwarz: *Surg. Gynec. and Obstet.*, 1910, *11*, 423.
[8] For a discussion of this question see Mitchell: *J. Am. Med. Assn.*, 1911, *57*, 709, where a review of the subject is given with reference to the views of physiologists and surgeons.

We owe to Lennander[1] the determination of the following facts, which, though disputed in part by physiologists and psychologists, still form the best working basis for the guidance of the surgeon in intra-abdominal work under local anesthesia. The parietal peritoneum is intensely sensitive to pain, but not to pressure, heat, or cold. The abdominal viscera, on the other hand, possess no sense of pain. In other words, the visceral peritoneum and the abdominal organs, innervated only by the vagus or sympathetic nerves, are not sensitive to pain, and

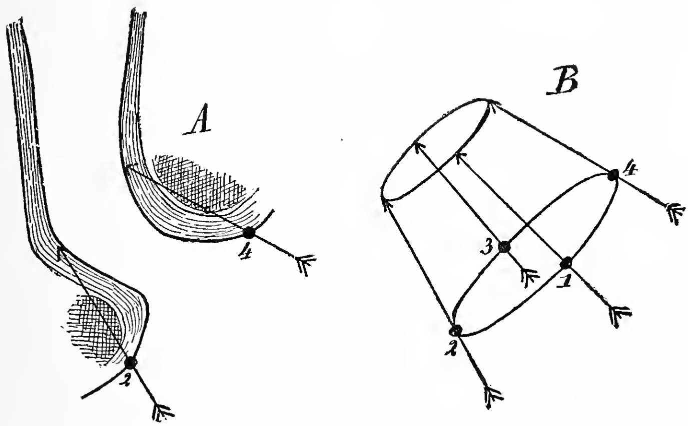


Fig. 214.—Sagittal Section of Rectum, Showing the Direction of the Needle in Anesthetizing the Rectum. A, cross-section, in a vertical plane, of the anus and rectum; in diagram B are shown the four points (1, 2, 3, 4) where the needle should be inserted. (After Braun. "The American Practice of Surgery," Vol. IV.)

painful abdominal sensations are transmitted only by the phrenic, the lower six intercostals, and the lumbar and sacral nerves, which supply the parietal peritoneum. For the mesentery, his findings are not absolute, though he considers it also insensitive.

No one should invade the abdomen without having in mind these points. It can be readily seen that an especially careful technique is necessary and that the parietal peritoneum is to be treated with the greatest respect. Before incising the parietal peritoneum, it, or its subserous connective tissue, should be widely infiltrated to allow retraction, and dragging on it should as far as possible be avoided. The placing of retractors and the force with which they are drawn upon should be carefully regulated. In introducing or removing gauze pads, care should be taken not to rub them over unanesthetized parietal peritoneum. By depressing the viscera in introducing the pads, and then allowing them to come up against the parietes, they may be painlessly placed. In han-

[1] Lennander: *Centralbl. f. Chir.*, 1901, *8*; also *Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1902, *10*, 38; 1906, *15*, 465; 1906, *16*, 19; 1906, *16*, 24; see, also, "Tr. Sect. on Surg.," *J. Am. Med. Assn.*, 1907, 211.

dling the viscera, avoid dragging on the mesenteries or parietal attachments. Incising, suturing, burning, or crushing any part of the gastro-intestinal tract does not cause pain so long as there is no dragging on the parietal peritoneum directly or through the mesentery.

It is evident, then, that in organs lying in apposition to the anterior abdominal wall operations under local anesthesia offer little difficulty. The liver may be painlessly incised with knife or cautery and the gall-bladder opened for the removal of stones or for drainage. The region of the common duct, however, is most sensitive and difficult of approach. Gastrostomy is practically always possible, and gastro-enterostomy, in the absence of adhesions, is not difficult. Adhesions between viscera can be painlessly separated, while the separation of organs adherent to the parietal peritoneum is very painful. The intestines are available for suture, anastomoses, resections, etc. In suspected perforation of the intestine in typhoid fever, an exploratory laparotomy under local anesthesia is acomplished with no risk, and should always be done rather than subject the patient to the dangers of delay while awaiting a definite diagnosis. Typhoid patients make ideal subjects as a rule, and the whole operation, including suture of the perforation, can ordinarily be completed without any further anesthetic. The appendix in interval cases, when free, can be readily removed, as we have demonstrated in many cases. The only pain experienced is in clamping or pulling on its mesentery, when it is referred to the region of the umbilicus. I have been able also by very careful technique to remove some acutely inflamed appendices and even drain deeply situated abscesses after packing off the rest of the abdomen. Inflammation does not alter the sensitiveness of the viscera to operative procedures, but greatly increases that of the parietal peritoneum. In abdominal surgery the combination of local and general anesthesia is often a most valuable one. A little nitrous oxid may be given while those procedures involving the parietal peritoneum or necessitating mesenteric traction are carried out and the rest of the operation done under local anesthesia.

We have found this especially useful for various anastomoses for the relief of ineradicable malignant disease in greatly exhausted patients. In gastro-enterostomy for such a condition of the pylorus, the exploration and demonstration of the condition are made under local anesthesia. Whiffs of nitrous oxid are given while the anastomosis clamps are applied and the stomach and intestines brought into position for suture. The suture itself is painless, and the local anesthesia induced for the incision is sufficient for the closure of the abdomen. Lennander's article is replete with brilliant abdominal work under local anesthesia, and Schley [1] cites some interesting cases, showing what extensive operations may be done in this way. Laewen's method of paravertebral nerve-

[1] Schley: *Med. Rec.*, Dec. 19, 1908.

blocking, reaching the nerves just after their exit, has been applied by Finsterer[1] to abdominal work, and Kappis[2] by the same method has several times removed the kidney. Kappis found that absolute anesthesia could thus be obtained for operations on the gall-bladder and stomach, thus supporting Lennander's view that the vagus is not concerned in the sensory innervation of this region.

Hernia in all its external forms belongs by choice to local anesthesia. When strangulation is present local anesthesia is imperative, for the question of hurry is eliminated, as well as the shock of general narcosis and the danger of drowning from fecal vomitus. Local anesthesia is the rule in our clinic. It is usually demanded by patients, and the knowledge of the method is passed on from one to another. For anatomical reasons simple inguinal hernias are best adapted to the method, but femoral and umbilical are easily maneuvered. Recurrent hernias are often difficult, but with experience comes ease in their management. Age is no bar except for early childhood, my youngest case being a boy of ten. I have recently had a successful and painless operation with uneventful recovery and cure in a man of 96 with a strangulated inguinal hernia. The greatest obstacles are fat and adhesions, because of technical difficulties in the first instance and pain in the latter. As to the thoroughness of the operation, there is no necessity for the altering of any step under the local method, and any particular type of operation can be utilized. The post-operative period is much more comfortable, from the absence of nausea and vomiting. Healing is if anything better. Nerves are respected, thus leaving stronger muscles, and recurrences are no more frequent. Why, then, should a patient be subjected to the added risk and discomfort of an unnecessary general anesthesia? The only reason could be to save time and trouble for the surgeon.

Inguinal Hernia.—The radical cure of inguinal hernia as described by Cushing[3] is one of the most practical demonstrations of the neuro-regional method. With some slight modifications we use this in all inguinal hernias. The skin in the line of proposed incision is infiltrated with cocain (1: 1000) or novocain (0.5 per cent) and adrenalin, producing a wheal. Through this an injection of the same solution is made along its whole length into the subcutaneous tissues. Gentle massage is administered over this injected region for a few minutes—usually while the operator is putting on his gown and the towels are being arranged. The incision at its upper angle is carried through skin and subcutaneous tissue to the aponeurosis of the external oblique. If the incision is completed throughout its whole length at this period, unanesthetized nerve fibers with one or two large vessels will be encountered in the fat, divi-

[1] Finsterer: *Zentralbl. f. Chir.*, 1912, *39*, 601.
[2] Kappis: *Zentralbl. f. Chir.*, 1912, *39*, 249.
[3] Cushing: *Ann. of Surg.*, 1900, *31*, 1.

sion of which is painful. When the external oblique is exposed, the line of the inguinal canal can be seen as a thinned-out area or weak line, which leads to the external ring. An incision is made in this in the line of the fibers of the external oblique, which exposes immediately the ilio-inguinal and ilio-hypogastric nerves. Into each of these, at as high a point as possible, the needle is thrust, pointing centrally, and a few drops

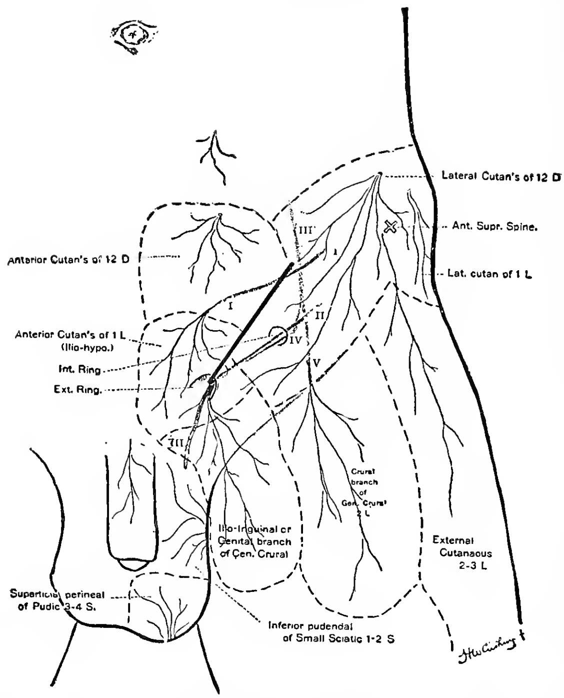


FIG. 215.—RELATIONS OF THE INGUINO-SCROTAL NERVES TO THE HERNIA INCISION. I, Iliohypogastric; II, ilio-inguinal; III, genito-crural; IV, genital branch; V, crural branch. (After Cushing. "The American Practice of Surgery," Vol. IV.)

of one per cent cocain or novocain plus adrenalin injected. From this point on we usually abandon the knife for blunt-pointed dissecting scissors. The skin incision can now be completed as desired, with no discomfort. The division of the external oblique is completed according to the operator's method. We carry it directly through the external ring. The flaps of external oblique are cleared by dissection with scissors and retracted by clamps. The nerves are freed and held aside by one of the clamps on the edge of the external oblique to preserve them from injury. The cremaster is divided in the same line and retracted, thus exposing the sac and cord. An injection of the weak solution is made about the exposed front and sides of the neck of the sac; and between the elements of the cord a few drops of the strong solution are diffused. In small hernias the neck of the sac may be completely injected at this point, but in larger ones it is impossible to reach the deeper part. The sac is now opened in front, its edges held apart with clamps, and the contents inspected and reduced or excised as occasion demands. We have frequently excised large portions of omentum or removed the appendix, and in cases of strangulation have resected the intestine. The posterior line of the neck of the sac can now be seen as a thickened white band. This is injected with the weak solution, completing the injection of the neck. The injection is carried well up above the neck of the sac. The sac is now divided at its neck, the neck is freed and closed with a purse-string suture. Traction on the neck of the sac is to be carefully avoided; for being parietal peritoneum it is exquisitely sensitive, and its disturbance causes not only pain, but often nausea and vomiting. The removal of the lower part of the sac after this division is not painful. The subsequent steps of the operation, depending on the surgeon's choice of method, may be carried out as under general narcosis, once the sac is disposed of. Bodine [1] considers the ilio-inguinal nerve as the only one necessary to inject. Bier [2] and Braun [3] hold that injection of nerves at all is superfluous and unnecessary, and prefer to make an injection of the whole area through the skin and to wait fifteen minutes or more to obtain anesthesia by diffusion of the fluid about the nerves and sac. I have not found

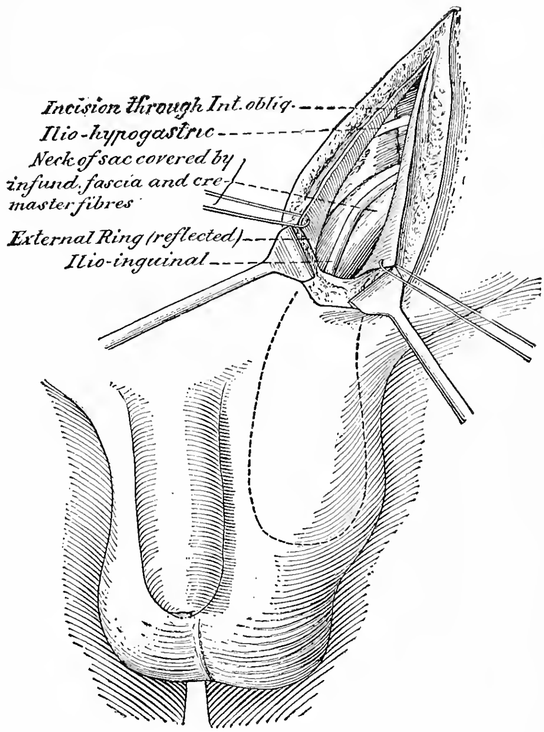


Fig. 216.—Sketch Showing Usual Situation of Nerves as Exposed After Division and Reflection of the Aponeurosis of External Oblique Muscle. (After Cushing. "The American System of Surgery," Vol. IV.)

[1] Bodine: *Med. Rec.*, 1905, *68*, No. 17.
[2] Bier: *Archiv f. klin. Chir.*, 1909, *90*, 349.
[3] Braun: "Die Lokalanæsthesie," Leipzig, 1913.

this method as satisfactory as that of Cushing. The injection of the individual nerves adds little trouble. The nerves are subject to variation in their course, but not enough to materially interfere, and can usually be located with little difficulty. Cushing's sketch shows their usual distribution. An advantage in Cushing's method is that the operation can be begun almost immediately after the skin injection is completed.

Recurrent hernias were formerly considered as necessitating general narcosis. For the past few years we have been doing them all under

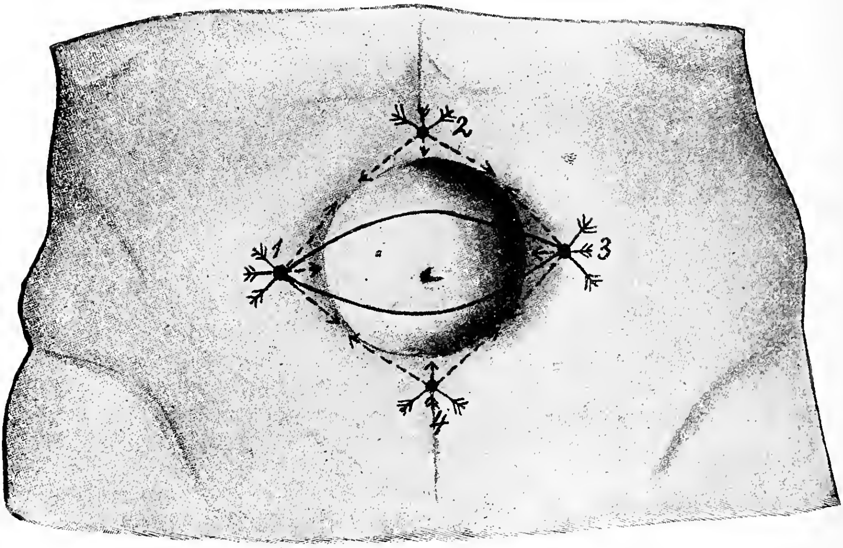


Fig. 217.—Scheme of Injection in Large Umbilical Hernia. The figures indicate the injection points; the arrows and dotted lines show the directions of the needle, and the solid lines the incision. This represents a characteristic example of the circumscribing blocking method of Braun. ("The American Practice of Surgery," Vol. IV.)

local anesthesia, and find them a little more troublesome, although, in most cases the method of the original operator being unknown, the anatomical relations may be at first a little confused. In such cases it is best to carry the incision higher and block the nerves well above the former field of operation. The region is then anesthetized, and the dissection of scar tissue made easy and painless.

Femoral hernias, if small, can be readily treated by simple layer infiltration. In larger hernias, or where strangulation is present, the incision is carried up above the external ring, a small incision made in the external oblique, and the ilio-inguinal nerve blocked with 1 per cent cocain. With the anesthesia produced in this way and a generous infiltration with the weak solution above the sac, no difficulty is experienced.

Umbilical hernias can practically always be repaired under local anesthesia, and the large ones in very fat women demand it. For ordinary ones the circumscribing injection of Braun with separate injection of the skin is satisfactory. I prefer local anesthesia in all cases, and use the layer method of infiltration with the overlapping closure of Mayo. Even the largest are adapted to this form of treatment. Occurring as they do in very fat individuals—bad risks under general narcosis—they make a striking tribute to the value of local anesthesia. I did such an operation four years ago on a woman weighing over three hundred pounds, using throughout a solution of 1:2000 cocain plus adrenalin. Two skin incisions over 30 cm. long, including between them a large area of skin and fat to be excised, were made transversely. The sac was opened without attempting to free it from the overlying skin. It was filled with many feet of adherent large and small intestine and omentum. The neck of the sac, about 15 cm. in diameter, was thoroughly infiltrated with the cocain solution. The contents were freed and reduced. The sac was then divided near its neck, and after being dissected from the skin was removed. The opening was repaired by the Mayo overlapping method, the peritoneal site of each suture being injected with cocain before introducing the needle. Although this operation consumed over three hours, the patient suffered no shock, had no nausea, made a good recovery, and has remained cured of this condition.

In the same way most post-operative *ventral hernias* can be handled under local anesthesia. They consume a great deal of time, and are a source of wear and tear on the surgeon, but the results are ample reward. The repair of hernias is one of the most satisfactory applications of local anesthesia if the surgeon will have ever in mind the cardinal principles: the differences in the sensation of tissues, a sufficient and suitable application of properly prepared anesthetizing solution, and, above all, patience and plenty of time.

PART II

INTRAVENOUS ANESTHESIA

William F. Honan, M. D. and J. Wyllis Hassler, M. D.[1]

Physiology.
Technique.
Mixed Forms of Anesthesia.
Blood Changes.
Urinary Examination.

General anesthesia by the intravenous route was demonstrated as a possibility by Ore of Lyons in 1872, chloral hydrate in solution being the

[1] Surgeons to the Metropolitan Hospital, N. Y. City. Abstract from a paper read before The American Association of Anesthetists, June, 1913; published in *Ann. of Surg.*, Dec., 1913, J. B. Lippincott Co., N. Y. With permission of Dr. Honan.

hypnotic agent employed. The method seemed very successful in 51 cases, but subsequent fatalities, due, perhaps, both to the drug used and the method employed, led to its discontinuance.

At the Berlin Surgical Congress, in 1910, six surgeons of prominence corroborated the success of Burckhardt, who led in perfecting the technique of this method. Kümmel reported 90 cases in his own experience. Later, Fedorow, of St. Petersburg, collected 530 cases from three Russian clinics, in which hedonal was used with no deaths attributable to the anesthetic. Fedorow and his colleagues used a 0.75 per cent solution of hedonal in normal saline solution.

Physiology.—The correct interpretation by the anesthetist of the physiological effect is that, when once a level of narcosis sufficient for the purposes of the surgeon is reached, very little anesthetic is necessary to maintain the anesthetic tension, and that so long as the tissues are not overnarcotized the cells will part with the anesthetic and regain their normal physiological status when the administration of the drug is withdrawn.

In the employment of intravenous anesthesia, the agent is directly introduced into the blood, and is maintained there at the desired anesthetic tension. In this method, the production of anesthesia is very rapid, the preliminary state of excitement is nearly always absent, the patient breathes almost naturally, the color of the skin remains good, and the relaxation and flexibilty of the muscles are absolutely satisfactory to the operator. The degree of narcosis can be maintained to a nicety, and at the completion of the operation the patient often answers questions rationally before leaving the operating table.

For the safe and satisfactory induction of anesthesia by the intravenous route, it is highly essential that the details of the technique, which is remarkably simple, be carefully and systematically observed.

Honan's own work has embraced about all of the operations usually employed in a large general surgical service, males, females, and children, and, at the present time, we can recall only one death in about 350 administrations that could be justly attributed to the method of anesthesia, and in that single instance the regrettable fatality was due to the unfortunate misunderstanding of a verbal order as to anodynes after the operation.

Technique.—For the intravenous use of ether, the patient, having been prepared for operation, is taken to the anesthetizing room about thirty minutes before the time for operation, and placed preferably upon the operating table which is to be used during the operation. A subcutaneous injection of morphin sulphate, gr. 1/6; atropin sulphate, gr. 1/100; and scopolamin, gr. 1/1000, is given at one dose—preferably in the loose tissues of the chest, abdomen, or thigh. From this time until the actual anesthesia is accomplished, it is extremely advisable to keep the patient as quiet as possible, so that when the administration begins the patient is in a condition of reposeful relaxation of mind and body. No matter how anxious or fearful of the result of the operation, the patient in thirty minutes is sustained and supported by the hypodermic medication, and the injurious effects of acute fear, which Crile has demonstrated are identical with those of acute shock, are successfully combated. A five to seven and one-half per cent solution of ether with filtered sterile Ringer's solution (normal saline solution may be used if the other is not available) at a temperature of 85° F. is poured into a reservoir which has a capacity of 2000 c.c. The solution is thoroughly mixed, and care should be taken to see that the ether is dissolved; for even after violent succussion there may be some stratification, the lighter ether floating upon the surface of the solution.

The solution having been prepared, the reservoir is adjusted on a stand eight feet above the floor level, at which point it remains during the administration. The fluid flows through an indicator which con-

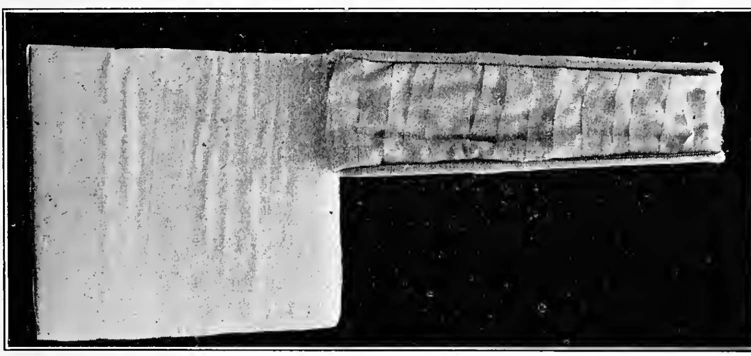


Fig. 218.—Holder for Arm.

tains a pipette, then through a rubber tubing into a blunt cannula, and so into the vein. The indicator consists of a cylindrical or globular bulb of a capacity of from two to four ounces with an inside pipette very similar to that used in the Murphy apparatus for protoclysis. When the apparatus is working properly, the lower half of the indicator is filled with solution, while the upper half contains air. The solution flows from the tank through the pipette, and drops on the surface of the fluid in the lower half of the indicator. By means of a compression top, placed below the indicator, the rate of flow can be accurately controlled, and, if the fluid in the bulb is kept at a proper level, a satisfactory index is furnished as to the rate the solution enters the vein. Usually the arm furthest from the operator is selected and the median basilic or cephalic vein exposed, but should the operative field be the skull, face, neck, or chest, where the infusion apparatus would inconvenience the surgeon or his assistant, the internal saphenous at the internal malleolus is selected. As a matter of fact, any vein, in any locality remote from the operator, may be utilized, the simple precaution being that it is superficial, free from varicosities, and sufficiently large to be readily exposed and to admit the small cannula through which the anesthetic solution is to be introduced into the system. If the elbow is selected, a padded splint, large at one end and tapering to a size somewhat wider than the forearm, is placed beneath the patient, extending from beyond the tips

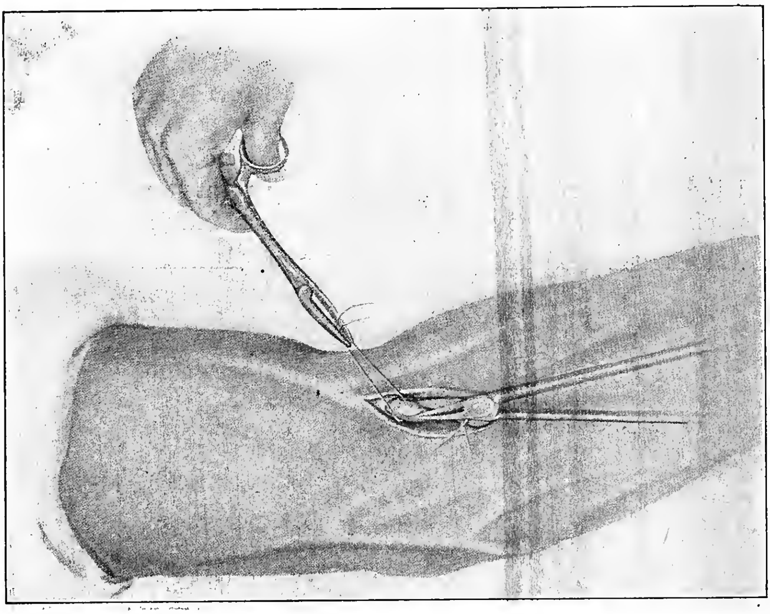


Fig. 219.—Vein Exposed and Ligated Distally. This ligature not shown in illustration. Vein is being opened with scissors. (*Annals of Surgery.*)

of the fingers to the opposite side of the body; a few turns of a three-inch rubber bandage just above the wrist will maintain extension of the forearm and prevent involuntary movements which might occur in the first stage of anesthesia and dislodge the cannula from the vein, an embarrassing but easily preventable accident. A space of about four to six inches over the bend of the elbow is now firmly wiped once over with a 5 per cent solution of thymol in carbon tetrachlorid on a piece of gauze. This is sufficient to thoroughly sterilize the skin, which has not received any previous preparation. It has an advantage over iodin, which is usually employed, in that it is more efficacious and, as an antiseptic, does not discolor the skin, a great advantage when superficial veins are to be dissected. It is not advisable to bandage the distal extremity of a limb to render the veins more prominent, as the compressor must be very quickly removed when the cannula is introduced, and that often adds to the difficulty. If the veins are not particularly prominent, an assistant may make some pressure with the hand on the upper and inner aspect of the arm while the vein is being exposed. There should be no blundering at this point, since nothing so disturbs the *morale* of the patient, destroys confidence, and adds fear and anxiety, when composure should be supreme, as the futile, clumsy attempts to find the vein by anesthetists not accustomed to doing surgical work.

We make it very emphatic that the exposure of the vein and the introduction of the cannula should be done with scrupulous regard to asepsis, since septic thrombosis at this point might lead to unpleasant after

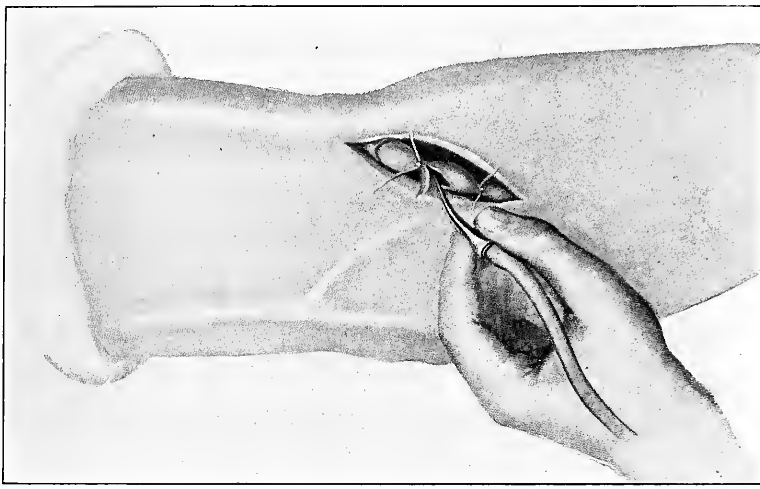


Fig. 220.—Cannula Introduced and Tied in the Vein. (*Annals of Surgery.*)

results. The skin over the vein selected is infiltrated with a few drops of one-half of one per cent solution of cocain, sufficient to make a blot one-half inch in diameter. The skin containing the blot is drawn aside from the vein with the thumb of the left hand so as not to be directly over the vein, and a small incision one-third to one-half an inch is made through into subcutaneous fat. The vein is now exposed by wiping with a bit of gauze for two or three firm strokes. A small hemostat, with a double ligature of No. 1 catgut, is now carefully thrust beneath the vein, and, by gently moving it horizontally in and out, the vessel is lifted from its bed and the exposure is complete. The ligature is cut, the lower half is tied tightly and attached to a hemostat, the upper half being tied loosely with half a knot and also clamped with a hemostat. The operator now takes the proximal ligature in his left hand, the assistant making slight tension on the one distal; the vein is lifted and put somewhat on the stretch. With a small rather blunt scissors an incision is made, embracing about two-thirds the caliber of the vessel. The operator now takes the cannula in his right hand, and, slightly relaxing tension on the proximal ligature which he holds, he is able usually to quickly insinuate

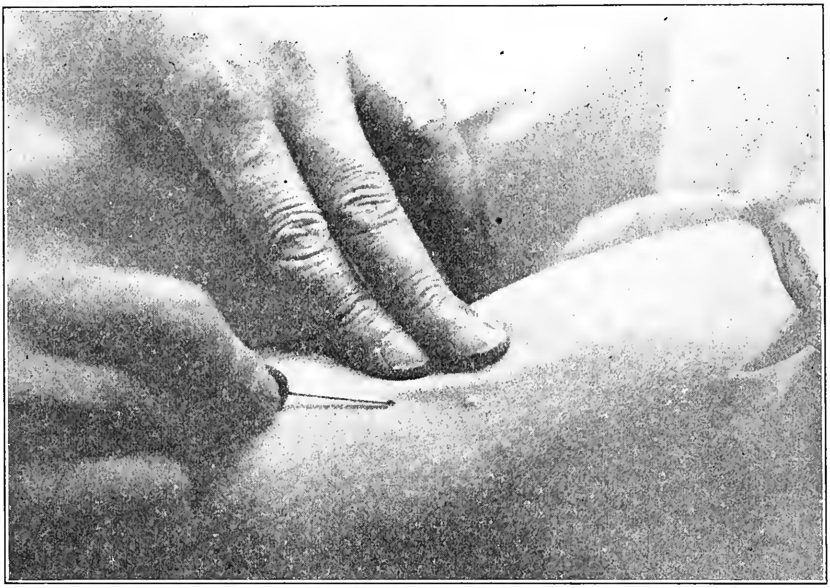


Fig. 221a.

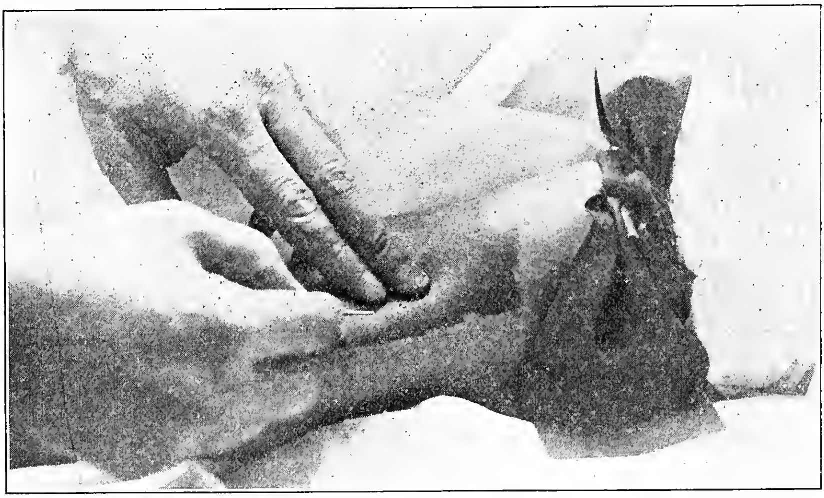


Fig. 221b.

Figs. 221a and b.—Salvarsan Method of Introducing the Needle.

it into the cavity of the vein. By manipulating the proximal ligature as to tension, he is able to facilitate this movement, though it is often advisable to have the assistant pick up the flap of the incised vein with a small pair of anatomical forceps which exposes the lumen, steadies the vessel, and very considerably facilitates the introduction of the cannula. The half loose knot in the proximal ligature is now drawn snugly down on the cannula, which is sufficient to hold it in place. A piece of adhesive plaster about 3 inches wide is placed about the rubber tubing connected with the cannula, which relieves all tension and tends more than anything else to prevent the accidental slipping of the tube from the vein. A large gauze pack is now placed over the incision, and the surgeon and assistant take their respective places to begin the contemplated operation. We have found that actual exposure of the vein and tying on of the cannula is the most satisfactory and safe procedure, many suggestions having been made as to the use of a technique similar to that employed in the salvarsan treatment; special needles have been made and tried only to return to the very satisfactory procedure described above.

The solution should be administered at a full flow at the beginning, the anesthetist reducing the stream at the appearance of the usual signs of surgical anesthesia. *It is quite as incumbent upon the anesthetist to take the usual precautions to secure and maintain an unobstructed airway and efficient respiratory act, as in the usual method of anesthesia.* Ether is rapidly eliminated by the lungs in this method, and, as is true of all methods, efficient respiration prevents accumulation and tension on the tissues, increases its output, and lessens its toxicity. In from one to five minutes anesthesia will be complete, and the operation may proceed.

It is highly important, as was noted above, to be economical in the use of the anesthetic solution; the patient should be placed in the appropriate position for the intended operation, the operative field draped, the skin disinfection completed, and the surgeon absolutely ready to make the initial incision when the cannula is inserted into the vein. There is a limit to the patient's tolerance for even salt solution, and it is very desirable that any portion of the period of anesthesia be not wasted upon preparation, but reserved solely for the actual operative technique. When the degree of narcosis is obtained, which varies somewhat with the nature of the operation, the flow into the vein is reduced by the control cock just below the indicator. It may be allowed to drip in a very fine stream or at the rate of 40 to 60 drops per minute, the corneal reflex affording a reliable guide for administration. The anesthetist readily becomes acquainted with the effects of the drug by this method, and, as narcosis can be absolutely and beautifully controlled, there is no need for any embarrassment to the operator from involuntary muscular contractions. Again, let it be urged that careful attention be directed to the maintenance of an open airway, and, as the muscles of the jaws and neck are very much relaxed, the tongue should not be allowed to drop back into the pharynx. It is more important to attend to these respiratory precautions than if the patient were being anesthetized by the inhalation method. The Hewitt breathing tube is very useful in assisting to maintain a proper airway and also as an aid to holding the tongue forward. Our usual practice is to fix the tongue with a pair of fine tenaculum forceps and let them hang by their own weight. We advocate a continuous flow in intravenous anesthesia, no matter what agent is employed as the hypnotic, though a few times we have interrupted the stream for a few

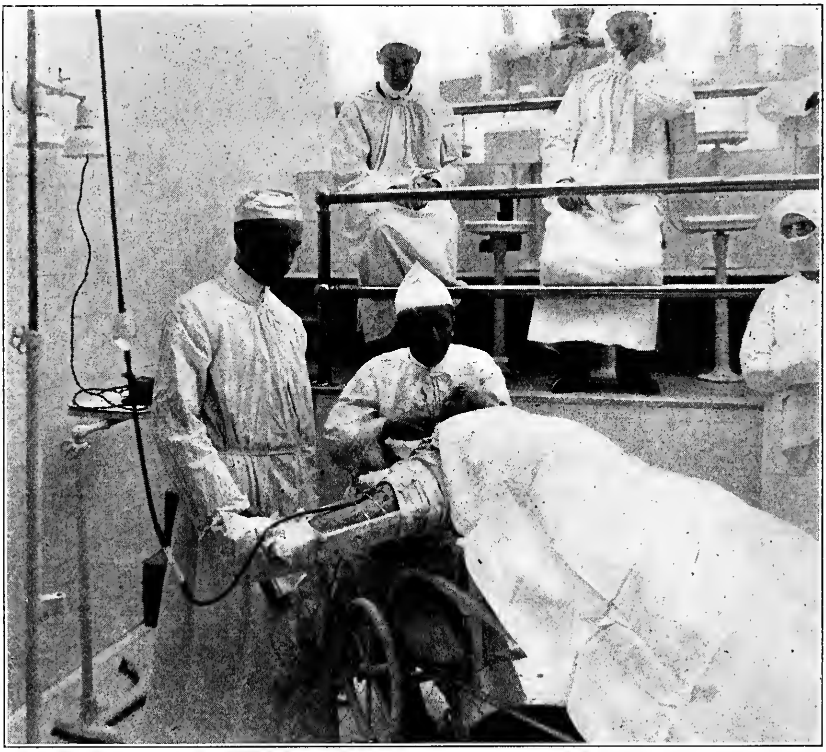


FIG. 222.—PATIENT UNDER ANESTHESIA BY THE INTRAVENOUS METHOD. Note globular indicator with control stopcock; also method of maintaining arm in proper position.

moments without any appreciably harmful effect at the conclusion of the operation, unless it has been quite prolonged; particularly if ether alone has been used, the dressings should be applied before the flow is actually stopped, as the return to consciousness often comes very promptly and the patient may resist efforts to finish the toilet of the incision properly. The blood pressure rises slightly with the use of ether in this way. We use it preferably in the old and cachectic patients, avoiding its use in young, full-blooded, or alcoholic subjects.

Oozing is more noticeable, perhaps, in the operative field, and, if the cavity of the abdomen is the seat of the operation, fluid quickly accumulates there. If extensive adhesions are to be dealt with, the fluid rapidly becomes blood-stained, and there might be instances where this might embarrass and delay the operator, but we have not been so troubled. The patient may be brought from one degree of anesthesia to another very rapidly by the judicious use of the control indicator, and it is well that the operation be entirely finished and dressings applied before the administration is stopped. If the administration has been skillfully performed, the patient will quietly drop to sleep without any appreciable indication of a stage of excitement. The face will flush, eyes roll, and some of the voluntary muscles stiffen for perhaps a few seconds, when suddenly the patient seems to have fallen into a quiet but deep sleep without the noisy stertorous respiration usually associated with narcosis. The usual signs, corneal reflex, pupillary indication, etc., are about as noted in the same degree of anesthesia by the inhalation method. At the conclusion of the operation, which may last from two to three hours, at the expenditure of about 1000 c. c. of solution per hour, the cannula is withdrawn by a quick jerk from the vein, the loose half knot of catgut is tied, which ligates the proximal portion of the vein. The wound is closed with a few fine silk sutures of 000 silk on No. 10 straight needles, wiped once with carbon tetrachlorid and thymol, 50 per cent solution, and an aseptic dressing applied. The patient is returned to bed, and, if much solution has been used and the operation prolonged, a semi-Fowler position is employed, and the

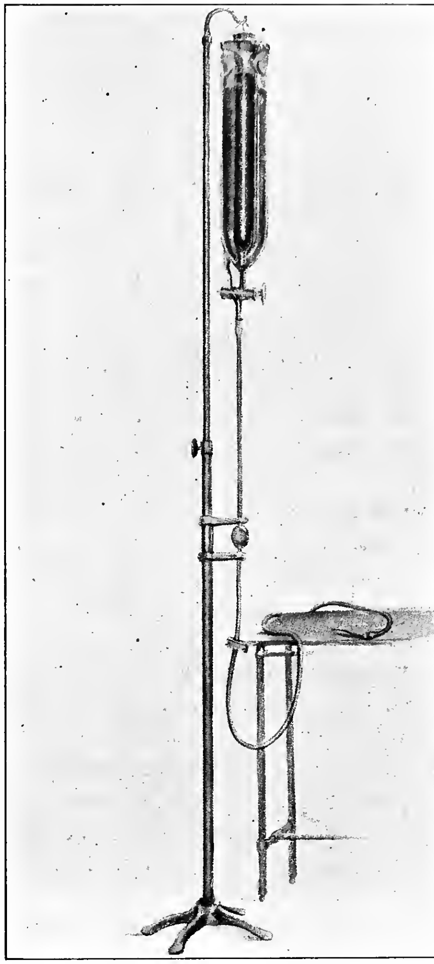


FIG. 223.—ANOTHER MODEL APPARATUS FOR INTRAVENOUS ANESTHESIA. The reservoir and tube for preliminary narcosis are in one piece, and the solutions are controlled by an ingeniously perforated glass stopcock. (*Annals of Surgery.*)

nurse instructed to turn the patient every one or two hours. This is a necessary precaution; for, if a very great quantity of fluid is used, there are naturally some possibilities of pulmonary edema, and curiously enough, certain spots on the back and buttocks often develop, looking like bruises. This is due to the anesthetic fluid settling in the loose fatty tissue of the most dependent portion of the body. Occasionally the patient will have a chill such as may occur when saline infusion is given to combat shock. This condition quickly subsides, particularly if hot-water bags are placed about the patient. It is a curious fact that this phenomenon will occur when solutions ten degrees higher than the body temperature are introduced into the circulation. The employment of ether in this way seems almost devoid of danger from either immediate or remote complications, and represents the basic type of intravenous anesthesia, from which have grown many modifications.

Mixed Forms of Anesthesia.—Experience has shown that in intravenous anesthesia better results are obtained, both as to the production of the narcosis and a state of anoci-association, if hypnotic agents are employed at the same time, which are of very widely different character, both as to chemistry and physiological action and which may be said to act synergetically. If the narcosis is first established by the use of a hypnotic, like hedonal or isopral, and the subsequent course conducted with the ether solution, the anesthesia is more satisfactory in every way. The method seems safer and more efficient; less solution is required to maintain the narcosis and the post-anesthetic history is free from incidents. Of the many substances employed in the preliminary narcosis, isopral seems to best fulfill the requirements. *Into the smaller reservoir is placed 250 c. c. of a one and one-half per cent solution of isopral in Ringer's solution, which has been boiled, filtered, and maintained at a temperature, approximately, of 85° F.;* into the larger, 2,000 c. c. of a five per cent solution of ether. Artery clips or compression tops are placed on the tubes leading from each reservoir to control the outlets. The apparatus, particularly rubber connections, is now carefully examined to see that all parts are secure, since the slipping of a rubber tube from its glass connection during anesthesia makes a very embarrassing situation, which may be easily prevented by a careful inspection before the apparatus is used. Everything being in readiness now, the vein examined, the solution from the smaller reservoir, which will be used first, is allowed to flow through the tubing to force out the air and to fill the indicator a trifle below the free end of the pipette. The cannula being introduced into the vein, the isopral solution is allowed to flow slowly into the vein, allowing four to five minutes for the entire 250 c.c. to enter the circulation. Usually, before that amount has been used, the patient has passed from a condition of consciousness to what is apparently a normal sleep, without a stage of excitement, and, if this preliminary narcosis has been skillfully conducted, there is nothing in the entire realm of anesthesia which so approximates normal sleep. The patient breathes quietly and naturally, there is no noisy respiration, the color remains good, and the transition from wakefulness to deep sleep has been so quietly accomplished that one is scarcely prepared to believe that narcosis is complete until examination shows complete muscular relaxation and absence of corneal reflex. This stage may be reached before the entire 250 c.c. of isopral solution has been used; often 100 c.c. is sufficient. However, in the very robust, and particularly in those addicted to the use of drugs or alcohol, this preliminary stage may be prolonged. Before the isopral solution is entirely exhausted, the clip is placed upon the tubing leading from the smaller reservoir and, simultaneously, the one from the larger reservoir is removed, allowing the ether solution to enter the circulation. Narcosis having been wholly or partially accomplished, the flow in this instance is just sufficient to maintain the degree already established, or such as may meet the demands of the operation. Hedonal may be used in the same way except that it is used in a 0.75 per cent solution. It is a more powerful respiratory sedative than isopral, and the precaution should be observed that it should enter the circulation slowly and especial attention be paid to its proper elimination by the maintenance of an adequate airway. It is possible to deeply narcotize a patient with hedonal in ten seconds after the cannula is introduced into the vein by allowing the flow full headway, but such effects are sensational in their rapidity, serve no useful purpose, and are not always devoid of danger.

Blood Changes.—In every case it was found that ether raised the blood pressure from 2 to 24 mm., this rise being followed by a fall of 2 to 20 mm. in from one to three hours and then gradually returned approximately to the point observed before operation.

Hedonal invariably lowered the blood pressure from 6 to 25 mm. of mercury, paraldehyd in about the same proportion, so also isopral. When mixtures were used, such as hedonal and ether, paraldehyd, or isopral and ether, the blood pressure was influenced to the extent of being about the same as before the operation, as only a small quantity of the hypnotics was used in the anesthetic mixtures. They, however, in every instance prevented the increased pressure noted when ether-scopolamin-morphin combination was used. It was singularly noted that female patients showed little or no changes in the blood pictures, neither did males in operations of short duration. Alcoholic habitués naturally required more anesthetic and, in one case, in which anesthesia was accomplished with a five per cent solution of paraldehyd in normal saline, there was decided crenation of red cells with some clumping crenation, and some crenation was noted when a mixture of ether 3 per cent and paraldehyd 25 per cent was employed. Some crenation was also noticed in one case where a large quantity (3,500 c.c.) of 7 per cent ether in normal saline was used. In every case the blood picture returned to normal in about four hours.

Hemoglobin, estimated by Tallquist scale, showed an average diminution of 5 per cent. There seemed to be no changes either in appearance or number of the leucocytes, and where an actual leucocytosis was observed before the infusion was given the blood picture was practically unchanged. The erythrocytes were not materially affected, except in three cases in which narcosis had been produced by paraldehyd.

Urinary Examination.—The urinary analyses made before the operation and for three or four days afterward showed no marked differences in the specimens. The total amount was increased and specific gravity lowered during the first twenty-four hours; often the specific gravity and solid content of the urine remained unchanged. In no case, even after employing 7.5 per cent ether solution, did blood, albumin or casts appear in the urine, though German observers have reported occasional cases of transient hemoglobinuria after the use of the stronger ether mixtures. It was quite surprising that there was not a large urinary output after the infusion of large quantities of fluid, so much so that the patients were regularly catheterized, thinking perhaps there might be some vesical paresis from overdistention, but we failed to find at any time a urinary output in proportion to the amount of fluid introduced into the circulation.

CHAPTER XIV

LOCAL ANESTHESIA AS APPLIED IN DENTISTRY

HERRMANN PRINZ, M.D., D.D.S.

HISTORY.

THE HYPODERMIC METHOD.

COLD.

MODE OF APPLICATION OF ETHYL CHLORID.

COCAIN: Preparation of Cocain Solutions; Sterilization of Solutions; Substitutes Proposed for Cocain; The Hypodermic Armamentarium.

TECHNIQUE OF INJECTION: The Subperiosteal Injection; Peridental Anesthesia; Intra-osseus Injection; Perineural Injection; The Injection Into the Pulp; Methods of Anesthetizing the Pulp.

History.—Probably the oldest known dental prescription that was used for the purpose of abolishing pain arising from an aching tooth is recorded upon a clay tablet that was found in Nippur. Its age may be approximately placed at 2250 B. C. Recent excavations that have been made near Nippur and Babylon have brought to light valuable information regarding the practice of medicine under Hammurabi, King of Babylon, a contemporary of Abraham. The clay tablet is written in the Babylonian tongue, which was the official language of diplomatic intercourse from the Euphrates to the Nile. The contents of this tablet refer to the "worm" theory of dental caries, and the treatment consists in filling the painful cavity of the tooth with a cement prepared by mixing powdered henbane seed with gum mastic. In Egypt the suet of the crocodile, locally applied, was believed to relieve pain, and Pliny refers casually to the mystic *lapis memphitis,* the stone of Memphis, which, when rubbed on the surface of the skin in conjunction with sour wine, was said to produce local anesthetic effects. In an early Cymric manuscript, which was probably written about the end of the fifteenth century, among a large number of conjectures we find the following: "How to extract a tooth without pain: Take some newts, by some called lizards, and those nasty beetles which are found in ferns in the summertime. Calcine them in an iron pot, and make a powder thereof. Wet the forefinger of the right hand, and insert it in the powder, and apply it to the tooth frequently, refraining from spitting it off, when the tooth will fall away without pain. It is proven."

In the early days of modern dentistry we meet with many feeble efforts to alleviate pain during trying operations. The search for new methods and means pressed the mysticism of the electric current into service, opening to the charlatan a prolific field, which, even to this day, has not lost its charm. Richardson's voltaic narcotism for a time attracted the attention of the medical profession; and Francis, in 1858, recommended the attachment of the electric current to the forceps for the painless extraction of the teeth. As dental depots still offer appliances of this nature for sale, it seems that the method is still in vogue with some operators.

Various drugs were employed, chloroform, alcohol, ether, opium, and the essential oils, either simply or as compounds, usually under fanciful names. Snape's "calorific" fluid, composed of chloroform, tincture of lemon balm, and oil of cloves; "nabolis," consisting of glycerite of tannic acid and a small quantity of chloral hydrate; Morton's "letheon," which was ether mixed with aromatic oils, are examples of proprietary preparations which enjoyed quite a reputation in their time.

In 1853 Alexander Wood introduced a method of general medication by means of hypodermic injections. It was at once suggested to employ such drugs as morphin or tincture of opium for the purpose of producing local anesthesia. The results were not encouraging, however, until Koller, in 1884, advocated cocain. With the introduction of this drug into therapeutics, local anesthesia achieved results which were beyond expectations, and its adoption created a new era in local anesthesia.

Local anesthesia may be obtained in two definite ways: (1) By inhibiting the function of the peripheral nerves in a circumscribed area of tissue, this process being called "terminal anesthesia"; (2) by blocking the conductivity of a sensory nerve trunk somewhere between the brain and the periphery, termed "conductive anesthesia." Conductive anesthesia may be produced by injecting into the nerve trunk proper—endoneural injection—or by injecting into the tissues surrounding a nerve trunk—perineural injection. The latter form is the usual method pursued when conductive anesthesia for dental purposes is indicated.

The Hypodermic Method.—The successful practice of local anesthesia in dental surgery involves the careful correlation of a number of important details, each one constituting a definite factor in itself, the neglect of which must necessarily result in failure. As a whole, the practice of local anesthesia by the hypodermic method represents the composite of the following factors: (1) A solution of active ingredients corresponding to the physical and physiological laws which govern certain functions of the living cell; (2) a carefully selected hypodermic armamentarium; (3) a complete mastery of the technique; (4) a proper selection of the method suitable for the case on hand; (5) good judgment of prevailing conditions.

Cold.—Physically reducing the temperature of the body by the application of cold (ice-pack, ice and salt mixture, cold metals, etc.) was practiced by the older surgeons. Arnott, in 1849, and Blumdell, in 1855, advocated ice-packs for the painless extraction of teeth.

Through the efforts of Sir B. W. Richardson, in 1866, this method was placed on a rational basis by the introduction of his ether spray. To obtain good results, an ethyl ether free from water is necessary.

Certain other carbon compounds possess similar properties in varying degrees, depending on their individual boiling points. In 1867 Rottenstein called attention to the use of ethyl chlorid as a refrigerating agent, and Rhein, in 1889, introduced methyl chlorid for the same purpose. In 1891 Redard reintroduced ethyl chlorid as a local anesthetic. It has since been marketed under various trade names, as antidolorin, kelene, locodolor, etc. Mixtures of methyl and ethyl chlorids, in various proportions known as anesthyl, anestile, coryl, meth-ethyl, etc., have been extensively used in minor oral and general surgery. A pure ethyl chlorid is best suited for this purpose, as it lowers the temperature of the tissues sufficiently to produce a short superficial anesthesia in a few minutes. Too rapid cooling or prolonged freezing by methyl chlorid or the various mixtures thereof produce deeper anesthesia, but such procedures are dangerous. They frequently cut off circulation in the affected part so completely as to produce sloughing (necrosis).

Liquid nitrous oxid, liquid or solid carbon dioxid (known as carbon dioxid snow), and liquid air have been recommended for similar purposes. However, they require cumbersome apparatus, and are extremely dangerous.

Mode of Application of Ethyl Chlorid.—For the extraction of teeth, immediate removal of the pulp, opening of abscesses, and other minor operations about the oral cavity, the ethyl chlorid tube should be warmed to body temperature by placing it in heated water, and its capillary end should be held about six to ten inches from the field of operation. The distance depends upon the size of the orifice of the nozzle, and complete vaporization should always be produced. The Gebauer tube[1] is fitted with a spray nozzle, which shortens the distance to one or two inches, and is especially well adapted for dental purposes. The stream is directed upon the tissues until the latter are covered with ice crystals and have turned white. For the extraction of teeth, the liquid should be projected directly upon the surface of the gum, as near to the apex of the root as possible, but care should be taken to protect the crown of the tooth on account of the painful action of cold on this part.

[1] See Figure 224, page 538.

The tissues to be anesthetized should first be dried and well surrounded by a film of vaselin or glycerin, and protected by cotton rolls and napkins, to prevent the liquid from running into the throat (Fig. 224). The patient should breathe through the nose. Occasionally light forms of general anesthesia are introduced by inhaling the vapor.

Precautions.—On account of the difficulty of directing the stream of ethyl chlorid upon the tissue in the posterior part of the mouth, it is not successfully applied to those regions. The intense pain produced

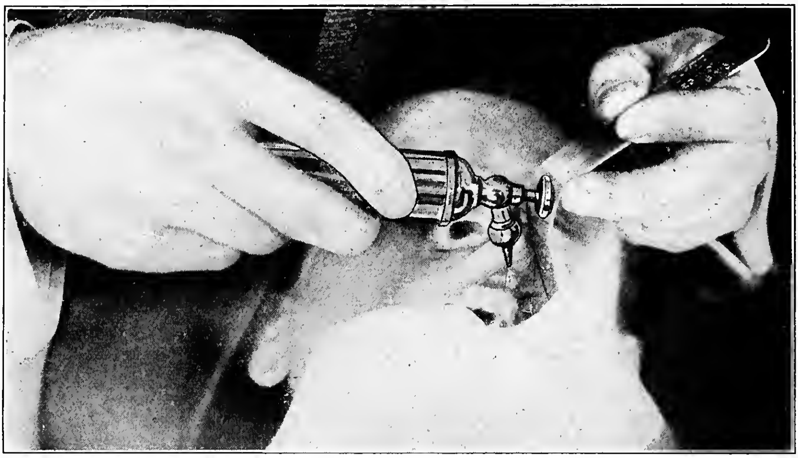


Fig. 224.—Application of the Ethyl Chlorid Spray.

by the extreme cold prohibits its use in pulpitis and acute pericementitis. To anesthetize the second and third branches of the fifth nerve, it is recommended to direct the stream of ethyl chlorid upon the cheek in front of the tragus of the ear, but the author has not seen any good results from such a procedure.

Caution should be exercised in using ethyl chlorid near an open flame or in conjunction with the thermo-cautery, as severe burns have resulted by setting the inflammable vapor on fire.

COCAIN

Cocain, when injected into the tissues, produces typical local and general effects. Locally, it possesses a definite affinity for the peripheral nerves; it causes constriction of the smaller arteries, producing light anemia in the injected area, with diminished action of the leukocytes. However, different parts of the organism require different doses to bring about the same reaction. Upon mucous surfaces, paralysis of the sensory nerves is produced; the senses of touch and smell are temporarily inhibited. The blood, as such, and the circulation suffer little. If cocain in sufficient quantities is absorbed by the circulation, general manifestations are produced from bringing other tissues in close contact with the poison. The principal disturbances of the central nervous system make themselves known by vertigo, a very slight pulse, enlarged and staring pupils, and difficult respiration. Vomiting may occur; the throat feels dry. Intense excitement is followed by epileptiform spasms; finally, complete loss of sensation and mobility results, which terminates in death from cessation of respiration.

Precautions.—With our increased knowledge of the action of cocain upon the tissues, and with proper technique of injection, dangerous results are comparatively rare at present. No direct chemical antidotes are known, and the treatment of general intoxication is purely symptomatic. Anemia of the brain, which is of little consequence, may be readily overcome by placing the patient in a recumbent position or by complete inversion if necessary. As a powerful dilator of the peripheral vessels, the vapors of amyl nitrite are exceedingly useful; it is best administered by placing three to five drops of the fluid upon a napkin and holding it before the nostrils for inhalation. The flushing of the face and an increase in the frequency of the pulse follow almost momentarily. For convenience, amyl nitrite may be procured in small glass capsules, holding the quantity necessary for one inhalation. Nausea may be remedied by administering small doses of spirit of peppermint, aromatic spirit of ammonia, or validol. To overcome the disturbances of respiration, quickly instituted artificial respiration is the alpha and omega of all methods of resuscitation. The only drug that has proved to be of value in this connection is strychnin in the form of sulphate, or the nitrate in full doses by means of hypodermic injections.

Preparation of Cocain Solutions.—The relative toxicity of a given quantity of cocain solution depends upon the concentration of the solution. Reclus and others have clearly demonstrated that a fixed quantity of cocain in a 5 per cent solution is almost as poisonous as five times the same quantity in a 0.5 per cent solution. From the extensive literature on the subject, we are safe in fixing the strength of the solution for dental purposes at 1 per cent. This quantity of cocain lowers the freezing point of distilled water just a little above 0.1° C. To obtain an isotonic solution, corresponding to the freezing point of the blood, 0.8 per cent of sodium chlorid must be added.

Having thus prepared a cocain solution which is equal to the blood in its osmotic pressure upon the cell wall, it is now necessary to aid the slightly vasoconstrictor power of the drug by the addition of a moderate quantity of adrenalin, thus increasing the confinement of the solution to the injected area by producing a deeper anemia. The purpose of this is twofold: (1) To act as a means of increasing the anesthetic effect of cocain; (2) to lessen its toxicity upon the general system by slower absorption. As stated above, one drop of adrenalin solution added to 1 c. c. of the isotonic cocain solution is sufficient to produce the desired effect.

A suitable solution for dental purposes may be prepared as follows:

℞	Cocain hydrochlorid	5 grains (0.3 gm.)
	Sodium chlorid	4 grains (0.25 gm.)
	Sterile water	1 fluid ounce (30.0 c. c.)

To each syringeful (2 c. c.) add two drops of adrenalin chlorid solution when used.

Sterilization of Solutions.—Ready-made cocain solutions may be sterilized only with difficulty; they will not keep when frequently exposed to the air. The ready-made anesthetic solutions found in the market usually contain preservatives such as phenol, naphthol, boric acid, iodin, essential oils, alcohol, etc., in variable quantities. Some of these solutions have a distinct acid reaction. While they may produce a serviceable degree of anesthesia, they usually damage the injected tissues sufficiently to retard the normal process of wound healing. For sterilization, see Chapters XV, XVIII.

Substitutes Proposed for Cocain.—Since the introduction of cocain into the materia medica for the purpose of producing local anesthesia, various substitutes have been placed before the profession, superiority in one respect or another being claimed for each over the original cocain. The more prominent members of this group are tropacocain, eucain B, acoin, nirvanin, alypin, stovain, novocain, and, very recently, quinin and urea hydrochlorid. (See Chapter XX.) None of these compounds, with the exception of novocain, has, in the opinion of the author, proved satisfactory for the purpose in view.

Novocain is about two to six times less toxic than cocain. It does not irritate in the slightest degree when injected; consequently no pain is felt from its injection *per se.* It is soluble in its own weight of water; it combines with adrenalin in any proportion, without interfering with the physiological action of the latter, and it is readily absorbed by the mucous membrane. The studies of Biberfield and Braun brought to light another extremely interesting factor concerning the novocain-adrenalin combination. Both experimenters, working independently of each other, observed that the adrenalin anemia on the one hand, and the novocain anesthesia on the other, were markedly increased in their total effects upon the tissues. Consequently a smaller quantity of this combination is required to produce a given therapeutic effect than is required of each individual drug. Very recently it has been shown by Esch that adrenalin possesses a specific action upon nerve tissue, viz.: it affects the latter tissue in a peculiar manner so that it will take up the anesthetic more readily. Its action may be compared to a mordant or fixing agent such as is used in tissue staining. The effects of the injection of such solutions of the combined drugs are usually confined to the injected area; general effects are therefore rarely produced.

A suitable solution of novocain for dental purposes may be prepared as follows:

Novocain	10 grains (0.6 gm.)
Sodium chlorid	4 grains (0.25 gm.)
Distilled water	1 fluid ounce (30 c. c.)
Boil	

To each syringeful (2 c. c.) add two drops of adrenalin chlorid solution when used. Fischer strongly advocates the following so-called "normal anesthetic solution," which, when prepared under strict aseptic precautions and when preserved in amber-colored bottles, will keep:

Novocain	23 grains (1.5 gm.)
Sodium chlorid	14 grains (0.92 gm.)
Thymol	1/3 grain (0.02 gm.)
Distilled water	3 fluid ounces, 1¾ fluid drams (100 c. c.)

To each cubic centimeter add one drop of synthetic suprarenin solution when used. A sterile solution may be made extemporaneously by dissolving the necessary amount of novocain-adrenalin in tablet form in a given quantity of boiled distilled water. A suitable tablet may be prepared as follows:

Novocain	1/3 grain (0.022 gm.)
Suprarenin hydrochlorid	1/1200 grain (0.000054 gm.)
Sodium chlorid	1/8 grain (0.008 gm.)

One tablet dissolved in 20 minims of sterile water makes a 2 per cent solution of novocain ready for immediate use.

Solutions for hypodermic purposes should preferably be made fresh when needed. A small glass dish and a dropping bottle constitute the simple outfit for such work. The dropping bottle should hold from one to two ounces, and should be provided with a dust cap. On one suitable bottle on the market, "a groove on one side of the neck of the bottle and a vent on the other connected with two grooves in the back of the stopper allow the contents to flow out drop by drop. A quarter turn of the stopper closes the bottle tightly." The water used for making the solution should be boiled and filtered distilled water.

Directions.—The hypodermic solution can be made extemporaneously in a few seconds, as follows: Place a tablet in a sterile glass dish, add

Fig. 225.—Outfit for Preparing the Hypodermic Solution.

20 minims (1 c. c.) of water, and to facilitate the solution mash the tablet. The solution is now ready for immediate use.

The Hypodermic Armamentarium.—The Syringe.—A hypodermic syringe that answers all dental purposes equally well is an important factor in carrying out the correct technique of the injection. The injection into the dense gum tissue requires from 15 to 50, or even more, pounds of pressure as registered by an interposed dynamometer, while in pressure anesthesia 100 or more pounds are frequently applied.

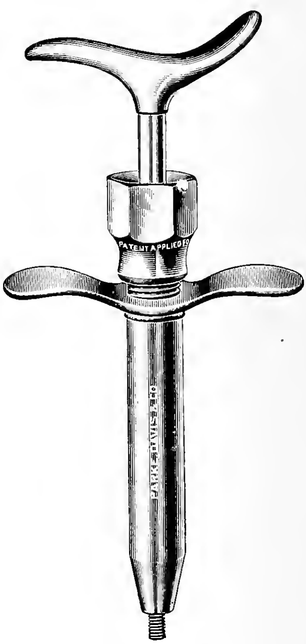


Fig. 226.—Dental Hypodermic Syringe.

The selection of a suitable hypodermic syringe is largely a matter of choice. All-glass syringes, glass-barrel syringes, and all-metal syringes are the usual types found in the dental depots. After testing most of the dental hypodermic syringes offered to the profession within the last five years by means of the pressure gauge, and in clinical work subjecting the syringes to routine wear and tear, the author has found that an all-metal syringe of the Imperial type is to be preferred to other makes. They are usually made of nickel-plated brass, which, however, is a disadvantage, as the nickel readily wears off from the piston, and exposes the easily corroded brass. The Manhattan all-metal platinoid syringe gives the best general service, and the author can conscientiously recommend it to his confrères. The syringe holds 40 minims (2 c. c.), is provided with a strong finger cross-bar, and is extremely simple in construction. The piston consists of a plain metal rod, without a thickened or ground piston end or packing. The piston rod is sufficiently long to allow about two inches of space between the cross bar and the piston top. This space is of importance, as it allows the last drop of the fluid to be expelled under heavy pressure without tiring the fingers.

NEEDLES.—Dental hypodermic needles should be made preferably of seamless steel, or, better still, of nickel-steel, 26 to 28 B. & S. gauge, and provided with a short razor-edge point. Thicker needles cause unnecessary pain, and thinner needles are liable to break. Iridio-platinum needles are preferred by some operators, as they may be readily sterilized in an open flame. The needle should measure from a quarter to a half inch. For infiltration anesthesia one-inch needles are necessary, and curved needles of various shapes are essential in reaching the posterior parts of the mouth. For pressure anesthesia special needles are required, and may be bought at the depots, or they may be quickly prepared by grinding off the steel needle at its point of reinforcement. The sterile needle should be kept in well-protected glass containers. The needles are sterilized after each use by boiling in plain water, dried with the hot-air syringe, and immediately transferred to a covered sterile glass dish. The sterile needles should not be again touched with the fingers, and the customary wire insertion is unnecessary.

TECHNIQUE OF INJECTION

Various methods of injecting the anesthetic solution about the teeth are in vogue. For the sake of convenience they may be divided as follows: (1) The subperiosteal injection; (2) the peridental injection; (3) the intra-osseous injection; (4) the perineural injection; (5) the injection into the pulp.

Preliminary Steps.—Before starting any surgical interference in the mouth, the field of operation should be thoroughly cleansed with an antiseptic solution. A thin coat of the official tincture of iodin painted over the surface is very useful for this purpose. After the diagnosis is made, the method of injection best suited for the case on hand is then decided upon.

The Subperiosteal Injection.—The subperiosteal injection about the root of an anterior tooth is best started by inserting the needle midway between the gingival margin and the approximate location of the apex. The pain of the first puncture may be obviated by using a fine, very sharp-pointed needle, by the simple compression of the gum tissue with the finger tip, by holding a pledget of cotton saturated with the prepared anesthetic solution on the gum tissue for a few moments, or by applying a very small drop of liquid phenol on the point of puncture. The needle opening faces the bone, the syringe is held in the right hand at an acute angle with the long axis of the tooth, while the left hand holds the lip and cheek out of the way. After puncturing the mucosa, a drop of the liquid is at once deposited in the tissue, and the further injection is painless. Slowly and steadily the needle is forced through the gum tissue and periosteum (Fig. 227) along the alveolar bone toward the apex of the tooth, depositing the fluid under pressure close to the bone on its upward and return trip. The continuous slow moving of the needle prevents injecting into a vein. A second injection may be made by partially withdrawing the needle from the puncture and swinging the syringe anteriorly or posteriorly, as the case may be, from the first route of the injection. This latter method is especially indicated in injecting around the upper molars. After removing the needle, place the finger tip over the puncture and slightly massage the injected area. A circular elevation outlines the injected field. The naturally pink color of the gum will shortly (Fig. 228) change to a white anemic hue, indicating the physiological action of the adrenalin on the circulation. No wheal should be raised by the fluid, as that would indicate superficial infiltration and, consequently, failure of the anesthetic.

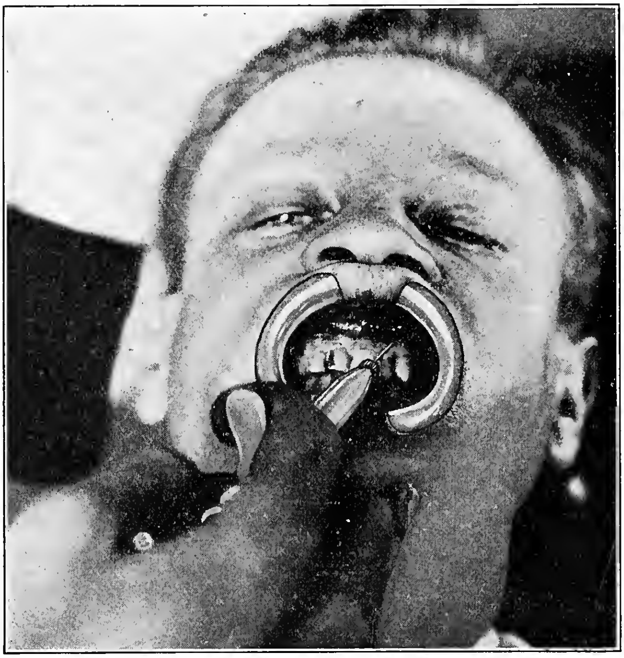


Fig. 227.—Method of Injection into the Labial Subperiosteal Gum Tissue.

Extraction.—As the liquid requires a definite length of time to pass through the bone lamina and to reach the nerves of the peridental membrane and the pulp, from 5 to 10 minutes should be allowed before the extraction is started. The length of time depends on the density of the surrounding structure of the tooth. The progress of the anesthesia may be tested with a fine-pointed probe, and its completeness indicates the time when the extraction should be started.

TECHNIQUE FOR DIFFERENT TEETH.—The *upper eight anterior teeth* usually require a labial injection only, while the molars require both a buccal and a palatine injection, using a slightly curved needle for this

FIG. 228.—METHOD OF INJECTING INTO THE PALATINE SUBPERIOSTEAL GUM TISSUE.

purpose. Buccally the injection is made midway between the mesial and distal root, and on the palatine side over the palatine root.

The *lower eight anterior teeth* are comparatively easily reached by the injection. The straight needle is inserted near the apex of the tooth, the syringe is held in a more horizontal position, and the injection proceeds as outlined above.

The *lower molars* require a buccal and lingual injection. The curved needle is inserted midway between the roots, the gum margin, and the apices. The external and internal oblique lines materially hinder the ready penetration of the injected fluid, and therefore ample time should be allowed for its absorption.

If *two or more adjacent teeth* are to be removed. the injection by means of infiltrating the area near the gum fold directly over the apices of the teeth is to be preferred. It is advisable to use a one-inch needle for this purpose, holding the syringe in a horizontal position, so as to reach a larger field with a single injection.

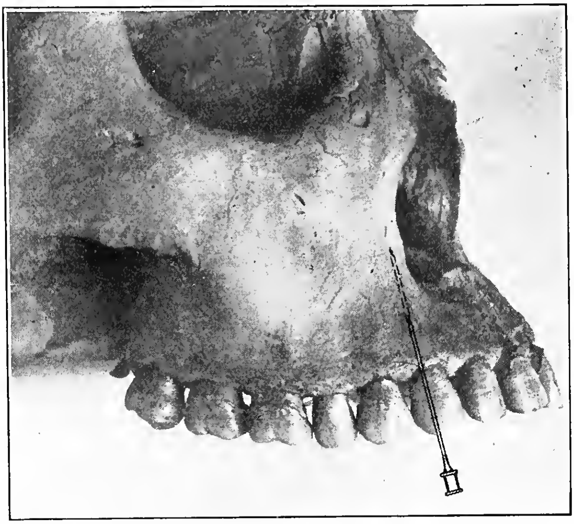


Fig. 229.—Subperiosteal Injection about an Upper Cuspid.

Abscesses.—Injection into inflamed tissues, into an abscess, and into phlegmonous infiltration about the teeth is to be avoided. Injec-

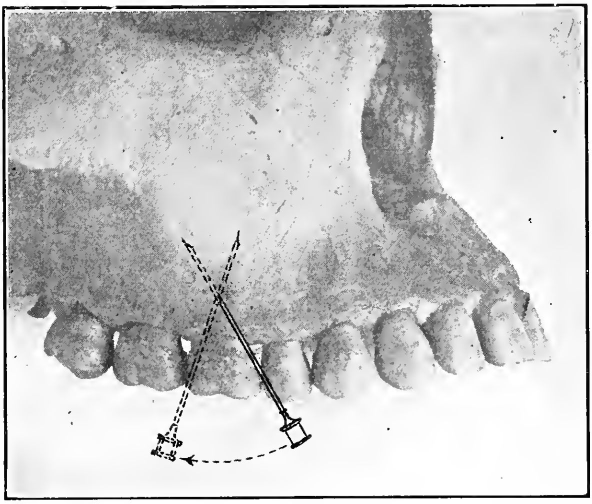


Fig. 230.—Subperiosteal Injection about an Upper Molar.

tion into engorged tissue is very painful; the dilated vessels quickly absorb cocain without producing a complete anesthesia, and general poisoning may be the result. In purulent conditions injection is decidedly dangerous, as it forces the infection beyond the line of demarcation. If the abscess presents a definite outline, the injection has to be made into the sound tissue surrounding the focus of infiltration. If a tooth is affected with acute diffuse or purulent pericementitis, a distal and a mesial injection usually produce successful anesthesia by blocking the sensory nerve fibers in all directions.

Peridental Anesthesia.—Teeth or roots standing singly, or teeth affected by pyorrhea, or similar chronic peridental disturbances, are frequently quickly and satisfactorily anesthetized by injecting the fluid directly into the peridental membrane. This method is known as peridental anesthesia, and its technique is very simple. In single-rooted teeth a fine and short hypodermic needle is inserted under the free margin of the gum, or through the interdental papilla, into the peridental membrane between the tooth and the alveolar wall. Sometimes the needle may be forced through the thin alveolar bone so as to reach the peridental membrane direct. To gain access to this membrane in teeth set close together, slight separation with an orange-wood stick or other suitable means is often found to be of advantage. Two, sometimes three, injections are necessary. To force the liquid into the membrane usually requires a higher pressure than that which is necessary for injecting into the periosteum covering the alveolar process, but the quantity of the anesthetic liquid is less than that which is required for the former injection. Acute inflammatory conditions of the peridental membrane and its sequelæ prohibit the use of this method. Peridental anesthesia is one of the most satisfactory forms of local anesthesia, since the seat of the nerve supply of the tooth is very quickly reached, and, as a consequence, the results obtained are in the majority of cases extremely satisfactory, provided that general conditions justify its application.

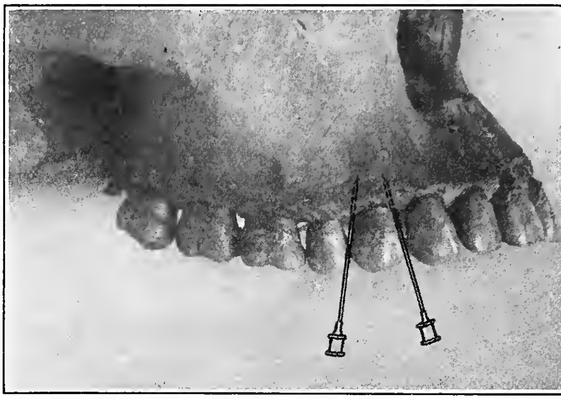


FIG. 231.—PERIDENTAL INJECTION ABOUT AN UPPER BICUSPID.

Intra-osseous Injection.—The gum tissue is thoroughly cleansed with an antiseptic solution, and is then anesthetized about the neck of the tooth in the usual manner. After waiting 2 or 3 minutes, an opening is made into the gum tissue and the bone on the buccal side with a fine spear drill or a Gates-Glidden drill. The opening should be made more or less at a right angle with the long axis of the tooth, a little below the apical foramen in single-rooted teeth or between the bifurcation in the molars. The right-angle hand piece is preferably employed for this purpose. The drill should be of the same diameter as the hypodermic needle. The gum fold is tightly stretched to avoid laceration from the rapidly revolving drill. As soon as the alveolar process is penetrated, a peculiar sensation conveyed to the guiding hand indicates that the alveolus proper is reached, and the sensation felt by the hand is about the same as that experienced when a burr enters into the pulp chamber. In this artificial canal the close-fitting curved needle of the hypodermic syringe is now inserted, and the injection is made in the ordinary way. The quantity of fluid used is much less than is usually needed for a subperiosteal injection. The roots of the teeth are imbedded in a sieve-like mass of bone tissue (diploë), which allows a ready penetration of fluid when injected under pressure.

Perineural Injection.—For the anesthetization of a number of teeth in the upper or the lower jaw, conductive anesthesia by means of peri-

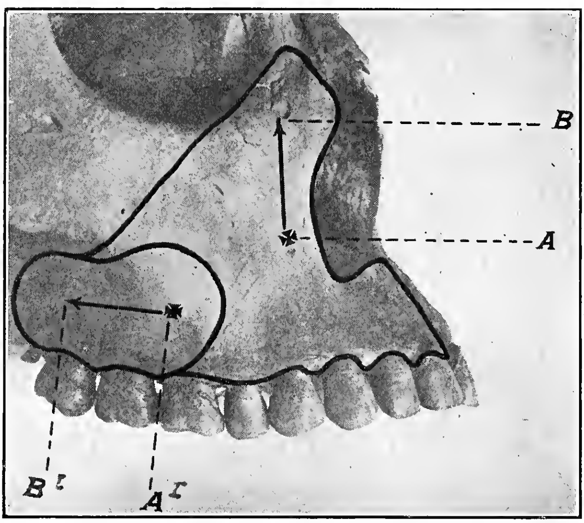


FIG. 232.—PERINEURAL INJECTION UPON THE BUCCAL SIDE OF THE UPPER JAW. A, B, injection below the infra-orbital foramen; A¹ B¹, injection over the region of the tuberosity.

neural injection is preferably employed. The perineural injection is made near the point of exit or entrance of the various nerves about their respective foramina. To anesthetize all the teeth of one-half of the upper jaw, 4 injections are necessary, i. e., 2 buccally and 2 on the palatine side of the bone. A 1-inch needle is required for such work. To reach the many small branches of the posterior dental nerves at the alveolar foramina, the injection is made buccally over the region of the tuberosity about ½ inch above the gingival line between the first and second molar teeth. The second injection is made below the intra-orbital foramen, so as to reach the middle and anterior dental nerves. With the index finger of the left hand the foramen is approximately located by exerting pressure upon the nerve exit. The lip is lifted up with the middle finger of the same hand, and the needle is now inserted between the apices of the cuspid and first bicuspid teeth. The needle is slowly pushed forward until its point is felt beneath the finger tip. To reach the nerve supply of the hard palate, one injection is made near the posterior palatine canal, and the other near the foramina of Scarpa. The great palatine nerves pass through the posterior palatine canals on both sides of the hard palate. The canals lie about ⅜ of an inch above the edge of the alveolar process and the last molar tooth. They move posteriorly with the eruption of the successive teeth. The nasopalatine nerves pass through the foramina of Scarpa (incisive foramen), which are situated in the line of the suture of the maxillary bones. If an imaginary line is drawn from the distal borders of the two cuspids, passing over the hard palate, it will ordinarily pass through the foramina. The needle should be inserted directly back of the papilla, which lies posteriorly between the central incisor teeth.

To anesthetize one-half of the mandible, three injections for the deposition of the anesthetic solution are necessary. The first injection is applied near the mandibular foramen, the second near the mental foramen, and the third into the incisive fossa. To locate the mandibular foramen in the mouth the lingual surface of the ramus is palpated with the finger, the anterior sharp border of the coronoid process is easily felt about ⅝ of an inch posterior to the third molar. The process passes downward and backward from the third molar, and enters into the external oblique line. Mesially from this ridge is to be found a small triangular concave plateau, which is facing downward and outward, being bound mesially by a distant bony ridge and covered with mucous membrane. As there is no anatomical name attached to this space, Braun has called it the retromolar triangle (trigonum retromolare). In the closed mouth it is located at the side of the upper third molar, and in the open mouth it is found midway between the upper and lower teeth. Immediately back of the mesial border of this triangle, directly beneath the mucous membrane, lies the lingual nerve, and about three-eighths of an inch further back the mandibular nerve is to be found. This last nerve lies close to the bone, and enters into the mandibular foramen, which is partially covered by the mandibular spine.

Before starting the injection, the patient should be cautioned to rest his head quietly on the headrest of the chair, as any sudden movement or interference with the hand of the operator may be the cause of breaking the needle in the tissues. The syringe, provided with a 1-inch needle, is held in a horizontal position, resting on the occluding surfaces of the teeth from the cuspid backward and slightly toward the median line. The needle is to be inserted three-eighths of an inch above and the same distance back of the occluding surface of the third lower molar,

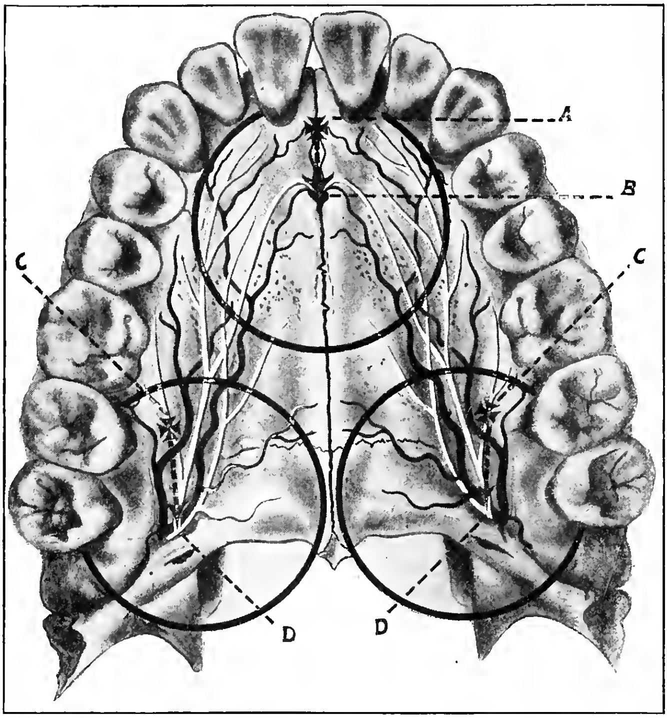


FIG. 233.—PERINEURAL INJECTION UPON THE HARD PALATE. A, B, injection near the foramina of Scarpa; C, D, injection near the posterior palatine canals.

the needle opening facing the bone. This position will insure the correct direction of the needle point, so as to reach the tissues immediately surrounding the nerves, and not lose the injection in the adjacent thick muscle tissue. The needle must always be in close touch with the bone, and is now slowly pushed forward, depositing a few drops of fluid on its way until the ridge is reached. About five drops of fluid are injected in this immediate neighborhood for the purpose of anesthetizing the lingual nerve. The needle is now pushed very slowly forward, always keeping in close touch with the bone and depositing fluid on its way, until it is pushed in about five-eighths of an inch. It is important to carefully feel the way along the bony wall of the ramus, as the needle may have to pass over the roughened and bony elevations which afford attachment to the internal pterygoid muscle. During the injection the syringe should remain in the same horizontal position as heretofore outlined. Soon after the injection, paresthesia of one-half of the tongue on the side of the injection occurs, which is soon followed by anesthesia of the mandibular nerve. Paresthesia of the mucous membrane and half of the lower lip is also established. The pulps of the lower teeth, including the cuspid and lateral incisor, the gum tissue on both sides of the jaw, and a part of the anterior floor of the mouth are anesthetized. The complete anesthesia of the two nerves also anesthetizes the whole alveolar process in this region. About five minutes are required for the complete anesthetization of the lingual nerve, and at least fifteen min-

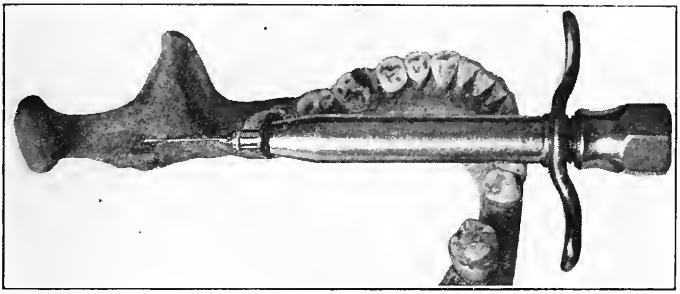


Fig. 234.—Perineural Injection Near the Mandibular Foramen.

utes for the mandibular nerve. Braun claims that the injection is absolutely free from danger, while Roemer states that danger may arise if the whole quantity of the solution should accidentally be injected into a vein.

The mental foramen lies midway between the superior and inferior border of the body of the mandible on its external surface, usually below the second bicuspid teeth. Its opening always faces posteriorly. An injection near this point increases the anesthesia in the cuspid region. The incisive fossa is a shallow depression on the external surface of the mandible between the cuspid teeth. It may be located by the palpating finger immediately above the chin. A number of small foramina are found in this region for the passage of nerves and nutrient vessels. The lower incisors may be anesthetized by making injections anteriorly into the incisive fossa, and one posteriorly in the region corresponding to the fossa. Usually peridental anesthesia is to be preferred for these teeth.

Precautions.—Conductive anesthesia is serviceable if a number of teeth have to be removed at one visit. It should be borne in mind, however, that in the average case *only one-half of either jaw should be anes-*

thetized at one sitting, so as to keep the quantity of the injected anesthesia solution within the limits of ordinary dosage.

The Injection into the Pulp.—By pressure anesthesia, pressure cataphoresis, or contact anesthesia, as the process is variously termed, we understand the introduction of a local anesthetizing agent in solution by mechanical means through the dentine into the pulp for the purpose of rendering it insensible to pain. Simple hand pressure with a suitable instrument, the hypodermic syringe, or the so-called high-pressure syringe, is recommended for such purposes.

Methods of Anesthetizing the Pulp.—(1) The pulp is wholly or partially exposed. The tooth is isolated with rubber dam, and cleaned with water and alcohol. The cavity is excavated as much as possible, and, if the pulp is not exposed, it is dehydrated with alcohol and hot air. A pledget of cotton or a piece of spunk is saturated with a concentrated cocain or novocain solution, placed into the prepared cavity, and covered with a piece of vulcanizable rubber. With a suitable burnisher, slowly increasing, continuous pressure is applied for from 1 to 3 minutes. The pulp may now be exposed and tested. If it is still sensitive, the process is repeated. Loeffler states that "this pressure may be applied by taking a short piece of orange wood, fitting it into the cavity as prepared, and directing the patient to bite down upon this with increasing force. In this way we can obtain a well-directed regulated force or pressure with less discomfort to the patient and operator." Miller describes this process as follows: "After excavating the cavity as far as convenient, and smoothing the borders of it, take an impression in modeling compound, endeavoring to get the margins of the cavity fairly well brought out; put a few threads of cotton into the cavity and saturate them thoroughly with a five to ten per cent solution of cocain; cover this with a small bit of rubber dam, and then press the compound impression down upon it. We obtain thereby a perfect closure of the margin, so that the liquid cannot escape, and one can then exert pressure with the thumb sufficient to press the solution into the dentin."

(2) The pulp is covered with a thick layer of healthy dentin. With a very small spade drill, one bores through the enamel or direct into the dentin at the most convenient place, guiding the drill in the direction of the pulp chamber. The chips are blown out, the cavity dehydrated with alcohol and hot air, and the syringe, provided with a special needle,—making as nearly as possible a water-tight joint,—is applied. Slow, continuous pressure is applied for from two to three minutes. With a round burr the pulp should not be exposed, and, if still found sensitive, the process is repeated.

Recently a method has come into vogue which allows successful anesthetization of the pulp by injecting the anesthetic solution around the apex of the tooth. The spongy alveolar process, which contains lymph channels, allows the ready penetration of the fluid. The injection should be made close to the bone, the needle being pushed slowly toward the apex, while the fluid is deposited drop by drop. No wheal should be raised by the injection, otherwise the benefit of the pressure from the dense gum tissue is lost.

CHAPTER XV

SPINAL ANALGESIA AND SPINAL ANESTHESIA

William Seaman Bainbridge, Sc.D., M.D.

Introduction.

History: Discovery of and Experimentation with Cocain; Experimentation with Cocain from the Neurological Point of View with Regard to Its Analgesic Effects Upon the Sensory Nerves, Including the Spinal Cord; Application of the Analgesic Effects of Cocain Upon the Cord to Surgical Operations Below the Diaphragm; Extension of the Surgical Application of Spinal Analgesia to Parts of the Body Above the Diaphragm; Experimentation with Other Agents.

Anatomical and Physiological Considerations: Origin; Volume; Specific Gravity; Movements; Pressure; Diffusion.

Course, Extent, and Duration of Analgesia: Course; Extent; Duration.

Accompanying Phenomena: Subjective; Objective.

Postoperative Phenomena.

Indications and Contraindications.

Advantages and Disadvantages: Advantages; Disadvantages.

Deaths.

Analgesic Agents: Cocain; Tropacocain; Stovain; Novocain.

Sterilization of the Analgesic Agent.

Sites of Injection.

The Patient: Preliminary Preparation of Patient; Position of Patient.

Apparatus and Materials.

Technique of Injection.

Additional Illustrative Case Reports.

Conclusion.

INTRODUCTION

In the pages which follow the term *analgesia* (ἀν + αλγος) is employed with its strict etymological significance—*absence of sensibility to pain.* The broader term, *anesthesia* (ἀν + ἄισθησις)—*without sensation*—is purposely avoided, except when quoting from authors who make no differentiation, and when referring to the exceptional cases in which analgesia merges into anesthesia.

Complete loss of sensation comes only with narcosis (νάρκωσις)—a state of profound unconsciousness. In some instances, with heavy dosage, an analgesic agent injected into the subarachnoid space may produce a state of mental lethargy bordering upon that which follows the inhalation of an anesthetic agent, with the loss of all forms of sensation—a real anesthesia. As a rule, however, with moderate dosage, the analgesic agent introduced into the spinal canal gives rise only to analgesia—loss of sensibility to pain. Tactile sense, the sense of heat and cold, of pressure and of traction, are not completely destroyed in the latter case.

The operator who fails to bear in mind the above differentiation is apt to experience more or less difficulty at times, and to feel that he has a right to chronicle dissatisfaction or failure with the method under discussion.

It has been our purpose to give, as briefly as possible, in the pages which follow, a cursory review of the work of others, rather than to confine ourselves strictly to the limits of personal experience. With spinal analgesia, as with every other form of analgesia or anesthesia, the method has its enthusiastic adherents and its uncompromising opponents. We have endeavored, in the light of personal experience, to examine the evidence *pro* and *con*, and to give a fair and impartial statement of our findings.

HISTORY

The history of spinal analgesia may be divided, for purposes of convenience, into four periods, which are more or less overlapping in time and achievement: (1) Discovery of and experimentation with cocain; (2) experimentation with cocain from the neurological point of view, with regard to its analgesic effects upon sensory nerves, including the spinal cord; (3) application of the analgesic effects of cocain upon the cord to surgical operations below the diaphragm; (4) extension of the application of spinal analgesia to parts of the body above the diaphragm. Experimentation with other agents.

Discovery of and Experimentation with Cocain.—The discovery by Niemann, in 1859, of the alkaloid of coca leaves, to which the name *cocain* was given, may be said to mark the first event in the history of spinal analgesia.

The discovery by Schraff, in 1862, of the local analgesic properties of this substance when placed upon the tongue was the second step forward in the history of this method.

With the application of the latter discovery to surgical purposes, suggested by Koller,[1] in 1884, the history of spinal analgesia was fairly initiated.

Following immediately upon these discoveries and their announcement,[2] many experiments were undertaken by investigators throughout Europe and America, all having for their motive the production of local analgesia for surgical purposes. This particular phase of the general subject of anesthesia falls within the scope of the chapter on local analgesia. It concerns the history of spinal analgesia only in so far as the discovery and application of cocain by others led to the sequence of deductive reasoning by Corning, and furnished the means for the application of the theories by which he gave to the world the discovery of spinal analgesia.

Experimentation with Cocain from the Neurological Point of View with Regard to Its Analgesic Effects Upon the Sensory Nerves, Including the Spinal Cord.—Corning's brilliant work [3] on the prolongation of the analgesic effects of cocain subcutaneously administered was the logical antecedent to his equally brilliant experiments with the local medication of the cord.[4]

In his first paper on spinal analgesia Corning was influenced in his deductions by the work of Harley,[5] who showed that a poison such as strychnin, injected under the membrane covering the cord, "can act only through the intermediation of the blood vessels, since, when the latter are separated from the cord, the solution remains entirely inert."

Corning concluded from this that, "in order to obtain the most immediate, direct, and powerful effects upon the cord with a minimum quantity of a medicinal substance, it is by no means necessary to bring the substance into direct contact with the cord; it is not necessary to inject the same beneath the membranes, as in the case of the frogs, since the effects are entirely due to the absorption of the fluid by the minute vessels. On the other hand, in order to obtain these local effects, it is first necessary to inject the solution in the vicinity of the cord; sec-

[1] Koller, Karl: "On the Use of Cocaine to Anesthetize the Eye," *Wiener med. Woch.*, Oct. 25, Nov. 1, 1884. Translated by H. Knapp: "Cocaine and Its Uses in Ophthalmic and General Surgery." Putnam's Sons, N. Y., 1885.

[2] Noyes, Henry D.: "A Few Cursory Notes on the Proceedings of the Meeting of the German Ophthalmological Society, Held at Heidelberg in the Middle of September of This Year." *Med. Rec.*, Oct. 11, 1884.

[3] Corning: (1) "On the Prolongation of the Anæsthetic Effects of the Hydrochlorate of Cocaine When Subcutaneously Injected. An Experimental Study." *N. Y. Med. J.*, Sept. 19, 1885; (2) "The Author's Method of Local Anæsthetization by Incarceration of the Anæsthetic in the Field of Operation," Part II, "Local Anæsthesia," 34.

[4] Corning: "Spinal Anæsthesia and Local Medication of the Cord," *N. Y. Med J.*, Oct. 31, 1885, Reprinted, 1909, *72*, 790. Also in "Local Anæsthesia," 85.

[5] See Ringer, Sidney: "A Handbook of Therapeutics," 1870, 387.

ondly, to select such a spot as will insure the most direct possible entry of the fluid into the circulation about the cord."

He reasoned that, if placed between the spinous processes of the vertebræ, "the anesthetic would be rapidly absorbed by the minute ramifications of the veins referred to, and, being carried by the blood to the substance of the cord, would give rise to anesthesia of its sensory and perhaps also of its motor tracts."

It was with this conception of the matter that Corning carried out his early experiments, first upon a dog and then upon a man.

In the case of the man, who was suffering from spinal weakness and seminal incontinence, 30 minims of a 3 per cent solution of cocain were injected between the spinous processes of the eleventh and twelfth dorsal vertebræ.

These experiments encouraged Corning to proceed with his investigations, and in 1888 he published a report [1] of his injection of cocain hydrochlorate in the immediate neighborhood of the cord.

The injections were made in the lumbar and dorsal regions, and thus Corning, antedated by three years the work of Quincke [2] with lumbar puncture.

Quincke found, independently, being unaware of Corning's work, that it was possible to remove the cerebrospinal fluid after lumbar puncture apparently without danger to the subject. He also demonstrated that a considerable amount of the cerebrospinal fluid may be withdrawn.

Quincke's experiments were made with a partly different object in view from that which actuated Corning, but the former's discovery undoubtedly had its effect in stimulating interest in the subject of spinal puncture, as it concerned the induction of spinal analgesia.

Following the work of Corning and Quincke, various experiments were made with reference to the effect of medicinal fluids upon the spinal nerves and cord.

Ziemssen [3] proposed the injection of such substances through lumbar puncture.

Sicard,[4] in 1898, published the report of a series of experiments in which he injected into the subarachnoid space normal salt solution,

[1] Corning: "Further Contribution on Local Medication of the Spinal Cord, with Cases." *Med. Rec.*, March 17, 1888; also "Headache and Neuralgia," 1888, 157.

[2] Quincke: "Die Lumbalpunktur des Hydrocephalis." *Berl. klin. Woch.*, 1891, No. 38.

[3] Ziemssen: *Wiesbaden Kongr.*, 1893.

[4] Sicard: "Essais d'injections microbiennes, toxiques et thérapeutiques, par voie céphalo-rachidienne." *Compt. rend. Soc. de Biol.*, Paris, April 30, 1898; also "Toxine et antitoxine tétanique par injections sous-arachnoïdiennes," *ibid.*, Nov. 12, 1898.

tetanus toxin, morphin, and other substances, and later he reported [1] the results of his investigations concerning the toxic effects of cocain when introduced into the subarachnoid space through the intracranial or spinal route.

From his first series of experiments Sicard concluded that the subarachnoid space could receive relatively large quantities of fluid, and that the effects of such fluid injected in this manner varied in proportion to the amount of dilution and to the rapidity with which the solution was injected.

Independent investigations by Jaboulay [2] confirmed Sicard's conclusions.

Corning, meanwhile, was still pursuing his experimental studies, and in 1894 he published the details of his method of irrigating the cauda equina with medicinal fluids.[3]

While he was engaged in testing his method of medicating the spinal cord, Corning became impressed with the desirability of introducing the remedies directly into the spinal canal, "with a view to producing still more powerful impressions upon the cord, and more especially upon its lower segment."

"There can be no doubt," he states, "especially if the injection be made between the second and third lumbar vertebræ, that the functions of the lower segments of the cord itself may be powerfully affected in this manner. We have only to conceive of the cerebrospinal fluid being at this point thoroughly impregnated with the medicinal fluid and lying in direct contact with the pia . . . to be convinced of the potency of such a procedure."

The dangers involved in such an operation were made a matter of consideration by Corning, and his own observations were in accord with the work of Mitchell [4] and Thoburn.[5]

Mitchell showed that a simple puncture of a nerve of an animal with a sharp needle causes little bleeding, which passes away without grave results.

Thoburn called attention to the harmlessness of such slight traumatism as the pricking of the cauda equina.

This work was later verified by Crile's investigations.[6] He found,

[1] Sicard: "Inoculations sous-arachnoïdiennes chez le chien; voie cranienne, voie rachidienne," *Compt. rend. Soc. de Biol.*, Paris, Oct. 29, 1898; also "Injection sous-arachnoïdienne de cocaïne chez le chien," *ibid.*, May 20, 1899.

[2] Jaboulay. "Drainage de l'espace sous-arachnoïdienne et injection de liquides médicamenteux dans les méninges," *Lyon méd.*, May 15, 1898.

[3] Corning: "Pain," 1894, 247 *et seq.*

[4] Mitchell, S. Weir: "Injuries of Nerves and Their Consequences," 1872.

[5] Thoburn, William: "Injuries of the Cauda Equina," *Brain, 10,* 381 *et seq.*

[6] Crile: "An Experimental and Clinical Research into Certain Problems Relating to Surgical Operations," 1901.

from a series of recovery experiments, that it was difficult to locate the point of injection, and that it was only in cases where no aseptic precautions had been taken at the time of the injection that the track of the needle could be traced by the unaided eye, careful inspection failing to reveal the point of injection in cases where such precautions had been taken.

Corning[1] emphasized the fact that serious disturbances of sensation and mobility, having their origin in the cauda equina, are always due to gross lesions, and not to insignificant circumscribed causes.

Application of the Analgesic Effects of Cocain Upon the Cord to Surgical Operations Below the Diaphragm.—The studies of Corning seem to have made little or no impression upon the minds of the various investigators to whose experiments reference has been made. Despite the fact that he had suggested, in his original contribution, the surgical application of the method,[2] no such application had been made until Bier, of Kiel, demonstrated its entire feasibility and published the results of his work.[3] Odier,[4] who injected cocain into the spinal cord of rabbits, noting the resulting protoplasmic changes in the nerve cells and the analgesia of the body below the point of the injection, failed to make any clinical application of the latter finding.

With the publication of Bier's paper the surgical application of spinal analgesia was definitely established.

Bier observed the effects of analgesia induced by this method upon himself, his assistants, and six patients. Lumbar puncture, after the method of Quincke, was employed. The passage of the needle was rendered painless by means of Schleich's infiltration. He used two cubic centimeters of a one per cent solution of cocain.

The appearance of Bier's paper led to the immediate adoption of the method by many surgeons throughout the civilized world, but especially in France and America. His findings were verified by Seldowitch,[5] experimenting upon dogs.

Tait and Caglieri[6] are credited with having performed the first sur-

[1] Corning: "Pain," 1894.

[2] Corning: *Op. cit.* (*N. Y. Med. J.*, Sept. 19, 1885)—"Whether the method will ever find an application as a substitute for etherization in genito-urinary or other branches of surgery, further experience alone can show."

[3] Bier: "Versuche über Cocainisirung des Rückenmarkes," *Deut. Zeit. f. Chir.*, Leipzig, 1899, 361.

[4] Odier: "Recherches expérimentales sur les mouvements de la cellule nerveuse de la moelle épinière," *Rev. Méd. de l. Suisse Romande*, 1898, *18*, 59.

[5] Seldowitch: "Ueber Cocainisirung des Rückenmarkes nach Bier," *Centralbl. f. Chir.*, 1899, *41*, 1110.

[6] Tait and Caglieri: "Experimental and Clinical Notes on the Subarachnoid Space," *Trans. Med. Soc. State of Cal.*, April, 1900, 266. Also, *J. Am. Med. Assn.*, July 7, 1900.

gical operation under spinal analgesia in America, on October 26, 1899. Osteëctomy of the tibia, in a patient fifty-four years of age, was performed without pain or discomfort, and with no unpleasant after-effects. One c. c. of a 3/4 per cent solution of cocain was employed.

The procedure was "popularized" by Tuffier,[1] who extended the application of the method from its original domain of the lower extremities, as practiced by Bier, to the genito-urinary organs and abdomen. He subsequently performed hysterectomy, salpingectomy, nephrectomy, pylorectomy, cholecystectomy, etc., under subarachnoid analgesia.

The position of spinal analgesia in the surgical world was established upon a firm basis by the work of Bier, Tait and Caglieri, Tuffier, and others of the early investigators, and the literature of the subject at once began to assume extensive proportions. The scope of the application of the procedure was quickly extended, and the method came to be employed in old and young, for divers conditions, and with varying degrees of skill and success.

It was not long until Bier felt called upon to protest[2] against the recklessness with which the method was being employed, regardless of the fact that no noteworthy improvement in technique had been evolved. He protested especially against the dangerously large doses of cocain which some operators used. New methods, he said, should be devised in an attempt to reduce the toxicity of the drug and to prevent the unpleasant by-effects so often noted. He suggested the application of the procedure to operations upon the entire trunk and arms, and made a plea for an effort to find less harmful drugs which would produce analgesia by this method.

In obstetrical practice subarachnoid analgesia was employed early in its history, Kreis[3] being credited with having first made this application of the method. Doléris,[4] Marx,[5] Dupaigne,[6] and others utilized the pro-

[1] Tuffier: (1) "Analgésie chirurgicale par l'injection sous-arachnoïdienne lombaire de cocaïne," *Soc. de Biol.*, Nov. 11, 1899, in *Semaine méd.*, 1899, 389; also, *La Presse méd.*, Nov. 15, 1899, 294; (2) "L'Analgésie chirurgicale par voie rachidienne," 1900. In *L'Œuvre médico-chirurgical*, Critzman, 1901-02, 24-30.

[2] Bier: "Bemerkungen zur Cocainisirung des Rückenmarkes," *Münch. med. Woch.*, Sept. 4, 1900, 1226.

[3] Kreis: "Ueber Medullarnarkose bei Gebärenden," *Centrlbl. f. Gyn.*, July 14, 1900, 724.

[4] Doléris: "Analgésie par injection de cocaïne dans l'arachnoïde lombaire," *Compt. rend. d. l. Soc. d'Obst., de Gyn., et d. Pédiat. d. Paris*, 1900, *2*, 328.

[5] Marx: (1) "Medullary Narcosis During Labor, a Preliminary Report," *Med. News.*, Aug. 25, 1900, 293; (2) "Medullary Narcosis During Labor," *Med. Rec.*, Oct. 6, 1900, 521; (3) "Analgesia in Obstetrics Produced by Medullary Injections of Cocain," *Phila. Med. J.*, Nov. 3, 1900, 857.

[6] Dupaigne: "Anesthésie rachidienne par le cocaïne," *Ann. de Gyn. et Obst.*, Paris, 1901, *55*, 44.

cedure for the same purpose. My own experience with spinal analgesia in obstetrical practice is limited to one case, but this was an excellent one in which to test the method in this class of cases. (See case description on page 593.)

In the early stage of the surgical application of spinal analgesia the author of this section began to employ the method, being particularly interested at that time in its use in young children. Seven cases operated upon under spinal analgesia were reported,[1] the youngest being 2½ and the oldest 11 years of age. The former case was apparently the youngest in which the method had been employed at that time. The youngest cases on record at that time were: One, 8 years, operated by Murphy; one each at 11 years, by Bier, Lugueu, and Kinderjy, and one, 12 years, by Tuffier.

An additional series of forty cases [2] was reported during the following year, the youngest of this series being 7½, and the oldest 19 years of age. Twenty-four of these cases were reported in detail.

Report [3] was published of twelve operations upon infants and young children ranging in age from 3 months to 5 years. Of this series the history of that case, No. XII, is detailed on page 588.

Tuffier [4] reported a case in an infant 3 months old.

Extension of the Surgical Application of Spinal Analgesia to Parts of the Body Above the Diaphragm. Experimentation with Other Agents.—It is impossible, within the limited space, to follow the work of the very large number of surgeons who have devoted attention to the subject of spinal analgesia during the years which have intervened since the appearance of Bier's original communication.[5] The historical contributions, other than those mentioned, have been largely in the nature of modifications of technique, and the verification of the earlier results by a large number of clinical cases.

With certain notable exceptions, both the experimental and the clinical investigations were concerned with the production of analgesia below the diaphragm and its application to the surgery of those regions.

Tait and Caglieri,[6] in 1900, reported 3 cases in which cocain was injected into the sixth cervical space without untoward effects. The

[1] Bainbridge: "Analgesia in Children by Spinal Injection, with a Report of a New Method of Sterilization of the Injection Fluid," *Med. Rec.*, Dec. 15, 1900.

[2] Bainbridge: "A Report of Twenty-four Operations Performed During Spinal Analgesia," *Med. News*, May 4, 1901.

[3] Bainbridge: "Report of Twelve Operations on Infants and Young Children During Spinal Analgesia," *Archives of Pediat.*, July, 1901.

[4] Tuffier: "Sur la rachicocainisation," *La Presse méd.*, Paris, June 8, 1901, 265.

[5] Bier: *Op. cit., Deut. Zeit. f. Chir.*, Leipzig, 1899, *51*, 361.

[6] Tait and Caglieri: *Op. cit., Trans. Med. Soc. State Cal.*, April, 1900, 266.

patients were examined weeks after the injection and found to be free from any complication.

Morton,[1] in 1900, also presaged the recent extension of spinal analgesia to surgical operations upon all parts of the body. "I think," he said, "we will soon find that, by injecting higher into the dorsal region, anesthesia can be extended all over the body with perfect safety. It has been demonstrated in the dog by making an injection in the upper part of the dorsal region. It does not interfere with motion, consciousness, or sense of touch."

In a later communication[2] Morton said: "I think we have a safe and reliable analgesic in the subarachnoid injection of cocain for the performance of any surgical operation on any portion of the body, regardless of age, sex, or disease, and one which has no contraindications." In this report Morton tabulated 253 cases operated upon by him, 24 in females, 229 in males, 8 of the operations being above the diaphragm. An additional series of 61 cases was added to the above report, 15 of which were upon the upper extremities or head. The analgesia was complete in all cases. One case in which the operation was above the diaphragm was reported in detail.[3]

Chaput and others performed operations on parts of the body above the diaphragm under spinal analgesia.

It appears that the work of Tait and Caglieri, Morton, and others, with high injection, has not been followed up with further published clinical application, for which reason, perhaps, originality in this regard has been generally accorded to Jonnesco.

In September, 1908, before the Congress of the International Society of Surgery, in Brussels, Jonnesco,[4] of Bucharest, described his new method of general spinal anesthesia, and reported 14 cases operated upon by this method. The method is detailed, and selected cases cited, 103 of which were high dorsal analgesias, and 295 dorso-lumbar analgesias.

In a later article[5] Jonnesco says: "It is an error to confuse lumbar rachianesthesia, conceived by Corning and popularized by Bier, with my method. As I have many times emphasized, my method is a new one and altogether distinctive, because I have generalized spinal anesthesia, adapting it to *all* operations on *any* part of the body. This has not yet

[1] Morton: "Is the Subarachnoidean Injection of Cocain the Preferable Anesthesia Below the Diaphragm?" *Pac. Med. J.*, Nov., 1900.

[2] Morton: "The Subarachnoid Injection of Cocain for Operations on All Parts of the Body," *Am. Med.*, Aug. 3, 1901.

[3] Morton: "Report of a Lipoma Removed from the Cheek under Medullary Narcosis," *Phila. Med. J.*, July 6, 1901.

[4] Jonnesco: "Remarks on General Analgesia," *Brit. Med. J.*, Nov. 13, 1909.

[5] Jonnesco: "Concerning General Rachianesthesia," *Am. J. of Surg.*, 1910, *29*, 33.

been done by others, although it is now a year and a half since I read a paper on this subject at the International Surgical Congress in Brussels. I secured this anesthesia by piercing the spinal column at all levels, and by adding strychnin to the anesthetic stovain, novocain, tropococain, etc."

Jonnesco holds that the fact that the respiratory nerves are not involved in the high injections, although all the other nerves of that spinal region are paralyzed, is due to the influence of the strychnin. To this latter statement reference will be made under the head of physiological action.

In the addition of the strychnin to the analgesic solution Jonnesco is evidently original. As early as 1903. however, the author of this section used strychnin hypodermatically in conjunction with spinal analgesia, with the same ends in view, of supporting the patient and preventing respiratory depression.

Following the suggestion of Bier concerning the desirability of discovering some more suitable drug than cocain for spinal analgesia (see page 560), a large amount of experimental work has been done with a view to accomplishing this end. Tropacocain, stovain, novocain, beta-eucain, beta-eucain lactate, alypin, nirvanin, holocain hydrochlorid, acoin, orthoform (new), and anesthesine are some of the drugs which from time to time have been made the subject of experimental or clinical investigation. (See page 599.) A full list of all substances which have been prepared is given in Chapter XX.

ANATOMICAL AND PHYSIOLOGICAL CONSIDERATIONS

With the discovery by Cotugno (Dominicus Cotunnius), in 1764, of the "collection of water about the brain and in the spine," a new interest was given to the cerebrospinal column. The observations of Cotugno upon the bodies of animals were confirmed by him upon human subjects, and his declaration that the nervous centers were bathed by this cephalo-spinal fluid called forth a brief but very good description by Haller, in 1766, and a complete study by Magendie, in 1825. Following these early investigators, a number of others continued the study of the anatomy and physiology of the cerebrospinal canal. Corning's experiments with reference to the local medication of the cord, and the discovery by Quincke that it is possible to remove the cerebrospinal fluid by lumbar puncture without danger to the subject, gave a still more definite interest to this region. The surgical application, made by Bier, of the discoveries of Corning and Quincke called forth an extensive series of investigations concerning the anatomical and physiological relations of the vertebral canal.

The extent of the experimental and clinical study devoted to this subject may be imagined when one realizes, as stated by Mott,[1] that in the ten years preceding 1910 there appeared in the *Revue Neurologique* abstracts of 187 papers on the physiology of the cerebrospinal fluid.

Despite the many contributions to the subject, there is a notable diversity of opinion with reference to certain practical points relating to the physiology of the cerebrospinal canal and its contents, as will be seen.

Among the more recent investigators of the anatomical relations of the canal, Gerstenberg and Hein [2] and Lusk [3] have given valuable practical contributions. Michelson [4] and others have emphasized the importance of bearing in mind that the spinal fluid bathes a number of cranial nerves, as well as the spinal roots, so that those nerves may also become exposed to the toxic action of the analgesic agent when it passes to a sufficient height in the dural sac. The *abducens, trochlear, motoroculi,* and *optic* are the cranial nerves primarily, and most frequently, involved in spinal analgesia.

It is to be taken for granted that the general anatomy of the parts involved is a matter of accurate knowledge on the part of the surgeon who undertakes spinal puncture, for which reason no space is given to this subject. Certain practical points which are directly concerned in the matter of the selection of the site for puncture, and in controversy relating to lateral or median puncture, are reserved for the section on Sites of Injection. (See p. 605.)

Physiological investigation has established certain facts with reference to the cerebrospinal fluid which have a practical bearing upon spinal puncture and spinal analgesia. The composition, origin, density, volume, pressure, drainage, and motion of the fluid have been made the subject of exhaustive research, formerly by physiologists and neurologists, and latterly by those especially interested in its utilization for therapeutic purposes, particularly with reference to spinal analgesia.

Origin.—Faivre, in 1854, suggested the intimate relationship between the choroid plexus of the central nervous system and the cerebrospinal fluid. Subsequent investigation has tended to support the view that the cerebrospinal fluid is a secretory product of the epithelial cells of the choroid plexus and of the ependyma membrane.

[1] Mott, F. W.: "The Cerebro-spinal Fluid," *Lancet,* July 2 and 9, pp. 1 and 79, 1910.

[2] Gerstenberg and Hein: "Anatomische Beiträge zur Rückenmarkesanästhesia," *Z. f. Geburtsch. u. Gyn.,* 1907-08, *61,* 524; also, *Verhandlungen der Gesellschaft f. Geburtsh. u. Gyn.,* zu Berlin, 1907-08.

[3] Lusk, William C.: "The Anatomy of Spinal Puncture with Some Considerations on Technic and Paralytic Sequels," *Ann. of Surg.,* Oct., 1911, 449.

[4] Michelson: "Der gegenwärtige Stand der Lumbal-anaesthesie," *Ergebnisse der Chir. und Ortho.,* 1912, *4.*

Volume.—There is abundant evidence of the fact that the cerebrospinal fluid is continually being secreted. The quantity in the subarachnoid space, the ventricles of the brain, and the central canal of the spinal cord is said to vary from 50 to 150 c. c., the average being from 100 to 130 c. c. (See pp. 619 and 624 Dry Spine.)

Specific Gravity.—According to Gray, who studied the cerebrospinal fluid in a series of normal children, from whom it was obtained on the operating table, the specific gravity varied from 1.0054 to 1.0071. In cases of extreme shock the specific gravity rose to 1.0076, 1.0080, and 1.0083. The fluid of older children tended to be of a higher density than that of infants and younger children.

The specific gravity of the fluid in adults is stated by Nogué [2] to vary from an average of 1.003 to as high as 1.020. By the majority of the writers consulted it is stated to vary from 1.004 to 1.007.

Movements.—The cerebrospinal fluid is in constant motion. Being constantly secreted, it is likewise continuously drained through the arachnoid sheaths of the nerves, the perivascular lymphatic sheaths, and, according to some observers, the Pacchionian bodies. This subject has been studied by Schwalbe, Key and Retzius, Tait and Caglieri, Klose and Vogt, and a number of others, and recently reviewed by Chambard.[3]

When sepia, India ink, or other colored fluid is injected into the canal, the colored corpuscles accumulate around the nerve roots and the cranial nerves near their exit orifices. The elimination in this manner of soluble substances injected into the fluid illustrates the meningeal permeability from within outward.

In addition to the constant drainage of the cerebrospinal fluid there are also pulsation, a systolic flux and reflux, and a transportation, under certain circumstances, of the entire bulk of the fluid, as when, in the horizontal position, the fluid is transported on to the medulla and the brain.

Pressure.—The pressure under which the fluid exists is dependent upon the cerebral circulation, and varies under certain circumstances and in different positions of the body. The actual pressure is taken by lumbar puncture in the sitting posture. This has been found by Quincke to vary from 50 to 150 millimeters of water.

Diffusion.—Tait and Caglieri,[4] in their valuable experimental and clinical work on the subarachnoid space, employed a large number of

[1] Gray, H. Tyrrell: "A Study of Spinal Anæsthesia in Children and Infants," *Lancet*, Sept. 25 and Oct. 2, 1909.

[2] Nogué: "Anesthésie," *Traité de Stomatologie*, 1912, *6*, Paris.

[3] Chambard: "L'Anesthésie Lombaire," *Thèse de Paris*, 1911.

[4] Tait and Caglieri: *Op. cit.*, *Trans. Med. Soc. State of Cal.*, April, 1900, 266. See, also, *J. Am. Med. Assn.*, July 7, 1900.

animals and a series of cadavers, and several patients were subjected by them to lumbar puncture for therapeutic purposes, with the hope of clearing up certain doubtful points relating to the physiology of the subarachnoid space.

By means of their experimental work on animals and their clinical studies on man, these investigators confirmed the theory that absorption and elimination occur when chemical substances are injected directly into the subarachnoid space, and that the osmotic current exists in only one direction; in other words, as shown by Sicard, that there is exosmosis, but no endosmosis.

The mode of diffusion of the cerebrospinal fluid was studied by means of colored mixtures, which enabled the workers to note with accuracy and facility both the miscroscopic and the macroscopic results. When injected without pressure, the colored fluid stained the space at the point of injection, then diffused in all directions, ascending and descending, following the meningeal prolongations along the spinal nerves, to the intervertebral foramina, where it stopped abruptly. The extent and the rapidity of the diffusion were influenced by the amount, the composition, and the specific gravity of the liquid injected, and chiefly by the pressure under which it was injected.

It was found that a slow injection of 1 c. c. of the colored mixture, in a rabbit weighing 900 gm., ascended rapidly, the fluid being found around the medulla oblongata and at the base of the brain when the animal was killed 10 hours after the injection.

The same amount of fluid injected under pressure was found 26 hours later to have diffused from the spinal subarachnoid through the foramen of Magendie to the fourth ventricle, through the *iter a tertio,* or aqueduct of Sylvius, to the third ventricle, and finally to the cortex of the brain. If 5 c. c. of the colored fluid were injected under great pressure in the lumbar space, the diffusion occurred instantaneously.

Experiments were instituted to determine the course followed by the fluid from the lumbar space to the cortex of the brain. It was found that the pia-arachnoid was colored in its entire course along the cord and brain, continuing along the sheath of the auditory, facial, and optic nerves, and following the prolongations through the cribriform plate of the ethmoid. The stain followed the meningeal sheath on the optic nerve, generally stopping at the junction with the sclerotic. In several of their specimens Tait and Caglieri found that the stain involved the sclerotic, choroid, papilla, and retina.

Halbreich,[1] from a series of experiments on dogs and frogs, concluded that the solution, when injected in the lumbar region, is the more liable to reach the medulla oblongata the larger the quantity of fluid injected and the more the head of the subject is lowered. The

[1] Halbreich: *Med. Obos.,* Russia. Abst. in *J. Am. Med. Assn.,* 1902, 603.

gray matter is penetrated, according to this investigator, by diffusion and osmosis, and by the lymphatics.

Crile,[1] in his studies upon the cord, injected a solution of cocain, which was colored with methylene blue. He found that an injection of ½ dram of this solution, made in the lumbar region, stained the entire cord and the under surface of the brain in 30 seconds. The various localized functions of the cord and medulla were rapidly anesthetized, the respiratory center in the medulla, for example, being anesthetized within a few seconds by lumbar arachnoid injection. A forcible injection was followed within a few seconds by a direct fall in blood pressure and by cessation of respiration. Crile found that the fluid ascended about as rapidly with the subject in a vertical position as in the horizontal, and he concluded that the effect of the anesthetic was due to local contact with the nerve structure, and not to absorption. This view, he held, is in full accord with the general action of cocain on other nerve structure. Crile purposely employed large doses in these experiments in order to determine the control, or, as he expresses it, the want of control, the operator can have over the extent of the analgesia.

The attempt to ascertain to just what physiological action of the analgesic agent the analgesic state may be attributed in the case of subarachnoid injection has led to various theories of more or less contradictory character.

Bier [2] held that the sequence of symptoms following the injection is the result of changes in the circulation caused by the introduction of a heterogeneous substance into the spinal canal, and that it is not due to any toxic action of the cocain.

Nicoletti [3] attributed it to the vasomotor constrictive action of the injected agent.

Goldan [4] held that the circulation is no factor in the production of analgesia when cocain is injected into the subarachnoid space, the effects being due, in all probability, to the passage of the cocain from the subarachnoid space along the perivascular spaces in the tunica adventitia of the blood vessels to the sensory columns of the cord, also directly into the lymph spaces of the nerves themselves.

The investigations of Dönitz and Barker seem to have led to different conclusions with respect to the manner of extension of the analgesia.

[1] Crile, George W.: "An Experimental and Clinical Research into Certain Problems Relating to Surgical Operations." Phila., 1901, 145 *et seq.*

[2] Bier: "Bemerkungen zur Cocainisirung der Rückenmarkes," *Münch. med. Woch.*, Sept. 4, 1900.

[3] Nicoletti: "L'analgesia cocainica del midollo spinale nella chirurgia ginecologica," Treizième Congrès International de Méd., Paris, Sec. de Chir. Gén., 1900; see, also, *Archiv. Ital. di Ginicol.*, Aug. 1900, 512.

[4] Goldan: "Intraspinal Cocainization for Surgical Anesthesia," *Med. News*, Nov. 3, 1900.

Dönitz[1] maintains that it is not a question of diffusion, but simply one of shifting the balance in the liquor spinalis, which takes place at the moment of the change of posture; that "it is not a question of the action of gravity on the analgesic compound at all, nor is it one of hypothetic currents."

Barker,[2] on the other hand, in his interesting series of clinical experiments, makes use of gravity by employing an injection compound of much greater specific weight than that of the liquor spinalis. Assuming that there are only three ways in which an analgesic fluid injected in the second lumbar interspace can make its direct effects felt in the mid-dorsal region or higher, Barker says with reference to these, in sequence:

"(1) Diffusion *alone* of one fluid in another is a slow process, and, as we shall see, is unlikely to be the mode of spread of the injected fluid in this procedure.

"(2) Bier and his followers have aimed at shifting the whole injected compound upward or downward with the whole mass of the liquor spinalis by raising or depressing the pelvis. That the cerebrospinal fluid does recede somewhat toward the head on elevation of the pelvis is undoubted, but it is hard to imagine its doing so to such an extent as to carry with it a cloud of fluid lighter than itself from the second lumbar to the fifth dorsal vertebra, some 8 to 10 inches. I venture to think that with such a fluid as he has used, whose specific gravity is 1.0058, suspended in the liquor spinalis, whose specific gravity is 1.0070, what he has achieved by elevation of the pelvis has rather been a more rapid diffusion of the injected drug, due to the consequent oscillation of the spinal fluid, aided, perhaps, by vascular pulsation. But this rapid diffusion would, of course, dilute the injection, and perhaps carry it further than desirable.

"(3) There remains, then, the third possibility, namely, that an injected compound heavier than the liquor spinalis may be affected by gravity, and sink through the latter in a way quite different to the behavior of a fluid of less specific gravity, such as that referred to."

Other investigators, notably Babcock,[3] by using an injection fluid lighter than the cerebrospinal fluid, seek to affect the sensory nerves without involving the motor nerves. The regulation of the position of the patient's body, with such a fluid, controls the area affected by the

[1] Dönitz: "Die Hohenausdehung der spinal Analgesie," *Münch. med. Woch.*, Nov. 27, 1906.

[2] Barker: "A Report on Clinical Experiences with Spinal Analgesia," *Brit. Med. J.*, March 23, 1907.

[3] Babcock, W. Wayne: (1) "Spinal Anesthesia. A Clinical Study of 658 Administrations," *Penn. Univ. Med. J.*, Aug., 1909; (2) "The Range of Activity and the Untoward Effects of Certain Spinal Analgesics; Based on Two Thousand Administrations," *Trans. Am. Ther. Soc.*, 1910, 57.

analgesia. The rate of diffusion of the lighter fluid is controlled by the addition of a larger or smaller percentage of alcohol. Babcock holds that the analgesic drug is decomposed by the cerebrospinal fluid, which still further limits its field of activity. The less the alcohol used, the more rapid is this decomposition; hence, as the fluid diffuses, it decomposes, and the anesthetic effect can be limited very largely to any desired portion of the spinal canal.

Tuffier,[1] considered the analgesic action of the agent to be local, whether it be exerted upon the cord, the nerve roots, or the spinal ganglion, being not determined. He inclined to the belief, however, that it is confined exclusively to the nerve roots. The early symptoms, such as malaise and trembling, he attributed to the direct action of the anesthetic agent upon the spinal axis.

Spiller and Leopold[2] experimented with stovain in an effort to determine certain points with reference to the action of this agent upon the nervous system. They thought that perhaps stovain, which produces temporary anesthesia, might, by repeated injections, produce anesthesia of gradually increasing duration until a finally persisting loss of sensation, resulting from organic change, might ensue. They desired to ascertain whether a systemic degeneration of the posterior roots and their continuation in the posterior columns of the cord is the common result of the repeated use of stovain. They also desired to determine whether the paralysis that occurs in stovain anesthesia is of a motor or sensory type, i. e., whether it is produced by changes in the peripheral motor neurons, or is the result of ablation of all afferent impulses which normally pass over the posterior roots. They called attention to the fact that reflex action and all recognition of toxicity of the limbs, and necessarily of the position of the limbs, are lost if all peripheral afferent impulses are cut off.

In order to satisfy themselves upon these points with reference to stovain, Spiller and Leopold experimented upon dogs, 5 subjects being employed. They performed lumbar puncture, using stovain in doses of 0.05 gm. to 2 gm., the injections being usually at intervals of 2 or 3 days.

They divided the symptoms into temporary and permanent. The temporary symptoms consisted of flaccid paralysis and complete or partial sensory loss. The permanent symptoms consisted of ataxia, decreased sensation, and, in one case, loss of patellar reflex. The symptoms became permanent after the third injection, remaining until the end of the experiment.

These investigators considered that their experiments clearly demonstrated that stovain affects especially the anterior and posterior roots of

[1] Tuffier: *Op. cit., La Presse médicale,* June 8, 1901.

[2] Spiller and Leopold: "The Effects of Stovain on the Nervous System," *J. Am. Med. Assn.,* June 4, 1910, 1840.

the cord. The degeneration of the posterior root fibers was intense, as was likewise that of the intramedullary portion of the lumbar and sacral posterior root fibers in the thoracic region. The posterior thoracic roots were unaffected. Stovain evidently causes slight degeneration in the periphery of the anterolateral columns, but has less effect here than on the nerve roots.

The lesions obtained by them could not have been produced, they hold, by the trauma of the needle, as the sections of the lumbar region examined were ½ to 2 inches above the point of injection, and yet the posterior and anterior roots were greatly degenerated.

"It would be unwarranted," they conclude, "to apply these findings too strictly to man, as no grave changes have been found as yet in the human cord. At most, our findings would show that repeated injections of stovain might be injurious, and would make one cautious in employing several injections within a short time in the same subject."

Spielmeyer [1] examined human spinal cords in his study of the pathologico-anatomical considerations involved in spinal analgesia. He examined the central nervous system of 13 patients who had died from various causes within from 2 to 8 days after spinal analgesia with stovain. In all except 1 case death was in no way related to the spinal analgesia. In 1 case death was due to respiratory paralysis 40 hours after the operation.

Upon examination of the woman who died from respiratory paralysis advanced changes in the cells of the spinal cord were found. Spielmeyer did not regard these as a direct effect of the analgesic agent, similar changes having been found in other cases in which death was due to respiratory paralysis of different origin. In three other cases Spielmeyer was enabled to demonstrate characteristic changes in the polygonal motor cells of the cord. The cells of the posterior horn and the spinal ganglia presented no changes. Spielmeyer was able to produce, experimentally, similar changes in the motor ganglion cells of dogs and monkeys.

Michelsson holds the view that, as this histological picture exactly corresponds to the phenomena which usually follow upon the destruction of the axis cylinder, it must be left undecided whether a primary or secondary effect of stovain upon the ganglia is responsible, although animal experiments rather favor the first assumption. It is certainly remarkable, he says, that these changes can be observed only on the motor ganglion cells, high up in the cervical cord, and that there is always a predominating number of normal polygonal cells, besides the affected cells. This probably accounts for the fact that motor disturbances were

[1] Spielmeyer: "Pseudosystemer-krankungen des Rückenmarkes nach stovainanästhesie," *Neurol. Centrlbl.*, Jan. 16, 1909, 69; see, also, *Münch. med. Woch.*, Aug. 4, 1908, 1629.

not noted in any of Spielmeyer's cases in man or in animals. In the 13 cases Spielmeyer employed stovain in doses of 0.12 gm. Patients who had received the customary dose of 0.05 gm. to 0.07 gm. presented no changes in the central nervous system, so that the assumption would seem to be justified that this stovain dose as a rule does not produce any lesions of the ganglion cells.

Klose and Vogt [1] employed tropococain and novocain in a series of experiments, which led them to the same results as those obtained by Spielmeyer with stovain.

These investigators found that the injected agents are distributed over the entire space occupied by the cerebrospinal fluid within half an hour at the latest. The specific gravity of the solution, and the position of the animal, are of subordinate importance. The alkaloids remain for a disproportionately long time in the cerebrospinal fluid. Among the agents examined by them, tropococain persisted for relatively the shortest time, stovain for the longest, novocain ranking midway between. In this scale of excretion the duration of the absorption, the sojourn in the blood, and the duration of the analgesia stand in direct proportion to the time after which absorption begins.

Following the work of Klose and Vogt, Barker [2] conducted a series of experiments to determine how long stovain remains in the dural sac after injection, unabsorbed, fixed, or destroyed; what effects, apart from analgesia, the agent produces; what immediate and remote effects, if any, the drug has upon the structures with which it comes in contact; and how the agent is eliminated from the system generally. Attention is directed by him to the importance of determining these points with reference to the various analgesic compounds or agents before this method of inducing analgesia can be put in its proper place among surgical procedures.

In nine of his cases previously injected with stovain Barker withdrew the cerebrospinal fluid, for various reasons, at periods varying from half an hour to forty-six hours after injection. Stovain was found to be present in six cases, the time after injection ranging from one-half hour to twenty-four hours; negative in one case at forty-four hours; and doubtful in two at forty-five and forty-six hours respectively.

The question whether any immediate effect is produced upon the structures within the dura by the stovain injection was answered, in Barker's experience, in the affirmative. In all the cases in which he withdrew cerebrospinal fluid within 46 hours of the injection of stovain

[1] Klose and Vogt: "Physiologische und anatomische Untersuchungen zur Lumbalanästhesie und zur Frage ihrer klinischen Verwertharkeit," *Münch. med. Woch.*, March 9, 1909.

[2] Barker: "Elimination of Stovain After Spinal Analgesia," *Brit. Med. J.*, Sept. 18, 1909, 789.

into it the fluid was distinctly turbid. The turbidity was found on microscopical examination to be due to the presence of leukocytes of various forms. The theory that the headache which sometimes follows spinal analgesia is due to aseptic irritation and hypersecretion within the dura did not seem to Barker quite satisfactory.

Barker found from the study of his cases that, long after the analgesic effect of the drug has passed off, stovain or its base can be shown to be unmistakably present in the cerebrospinal fluid. No satisfactory answer could be given to the question, Why does the analgesia last for only a couple of hours? He suggested that only perfect stovain is analgesic, and that its base split off by the alkaline cerebrospinal fluid is not, and that this base is what is recovered in subsequent tappings.

From his clinical studies he thought it clear that no permanent structural change in the nervous structures leading to definite symptoms has been proved to be due to the injections.

From the foregoing references to the experimental work of various investigators it will be noted that the physiological action of cocain and other analgesic agents when injected into the subarachnoid space was not clearly understood in the earlier stages of the development of spinal analgesia, and that the studies of later investigators have not served to fully settle these problems.

COURSE, EXTENT, AND DURATION OF ANALGESIA

Course.—The course of the analgesia, or the sequence in which the various parts of the body are affected, varies with the individual, the point of injection, the agent employed, and the technique.

As a rule, in lumbar analgesia, after a minute or so, sensibility to pain is lessened in the perineum, external genital organs, and the inner side of the thigh. The first reflex to disappear is the patellar, which is quickly followed by the disappearance of ankle clonus. Loss of sensibility to pain follows, in the order named, in the posterior surface of the thighs and legs, the soles of the feet, and the anterior surface of the legs, and the thighs up to Poupart's ligament. The analgesia then gradually extends to the umbilical region, and from that zone on, in some instances, higher and higher, until universal analgesia, as this may be determined from superficial tests, supervenes. In some instances this includes the mucous membranes of the mouth, nose, and larynx.

The course of the disappearance of sensibility to pain is segmental, proceeding from the fourth or fifth sacral, segment by segment, to whatever limit it reaches in the individual case.

Extent.—Analgesia may be partial or complete, with reference to

Fig. 235.—Operation Under Way for Removal of Tumor of Abdominal Wall Under Spinal Analgesia. Ten minutes after puncture. Face screen in position.

Fig. 236.—Second Operation, Same Analgesia, Same Patient as in Figure 235. Exsection of varicose veins, both legs; patient reading, resting paper against face screen.

the extent of the body involved, as well as to the degree to which sensation is abolished. The term *complete* is generally employed to signify the degree of loss of sensation, particularly pain sense, though the word is not infrequently used with reference to the extension of the analgesia over the entire body. For the latter purpose the word *universal* is perhaps preferable. When the cerebral cortex becomes involved, the analgesia merges into true anesthesia, during which the patient loses consciousness, or lapses into a deep sleep with snoring.

In the majority of instances in which the analgesic agent is injected

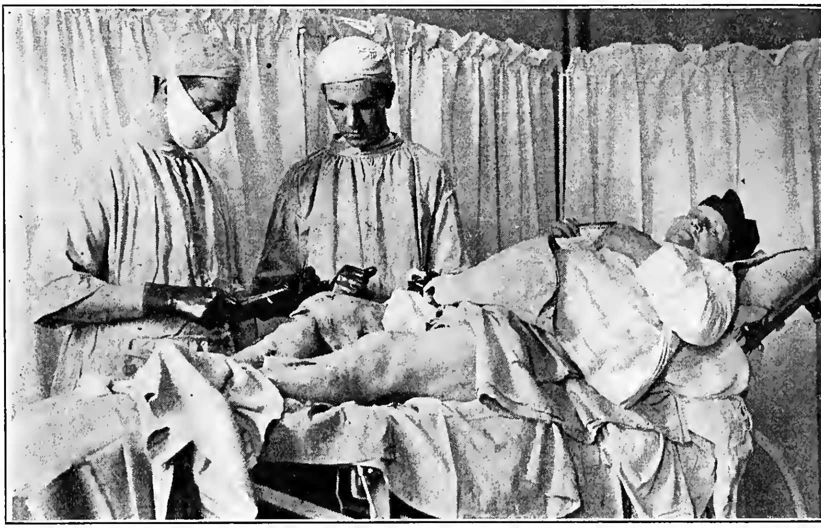


Fig. 237.—Same Patient as in Figures 235 and 236. At End of Operation. While the wounds are being sutured, She drinks a cup of tea; facial expression shows absence of pain or discomfort.

into the lumbar or lower dorsal region the analgesia extends to the umbilical region. Under different circumstances the height to which this goes varies, as previously noted.

It not infrequently happens that complete analgesia to a very high level, or even universal analgesia, follows the introduction of moderate doses of the analgesic agent into the lumbar region.

Morton,[1] in 1903, published a record of 929 cases operated upon below the diaphragm and 76 above it. In one case he removed the entire superior maxilla for carcinoma, the analgesia being complete. He introduced in this case half a grain of cocain between the third and fourth lumbar vertebræ.

[1] Morton: "Excision of the Superior Maxillary Under Medullary Narcosis," *Am. Med.*, March 21, 1903, 451.

Chaput[1] noted that in 53 of 102 cases the analgesia extended above the diaphragm, the arms being involved in 31, the face in 13; while in 9 cases the analgesia of the head was complete. This high analgesia was obtained by the rapid and forcible injection of large doses of cocain.

Pedeprade[2] noted 5 cases in which analgesia was complete throughout the body.

Tuffier[3] reported the removal of a cyst of the lung under medullary analgesia.

In 4 of the writer's early cases the analgesia extended over the entire body, even the mucous membrane of the mouth and larynx being com-

FIG. 238.—ENLARGED PICTURE OF PATIENT'S FACE SHOWING FACIAL EXPRESSION.

pletely analgesic, as recorded in a personal letter to Patterson and incorporated by the latter in his admirable résumé of the literature of spinal analgesia.[4] In 27 other cases, operated upon under lumbar analgesia, with moderate doses, the analgesia was sufficiently extensive to have rendered painless operation upon the upper part of the body.

A typical instance of universal analgesia[5] was that of a female patient, aged 11½ years, who was suffering from tuberculous abscesses of the foot, with tarsal necrosis. On February 7, 1901, she was operated upon under cocain spinal analgesia. The injection was made between

[1] Chaput: "Sur la Cocaïne Lombaire," *Bull. et Mém. d. l. Soc. d. Chir. de Paris*, 1901, 883.

[2] Pedeprade: "L'Analgesie par injection de cocaïne sous l'arachnoïde lombaire en chirurgie." Paris, 1901.

[3] Tuffier: *Op. cit., La Presse méd.*, June 8, 1901.

[4] Patterson: "Spinal Analgesia. The Present Status of the Method Based on a Review of the Literature," *Archiv Internat. d. Chir., 1*, 502; *2*, 53.

[5] Bainbridge: "A Report of Twenty-four Operations Performed During Spinal Analgesia," *Med. News*, May 4, 1901, Case IX.

the third and fourth lumbar vertebræ, the amount of cocain being 15 minims of a two per cent solution. Analgesia extended to the level of the diaphragm in 2 minutes. The operation lasted 20 minutes, and included the opening of the abscesses and the removing of carious bone and tuberculous tissue. At the close of the operation, 25 minutes after the injection, there was absolute absence of pain sense over the entire body. Tests proved that the analgesia was present in the conjunctiva, the mouth, on the tongue, and over the posterior pharyngeal wall.

A similar instance of complete analgesia occurred in a child five years of age,[1] upon whom circumcision was performed. Other cases of analgesia extending practically over the entire body are cited.[2] In one case (No. XXII) a tuberculous sinus extending into the external condyle of left humerus was enlarged and dead bone removed. In another (No. XXIV) the left thumb was amputated at the lower third of the metacarpal bone. In the former case 8 minims of a two per cent solution of cocain were injected between the third and fourth lumbar vertebræ; in the latter 32 minims of a two per cent solution were injected between the second and third lumbar.

In a number of recorded instances the analgesia was unilateral, presumably, according to Dönitz,[3] because the injection was made at the beginning of the cauda equina, in the right or left group of nerve fibers, instead of the cisterna terminalis. Diffusion is thus incomplete, the solution reaching only the contiguous nerve roots, hence producing only partial analgesia, or analgesia of a given side.

Duration.—The duration of analgesia induced by subarachnoid injection is generally from 3/4 of an hour to 1½ hours, with cocain, stovain, and tropococain, the last named being shorter than the other two, and from 2½ to 3 hours, with novocain and adrenalin. Instances have been recorded where the analgesia lasted from 17 minutes to 8 hours. Jonnesco states that with his method analgesia lasts from 1½ to 2 hours.

The writer has found the analgesia to vary in duration from 45 minutes to 3 hours and 20 minutes. This has reference to the complete return of pain sense. During the early days, when the dosage was so uncertain, when cocain was used exclusively, and when so much was being said concerning the dangers of this agent, very conservative doses were employed, and the analgesia was often of shorter duration than obtains at the present time, when the method is more thoroughly understood in all its phases. It may be said, however, that, with all the added knowledge gained from experience, the duration of analgesia is still

[1] Bainbridge: "Report of Twelve Operations on Infants and Young Children During Spinal Analgesia," *Archives of Pediat.*, July, 1901, Case I.

[2] Bainbridge: *Op. cit.*, *Med. News*, May 4, 1901, Cases XV, XXII and XXIV.

[3] Dönitz: *Verh. d. deutsch. Gesell. f. Chir.*, 1905, 536.

problematical, and will doubtless continue to be so until some definite scientific basis for dosage is formulated.

ACCOMPANYING PHENOMENA

Subjective.—The manifestation of subjective symptoms begins within from two to eight minutes after the injection is made, varying with different patients. As a rule, the first subjective symptom noted is a tingling sensation and numbness in the feet and sometimes in the legs. During the first ten minutes or so there is a sense of malaise, characterized by a feeling of epigastric heaviness, thirst, and air-hunger. A sensation of cold, or of heat, with sweating, and sometimes salivation, follow the vasomotor reaction to the analgesic agent. In a certain proportion of cases there is a trembling of the legs amounting to clonic contractions. There may be cramps in the muscles of the legs.

Nausea occurs in about thirty per cent of cases, as culled from the literature by Patterson.[1] It seems to bear no relation to the preceding meal. The size of the dose of the analgesic agent injected bears a relation to the nausea, the larger the dose the more certain the nausea. The bulk or volume, rather than the strength, of the injected fluid is held by Gray and others to be the main factor in the production of nausea.

Vomiting, which occurs in about forty per cent of cases, begins, as a rule, in from five to ten minutes after the injection, sometimes earlier. It occurs in women more frequently than in men. It is seldom repeated more than 3 or 4 times. There may be late vomiting, coming on in from 2 to 3 hours after operation, and continuing for 2 or 3 days, according to some writers. Personal experience, and that of all but a few operators, is at variance with this observation.

An interesting study of the subjective symptoms has been furnished by Fraicou,[2] who operated upon himself for hernia under spinal analgesia with strychninized stovain.

The injection was made by an assistant, between the twelfth dorsal and first lumbar vertebræ, 1 c. c. of water, containing 5 centigrams of stovain and 1 milligram of strychnin, being employed. In addition to this, 2 centigrams of stovain were employed locally in the iliac fossa and external portion of the inguinal region.

During the entire operation, which was performed without assistance, the analgesia was complete below the anterior superior iliac spines. The body above this level remained unaffected throughout. The anal-

[1] Patterson: *Op. cit.*

[2] Fraicou: "Auto-observation d'une auto-opération de hernie sous la rachi-strychno-stovainization," *La Presse méd.*, Feb. 11, 1911, 105.

gesia disappeared as the work was drawing to a close, and the suture of the skin was slightly painful.

The conclusions formulated from this experience are in part as follows: (1) The pain produced by the spinal puncture is greater than that caused by a simple subcutaneous injection with the Pravaz syringe. The pain, however, is less disagreeable than the sensations experienced by the majority of patients at the beginning of chloroform anesthesia. (2) The anesthesia became established with pleasant sensations, and disappeared imperceptibly.

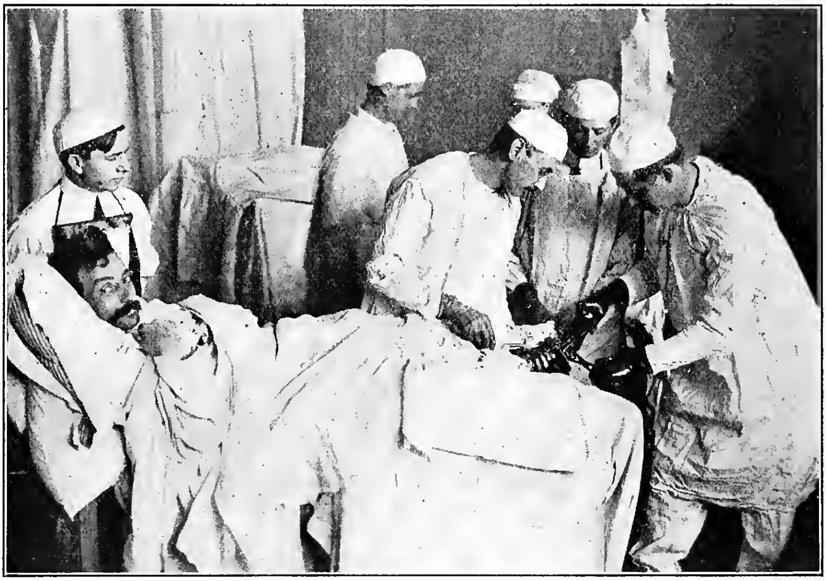


Fig. 239.—Amputation of Foot Just Above Ankle Joint Under Spinal Analgesia. Operator with clamp grasping sensory nerve and cutting it short; note absence of pain in expression.

(3) The mild excitement at the beginning of the anesthesia, and the vertigo which was felt on making sudden movements, are proof of the anesthetic fluid having slightly spread toward the cerebral hemispheres. The intellectual faculties remained absolutely intact, and consciousness was entirely preserved. This is conclusively proven by the fact that the surgeon also conducted a delicate operation upon himself to a successful outcome.

(4) The technique of the anesthetic method and the patient's position after the injection are the essential factors on which depend the degree and intensity of the anesthesia.

(5) The anesthesia has a great tendency to remain segmental.

(6) The harmlessness of the method of rachi-strychno-stovainiza-

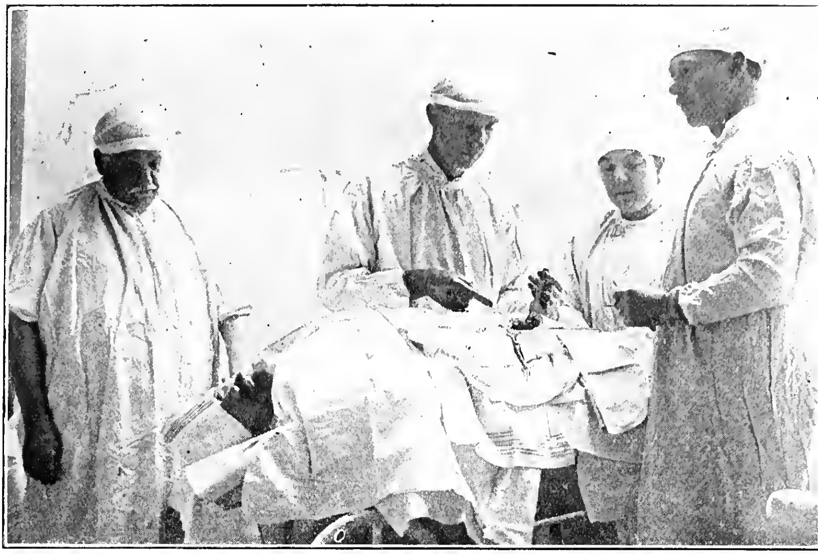


Fig. 240.—Inguinal Hernia, Inherent Intestine, Adhesions Being Pulled Apart Under Spinal Analgesia. Babcock's diffusible solution. Head lowered.

Fig. 241.—Same as Figure 240, Head Elevated. Patient reads to surgeons during operation.

tion is illustrated by the fact that during the entire anesthesia no unpleasant incident or phenomenon occurred, aside from vertigo caused by all sudden movements, despite the sitting position which it was necessary for the operator to maintain throughout.

(7) The contrast between the absence of any accident during the anesthesia and the onset of transitory postoperative and postanesthetic symptoms is accounted for by the fashion in which the operation was performed. Although in the upright position, and although the move-

Fig. 242.—Same Patient at End of Operation. Patient drinking water.

ments during the operation had no influence upon the onset of immediate symptoms, they gave rise at least to secondary disturbances.

Another instance of auto-observation of the symptoms caused by spinal analgesia was the operation for appendicitis recently performed upon himself by Dr. Bertram F. Alden, chief surgeon to the French Hospital, San Francisco.

The following history embraces the auto-observations of a patient operated upon by the author:

Miss E. F., 47 years of age, trained nurse. According to her own statement, she had had chronic nephritis for a number of years, with albumin as high as 25 per cent by volume at times, with hyaline, granular and blood casts, crystals of triple phosphate, and kidney and bladder epithelia. This statement was verified by urinalysis previous to operation. For 35 years she had had goiter, which was found to be of the cystic variety. The goiter developed with puberty, since which time she had always been extremely nervous, with more or less functional irregularity of the heart. Referred to me, January 5, 1911, by Dr. E. M. Mosher, of Brooklyn, for multiple uterine fibroids which filled the entire pelvis. On January 14 panhysterectomy and appendectomy were performed under spinal analgesia, one-half dram of a 3 per cent solution of stovain being injected between the second and third lumbar vertebræ.

The patient's description of her experience follows: "In a few minutes (5) after the injection the lower extremities became lifeless. Just as the incision was made into the skin of the abdomen my head was raised in order to put a pillow under it. I saw the incision, and felt the doctors working, but experienced absolutely no pain until the last 3 stitches were applied. These caused slight pain. By this time the analgesia was gradually disappearing. I slept at short intervals during the operation. I was given during the operation by hypodermic injection 1/100 gr. nitroglycerin and 1/6 gr. morphin, and at intervals small quantities of brandy and water by mouth. After the operation I drank lemonade to the health of the doctors. I was removed to my room perfectly conscious and free from pain. I had no unpleasant after-effects from the analgesia. The wound healed by primary union."

On February 11, 1911, half of the cystic thyroid gland was removed under local cocain analgesia. Since that time the patient has been perfectly well, resuming her work as a professional nurse.

Objective.—Tests elicit the fact that the sense of pain is the first to disappear, while the senses of touch and posture are gradually lost to a greater or less extent, according to dosage. Motor pareses manifest themselves first in the muscles of the feet, gradually extending upward. The extensors are more pronouncedly involved than are the flexors.

From Patterson's [1] investigation of the subject, it appears that in about 30 per cent of the cases there is incontinence of feces, due to the direct insensibility of the rectum. In about 10 per cent of the cases there are urethrovesical symptoms. In all cases the sense of distention, as well as of contact, with reference to the bladder is lost.

Pallor of the face and profuse perspiration are sometimes noted.

The general observation seems to be that there is a fall of blood pressure following immediately upon the injection, and that this varies with the completeness of the analgesia and with the parts affected. The pulse rate varies from 80 to 129 beats per minute, but the cardiac rhythm is regular.

Babcock [2] holds that surgical shock is less apt to occur with spinal analgesia than with general anesthesia, because of the blocking off of the nerves of sensation in the former. "The shock of the later stages of

[1] Patterson: *Op. cit.*

[2] Babcock: "Spinal Anesthesia, a Clinical Study of 658 Administrations," *Penn. Med. J.*, Aug., 1909.

the operation," he says, "is negatived by the emergence of the spinal centers from the depression of the anesthetic. For this reason, under spinal anesthesia it is not unusual to find the pulse stronger and fuller and the patient in better general condition at the end of an operation than at the beginning."

In low analgesia the effect upon the respiration is shown in a greater or less increase in rapidity, while the rhythm is practically unchanged. The greatest danger of so-called high analgesia is paralysis of the muscles concerned in respiration. This may vary from slight and temporary respiratory embarrassment to complete and lasting respiratory paralysis.

Jonnesco [1] holds that such phenomena as pallor, nausea, and sweating rarely occur when the stovain-strychnin solution recommended by him is used. The face, in such cases, retains its normal aspect; nausea occurs in 2.25 per cent, vomiting in 1.25 per cent, and sweating in 2 per cent. He has noticed fecal incontinence in 4 per cent of cases in cachectic, feeble individuals. The pulse, which is slowed by stovain alone, is usually normal in rapidity and strength when the stovain-strychnin solution is employed. Sometimes, according to Jonnesco, it rises to 80 or 90, but always remains strong. The 5 cases in which he noted temporary stoppage of respiration were cases in which he departed from his usual method in some detail. The addition of the strychnin is claimed by him to obviate this difficulty.

POSTOPERATIVE PHENOMENA

Alessandri [2] contributes a compilation, from the Neuro-pathological Institute in Rome, of the unfavorable accidents and complications following spinal analgesia with stovain injections.

The nervous system, according to this observer, which has a great affinity for stovain, presents chromatolysis of the nerve cells, which may affect all parts, inclusive of the bulb. In this way paresis of all descriptions may follow. Nausea and vomiting are not uncommon, as the immediate result of the effect upon the bulb. Syncope and severe respiratory disturbance are equally frequent.

Among the remote results of stovain analgesia mentioned by Alessandri are: Hyperthermia, up to 40° C., lasting several days, referred by some observers to shock due to operation; disturbance of the sensory nerves, represented by headache, and pains of the spinal nerves; trophic disturbances in the form of bed sores; psychic disturbances in the form of delirium and persistent insomnia.

[1] Jonnesco: *Op. cit., Brit. Med. J.*, Nov. 13, 1909, 1396.

[2] Alessandri: "Gli accidenti nervosi rachianestesia," *Il Morgagni*, Aug. 24, 1909.

Attention is called to the fact that certain disturbances which have been attributed to the stovain may also be referable to faulty puncture of the medullary canal or puncture at an unsuitable spot.

Intense headache, dizziness, nausea, vomiting, rigidity of the neck, tenderness to pressure over the cervical vertebræ, and pain in the small of the back constitute a symptom-complex known as meningism—due to irritation of the meninges.

Sleeplessness, lasting sometimes for as long as 7 nights, has been reported as following subarachnoid analgesia.

Postoperative fever, with or without chills, the temperature sometimes running as high as 102° F., in some instances follows the injection of tropococain, the fever being a manifestation of irritation of the heat center of the brain.

Headache, retention of urine, and rise of temperature are seldom noted, according to Jonnesco, when his method is employed, and when they do occur they are of short duration. He has observed headache in 6.25 per cent of cases, but it is not severe, and disappears in a few hours after operation. Transitory retention of urine was observed in 4.5 per cent of cases. In no case did the temperature reach 104° F. Postoperative vomiting has rarely been observed by him, and he has never seen postoperative analgesia paralysis.

Hoseman,[1] in discussing the after-effects of lumbar analgesia and their control, calls attention to the importance of measuring lumbar pressure. This serves to show that headache as a sequel to lumbar analgesia is always associated with changes of pressure, which is rarely increased, but frequently diminished. Where the pressure is increased the headache is favorably affected by the withdrawal of spinal fluid; when it is decreased, the introduction of fluid in the form of subcutaneous salt infusion and enemata is serviceable. The introduction of these measures in the Rostock Surgical Clinic obviated the severe after-effects of lumbar analgesia.

It has been claimed by a number of writers that albuminuria is one of the after-effects of spinal analgesia. Babcock [2] failed to corroborate this statement, never having observed any clinical evidence of irritation of the kidneys.

My own experience is in keeping with that of Babcock. As a routine practice the urine is examined on the day following the injection, and the findings, with regard to albuminuria, are uniformly negative.

Various motor manifestations have been noted. Among these may be mentioned paralysis of one or both abducens, the trochlearis, and sometimes the oculomotor muscles, coming on from 4 to 18 days after the

[1] Hoseman: *Verhandl. d. deutsch. Ges. f. Chir.*, 38 Kongress 1909, 17.

[2] Babcock: "Spinal Anesthesia, a Clinical Study of 658 Administrations," *Penn. Med. J.*, Aug., 1909.

analgesia, and disappearing spontaneously in from 21 to 36 days. Pareses of the legs sometimes remain for a number of hours, as may also those of the rectum and bladder.

Lusk[1] correlated the reported cases of paralytic sequels of the lumbar injection of spinal analgesic agents, finding quite a number of instances. "These paralyses," he says, "became apparent either closely consecutive to the recovery of the patient from the effects of the anesthetic, or else later after an interval of complete restoration of function to the patient. They are regarded as due either to trauma inflicted on the nerve structures by the puncturing needle, or to some irritative action of the solution injected. It can be seen that paralyses attributable to the former cause must be limited to the lower half of the body, and that their onset, as in the case of any severe nerve injury, ought to be immediate. The late occurrence of a paralysis would seem to be at total variance with a traumatic origin, and might consequently be regarded as characteristic of an irritation by the anesthetizing drug. In support of the latter proposition is the fact that paralysis of the upper extremity and more frequently of the eye muscles, following the lumbar injection of a spinal anesthetic, which could by no possible logic be attributable to the traumatism of a lumbar needle puncture, are characterized by a late onset. These late occurring paralyses are sometimes permanent."

Persistent paralyses are very rare, according to Fisher.[2] When they do occur, according to this writer, they are referable to imperfect asepsis (spinal meningitis), or to the injection of a too highly concentrated, irritative solution.

In my first paper,[3] under the head of after-effects, the statement is made that in all cases whatever after-effects were noted were of a temporary nature. In only one case (cited by Lusk) were there any serious symptoms following operation.

In the case referred to the patient, a male child 7 years of age, was in a very poor general condition, with a marked lumbar kyphosis, and a large psoas sinus with small inguinal opening. Operation consisted in the enlargement of the sinus, curettage of the bodies of the third and fourth lumbar vertebræ. The cocain solution, 9 minims of a one per cent solution, was injected to the right, between the twelfth dorsal and first lumbar vertebræ, thus avoiding the site of the spinal curvature. In 9 minutes after the injection, analgesia was present over the entire body, with the exception of a space bounded behind by the posterior fontanelle, in front by the point of the chin, and laterally on each side by the angle of the jaw, the malar bone, the temporal ridge, and the parietal boss.

[1] Lusk, William C.: "The Anatomy of Spinal Puncture, with Some Considerations on Technique and Paralytic Sequels," *Ann. of Surg., Oct.,* 1911.

[2] Fisher: "L'Anesthésie rachidienne," *Thèse de Paris,* 1911.

[3] Bainbridge: *Op. cit., Med. Rec.,* Dec. 15, 1900.

Some nausea and vomiting occurred for a few minutes after the injection. During the operation the patient was free from pain, and showed no sign of nervousness. He answered questions and manifested a full command of his faculties. Analgesia disappeared in 1¾ hours. Before operation, the temperature was 98.4°; pulse, 126; respiration, 34. One hour after operation, temperature, 100.6°; pulse, 108; respiration, 36. The patient vomited twice during the night. The pulse was good.

The day following the operation the child was restless at intervals, and cried out. An ice cap was applied, sodium bromid given in small doses, and the bowels thoroughly opened. The second day after operation the patient seemed stupid, and was apparently unable to express his desires in words. He did not move the right arm and hand, and the legs were drawn up. There was a slight elevation of temperature, with weak and rapid pulse. The third day was marked by a continuation of the stupidity, failure to talk, and slight movement of the right arm. Strychnin and digitalin in small doses were administered hypodermatically. Improvement then began to be noted, ability to move the right arm slowly returned, the legs could be extended, and the patient began to talk. One month after operation he was in excellent condition, and better than before operation.

In a later paper [1] the following statement occurs: "Of the many scores of cases upon which I have operated in this way, the ages have varied from 4 months to 67 years. With cocain as an agent, and with my present technique, I have had no failures and no serious after-effects. Many of the patients have been under my observation for several years after the operation without any deleterious effects being noted. The prophesied evil to the cord—which the needle should never touch—has not been seen in any cases coming under my observation."

This early experience, which was almost exclusively with cocain, has been corroborated, in the main, during the years which have elapsed since the introduction of the method. In 1,065 cases, in hospital and private practice, and with other agents as well as with cocain, I have had only 1 death (with the diffusible stovain solution, probably due to status lymphaticus; one case of temporary partial paralysis (see p. 584); one case of failure to induce analgesia, due to idiosyncrasy (see p. 623); one case of failure due to so-called "dry spine" (see p. 624); and two cases, with alypin, in which there was considerable respiratory depression. In all the other cases there were no accompanying or postoperative symptoms of permanent or serious moment.

[1] Bainbridge: "Further Remarks on Spinal Analgesia." Read before the Med. Soc. of the Co. of Westchester, Yonkers, March 15, 1904.

INDICATIONS AND CONTRAINDICATIONS

The extremes of opinion with reference to the safety of spinal analgesia have been expressed by Murphy[1] and Jonnesco.[2] The former said: "The mortality of spinal analgesia is such as to cause it to be abolished as an analgesic of choice, if not sufficient to cause statutory enactments against its use." The latter holds that there are no contraindications for "general spinal anesthesia," which, according to his belief, is absolutely safe, has never caused a death nor produced any important complications, early or late, is infinitely superior to inhalation anesthesia, is within the reach of all, and may be employed with any patient.

Between these two extremes of opinion may be found various degrees of conservatism and radicalism. Reference to the views of a few who have written upon the subject will serve to show how widely divergent they are concerning the indications and contraindications for spinal analgesia.

Bier, speaking before the German Medical Congress in April, 1909, cautioned against indiscriminate resort to spinal analgesia, and advised its restriction to pelvic operations and operations upon the lower extremities.

According to Buxton,[3] the consensus of opinion narrows the limits of the employment of this method, excluding from its use the following individuals: "The wounded in war, children, persons over 65, syphilitics, those who have some infective or septic disease, sufferers from serious heart or nerve lesions, arteriosclerosis, the nervous and the alcoholic, those who have albuminuria, and diabetics." "This list," he continues, "comprises the opinions of various experts and narrows the field very considerably, but it is only fair to say that many able surgeons who adopt the spinal puncture are prepared to risk the dangers of the conditions named and do not select their cases."

Matas[4] limited the indications: (1) To adults, and to reasonable persons who have good self-control, thereby excluding children, hysterical patients, and the insane; (2) to patients in whom the methods of local or regional anesthesia are inapplicable; (3) to patients suffering from emphysema, advanced asthma, chronic bronchitis, and other res-

[1] Murphy, John B.: "The Practical Medicine Series," *2*, Editorial note, 28; "General Surgery," 1909.

[2] Jonnesco: *Op. cit., Brit. Med. J.*, Nov. 13, 1909.

[3] Buxton, Dudley W.: "Discussion on Spinal Analgesia," Section on Pharmacology and Therapeutics, Brit. Med. Assn., *Brit. Med. J.*, Sept. 18, 1909, 786.

[4] Matas, Rudolph: "Local and Regional Anesthesia with Cocain and Other Analgesic Drugs, Including the Subarachnoid Method, as Applied in General Surgical Practice," *Phila. Med. J.*, Nov. 3, 1900.

piratory affections in whom a general inhalation anesthetic is absolutely contraindicated; in advanced cardiac cases with degenerative lesions (on account of the possible depressing effects of the injection and excitement of the circulation); (4) in the majority of cases in which the painful part of the operation is not likely to be prolonged beyond one hour and a half. Matas also acknowledges its indication in labor, especially in nephritic patients.

Babcock [1] employed spinal analgesia "in the most serious types of disease requiring operation below the level of the diaphragm where the patient suffered from severe shock, hemorrhage, marked sepsis or toxemia, or in conditions of extreme debility."

Gray [2] has found the method to be particularly indicated in many cases of abdominal surgery, preventing shock and reducing mortality 25 or 30 per cent.

Leedham-Green,[3] after an exhaustive experience with the method, found it to be indicated in dealing with gravely debilitated patients, such as those suffering from chronic intestinal obstruction, extravasation of urine, senile gangrene, and the like, where the disturbance occasioned by a general anesthetic often robs the patient of his chance of recovery. He also found it to be of great value for catheterization of the ureters in patients with highly sensitive bladders, as in cases of tuberculosis.

Canny Ryall [4] uses the method for operations on all parts of the body. Craniotomy, excision of the sympathetic ganglia, extirpation of the larynx, and excision of one-half of the tongue, with removal of the glands from both sides of the neck, are some of the operations performed by him under spinal analgesia.

Summing up the findings of many surgeons, it would seem that the method is generally conceded to be contraindicated in persons suffering from concomitant affections of the heart, lungs, and kidneys; from definite lesions of the nervous system, especially of the spinal cord; from sepsis or pyemia; from recent lues, and, according to some, from the later manifestations of this disease. Persons already in shock, or collapse, are not suitable subjects for this method, and for this reason it is considered by some to be unsuitable for war surgery.

It may be generally conceded, also, that, as a rule, the method should be employed for operations below the costal border, being especially indicated for operations upon the genital organs, perineum and rectum, and

[1] Babcock: *Op. cit.*, *Penn. Med. J.*, Aug., 1909.

[2] Gray: "Indications for the Employment of Spinal Anesthesia in Abdominal Surgery," *Brit. Med. J.*, Sept. 2, 1911.

[3] Leedham-Green: "Discussion on Spinal Analgesia," Section on Pharmacology and Therapeutics, Brit. Med. Assn., *Brit. Med. J.*, Sept. 18, 1909, 789.

[4] Ryall: *Brit. Med. J.*, June 19, 1909.

upon the lower extremities. As is well known, many surgeons do not subscribe to these limitations.

The method has been found uniformly satisfactory in a considerable number of infants and young children in whom I have employed it. The youngest child operated upon by me under spinal analgesia [1] was a male 3 months old, in very poor general condition, suffering from double inguinal hernia, with danger of incarceration. Incarceration finally occurred, and the patient was operated upon under chloroform anesthesia. Active stimulation was necessary during the narcosis. The patient recovered from this operation, but the other side became strangulated some days later. The patient was in such poor general condition, in addition to having developed bronchitis and having undergone an operation so shortly before, that it was deemed unwise to resort to a second general anesthesia. Spinal cocain analgesia was employed March 19, 1901. Point of puncture, between third and fourth lumbar vertebræ; amount of cocain, 6 minims of a one per cent solution. Injection, 11:32 A. M. Analgesia to the level of the diaphragm at 11:40. Operation begun at 11:40½. Infant began to cry before the needle was inserted in the back, and continued to cry until the feeding bottle with a small quantity of milk was allowed. Vomited once. There was no pain, and the patient remained quiet the greater part of the time. The sac was separated and opened, exposing intestines, the appearance of which confirmed the necessity for operation. When the constricted neck of the sac was enlarged a coil of intestine came down. Difficulty was experienced in reducing the intestine, and a few breaths of chloroform were given for the purpose of still further relaxing the muscles and quieting the child, who, by this time, had become frightened at the efforts to place the loop of intestine back in the abdominal cavity. The suturing of the abdominal wall and the completion of the operation were accomplished under the analgesia from the cocain.

At the end of the operation, at 12:15, the loss of the pain sense was complete to the level of the diaphragm. There was no vomiting from the time of the initial emesis until the chloroform was administered. To those present at the operation, it was apparent that a general anesthetic would have proved fatal to the child. Perfect recovery resulted.

The most striking report of the application of spinal analgesia in children comes from Gray,[2] who published an interesting series of observations in 300 cases in infants and young children, the youngest being 12 hours old, the oldest 13 years. Of the operations performed, 190

[1] Bainbridge: *Op. cit.*, *Archives of Pediat.*, July, 1901, Case XII.

[2] Gray, H. Tyrrell: (1) "A Study of Spinal Anæsthesia in Children and Infants, from a Series of 200 Cases," *Lancet*, Sept. 25, Oct. 2, 1909; (2) "A Further Study of Spinal Anæsthesia in Children and Infants," *Lancet*, June 11, 1910.

were upon the trunk, and 104 upon the extremities. Failure to obtain anesthesia resulted in 10 out of the 300 cases.

Of the first 100 cases, 9 children died subsequently from diseases for which they were operated upon. Necropsy showed no abnormality in the nerve roots, the cord, or its membranes.

In the second series of 100 cases there were no deaths from the spinal analgesia.

In the third series of 100 cases the author reports one death under analgesia. The patient was in such condition that operative relief seemed imperative, and death was practically certain under general anesthesia. Necropsy in this case showed that both lungs were completely collapsed; that there was pneumothorax on both sides; that the left side of the diaphragm was extensively infiltrated, with malignant new growth extending into the left pleura; that there were several nodules on the under surface of the right side of the diaphragm and metastatic deposits in various other regions; and that the growth from which the patient was suffering was a retroperitoneal sarcoma, involving kidney, pancreas, etc. The outcome in such a case cannot be considered as corroborative evidence of the alleged contraindication of infancy and childhood.

In concluding his last report, Gray says: "Such disadvantages as are consequent on the use of this method are very greatly overshadowed by the advantages to the patient and surgeon in certain cases. I believe that spinal analgesia is urgently called for on all occasions where the after-progress of a case is likely to be influenced by shock during operation, and often in cases when its employment is of definite assistance to the surgeon in doing his work as perfectly as possible."

Waugh,[1] of the Great Ormond Street Hospital for Sick Children, says concerning spinal analgesia in children: "So striking is the immediate result, as witnessed by the surgeon, that for my own part all operations on children below the level of the fifth thoracic nerve involving considerable shock are unhesitatingly performed under spinal anesthesia as the anesthesia *par excellence* for such cases." "That I have been able," he continues, "to resect six inches of intestine for acute obstruction in a baby eighteen hours old, perform a lateral anastomosis by suture in the ordinary way, and send the child out of the hospital in a fortnight's time is a striking testimony to its value." He adds that he has completely abandoned the use of general anesthesia for children in all cases of acute appendicitis, intussusception, and acute intestinal obstruction, which cases form no small share of the operative work in a large children's hospital.

Prelcitner,[2] in Escherich's clinic, had an experience of 40 cases in

[1] Waugh, George E.: Personal communication, 1911.

[2] Preleitner: *Münch. med. Woch.*, 1905, *52*.

children, with discouraging results. Fraenkel,[1] discussing Preleitner's paper, held that spinal analgesia does not eliminate the psychical factors, for which reason the method had not obtained a foothold in the surgery of children.

Barker [2] excluded children from his list of patients, along with "obviously nervous and excitable people."

Gray,[3] commenting upon such experiences, stated that they are entirely contradicted by his own experience. "From the psychical aspect," he says, "no more suitable patients for spinal anesthesia could be found, since ignorance is their safeguard against panic, and it may be stated generally that the younger the children the more satisfactory are they in this respect." The most troublesome age, in his experience, is between 2 and 5 years, children of this age being with greater difficulty kept quiet.

Personal experience is in accord with that of Gray. As Attending Surgeon, New York City Children's Hospitals and Schools, ample opportunity has been afforded me to test the utility of spinal analgesia, not only in infants and young children, but in the highly neurotic, epileptic, and idiotic.

In one instance,[4] the patient, female, aged 4 years and 10 months, of very nervous temperament, being operated upon for umbilical entero-epiplocele, gave some hysterical manifestations during the operation, and cried as if in pain. Careful tests proved, however, that the analgesia was complete with reference to pain sense. No serious accompanying or post-operative symptoms occurred in this case.

In another case [5] of the same series, the patient, male, aged 9 years, was an epileptic, operated upon for congenital malformation of the glans and prepuce, with hypospadias. No pain or nervousness was noted in this instance.

Of the cases reported in another paper,[6] the following features were noted: epileptic; highly neurotic; nervous temperament; feeble-minded, deaf and dumb, hydrocephalic; marked idiocy, with epilepsy; highly neurotic; marked idiocy, with epilepsy; highly neurotic; idiocy.

Among the conclusions formulated in the last-named paper is the following: "In neurotic patients there are often hysterical symptoms directly following the completion of the injection, but, as a rule, in a few

[1] Fraenkel: *Münch. med. Woch.*, 1905, *52*.

[2] Barker: *Op. cit.*, *Brit. Med. J.*, March 23, 1907.

[3] Gray: *Op. cit.*, *Lancet*, Sept. 25, 1909.

[4] Bainbridge: *Med. Rec.*, Dec. 15, 1900, Case II.

[5] *Ibid.*, Case V.

[6] Bainbridge: *Med. News*, May 4, 1901, Cases I, II, VIII, XIII, XV, XVI, XIX, XXI, XXIV.

moments a calm follows and the patient lies perfectly still." Subsequent experience bears out this statement.

It has been claimed that convulsions are apt to follow spinal puncture in epileptics. In personal experience with 16 epileptic patients operated upon under spinal analgesia, not one instance of convulsion on the table has been witnessed. No increase in nervous symptoms was noted in any case, and several patients were distinctly better for days after the injection. Many of these children have lived for years afterward, and have died of other diseases, nothing being found abnormal with the cord or the nerve roots.

The contraindication of age beyond 65 years does not hold in all cases. Weber [1] reported a case in which he operated upon a man of 84 years. Jonnesco's oldest recorded case in 1909 was 75. Barker operated upon one patient 71 years of age. Many other instances are on record of operations under spinal analgesia in patients far past middle life.

An early personal case [2] was that of a woman 67 years of age, who was suffering from complete procidentia, with beginning gangrenous changes in the lower part of the uterus, fatty heart, edema of the lower extremities and marked edema of the local parts, and suppression of the urine for twenty-four hours previous to operation. Ether was thought to be contraindicated because of the absence of urine; chloroform had been tried, but the patient collapsed under it. Cocain spinal analgesia was resorted to, 35 minims of a two per cent solution being injected between the second and third lumbar vertebræ. Analgesia was complete below the clavicles in 15 minutes, and lasted 2 hours and 50 minutes. The operation lasted only 30 minutes, as, after scarification of the cervix and curetting, it was found possible to reduce the uterus inside the pelvis and to retain it there without further operative procedure.

The only unpleasant symptoms in this case were nausea a few minutes following puncture, retching once or twice, and slight headache, with 2 degrees elevation of temperature the night after the operation. Recovery was uneventful.

Another patient, male, 66 years of age, was operated upon for inflamed, irreducible right inguinal hernia, January 24, 1911. The hernia could not be held by truss, and gave repeated symptoms of impending strangulation. In addition to this the patient was suffering from advanced arteriosclerosis, enlarged prostate, cystitis, and a double cardiac lesion, and gave evidence of an old healed process in the right lung. The operation was successfully performed under spinal analgesia, with

[1] Weber: *J. Am. Med. Assn.*, Feb. 9, 1900.

[2] Case IV, of paper read before the Med. Soc. of the County of Westchester, Yonkers, March 15, 1904.

2 c. c. of a three per cent stovain-dextrin solution, injected between the third and fourth lumbar vertebræ. There was no nausea, no vomiting, or other untoward symptom, the patient read throughout the operation, and recovery was uneventful.

A man 70 years old was operated upon by me August 4, 1911, under cocain spinal analgesia, with 18 minims of a two per cent solution, injected between the third and fourth lumbar vertebræ. The patient for years had suffered from hypertrophy of the prostate, with the usual symptoms. He had had electrical treatment for 5 years, with temporary benefit. For a year he had been in a pitiable condition, passing urine almost constantly, in dribbles, with retention in the bladder of from 24 to 36 ounces of urine, and having to wear a urinary receptacle night and day. The urine was about 25 per cent by volume of pus and detritus, with blood casts and albumin. He was running several degrees of temperature when first seen, early in July, and was in very poor general condition. Arteriosclerosis of moderate degree added to the complications.

The patient was put to bed, the bladder washed out for a time, and the alimentary canal cleared. With preliminary medication of 1/4 gr. morphin and 1/200 gr. nitroglycerin, Young's operation for prostatectomy was performed without difficulty. Analgesia was complete to the clavicles in 3 minutes, and remained so during the entire operation, which lasted an hour. There was slight nausea for a moment at the beginning of the operation, but this quickly subsided. There were no other unpleasant symptoms. The operation was at 12:30 P. M. At 7 P. M. the temperature was 102.8°; pulse, 112; respiration, 24. At 10 P. M. the temperature was 101°; pulse, 114; respiration, 30. At 2 P. M. the following day, temperature, 100.6°; pulse, 110; respiration, 28. At 6 A. M., temperature, 99°; pulse, 100; respiration, 22. At 3 P. M., temperature, pulse, and respiration were normal. Recovery uneventful.

Spinal analgesia has been employed in the most elaborate gynecological and general surgery, the variety of operation, in suitable subjects, being no contraindication.

Wertheim,[1] in a paper read before the joint session of the Chicago Medical and Gynecological Societies, October 10, 1906, said: "For over a year we used, with exceptionally good results, lumbar anesthesia. We use for this purpose stovain with the addition of adrenalin. Even very old cachectic women with badly degenerated hearts bear this operation well by this procedure."

Barker,[2] in his third series of 100 cases, a number of which were very

[1] Wertheim: "The Radical Abdominal Operation in Carcinoma of the Cervix Uteri," *Surg., Gyn. and Obst.*, Jan., 1907.

[2] Barker: "A Third Report on Clinical Experiences with Spinal Analgesia," *Brit. Med. J.*, Aug. 22, 1908.

grave conditions, cited, as the worst general condition to be contended against, the case of a woman 48 years of age, operated on in the country for gangrene of nearly 5 feet of the small intestine strangulated by bands. The patient was pulseless, and cyanosed in face and hand, with pulse between 120 and 130. About 6 cg. (0.92 gr.) of stovain placed her in comfort in 5 minutes, 4 feet and 9 inches of black gangrenous bowel were excised, and the healthy gut anastomosed above and below, with perfect recovery.

In obstetric practice the method is not infrequently indicated, and has been successfully employed by a number of European and American obstetricians, as stated in the section on history.

Doleris and Malartic[1] conclude that the uterine contractions become painless in from 5 to 10 minutes after the injection of from 1 to 2 centigrams of cocain, remaining practically painless, though perceptible, for a period of about 27 minutes after an injection of 7½ milligrams. Complete analgesia, according to these authors, has a duration of from 1 hour and 23 minutes to 2¼ hours, with a dose of from 1 to 2 centigrams. The uterine contractions become energetic, more frequent, and of longer duration after the injection than before it, and in the interval between the contractions the uterus remains in a condition of tension during a variable period.

They found the bleeding to be much less than usual, and in a case of placenta prævia the hemorrhage spontaneously ceased before the rupture of the membranes. The action of the cocain on the fetus, in their experience, was *nil.*

Cesarian section has been successfully performed under spinal analgesia by Sinclair,[2] Hopkins,[3] and Doleris.[4]

Marx[5] recommended spinal analgesia in all cases in which the first stage of labor is prolonged. By the use of small doses, used as required, he has been able to carry a patient painlessly through labor of 8 hours' duration.

The only case[6] in which I have employed spinal analgesia in obstetrics was for the delivery of a full-term child by means of high forceps operation. The patient, Mrs. H., 26 years of age, lived in a tene-

[1] Doleris and Malartic: "Analgésie obstétricale par injection sous-arachnoïdienne de cocaïne," *La Semaine méd.*, 1900, 243.

[2] Sinclair: "Cæsarian Section under Cocaine Anæsthesia," *J. of Obst. and Gyn. of Brit. Emp.*, Sept., 1902, 221.

[3] Hopkins: "Case of Cæsarian Section under Spinal Anæsthesia," *J. Am. Med. Assn.*, May 24, 1902, 1355.

[4] Doleris and Malartic: *Op. cit.*, *Compt. rend. d. l. Soc. d'Obst., Gyn. et Péd. d. Paris*, 1900, 328.

[5] Marx: *Med. Rec.*, Oct. 6, 1900, 521.

[6] Bainbridge: Reported before the Surgical Section, Am. Med. Assn., Atlantic City, June 4-7, 1912.

ment house, and this was her fifth confinement. Labor began at 6:30 on the evening of February 23, 1901, the weak and ineffectual pains continuing until 2:30 A. M. of February 24. The membrane then ruptured, and the infant's heart beat became very weak, then practically inaudible. It was determined to deliver the child by forceps, under spinal analgesia. The injection was made at 3:35 A. M., 20 minims of a two per cent solution of cocain being introduced between the third and fourth lumbar vertebræ. At 3:48 analgesia was complete to the level of the chin, and at 4:20 the child was born. By 6:55 analgesia had fully disappeared. The analgesia was so perfect that the mother went to sleep during the delivery, being unconscious of the birth of the child until she was awakened by its cry.

Ehrenfest [1] calls attention to the following objections which may be urged against spinal analgesia for general obstetrical use: (1) It is not a harmless procedure. (2) Disagreeable symptoms inevitably follow the injection. (3) It may have a toxic effect on the child, such cases having been reported. (4) The analgesic effect may disappear just at the moment when it is necessary and only the unpleasant sequelæ, such as vomiting and extreme nervousness, remain. (5) The loss of the active help of the abdominal muscles is a very decided disadvantage.

From the weight of conflicting testimony with reference to the indications and contraindications for spinal analgesia, it may be deduced, in a general way, that, granting the need of operation, and the impracticability of local or regional analgesia, the indications for spinal analgesia are the contraindications for general inhalation anesthesia. So far as the character of the operative procedure is concerned, there are practically no contraindications to the employment of spinal analgesia. With the modifications of injection fluid now in use, it may be said that no part of the body is under the ban of contraindication. Despite the improvements of technique and the extension of domain, the method is employed more often as one of expediency than as one of choice.

ADVANTAGES AND DISADVANTAGES

Advantages.—The advantages of spinal analgesia may be stated categorically and briefly as follows:

(1) Very little apparatus is required.

(2) The operative technique presents few difficulties, hence the method is easy of application.

(3) The injection may be made by the surgeon himself, thus obvi-

[1] Ehrenfest: "A Few Remarks on the Use of Medullary Narcosis in Obstetrical Cases," *Med. Rec.*, Dec. 22, 1900, 967.

ating the necessity of an assistant. For emergency, military, and naval surgery this is a distinct advantage.

(4) Analgesia is quickly induced, from 4 to 10 minutes being sufficient, as a rule, for the induction of analgesia as far as the diaphragm.

(5) The relative safety, as regards life, with good technique, skilfully executed, is high.

(6) Does not depress the heart, like chloroform, or cause pulmonary and renal complications, like ether, as these anesthetics are ordinarily administered.

(7) Insures physical quietude during operation, which is of distinct advantage to the surgeon.

(8) Insures the patient's aid, which may be desirable, as in coughing mucus or blood from the throat.

(9) May save the life of patients who, because of contraindications to inhalation anesthesia, would be consigned to their fate without operative relief.

(10) Controls surgical shock by blocking off reflexes.

(11) Obviates persistent postoperative retching and vomiting, which is of especial advantage in abdominal work.

(12) Lessens postoperative pain.

(13) Lessens postoperative restlessness which results from postoperative pain.

(14) Diminishes the danger of postoperative pulmonary complications.

(15) Gives "abdominal stillness," emphasized by Jonnesco, Gray, and others, in connection with laparotomies.

(16) Decreases mortality.

Busse,[1] upon the basis of experience with 1,232 cases of lumbar analgesia, points out the following advantages of this method as compared with inhalation anesthesia:

(1) The blood pressure is not seriously affected.

(2) Asphyxia is considerably less frequent.

(3) Vomiting during the operation is less common and less profuse.

(4) Vomiting after operation occurs less frequently.

(5) Vesical disturbances are reduced to about one-third to one-half.

(6) Deaths from pulmonary embolism seem to become less common.

Babcock[2] emphasizes the following advantages of this method over general anesthesia:

[1] Busse: *Prakt. Ergebnisse der Geburts. u. Gyn.*, 1909, *1;* also, *Centralbl. f. Gyn.*, 1910, No. 42, 1363.

[2] Babcock: *Penn. Med. J.*, Aug., 1909.

(1) It reduces the mortality and morbidity of operations.

(2) It insures physical quietude before, during, and after the operation.

(3) It secures complete muscular relaxation and a desirable peristaltic stimulation.

(4) It increases the patient's comfort and resistance.

Disadvantages.—The disadvantages of spinal analgesia have been variously estimated, from none at all to an overwhelming number, by the enthusiastic advocates of the method on the one hand, and its unqualified opponents on the other. By conservative opinion they may be summed up categorically and briefly as follows:

(1) Unpleasant accompanying and postoperative phenomena, which, despite all precautions, may occur.

(2) Possible dangers from the analgesic agent *per se,* which, though not so frequent as formerly, do nevertheless occur, and have always to be borne in mind.

(3) Uncertainty as to the length of the analgesia, which may wear off before the operation is completed.

(4) Uncertainty as to the exact amount necessary to produce the desired effect in a given case.

(5) Absolute commitment of the surgeon to the consequences of the dose injected, the effects of which, if untoward, cannot be controlled, as in the case of a general anesthetic, the dose of which may be regulated to suit the exigencies of the individual case.

(6) Consciousness on the part of the patient, and the consequent possibility of psychic pain, nausea, and other disturbances, especially on the part of nervous individuals.

(7) Incomplete muscular relaxation, which may occur when relaxation is desirable.

(8) Failure to obtain sufficient cerebrospinal fluid to warrant making the injection, sometimes attributed to so-called "dry spine," and occurring at times in the experience of skillful operators.

(9) Possible injury to and irritation of the spinal cord and nerve roots.

DEATHS

It has been repeatedly stated that death statistics are of no practical value in determining the direct toxic working of the drugs employed for the induction of spinal analgesia, the question being mainly one of dosage. Deaths have been reported in connection with each of the drugs in common use, whether justly attributable directly to the action of the drug in any case being a debatable point. It is fair to assume that other factors are to be considered in connection with fatalities resulting from spinal analgesia. For all surgeons, except, possibly, the few peculiarly expert operators who recognize no limitations to the method, the selection of the subject for spinal analgesia must exert considerable influence over the mortality record. The entire management of the case, including the surgical interference, bears a direct relationship to the safety of the method. Despite every possible safeguard, however, deaths have occurred, and will doubtless continue to occur, with this as with every other method.

Chiene [1] collected the reports of over 12,000 cases, with 22 deaths, or, roughly, 1 death in 570. He holds that, if the cases be analyzed in which death occurred, it will be found that very few can be attributed solely, or even partially, to the anesthetic. In analyzing the table of statistics given by Strauss,[2] in which the latter collated 22,717 cases, with 46 deaths, Chiene found that 25 of the 45 deaths reported occurred when cocain was used, which works out at 21 deaths in 15,842 cases where other drugs were employed, or 1 in 754. Only 3 of these were stated to be clearly due to the analgesic agent, or 1 in 5,282, and 9 more seemingly in connection with the agent; in all, 1 in 1,320.

Compared with results obtained in a similar number of cases by general anesthesia, Chiene considered the above figures not so unfavorable as some writers have claimed.

Jonnesco [3] gives the following statistics: From July 5, 1908, to Nov. 8, 1909, 758 cases were operated upon by Jonnesco or his assistants. Two cases in London and 23 in America bring the total to 783, of which 195 were superior dorsal and 588 dorsolumbar injections. If to this number be added 603 earlier lumbar analgesias, he has a record of 1,386 rachianesthesias, without mortality.

In a later communication Jonnesco [4] gives the following personal statistics: One thousand and five cases, from July 8, 1908, to September 29, 1910, including 238 high analgesias (operations on the head, neck, superior extremities, and thorax), and 267 low analgesias (operations on the abdomen, pelvis, perineum, and inferior extremities). These statistics include 2 cases operated upon by Jonnesco in London and 23 in America. The ages of the patients varied from 1 month to 82 years. He had no deaths, he avers, due to the method, in the 2 years. Two fatal cases among high analgesias occurred among his Roumanian colleagues, but these were referable to overdoses of stovain or strychnin.

[1] Chiene: *Op. cit., Brit. Med. J.*, Sept. 18, 1909, 785.

[2] Strauss: "Der Gegenwärtige Stand der Spinalanalgesie," *Deutsch. Zeit. f. Chir.*, July, 1907, 275.

[3] Jonnesco: *Am. J. of Surg., op cit.*, 1910, *29*, 33.

[4] Jonnesco: "La rachi-anésthesie générale," *Rev. de Thérapeut. méd.-chir.*, Dec. 1, 1910, 798.

Kohler[1] collected 7,780 cases, with 12 deaths. Chaput[2] knew of no deaths among 7,000 cases. Tuffier[3] reported one death (not positively attributable to the analgesia) in 11 years. Gray[4] reported one death in his series of 300 cases in children. Barker[5] formulated a table of the results at 5 British hospitals working on exactly the same principles and technique, and with the same instruments and solutions carefully prepared. This table represents 2,354 cases, including 775 cases under his own observation, in which there were only 3 deaths, or 0.1 per cent.

Michelsson,[6] discussing the various attempts to calculate the mortality of spinal analgesia on the basis of statistical compilations, gives the following divergent results: Tomachewski calculates the mortality of spinal analgesia as 1:17847; Strauss, 1:2524; Chiene, 1:570; Hohmeier, 1:200. The figures of Strauss are held by Michelsson to be nearest the truth of the matter, although the mortality percentage is stated a little too high, omitting cocain analgesia, the mortality amounting to about 1:3500.

In a personal experience of 1,065 cases, covering an extensive variety of operations upon patients ranging in age from 3 months to 70 years, there has been one fatality.[7] This might easily be attributed to other causes (see pp. 585, 625).

It is worthy of note, in connection with the subject of mortality due to the subarachnoid injection of anesthetic agents, that Engsted[8] has reported the successful use of ether as an antidote to cocain and other drugs employed as local or spinal analgesics. He has been able, by this means, to revive patients who were practically *in extremis.* The best results are obtained, he holds, when ether is administered to the degree of mild surgical narcosis, or even less. A mask is employed, and the vapor given by the drop method, thus preventing adding to the danger by excluding air from the lungs already engorged with venous blood.

[1] Kohler: *Deutsch. Zeit. f. Chir.,* 1909, 16.

[2] Chaput: *Brit. Med. J.,* May 30, 1908, 1330.

[3] Tuffier: Personal communication, March, 1911.

[4] Gray: *Op. cit., Lancet,* June 11, 1910.

[5] Barker: *Brit. Med. J.,* March 16, 1912, 597.

[6] Michelson: *Op. cit., Ergebnisse d. Chir. und Ortho., 4,* 1912.

[7] Bainbridge: "Spinal Analgesia—Development and Present Status of the Method, with Brief Summary of Personal Experience in 1,065 Cases," *J. Am. Med. Assn.* Read before the Section on Pharmacology and Therapeutics, in joint session with the Section on Pathology and Physiology, American Medical Association, Atlantic City, June 6, 1912.

[8] Engsted, J. E.: "Ether: An Antidote of Cocain and Stovain Poisoning," *J. Am. Med. Assn.,* March 19, 1910, 964.

ANALGESIC AGENTS

The Therapeutic Committee of the British Medical Association[1] investigated the following local analgesic agents: stovain, novocain, tropacocain, beta-eucain, alypin, beta-eucain lactate, nirvanin, holocain hydrochlorid, acoin, orthoform (new), and anesthesine. (See Chapter XX.)

Among the points to which especial attention was directed in this investigation was the suitability of the agent for medullary narcosis. Preliminary experiments reduced the list to 4, viz.: stovain, novocain, tropacocain, and beta-eucain lactate, which were subjected to further investigation. After comparing these drugs one with the other, the conclusion was reached that novocain is the most satisfactory for general use. "Its anesthetic action is equal to that of cocain, and its toxicity and general destructive power on the tissues are very much less."

Of the four drugs mentioned in the above report, stovain, novocain, and tropacocain are most generally used, though some operators, myself among the number, still find, at times, a place for cocain. Various modifications of the analgesic solution and its preparation have been adopted. A few are mentioned here, but more are given in Chapter XX.

Cocain, tropacocain, stovain, and novocain are considered in the order of their introduction for purposes of spinal analgesia, and not with reference to their relative merits. Personal experience with other agents, eucain and alypin, for example, does not warrant devoting to them further consideration. Eucain was discarded because it gives a "patchy" analgesia, and alypin because it depresses respiration.

The analgesic agents most commonly employed are variously modified, the purpose being to produce a fluid of the same, heavier or lighter specific gravity, as compared with the cerebrospinal fluid. The injection fluid, thus modified, is more or less diffusible, according to its relative specific weight, and, as a consequence of the relative diffusibility, the analgesia produced is more or less controllable as regards its extent.

The various analgesic solutions may be classed, according to their relative specific gravity, as follows: (1) Analgesic agent, plus water, plus alcohol; (2) analgesic agent, plus water; (3) analgesic agent, plus water, plus cerebrospinal fluid; (4) analgesic agent, plus cerebrospinal fluid alone; (5) analgesic agent, plus water, plus normal salt solution; (6) analgesic agent, plus water, plus dextrin, glucose, or gum arabic.

To any of the above may be added, if desired, adrenalin or some similar product, as employed by Bier, Gray, and many others, or strychnin, as suggested by Jonnesco.

[1] Le Brocq: "Report on the Local Anæsthetics Recommended as Substitutes for Cocaine," *Brit. Med. J.*, March 27, 1909.

Solutions of lighter specific gravity than the cerebrospinal fluid are generally called diffusible, whereas those of heavier specific gravity are called non-diffusible solutions. To the former class belongs No. 1; to the latter, No. 6.

Cocain.[1]—During the early days of spinal analgesia cocain was the agent most commonly employed, but because of the various fatalities and the many unpleasant accompanying and postoperative phenomena which marked the experimental stage it has been pretty generally abandoned.

Allen[2] says: "Since 1899, when Bier's first work appeared, cocain has gradually given way to the less toxic and equally effective stovain, novocain, or tropacocain, and it is now never used." He considers that it has no place in spinal analgesia. With this view probably the majority of surgeons are in accord.

A more favorable opinion of cocain is expressed by Filliatre,[3] who declares that this agent, employed by his method, is absolutely devoid of danger. His method, which he has employed in 1,500 cases, consists in first withdrawing 30 c. c. of cerebrospinal fluid, then injecting from 0.5 to 2 c. c. of a 2 per cent solution of cocain. This gives a dosage of from 1 to 4 cg. (0.15 + to 0.6 + gr.) of cocain.

J. Garland Sherrill, of Louisville, Kentucky, has always found a two per cent solution of cocain quite satisfactory, never using over 15 minims as a dose.

Charles Chassaignac (private communication), of New Orleans, has used cocain in doses ranging from 1/5 to ¼ gr.

E. Denegre Martin (*idem*), New Orleans, gives cocain the preference, employed in doses of 5 minims of a 4 per cent solution.

Simon Marx (*idem*), New York City, mentions cocain as his second choice, stovain being first. He uses cocain in doses of ¼ gr.

In a rather extensive experience with cocain the results of Bainbridge with this agent have been uniformly successful when the solution has been prepared according to his method. The dose employed ranges from 5 to 20 minims of a two per cent, and from 5 to 30 minims of a one per cent, solution.

Cocain has been largely employed as a standard by which to gauge the toxicity of other analgesic agents. It is considered twice as toxic as tropacocain, about 7 times more toxic than novocain, and 6 times more toxic than stovain.

While cocain is more toxic than other agents, needing, in consequence, more safeguarding, the resulting analgesia is more profound, and lasts longer, with correspondingly moderate dosage.

The toxicity of cocain has been attributed by many writers to harm-

[1] For further data, see Chapter XX.

[2] *Boston Med. and Surg. J.*, *163*, No. 19.

[3] *Ann. d. mal. d. org. génito-urin.*, 1909, No. 13.

ful by-products resulting from its decomposition by the heat used in sterilizing this agent. Others contend that cocain is not decomposed by heat, and that the unpleasant phenomena which accompany its use in some cases result not from the cocain or its decomposition products, but from the water used in making the solution.

Tropacocain.[1]—It is claimed by some that analgesia occurs sooner with tropacocain than with cocain, and that it is of longer duration. Personal experience is that there is very little difference in these regards.

The solution recommended by Willy Meyer [2] is as follows:

Tropacocain hydrochlorate................	0.15 gm. (2½ grs.)
Sodium chlorid..........................	0.06 gm. (1 gr.)
Distilled water..........................	10.00 gm. (2½ drs.)

Fifty minims of this solution contain 5 centigrams (5/6 gr.) of tropacocain, which is the dose usually required. This dose gives an analgesia sufficient for an operation lasting 1 hour or longer.

The Bier solution of tropacocain, so largely used, is put up in ampules containing 1.3 c. c. of a 5 per cent solution of tropacocain, with adrenalin hydrochlorid, 0.00013 per c. c. The dose of tropacocain usually given is 5 cgm. (5/6 gr.).

Slajiner [3] employed spinal analgesia in 2,700 cases, during the years 1901-1909, in his capacity as chief physician to the Surgical Department of the Laibach General Hospital. In all these cases tropacocain was used (Merck's sterilized flasks), the usual dose being 0.07 gm. (1 + gr.).

Colombani,[4] on the basis of 1,100 operations performed under tropacocain analgesia, advocates as the usual dose 0.08 gm. (1½ + gr.).

Erhardt [5] recommends the addition of gum arabic to the tropacocain solution used for spinal analgesia, in a dosage of three per cent gum to a one per cent tropacocain solution. The advantages of the addition are unmistakable, consisting in the diminution of the general toxic manifestations, and the prolongation of the anesthetic effect. The essential cause for the lessened toxic action is referable to the delayed absorption and the less immediate contact with the central nervous structures.

Hertel,[6] after having performed lumbar analgesia with watery solutions of tropacocain, recommends the addition of gum arabic, which he has already employed in 82 cases. Apparently the danger is diminished,

[1] See Chap. XX, for a fuller discussion of tropacocain.
[2] Meyer, Willy: *Med. News,* April 13, 1901.
[3] Slajiner: *Beit. z. klin. Chir.,* 1910, *67.*
[4] Colombani: *Wiener klin. Woch.,* 1909, No. 39.
[5] Erhardt: *Münch. med. Woch.,* 1908, No. 19, 1005.
[6] Hertel: *Münch. med. Woch.,* 1910, No. 16, 844.

although not entirely excluded; the analgesia seems to reach higher, and the number of failures is also apparently diminished.

Stovain.[1]—The Bier compound of stovain is as follows:

Stovain	4 per cent
Sodium chlorid	0.11 per cent
Epirenin borate	0.01 per cent

Tuffier recommends a 10 per cent solution of stovain in normal salt solution.

Chaput uses the following:

Stovain	10 per cent
Sodium chlorid	10 per cent
Distilled water	80 per cent

The Stovain-Billon solution so largely employed is marketed in ampules of 2 c. c., each cubic centimeter containing:

Stovain	0.04 gm. (6/10 gr.)
Adrenalin borate	0.00013 gm.
Sodium chlorid	0.0011 gm.

Each ampule contains 8 cgm. of stovain (1 1/5 gr.), so that a minimum or a maximum dose may be given.

Barker's compound (stovain-glucose) is:

Stovain	10 per cent
Glucose	5 per cent
Distilled water	85 per cent

The glucose was added by Barker for the purpose of obtaining a fluid of heavier specific gravity than the cerebrospinal fluid. By this means he believed it would be possible to localize the analgesia.

Houghton [2] has contributed a report of 400 cases operated upon under spinal analgesia induced with the Barker stovain-glucose solution. From his previous experience[3] with other drugs, followed by the series of cases in which he confined himself to the use of the Barker solution, he concludes that the 5 per cent solution of stovain and glucose has given the most consistent and reliable results. In this series there was no case of failure to enter and to inject the spinal sac, no case in which the injection failed to induce adequate analgesia, and no case which gave cause for any anxiety as to the safety of the method. In life-saving operations, such as amputation of the leg for diabetic gangrene, or

1 For further information on Stovain, see Chapter XX.

2 Houghton, J. W. H.: "Spinal Analgesia. Report of 400 Operations at the Military Hospital, Aldershot," *Lancet*, Oct. 12, 1912, 1008.

3 *Royal Army Med. Corps. J.*, Aug., 1908, and Oct., 1909.

operation upon a patient with advanced cardiac disease, in which neither chloroform nor ether is admissible, stovain can be used. In Houghton's experience there was absence of shock during operation, and the muscular relaxation was so complete that much less time was required for the completion of the operation than with chloroform.

The dextrin-stovain solution employed by Gray consists of stovain, 3 per cent, with dextrin and suprarenin in saline solution. This solution is placed upon the market in ampules of 2 c. c. each, one ampule being sufficient for the induction of analgesia to the diaphragm, and often above.

The dose is 0.015 to 0.04 gm. (1/5 to ½ gr.) of stovain.

The stovain-strychnin solution suggested and so extensively used by Jonnesco in the so-called high analgesia must be prepared in advance of the time of operation, inasmuch as the strychnin sulphate takes some time to dissolve.

The amount of strychnin and stovain in the solution varies with the site of injection, the patient's age, and general condition. Jonnesco uses from 1 to 10 cgm. of stovain.

Babcock, who advocates a solution of lighter specific gravity than the cerebrospinal fluid, uses the following combination, made by Morgan, of Philadelphia:

Stovain	.08 p. c.
Ac. Lactic	.02
Abs. Alcohol	.20
Aq. dest.	q. s. 2.00

The alcohol content of this solution is reduced in strength about one-half by the admixture of the solution with the cerebrospinal fluid before it is thrown into the spinal canal.

Lambotte, of Antwerp, and his assistants have employed stovain in over 1,800 cases, with uniformly satisfactory results.

It may be of interest to note that at Sing Sing, the New York State prison at Ossining, stovain has been used exclusively since August, 1908, for operations below the level of the umbilicus.[1] The results have been uniformly successful, with no deaths due to the anesthetic, in approximately 400 operations performed by H. E. Mereness, Jr., and F. E. Lettice. The Billon preparation is employed.

Novocain.[2]—The novocain-suprarenalin solution advocated by Braun,[3] who first suggested the addition of adrenalin to analgesic agents, is put up in ampules of 3 c. c. each, containing:

[1] Personal communication from Mereness, Feb. 23, 1913.

[2] For further information on Novocain, see Chapter XX.

[3] Braun: *Deutsch. Monatsh. Jahnheilk.*, June, 1906.

Novocain	0.15 gm	(1 to 1½ gr.)
Suprarenalin	0.000325 gm.	(1-250 gr.)

This is equal to five minims of suprarenalin solution, 1-1000, to 3 c. c. of sterilized distilled water. Of this solution 2 to 3 c. c. may be used.

Meissner [1] reports 600 lumbar analgesias from the Tübingen Surgical Clinic, in all but 40 of which novocain was employed, first in 5 per cent solution (2 to 3 c. c.), later in 1 per cent solution (6 to 7 c. c.).

Ryall [2] reports having used novocain with the addition of strychnin, according to the Jonnesco method.

Chaput [3] reports 405 cases treated with novocain, a 4 per cent solution being used, without addition. The dose was from 0.06 to 0.08 gm.

Hypodermic tablets, novocain, 1/3 grain, are on the market. Each tablet contains novocain 0.020 gm.

In 988 of my 1,065 cases simple solutions of the analgesic agent—cocain, stovain, tropacocain, etc.—with water, were employed. In the remaining cases I have used various modified solutions, heavier and lighter, with and without the addition of adrenalin or other similar product. With no intention of condemning any of these modified solutions, I must confess that my preference is decidedly in favor of the simple solution, with the analgesic agent sterilized according to the method herein detailed. With such a solution, prepared under personal supervision, I am sure of the fluid injected into the subarachnoid space. If it were possible, as with Waugh, Gray, Barker, Babcock, and those who employ the ready-made solutions, to obtain the modified solutions *fresh* and *dependable,* the matter would be different. The fact remains, however, that all of the solutions prepared and dispensed in ampules deteriorate with time, and unless one is convenient to the source of supply there is always a doubt concerning the potency of the agent.

STERILIZATION OF THE ANALGESIC AGENT [4]

Many of the unfortunate results obtained in the early history of spinal analgesia were presumably due to improper methods of sterilizing the analgesic agent. This was certainly true of cocain. In order to overcome this difficulty various methods of sterilization have been devised, of which those of Tuffier, Roux, Murphy, and Bainbridge are examples.

[1] Meissner: *Beit. klin. Chir., 64,* No. 1.
[2] Ryall: *Brit. Med. J.,* June 19, 1909.
[3] Chaput: *Gaz. des Hôpitaux,* 1910, No. 48.
[4] See Chapter V and Chapter XIII.

The numerous special compounds have each a special method of preparation, which need not be detailed here.

In 1899 the following method [1] for the sterilization of cocain was first employed by me, and since that time it has been found equally satisfactory for the other analgesic agents in general use. The simplicity of the procedure renders it valuable for emergency work, as well as for other surgical cases in which spinal analgesia is indicated.

The method is as follows: Five grains of fresh cocain hydrochlorid crystals, carefully weighed, are placed in a sterilized measuring glass. Two drams of strong ether are added, and mixed thoroughly with the cocain crystals by means of a sterilized glass rod. The mixing process is continued until all the ether is evaporated. One-half to 1 ounce of warm boiled or filtered water or normal salt solution is then added. One-half ounce makes practically a 2 per cent solution, and 1 ounce a 1 per cent solution. Of the former solution 10 to 20 minims may be employed; of the latter, 10 to 30 minims.

The drug is practically sterilized in its manufacture, and all that infects it is apt to be on the outside of the crystals. Careful bacteriological tests were made by me to determine the extent to which this process sterilized the cocain, and it was found that practically all ordinary organisms are destroyed. (See Fig. 256, p. 616.)

The crystals do not deteriorate, as do the cocain and other solutions. It is advisable, however, if possible, to employ only fresh crystals, or to be sure that the crystals employed have been kept perfectly dry.

In the preparation of the diffusible solution employed by Babcock pasteurization is resorted to instead of sterilization.

SITES OF INJECTION

The routes commonly adopted for spinal puncture are the lumbar and the sacrolumbar, the former being preferable in human beings and the latter in animals. For purposes of spinal analgesia the points of election are generally conceded to be between the spinous processes of the third and fourth or fourth and fifth lumbar vertebræ. It is easier to enter the canal at these sites, and the danger of injury to the cord is minimized.

Lusk [2] emphasizes the conclusion, drawn from a series of anatomical studies, that "the only vertebral interspaces through which puncture of the subarachnoid space can be made with practical assurance that nerve structure will not be penetrated are the fourth lumbar and the lumbosacral, preferably the former."

[1] Bainbridge: *Op. cit., Med. Rec.,* Dec. 15, 1900.

[2] Lusk: *Op. cit., Ann. of Surg.,* Oct., 1911.

According to this author, "The anatomical findings in eleven dissections of the arachnoid membrane, from the conus medullaris up into the cervical region, were condemnatory of the procedure of puncture within

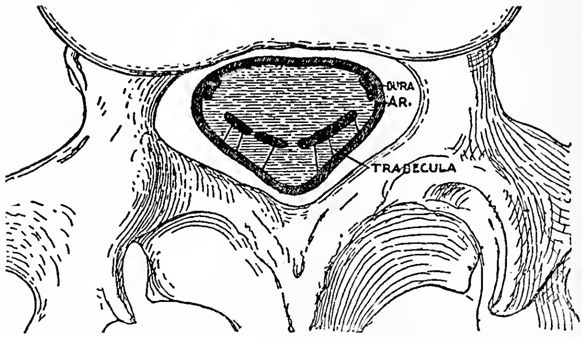


FIG. 243.—DIAGRAM OF CROSS-SECTION OPPOSITE THE FOURTH LUMBAR INTERSPACE. Below the lower border of the fifth lumbar vertebra nerve-roots were adherent to the arachnoid. Above this level the arachnoid was firmly adherent over the posterior surfaces of the laterally situated nerve-roots of the cauda equina, while mesially it lay loosely over the posterior surface of the nerve structures, to which it was connected by delicate trabeculæ from about one-eighth to one-quarter inch in length, the shorter trabeculæ occupying the more lateral position. (Lusk.)

this area, as one attended with the greatest liability of penetrating the cord."

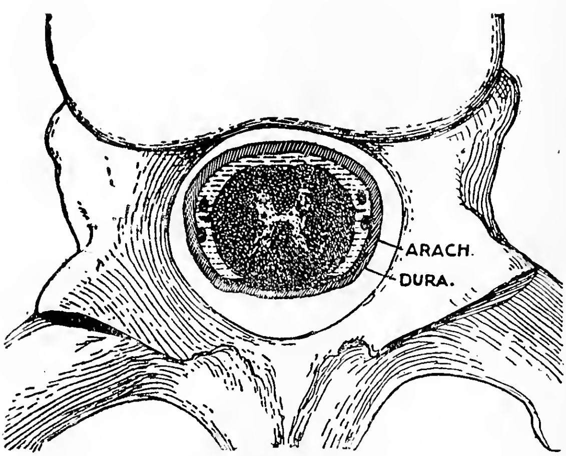


FIG. 244.—DIAGRAM OF A CROSS-SECTION THROUGH THE DORSAL SPINE. Showing how the arachnoid membrane may be adherent to the posterior surface of the cord, which was the predominating anatomical arrangement in this and the lower cervical regions in six out of ten dissections. The close contact between the arachnoid and dura is here illustrated. (Lusk.)

In fifteen dissections the conus medullaris was found by Lusk to terminate in 11 cases at the level of the first lumbar vertebra, 3 times at the level of the junction between the twelfth dorsal and the first lumbar vertebra, and once it reached to the lower border of the second lumbar vertebra. The normal or usual termination is shown in Figs. 245 and 248.

Of 11 dissections of the arachnoid membrane above the conus, in only three was there a complete posterior arachnoid space present all the way up into the cervical region, the channel being interrupted at intervals by transverse septa. In three dissections the arachnoid membrane was adherent to the posterior surface of the cord all the way from the conus up to the cervical region; in one it was completely adherent above the level of two inches above the conus, and in two above the levels of the fifth and seventh dorsal vertebræ respectively. (See Figs. 243 and 244.)

From these findings Lusk concludes that, if the cerebrospinal fluid be constantly withdrawn as a result of mesial puncture at or above the level of the conus, in many instances the substance of the cord must be traversed by the needle and the fluid taken from the anterior portion of the arachnoid space.

In all the 15 dissections Lusk found that the one site at which lumbar puncture of the arachnoid space could have been made without liability of injury to the nerve roots was mesially in the interval between the fourth and fifth lumbar vertebræ. The great tendency of the nerve roots to become adherent to the posterior wall of the arachnoid sac in the lumbosacral interspace, as well as for the subarachnoid space to become shallower in this region, rendered this the site of second choice.

Despite the anatomical findings of Lusk and others who have studied the subject from this point of view, injections have been successfully made at higher levels than those above indicated.

Morton,[1] in two cases, injected between the last dorsal and first lumbar, but abandoned this site as being unnecessary.

Tait and Caglieri [2] (see p. 561) reported having injected cocain into the sixth cervical space, without untoward effects.

Jonnesco,[3] who at first advocated piercing the column "at all levels," later abandoned this procedure and confined himself to two sites: (1) superior-dorsal, between the first and second dorsal vertebræ, and (2) dorsolumbar, between the twelfth dorsal and first lumbar vertebræ. "I had already been convinced by experience," he said, "that spinal anesthesia was not so regional as I had believed, and that mediocervical puncture was as useless as it was dangerous. It favors the appearance of bulbar phenomena—nausea, vomiting, pallor of the face, momentary

[1] Morton: *Am. Med.*, Aug. 3, 1901.

[2] Tait and Caglieri: *Op. cit., Trans. of the Med. Soc. of the State of Cal.*, April, 1900; also, *J. Am. Med. Assn.*, July 7, 1900.

[3] Jonnesco: *Brit. Med. J.*, Nov. 13, 1909; also, *Revue de thérap. méd.-chir.*, Dec. 1, 1910, 798.

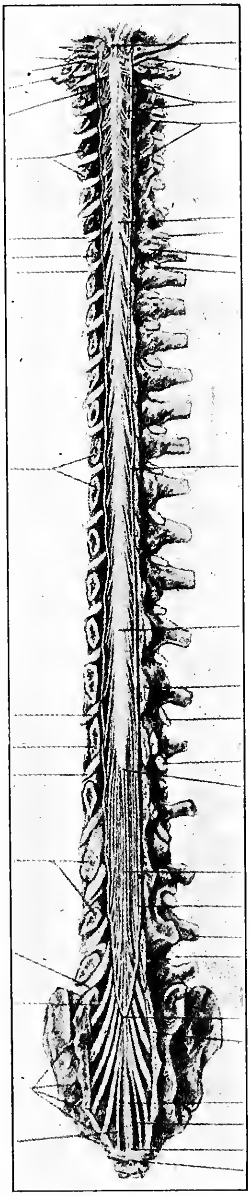


Fig. 245.—Spinal Cord Enclosed in Unopened Dural Sheath Lying Within Vertebral Canal. Neural arches completely removed on right side, and partially on left, in order to expose dorsal aspect of dura. (Piersol.)

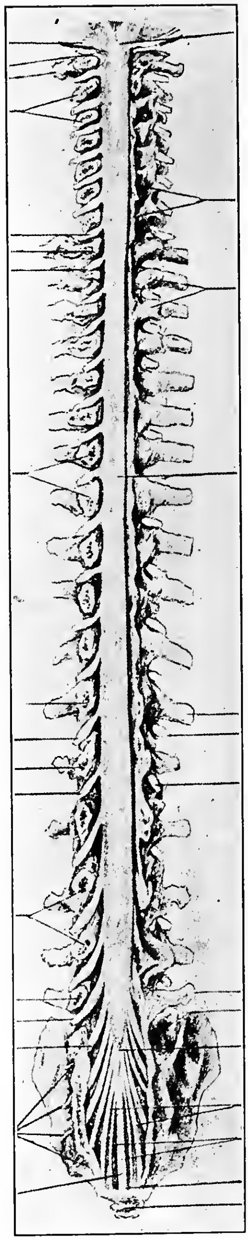


Fig. 246.—Posterior Wall of Vertebral Canal Has Been Removed and Dural Sheath Opened to Expose Spinal Cord and Dorsal Roots of Attached Nerves. (Piersol.)

stoppage of respiration, and so on—phenomena due to a too direct action of the anesthetic fluid upon the bulb. Their occurrence may be avoided by making the puncture lower down between the first and second dorsal vertebræ, which produces as perfect and deep analgesia for

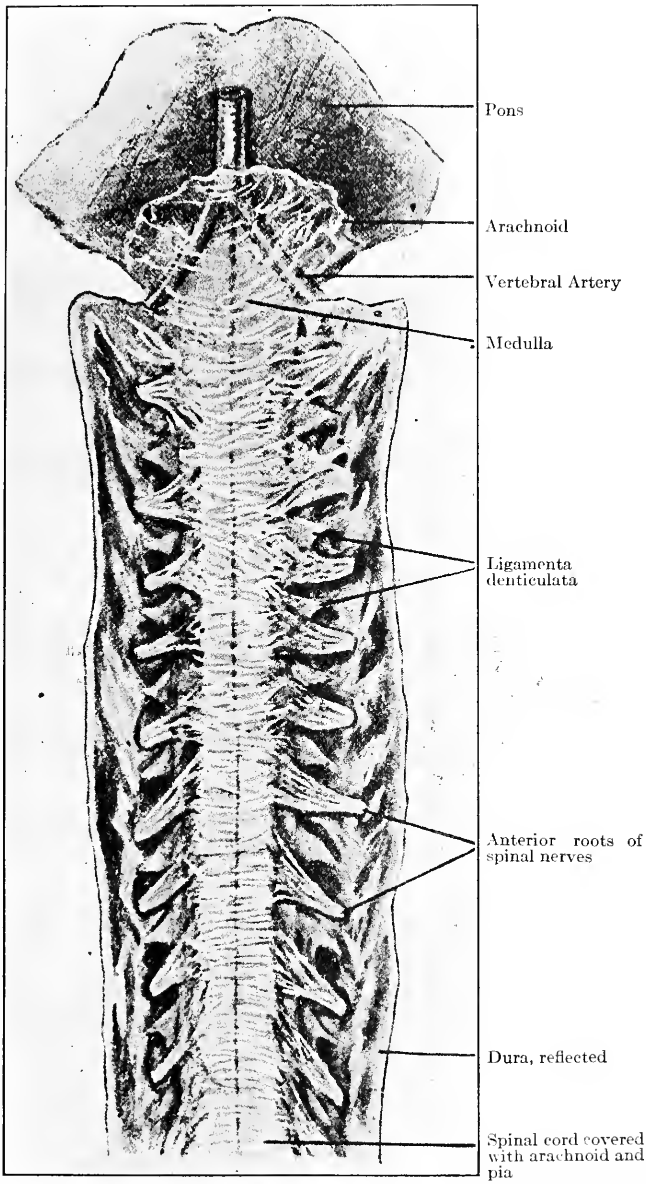


Fig. 247.—Upper Part of Spinal Cord Within Dural Sheath, Which Has Been Opened and Turned Aside. Ligamenta denticulata and nerve-roots are shown as they pass outward to dura. (Piersol.)

the segment of the body comprising the head, neck, and upper limbs as is produced by the mediocervical puncture. I have therefore reduced sites of election for puncture or two." These are stated above.

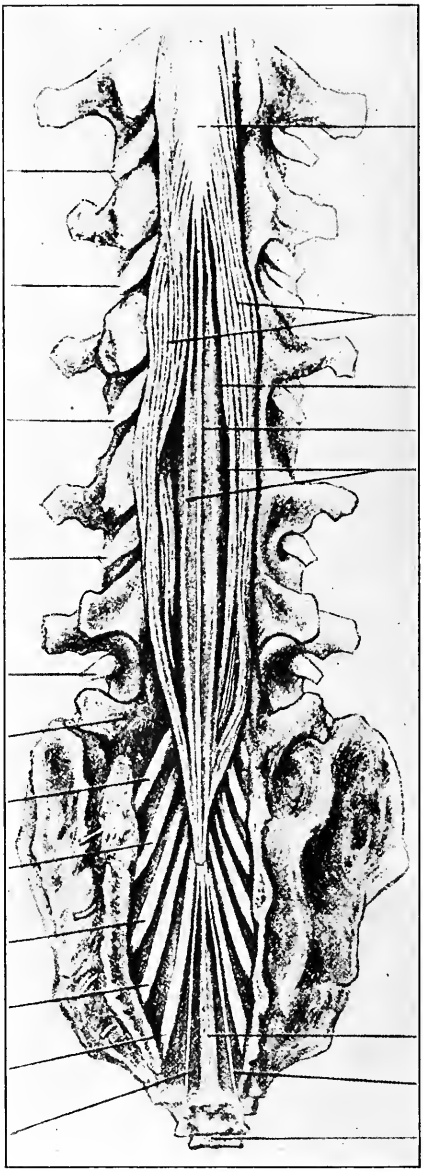


Fig. 248.—End of Spinal Cord With Roots of Lower Nerves Descending in Cauda Equina to Gain Their Respective Foramina. (Piersol.)

Canny Ryall,[1] one of the most enthusiastic advocates of the Jonnesco method for operations upon the upper part of the body, makes the injection into the first dorsal space, and for operations upon the lower part into either the eleventh or twelfth dorsal spaces. He rarely uses lumbar puncture, since, in his experience, better results are obtained by making the injection into the dorsal region. He finds no advantage in making a cervical puncture, for perfect analgesia lasting an hour or two can be obtained by injecting between the first and second dorsal spines.

Gray [2] considers it unnecessary to make the puncture higher than the interspace between the first and second lumbar vertebræ, the space between the third and fourth being best for routine work.

Avamresco [3] varies the site of puncture according to the operation, as follows: (1) For operations on the perineum, external genitals, and anus, between the third and fourth lumbar vertebræ; (2) for operations on the inguinal region and lower

[1] Ryall: *Op. cit., Brit. Med. J.,* June 19, 1909.

[2] Gray: *Op. cit., Lancet,* Sept. 25 and Oct. 2, 1909.

[3] Avamesco: *Lancet,* 1901, *1,* 637.

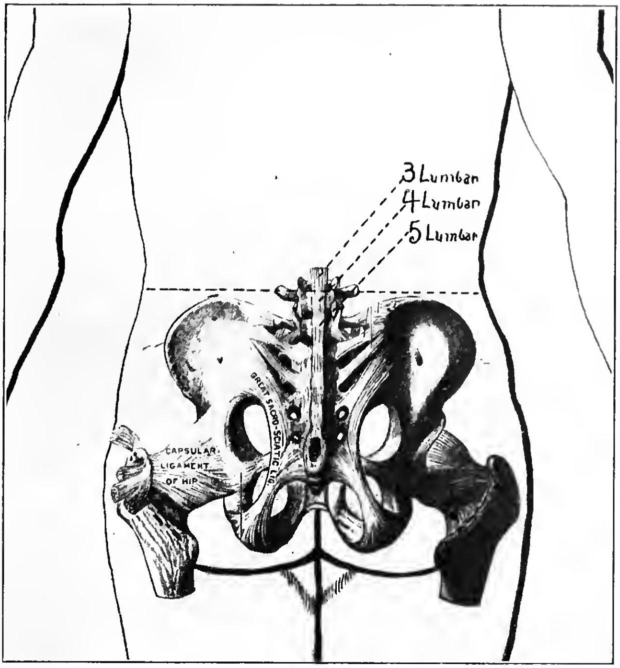


FIG. 249.—SCHEMATIC PICTURE SHOWING LANDMARKS USED IN LOCATING SPACE BETWEEN THIRD AND FOURTH LUMBAR VERTEBRÆ.

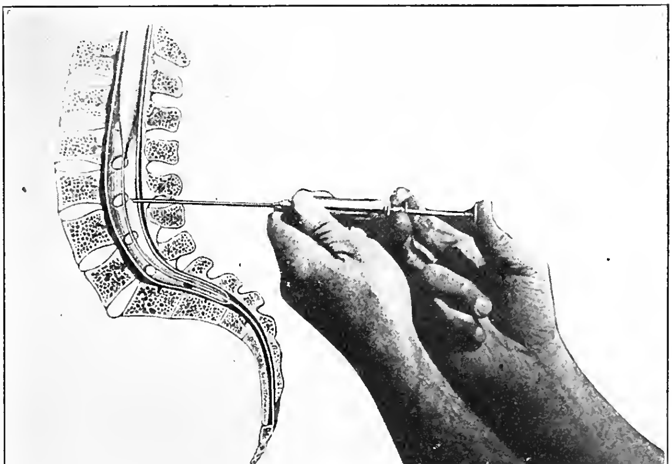


FIG. 250.—SCHEMATIC PICTURE SHOWING NEEDLE INSERTED BETWEEN THIRD AND FOURTH LUMBAR VERTEBRÆ OF THE SPINAL CANAL, BUT BELOW THE CORD.

extremities, between the first and second lumbar spines; (3) for operations on the abdomen below the umbilicus, between the ninth and tenth dorsal spines; (4) for operations on the abdomen above the umbilicus, between the sixth and seventh dorsal spines.

Babcock [1] injects in the second lumbar interspace for operations not involving tissues above the level of Poupart's ligament, or the first lumbar or twelfth dorsal interspace, if intra-abdominal manipulations are required.

Personally, I recognize no advantage by going into the subarachnoid space at a higher point than between the third and fourth lumbar vertebræ, though on several occasions, because of deformity of the spine, or for other reasons, the spaces between the first and second, and between the second and third lumbar vertebræ, have been successfully entered. In cases where there is to be much pulling and tearing of the tissues of the abdomen, particularly in the upper part, I sometimes inject between the twelfth dorsal and the first lumbar. Analgesia of any part of the body, however, may be obtained by lumbar injection, plus the use of an analgesic agent of equal or lighter specific weight than the cerebrospinal fluid, or by employing a fluid of greater specific weight, plus the lowering of the patient's head.

THE PATIENT

Preliminary Preparation of Patient.—The operator who is to make the injection should apply the principles of psychotherapy to the patient some time before the operation, if this is possible. The indications for the method in the given case should be explained, and emphasis laid upon the advantages of this method over inhalation anesthesia. A clear understanding of what is to be expected on the part of the patient is quite conducive to the successful application of the method. At any rate, the patient's confidence should be gained by the operator. This is particularly true of nervous and excitable persons. Even with children much can be accomplished in this way. Not infrequently a doll or other toy put into the hands of the child patient will divert attention and gain confidence, sometimes rendering an otherwise intractable patient quite docile.

A hypodermic injection of morphin (1/8 to 1/4 gr.), combined in some cases with atropin or hyoscin, may be given half an hour or an hour before injection. It serves to tranquilize the patient and to make him less susceptible to any possible pain or discomfort contingent upon the initial procedure. Bromids instead of morphin may be given the day before, or nitroglycerin (1/200–1/100 gr.), given coincidentally with the spinal injection, may be advantageous. Strychnin (1/60 gr.) given at the time

[1] Babcock: *Op. cit., Penn. Med. J.,* Aug., 1909.

of the injection is supportive. Combined with nitroglycerin, it lessens the danger of headache, shock, and other disagreeable symptoms.

No preliminary medication is given with children.

Preliminary preparation of the patient as regards diet, catharsis, etc., which is of so great importance in inhalation anesthesia, is not essential in spinal analgesia. Patients coming into the hospital from the street, with no preliminary preparation in these regards, have been operated upon as successfully, and with as few accompanying and postoperative phenomena, as have those who have been subjected to the most careful preparatory care. Generally speaking, however, attention to no details which conserve the patient's vitality and comfort should be neglected.

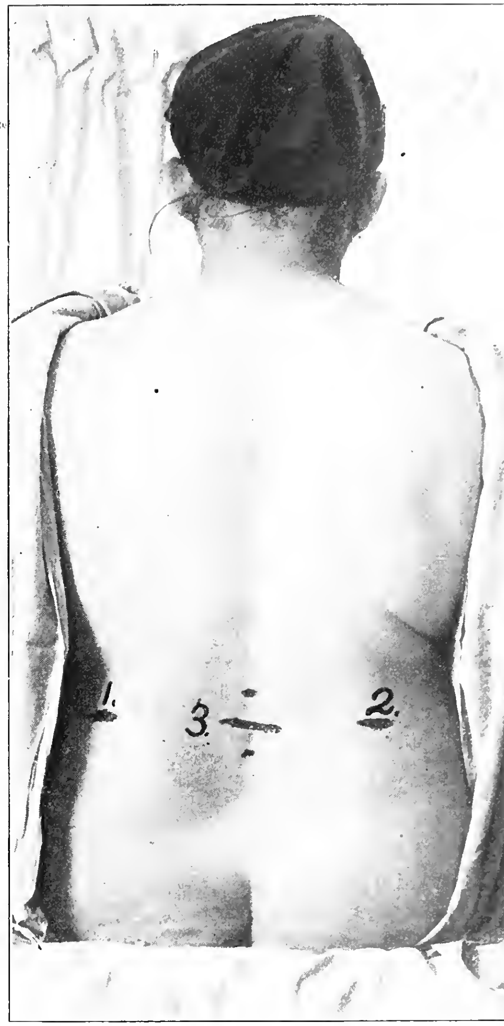


Fig. 251.—Patient in Sitting Posture Ready for Spinal Puncture. 1 and 2, Highest points of crests of ilia; 3, spinous processes of third, fourth and fifth lumbar vertebræ.

Position of Patient.—The position of the patient while the injection is being made is important. One should sit evenly on the edge of the table, the feet hanging down. The arms are folded against the abdomen. At the moment of the puncture the patient should bend the head down, as in Figure 259, and push against the abdomen with the arms in such way as to arch the back and separate the vertebræ as much as possible. In the case of children and infants, it is necessary for the attendant to see that this position is maintained.

The patient must be warned beforehand, and reminded at the time, to maintain this position, and not to straighten up or otherwise move until told to do so.

Fig. 252.—Injection Being Made With Patient in Recumbent Position.

If for any reason it is impossible to make the puncture with the patient in the above position, it may be done in the recumbent posture, as shown in Figure 252.

APPARATUS AND MATERIALS

The apparatus and materials employed in the induction of spinal analgesia are shown in Figures 253 and 254.

The apparatus for giving the injection of the analgesic agent consists of a syringe and two cannulæ.

The syringe, which is made by Ford & Co., of New York, is entirely of metal, including the piston, so that it expands uniformly upon boiling. It has a capacity of 5 c. c., the corresponding quantities in the two systems being graduated upon the piston.

The cannulæ are made in two sizes, of three lengths; the points are ground short and beveled, with a cutting edge all round. The shank is of flexible metal, so that it will bend without breaking.

The cannula slips on a ground joint, fitting accurately the handle, without washers or screws. The proximal end of the cannula is fitted with a handle which can be firmly grasped.

Through the cannula runs a stylet, the proximal end of which is rounded, knob-like, so that it can be pressed against the base of the index finger, adding firmness of grip.

FIG. 253.—TABLE CONTAINING INSTRUMENTS AND MATERIALS USED IN GIVING SPINAL ANALGESIA. (a) Glass with sterilized water; (b) empty glass in which to collect cerebrospinal fluid (c) bottle of iodin for sterilizing the skin; (d) graduate for preparing solution; (e) bottle of collodion; (f) bottle of ethyl chlorid wrapped in sterilized gauze; (g) sterilized gauze and sterilized cotton; (h) small can of strong ether wrapped in sterilized gauze; (i) dish of bichlorid solution: (j) two powders, 5 grains each, one of cocain and one of tropacocain; (k) two ampules containing stovain (suprarenin-glucose solution); (l) two needles and syringe (Bainbridge); (m) small scalpel for making puncture; (n) clamp with piece of sterilized gauze for painting the skin with iodin; (o) glass rod for mixing.

The instrument can be taken apart and thoroughly sterilized.

Figure 255 shows the fine needle employed by Babcock. The syringe is a Luer syringe of 2 c. c. capacity, graduated in cubic centimeters and

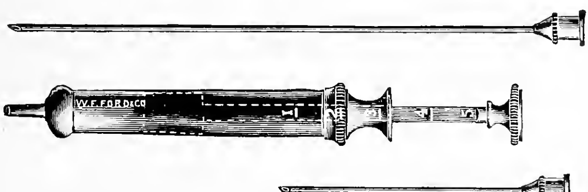


FIG. 254—BAINBRIDGE'S SYRINGE AND NEEDLE.

FIG. 255.—BABCOCK'S NEEDLE FOR SPINAL ANALGESIA.

millimeters. The obturator which comes with this needle fits perfectly around the opening at the end of the needle, thereby closing it entirely during the time it is being injected and until the obturator is withdrawn,

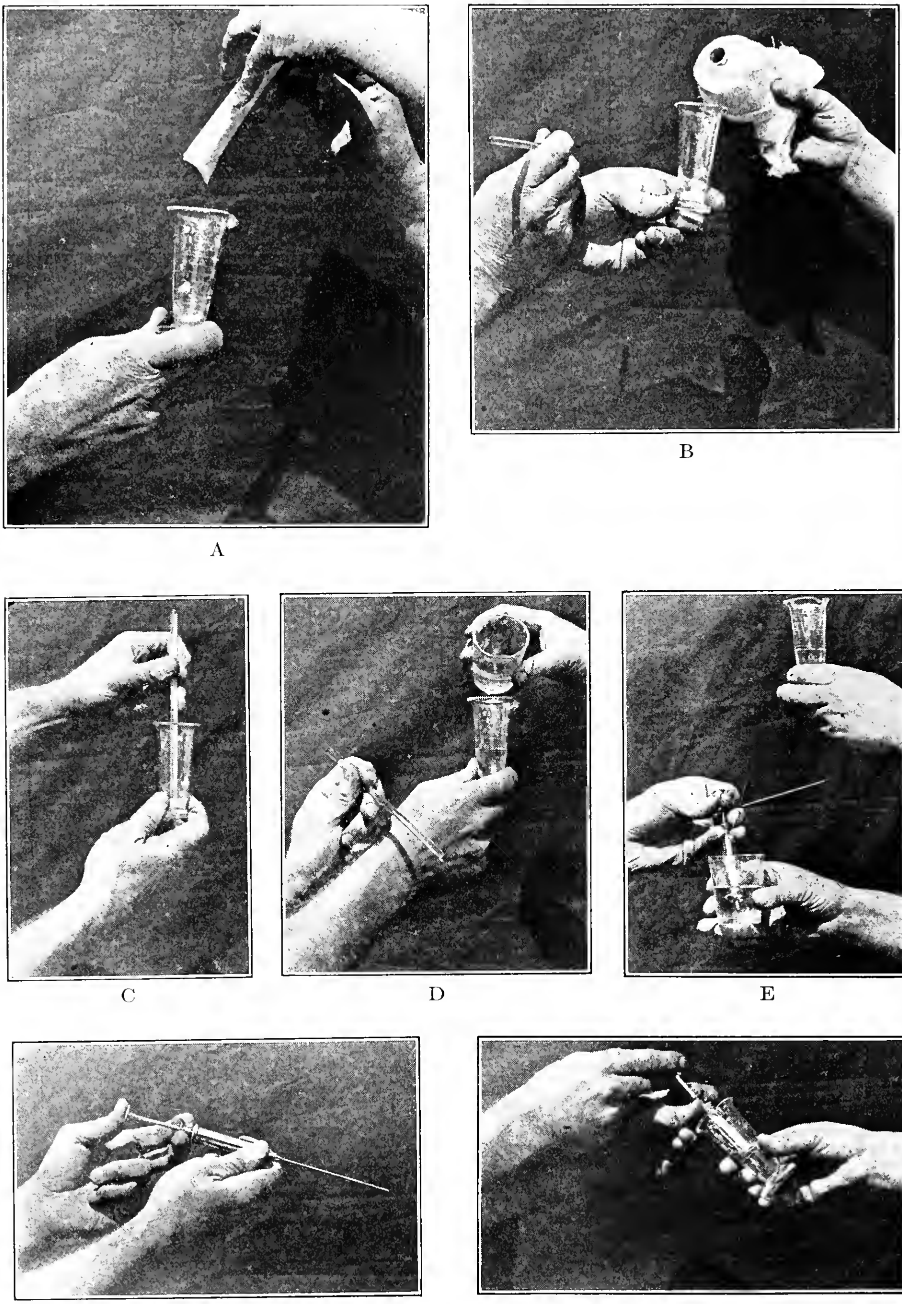


Fig. 256.—Sterilizing the Apparatus. A, placing the drug in the graduate; B, adding ether to sterilize; C, mixing ether with powder into a paste; D, adding required amount of water to make given solution; E, testing syringe with sterile water; F, testing syringe; G, filling syringe with injection material.

before the syringe is slipped into the hub for the injection of the analgesic agent. This needle is made by Charles Lentz & Sons, Philadelphia.

In sterilizing the apparatus no soda or other alkalies should be employed, nor should the analgesic agents be in any way allowed to come in contact with these substances, which destroy their analgesic properties.

The sterile implements and materials are placed upon a table covered with a sterile sheet until ready for use.

Various needles, syringes, etc., have been devised and advocated, and are readily obtainable. The apparatus described above will answer all requirements of spinal analgesia.

TECHNIQUE OF INJECTION

The operator's hands are made aseptic in the usual manner.

The site of puncture may be cleansed in the ordinary way, by scrubbing, etc., or, if desired, it may be rendered aseptic, after the patient has been placed upon the table, by painting the skin with tincture of iodin. If preferred, the area may be painted an hour or so before operation, and again after the patient is placed upon the table.

If the iodin method is employed, no preliminary washing should be resorted to unless it is done a sufficiently long time before the painting for the tissues to become thoroughly dry. If desired, the skin may be sponged with ether, which quickly evaporates, leaving a perfectly dry surface for the action of the iodin. This is not necessary, however, as the iodin is sufficient for purposes of antisepsis.

The patient, in the position shown in Figure 251, with the puncture site painted with iodin, as shown in Figure 257, is draped with the sterilized sheet, as shown in Figure 258.

This sheet has cut in it a hole or window (Fig. 258) large enough for purposes of injection. The operator, in making his examination and identification of landmarks, runs no risk of contaminating his hands by contact with skin surfaces which have not been rendered aseptic.

The site of puncture is now located in the following manner, as indicated in Figures 259, 260, and 261:

(1) The highest points on the crests of the ilia are located by the hands, as shown in the figures.

(2) The sites of the second, third, fourth, and fifth lumbar vertebræ are marked.

(3) The thumb of each hand is placed in the space between the second and third, third and fourth, or fourth and fifth lumbar vertebræ,

according to the selection of site, at the mid-point between the two. One-half inch to either side of this point is the site for the puncture.

The puncture point being located, the assistant plays ethyl chlorid on the area, or, if preferred, a preliminary injection of cocain or other local analgesic agent may be made. (See Fig. 260.)

Fig. 257.—Puncture Site Area Painted with Iodin.

A small incision is now made through the true skin, which is rendered hemostatic as well as analgesic by the ethyl chlorid.

The needle is passed through the incised skin and subcutaneous tissue, straight forward, as in Figures 250 and 261. It is then depressed, the point being made to go upward, forward, and inward, toward the median line. It is inserted from 1½ to 2 inches, according to the thickness of the patient's flesh.

When the needle is felt to impinge upon the bone surrounding the foramen, it is depressed a little more, and pushed forward, when it comes upon the ligamentum subflavum, then the dura mater. In piercing the ligament and dura there is a peculiar sensation like the popping of a membrane. This signifies the entrance to the subarachnoid space.

The cerebrospinal fluid escapes, as shown in Figure 262, under ordinary circumstances. If it does not flow freely, something is wrong. The needle may not have entered the right place, or it may be clogged. A stylet should not be inserted into the needle. Another syringe should be ready, and with this, if one cannot draw out blood or fluid, the needle should be withdrawn, and, after being rendered patent, be reinserted.

It should be noted that there is considerable difference in spines with reference to the amount of cerebrospinal fluid, some being what is called "dry," with little fluid escaping upon puncture; others, "wet," with an abundance of fluid under high tension. The quantity withdrawn depends upon the tension. If the fluid comes out with force more is withdrawn than when it is not under much pressure.

Fig. 258.—Sterilized Sheet, Patient Draped, and Window Made at Site of Puncture.

I prefer not to proceed with the injection unless the fluid issues with at least an approximate quantity and tension. Gray[1] does not hold to this point. Discussing the general opinion that satisfactory analgesia will not result unless there is a free flow of fluid, he says:

"This is true enough in the main, but if, after patience and perseverance, a free flow of fluid cannot be obtained, but only slow drops (or if slightly blood-stained fluid only appears), I consider that the injection *should* be attempted before making another puncture, provided cerebrospinal fluid has been seen. I have encountered this class of case on two or three occasions, when, in spite of failure to obtain a free jet, a perfectly satisfactory anesthesia has resulted from the injection."

Dönitz[2] and Dean[3] suggest that when the fluid flows scantily this is an indication for a larger quantity of the analgesic solution.

[1] Gray: *Op. cit., Lancet,* Sept. 25, Oct. 2, 1909.
[2] *Verhandl. d. deutsch. Gesellsch. f. Chir.,* 1905, 525-548.
[3] *Brit. Med. Jour.,* 1907, *2,* 869.

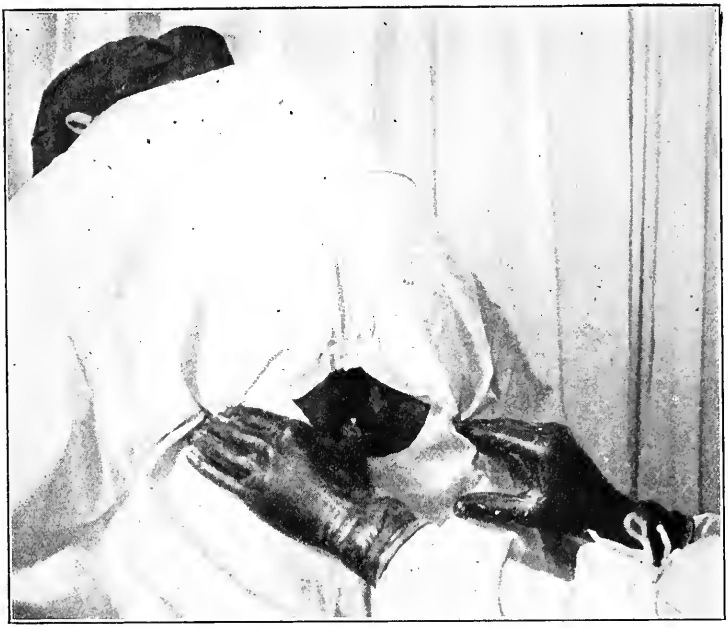


FIG. 259.—LOCATING THE SITE FOR PUNCTURE.

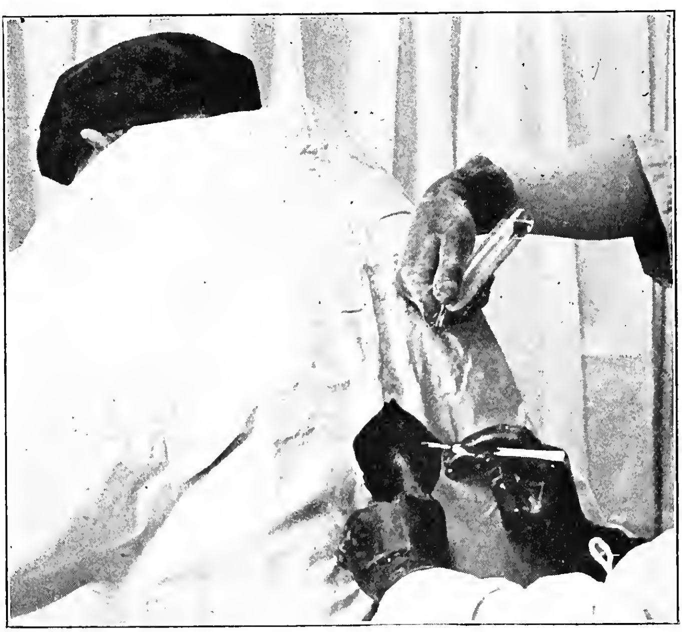


FIG. 260.—APPLYING ETHYL CHLORID AND INCISING THE SKIN.

In some cases, despite careful technique and repeated attempts, at different sites, no cerebrospinal fluid is obtainable. Such cases have doubtless led to the expression "dry spine," but it is rather to be inferred that they come under the category mentioned by Gerstenberg and Hein, Lusk, and others. (See pp. 564 and 605 *et seq.*) A personal experience with such a case is cited on page 624.

The first few drops of fluid may be bloody, which may signify merely that a small quantity of blood has been carried in with the needle. If it

FIG. 261.—SHOWING DIRECTION OF NEEDLE ABOUT TO ENTER SPINAL CANAL.

continues bloody, however, something more serious is to be considered. This rarely happens, but when it does the operation should be discontinued.

Sometimes, when the fluid does not flow freely, it will do so if the patient will cough, thus causing more tension upon it.

An uncontrollable patient, who will not remain still and quiet, should be held steadily while the puncture is being made, or the needle should be withdrawn at once. The injection of the analgesic agent should not be made unless the patient is perfectly quiet.

The fluid is injected slowly, as shown in Figure 263. The obliquity of the passage of the needle has the advantage that no tract is formed for the fluid to follow as the needle is withdrawn.

The body of the vertebra in front should not be touched with the needle, because of the presence there of a large plexus of blood vessels.

When the needle is withdrawn a cotton and collodion dressing is applied, as shown in Figure 264.

Fig. 262.—Cerebrospinal Fluid Escaping.

If low analgesia is desired, for operation upon the lower part of the body, the patient may be allowed to sit up for a few minutes after the injection, or the head may be elevated.

If high analgesia through lumbar puncture is desired, for operations upon the upper part of the body, the head is lowered, or a fluid with lower specific gravity than the cerebrospinal fluid is employed. Having had no personal experience with the Jonnesco method of inducing high analgesia, no statement can be made with reference to the relative merits of the so-called high analgesia for this purpose, as compared with lumbar injection plus modified agent or position of patient.

Fig. 263.—Injecting Solution.

Babcock[1] prefers to use a small needle (Fig. 255), and to go in without the preliminary nicking of the skin. If the patient has received no preliminary medication the area marked off on the back is frozen by a spray of ethyl chlorid. The needle is intro-

[1] Babcock: *Op. cit.*, *Penn. Med. J.*, Aug., 1909.

duced through the line marking the injection point, at right angles to the skin, and about 2 millimeters to one side of the median line. The needle is carried steadily forward until the resistance of the ligamentum subflavum is felt, when the mandrin is withdrawn from the needle, which is then carried on through the dura.

If high analgesia is desired, Babcock considers it advisable, before the injection is given, to so reduce the cerebrospinal fluid that it issues only in drops from the needle. The needle is cautiously rotated to make sure that the bevel point is entirely through the membrane. The syringe is then attached, and about 1 c. c. of cerebrospinal fluid is cautiously withdrawn to mix with and dilute the analgesic solution. The mixture is now steadily and rather rapidly injected, the needle with the attached syringe quickly withdrawn, and the patient immediately placed in the recumbent posture with the head slightly raised. This last point is of the utmost importance.

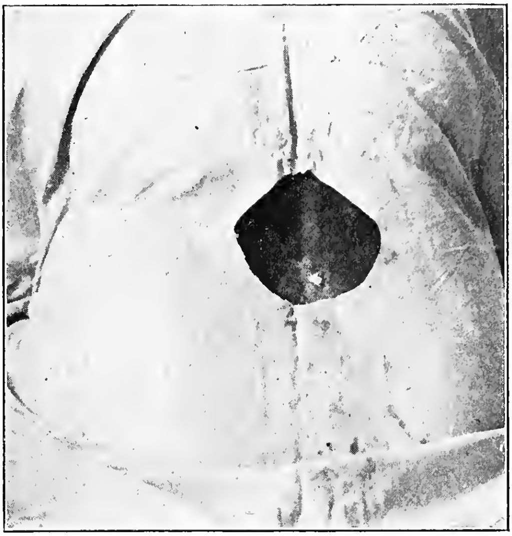


Fig. 264.—Cotton and Collodion Dressing on Puncture Point.

In testing for analgesia, which begins in from three to ten minutes after the injection, one should bear in mind the difference between analgesia and anesthesia. (See Introduction, p. 555.)

ADDITIONAL ILLUSTRATIVE CASE REPORTS

With the preliminary preparation, the necessary adjuvant medication, and the careful technique, as outlined in the foregoing pages, there should be no difficulty with spinal analgesia, unless some anatomical anomaly or an idiosyncrasy be encountered. Occasionally,—very rarely,—one encounters a patient who possesses an idiosyncrasy with reference to one or another, or perhaps all, of the spinal analgesic agents. Such a case was encountered by me recently, as was also one of so-called "dry spine.'

Case of Idiosyncrasy.—H. C., female, aged 24. Consulted me in February, 1911, with reference to hernia and displacement of the uterus. Patient was anemic and nervous, and had an old healed tuberculous lesion of the lung. Otherwise in fair general condition. She requested that operation be performed under spinal analgesia. This was undertaken on February 14, 1911, no preliminary medication being employed.

Spinal puncture was made, between the third and fourth lumbar vertebræ, and 30 minims of fluid withdrawn. An injection was made of 15 minims of a 3 per cent solution of novocain. After an interval of 15 minutes there was no analgesia, even in the feet. A second injection was made, this time with stovain, 12 minims of a 3 per cent solution being used. After waiting 20 minutes the site of operation was still sensitive. During all this time (40 minutes from the time of the first injection), the patient was in good condition, with only slight nausea and no vomiting. The pulse was 120, full and strong.

The operation was abandoned for the day, it being thought unwise to subject the patient to a third injection. During the next three days she suffered from slight headache, but was otherwise in good condition.

On February 17 another attempt was made to induce spinal analgesia. Cocain was used on this occasion, 15 minims of a 2 per cent solution being employed. After 25 minutes there was no evidence of analgesia so far as pain sense was concerned. The patient was nervous to begin with, and became nauseated after the injection, but the pulse (120) was fairly strong. A second attempt was made, but, as there was no escape of fluid, no injection was made.

On the assumption that the patient had an idiosyncrasy, it was decided to test the matter with local injections. Accordingly, 1 c. c. of a 2 per cent solution of cocain was injected at the site of operation, but without success. The patient became quite hysterical, and the entire matter was abandoned. Patient was subsequently operated upon under general anesthesia.

Upon further questioning, it was learned from the patient that in 1900 an attempt was made by Dr. Frederick Kammerer, of New York, to operate upon her for appendicitis under spinal analgesia, cocain being employed. No analgesia was obtained, and the operation was performed under general anesthesia.

Case of So-called "Dry Spine."—B. M., female, negro, aged 17. Operation, Woman's Hospital, Philadelphia, January 25, 1912, appendectomy. Gangrenous appendix found to be walled off by adhesions. Recovery uneventful.

This patient had Bright's disease and an old consolidation at the apex of one lung. For these reasons it was thought advisable to operate under spinal analgesia.

An attempt was made to operate in this case under spinal analgesia, but without success. Puncture was made between the fourth and fifth lumbar vertebræ, but, only a tiny drop of fluid being obtained, injection was not made. A second attempt with another needle proving futile, puncture was made successively in the spaces between the third and fourth and second and third lumbar vertebræ. No fluid being obtained, the effort at spinal analgesia was abandoned, and the operation was performed under inhalation anesthesia.

Case of a Typical "Satisfactory" Analgesia.[1]—L. L., female, aged 58, admitted to the New York Skin and Cancer Hospital, March 18, 1911, for operation for lipomata of the abdominal wall, papilloma of neck, angiomata of abdominal wall, and varicose ulcers of the legs. Operation, March 20, 1911. The various growths were removed, and the ulcers of the legs excised.

Adjuvant medication: Strychnin sulphate, 1/60 gr.; nitroglycerin, 1/200 gr.

Analgesic agent: Glucose-adrenalin-stovain, one ampule, 2 c. c.; stovain, 3 per cent.

Analgesia extended to neck, and lasted for 1 hour and 55 minutes.

There was no nausea, no vomiting, no headache, or other unfavorable symptom, and recovery was uninterrupted.

Case of Typical Analgesia, Injection in Recumbent Position.—Figure 262 represents the injection being given with the patient in the recumbent position. This patient was a male, B. N., aged 38 years. Operated upon for gangrene of the foot February 7, 1911, the foot being partially amputated.

No preliminary medication. Stovain, 8 minims of a 3 per cent solution, injected between the third and fourth lumbar vertebræ. Analgesia complete to the umbilicus in 8 minutes. No unfavorable symptoms.

On February 24, 1911, amputation of foot, leaving os calcis. Sixteen minims of a 3 per cent solution of stovain in water employed. Within 2 minutes after the injection the patient was analgesic to the nipple line, and 5 minutes after the injection the operation was begun. No unfavorable symptoms. Patient manifested an interest in the entire procedure.

An Additional Case (No. 1069), of Special Interest.[2]—During the Clinical Congress of Surgeons of North America, held in New York City in November, 1912, a patient at the New York Polyclinic Hospital died after a lumbar subarachnoid injection of stovain, preparatory to the performance of an operation for hernia.

P. H., Irish, male, age given as 50 years, probably 60 or more; chronic alcoholic. Came to my clinic at the New York Polyclinic Medical School and Hospital, October 18, 1912, seeking relief for a condition which

[1] This is the case with which the technique is illustrated, Figs. 251 and 257 to 264.

[2] Bainbridge: "Spinal Analgesia—Development and Present Status of the Method, with a Brief Summary of Personal Experience in 1,065 Cases." *J. Am. Med. Assn.*, Nov. 23, 1912, *59*, 1855-1859.

proved, upon examination, to be right inguinal hernia, at times irreducible, and causing great suffering. The man gave a history of having felt a sharp, tearing pain in the right groin, while operating a taxicab, about three months previous to coming to the clinic. Since that time he had been to several dispensaries in a vain search for relief. He had used a truss without success. Failing to obtain relief by other measures, he wished to be operated upon at once.

From the general physical examination the patient was found to be in a very bad condition, as the result of the prolonged excessive use of alcoholic stimulants. The following conditions were present: general atheroma of the arteries; renal insufficiency, due to chronic Bright's disease; marked enlargement of the liver; myocarditis, with systolic murmur at the base; emphysema; râles over the bases of both lungs. A history of chronic gastritis was also elicited.

The patient's general condition was such that immediate operation was not deemed advisable. He was told, accordingly, to abstain from the use of intoxicants, and to refrain from lifting or straining; he was put upon a diet, tonics, etc., and was kept under observation for about three weeks. Despite the fact that only slight improvement followed this régime, he insisted upon operation. He was then admitted to the hospital on November 14, and prepared for operation the next day.

Because of the man's general condition, inhalation anesthesia was considered contraindicated. He was prepared, accordingly, for operation under spinal analgesia. Before the members of the Congress of Surgeons present, I injected into the cauda equina twenty-six minims of a one per cent solution of stovain. The patient, who presented no symptoms differing from those of the average subject during the spinal injection, was then sent to another room to be operated upon by E. M. Foote and Claude A. Frink, of my staff, while I concluded my lecture before the Congress. The man's mind was perfectly clear, his pulse was good, there was no nausea, no cyanosis, no respiratory embarrassment—in fact, *none of the symptoms of stovain poisoning*. He suddenly turned pale, said, "I am dying," and instantly died.

The case was made a coroner's case, and an autopsy was performed the next day, with the following findings:

Marked edema of the brain, so-called "wet brain"; myocarditis; atheroma of aorta; aortic insufficiency; emphysema of lungs; chronic interstitial splenitis; chronic gastritis; chronic enteritis; chronic interstitial nephritis. Spinal cord showed no gross lesion.

The coroner's inquest was held on December 4, 1912. The jury, after listening to the testimony of the above facts and a number of experts as to the indications of death by stovain poisoning, did not find that the man died of stovain poisoning, but that death was caused "by pathological conditions" as described, and all concerned were exonerated from blame.

CONCLUSION

In summing up the entire subject of spinal analgesia, the author of this section wishes to reiterate that this method is not to be considered as replacing inhalation anesthesia. It has, however, a distinct place in surgery, and as the indications and contraindications are more clearly understood and the technique of the method improved, its field of usefulness has widened, and will doubtless continue to widen. It must nevertheless still occupy a limited sphere until further accurate and scientific experimentation has led to more certain conclusions with reference to the physiological action of the agents employed and the dosage in which they may be used to obtain a given result.

CHAPTER XVI

ELECTRIC ANALGESIA, SLEEP, AND RESUSCITATION

LOUISE G. ROBINOVITCH, B. ÈS L., M. D. (PARIS)

HISTORY: Electric Source and Technique; Application in Man; Contraindications; Electric Analgesia and Sleep in Wireless Circuits; Conclusions.

ELECTRIC ANALGESIA AND ELECTRIC RESUSCITATION AFTER HEART FAILURE UNDER CHLOROFORM OR ELECTROCUTION: Exclusion of the Head; Kind of Current Used; Procedure; Limitations; Application in Accidental Electrocution; Application in Surgery; Clinical Applications.

History.—In 1890 d'Arsonval found that high frequency currents above 2,500 and not over 10,000 periods per second caused a certain degree of anesthesia. In 1892, or earlier, Hutchinson found that induction currents, frequently interrupted with the ribbon vibrator that he had invented, caused anesthesia.[1] In 1901 Mlle Pompilian produced anesthesia in frogs by subjecting them to induction currents frequently interrupted by means of a revolving wheel with 12 insulated segments designed by herself.[2] In 1902 Leduc and Rouxeau experimented with direct currents interrupted by means of a revolving wheel designed by them. This wheel had 4 insulated segments.[3] There were 2 contact levers; one lever was fixed and the other adjustable. By changing the relative position of the movable level it was possible to change the period of the passage of the current. One-tenth of the entire period during a revolution was found to be the most favorable condition for producing what was then called electric "sleep" or "anesthesia."

In 1905 we found, while working in the laboratories of these two professors, that an induction current obtained by an induction apparatus in which the primary coil was run by means of a frequently interrupted direct current, 6,000 times per minute, period 1/10, produced deep anesthe-

[1] Verbal information given by the New York manufacturers of coils with the ribbon vibrator.

[2] Personal communication.

[3] Rouxeau did not know of the existence of Mlle Pompilian's models when he designed his wheel.

sia in rabbits. While working out the details of the physiology of electric "anesthesia" we pointed out the dangers of using induction currents on animals,[1] especially when the head was included in the circuit. In 1906 researches into the blood pressure, temperature, respiration, and duration of electric "sleep," as well as studies of the effects of the two polarities and of various electric currents, were conducted. In 1907-1908 we perfected the interrupter, general instrumentation, and technique of application.[2] In 1909 we pointed out that a certain degree of analgesia and sleep could be obtained in rabbits with currents generated by a Vreeland oscillator, the preferred form of current being a pulsating one.[3]

In December, 1909, we found that "sleep" could be produced by unipolar and even by wireless methods in paths of displacement currents. In 1910 we obtained myogram traces showing muscle-nerve reaction in paths of displacement currents by both the unipolar and wireless method. After we had registered these myogram traces, Law found a valuable reference to Danilevsky's remarkable experiments on muscle-nerve reaction in the vicinity of powerful electromagnetic fields.[4]

The first physiological investigations on electric sleep, or anesthesia, were made by Rouxeau.[5] The detailed physiologic researches into this sleep and anesthesia were made by us in his laboratory. Utilization of this anesthesia in laboratory surgery was made in 1906. To eliminate the muscular rigidity caused by the earlier models of interrupter, we perfected the wheel interrupter and pointed out the danger of using the city current, alternating, rectified, ordinary wet battery, and all sorts of irregular currents.[6] In 1907 we employed electric sleep and anesthesia in clinical work,[7] and electric analgesia was applied by us locally in 1910.

[1] Robinovitch: "Sommeil électrique, épilepsie électrique et électrocution," *Thèse*, Paris, 1906.

[2] Robinowitch: "Electric Anesthesia or Sleep," *Handbook of Med. Sci.*, N. Y., 1907; "Electric Anesthesia; Its Use in Laboratory Work," *J. Ment. Path.*, 1907, No. 3.

[3] Robinovitch: "Physiologic Effects of a New Variety of Electric Current," *J. Ment. Path.*, 1909, No. 4; also, *Med. Rec.*, Dec. 11, 1909, 1009.

[4] Danilevsky: "De l'excitation des nerfs par les rayons électriques," *Compt. rendu du XXIIème Cong. Inter. de Méd.*, Moscow, Aug., 1847, 59.

[5] Leduc and Rouxeau: "Du temps pendant lequel peut-être maintenu l'état du sommeil électrique," *Compt. rend. d. l. Soc. d. Biol.*, July 4, 1903; also, "De l'influence du rhythme et de la période sur la production de l'inhibition par les courants intermittents de basse tension."

[6] Robinovitch: "Electric Anesthesia, Its Use in Laboratory Work," *J. Ment. Path.*, 1907, No. 3; also, "Anesthêsie électrique; application clinique; presentation de malades et d'instruments," *Bull. d. l. Soc. Clinique d. Méd. ment.*, Nov., 1908, No. 4; also, "Motor-interrupter Supplying a Current of Frequent Interruption for Electric Anesthesia," *Bull. d. l. Soc. Clinique d. Méd. ment.*, Nov., 1908.

[7] Robinovitch: "Electric Anesthesia in Laboratory Surgery Successfully Applied During a Period of Three Years. Demonstration on an Animal and Clinical

Electric Source and Technique.—Pending further investigation of our findings and practical application of wireless electricity for producing sleep in man, we shall go over the matter, dealing with currents in wired circuits in relation to sleep and analgesia, as we have applied it in clinical work as well as in animal and in human surgery.

Nothing but storage batteries of large capacity, 100 to 200 amperes, should be used.[1] The current used for the patient and the motor should come from two separate sources. The current to be used for the patient is connected with the inlet binding posts of a graphite rheostat. A wire potentiometer should not be used because it brings troublesome inductance into the circuit, as is explained in Figures 265, 266, 267, and 268. The current is interrupted on the negative pole; this pole is connected as follows: a wire connects the outlet binding post of the potentiometer (negative pole) with the wheel interrupter, a milliamperemeter, a switch, and finally a resistance box (Wheatstone bridge or any graded resistance). The other binding post of the potentiometer (positive) is connected directly with the bridge. The resistance put into the circuit is from 300 to 500 ohms. The resistance represents the patient or the animal. The circuit is then closed by means of the switch. A voltmeter is connected in shunt; all the other instruments are in series. The wheel interrupter is put in such a position as to allow the passage of the direct current without interrupting it (the wheel is not revolving). The voltmeter indicates, say, 40 volts; the milliamperemeter indicates, say, 20 milliamperes. Now the wheel interrupter is made to revolve by means of the motor, say, 1,500 to 2,000 times per minute. Whatever the amperage is while the wheel is interrupting the direct current, it is the aim to regulate the period of the passage of the current so as to have it pass only 1/10 of the time, 9/10 being lost. This is accomplished by changing the position of the adjustable contact lever in relation to the fixed lever on the wheel, while the latter is revolving. Keep on adjusting the movable lever until the milliamperemeter that registered 20 milliamperes when the wheel was stationary now registers only 2 milliamperes while it is revolving. The period of the passage of the current is now 1/10. It is of the utmost importance in this work and should be regulated every time

Application, Presentation of Patients,'' *J. Ment. Path.*, 1909, No. 4; also, ''Presentation of Instruments: Motor-interrupter Supplying a Current of Frequent Interruption for Electric Anesthesia,'' *J. Ment. Path.*, 1909, *8*, No. 4.

[1] Robinovitch: ''Electric Anesthesia, Its Use in Laboratory Work,'' *J. Ment. Path.*, 1907, No. 3; also, ''Anesthêsie électrique; application clinique; presentation de malades et d'instruments,'' *Bull. d. l. Soc. Clinique d. Méd. ment.*, Nov., 1908, No. 4; also, ''Motor-interrupter Supplying a Current of Frequent Interruption for Electric Anesthesia,'' *Bull. d. l. Soc. Clinique d. Méd. ment.*, Nov., 1908.

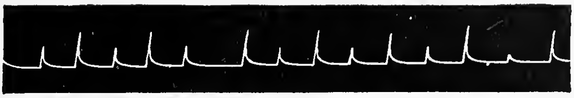


Fig. 265.—Myogram No. 5. Unipolar Method. Reaction at make and break of direct-current feeding field coils. At break of current reaction is more marked than at make. M, make; B, break.

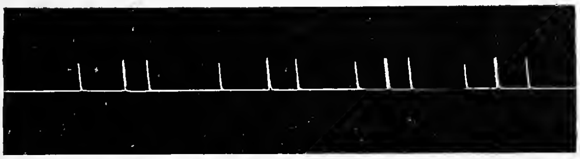


Fig. 266.—Myogram No. 6. Reactions at make of direct-current feeding field coils, at make of arc and at break of direct-current feeding field coils and vacuum tube. M, make; A, arc; B, break.

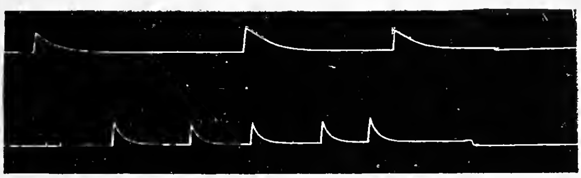


Fig. 267.—Myogram No. 7. Upper tracing; wireless; one end of wire connected with binding post of damp chamber. Other end of this wire held at a distance of fifteen centimeters from field coils and arc in vacuum tube; these coils and arc in vacuum tube in operation. No weight on muscle. Lower tracing: end of the wire three centimeters from tube anode. Reactions take place at make and break of arc in vacuum tube.

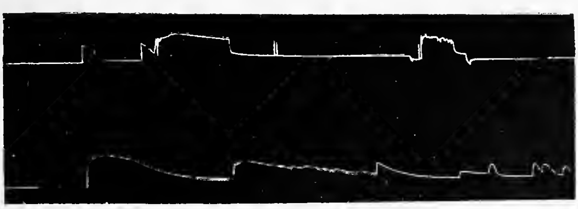


Fig. 268.—Myogram No. 8. Lower tracing: primary coil only; "wired" circuit with "gap" of five centimeters. M, reaction as soon as ribbon vibrator is in operation and magnetic flux brought into play. T, reaction while operator was touching base of stand holding muscle-nerve preparation. Rest of trace, spontaneous irregularity, while free end of wire was held in magnetic flux. Upper tracing: with a circuit "gap" of five centimeters and end of wire held near magnetic flux. No reaction when wires withdrawn from field.

before an experiment is commenced.[1] Now reduce the current to zero with the potentiometer, break the circuit by opening the switch, take out the bridge and substitute for it an animal or a patient. The wheel is

FIG. 269.—MYOGRAM NO. 9, "UNIPOLAR." Primary coil only (10 inches long, six layers of wire, of which diameter is $\frac{12}{16}$ mm., condenser in circuit. Core one inch in diameter. No weight on muscle); reaction when one end of the single wire is connected with damp chamber, the other end touching any part of the metal frame near magnetic flux. M, reaction when end of wire touches any part of metal frame; T, operator touching with hand base of drum on which trace is registered; S, operator touching base of stand holding muscle-nerve preparation.

made so that it can interrupt the current from 6,000 to 12,000 times per minute, according to the speed of its rotation.

It is dangerous to use any other current than that indicated above. Alternating, induction, rectified currents, or those supplied by ordinary

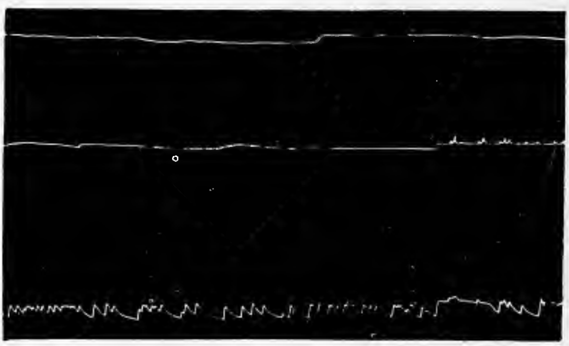


FIG. 270.—MYOGRAM NO. 10. "WIRELESS." No weight on muscle. From below upward; lowest line; Tesla high frequency. Preparation grounded; no spark across Tesla terminal apparatus one foot away from preparation. The two upper traces: oscillations conducted to preparation by operators' body, as explained in the text. Spark across Tesla terminals.

wet batteries are dangerous for this work. Irregular direct currents are equally dangerous. Bad results may be obtained in experiments in animal surgery by irregular currents, when laundries and elevators are run by power taken from the same main line as that supplying the laboratories. Unsuitable apparatus combined with such markedly uneven currents accounts for death and convulsions in animals, especially when too

[1] A firm in New York has constructed, under our direction, an interrupter with a fixed period of the passage of the current.

high amperage is used. Correct technical construction of the apparatus is of utmost importance.

When used with a wire potentiometer in the circuit, even our best model of interrupter caused muscular rigidity because of inductance. The myograms fully explain the difficulty.

We have found that substitution of a graphite rheostat for one made of wire eliminates this difficulty to a large extent.

Application in Man.—For Inducing Sleep.—Leduc was the first to submit himself to electric "sleep." Rouxeau and Malherbe applied the

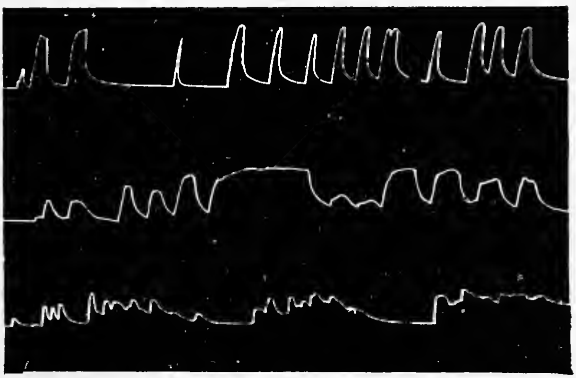


Fig. 271.—Myogram No. 11. "Wireless." Weight on muscle. From above downward: 1, reaction at a distance of 2 meters; each end of solenoid screwed into respective binding posts on disc of damp chamber; 2, reaction at a distance of 2 meters, one end of solenoid being free in the air; 3, reaction at a distance of 2½ meters, solenoid with one free end in the air reinforced.

current; the experiment was not pushed far enough to produce complete anesthesia; 35 volts and 4 milliamperes were used centrally.

In our work we distinguish between electric sleep and analgesia. We produce electric sleep in patients suffering from insomnia by applying to the forehead the negative electrode shaped to the forehead and the positive electrode to the palm of the right hand. The current is turned on slowly, generally, some 5 minutes being consumed in turning on ¾ of a milliampere. When this amount of current is reached, the patient feels a tingling sensation through his head and falls asleep within a few minutes. A small flag mounted on a little block of wood is placed upon the patient's chest; the flag moves with the movements of the chest, that are watched all the time while the patient is sleeping. We generally allow the current to course through the body for 1 hour, then turn it off; but the patient continues to sleep. On awakening the patient feels refreshed; if he is very sensitive, he may remark that he feels "a bit chilly." This chilly feeling is probably caused by the vasoconstriction during the passage of the current.

For Local Purposes.—In clinical work we have applied electric anesthesia in numerous cases. The chosen part of the body or limb is included in the circuit, the cathode always being nearer the central nervous system, the anode being the distal electrode. If the chest is in the circuit the amperage should be governed judiciously.

For Surgical Purposes.—We applied local electric analgesia in man for surgical purposes in 1910; the patient, a man twenty-three years old, was at the St. Francis Hospital, Hartford, Conn. M. M. Johnson, assisted by Edward Herr, operated. The patient talked with those near him while his toes were being amputated. The great toe of one foot and the great, second and third toes of the other were amputated. The operation was "bloodless." Four milliamperes of current and 54 volts were used in this case. Other surgical cases in which we applied electric analgesia locally are not yet published. One of these was a major operation of the lower limb and was also "bloodless." The vasoconstriction accounts for the insignificant loss of blood.

In some cases we used 9 milliamperes for amputation of the toes (one in a man, another in a woman) and 18 milliamperes for resection of the leg in a man. Neither one of these patients withdrew the limbs during the operation, although the surgeons urged them to do so if they felt pain. They only complained of the tingling sensation caused by these strong currents. We believe, therefore, that 4 milliamperes of current, applied with electrodes of the dimensions reported by Johnson, are most favorable.

Local analgesia depends entirely on proper technique in the application of the electrodes. In the lower extremities application of the electrodes is quite easy, because the anterior crural nerve and its accompanying vessels in Scarpa's triangle are readily reached with an electrode; so are the anterior and posterior tibial nerves in the leg. In the upper extremities it is rather difficult to hold the electrode applied over the large trunks of nerves and vessels. When the electrodes are properly applied to them the analgesia is good; but it is difficult to keep the electrodes in their proper places.

Locally, the amperage may readily be increased above 4 milliamperes; we do not recommend higher amperage than 4 milliamperes of the interrupted current; but 5 or 6 milliamperes may sometimes be necessary. Centrally, 4 milliamperes is as strong a current as should be applied. Currents slightly stronger than this should be used by none but the expert in this work. The major advantage of this analgesia is that it is not dangerous *when properly applied, with proper instruments and proper currents.*[1]

[1] This is part of a paper, "Electric Anesthesia and Electric Resuscitation After Heart Failure under Chloroform or Electrocution." Read in the Section of

Contraindications.—Electric sleep, and particularly analgesia, when applied centrally, causes abortion in pregnant animals. The current is contraindicated in cases of high arterial pressure, in the apoplectic and in the epileptic, because this current increases arterial tension.

Electric sleep or analgesia should not be combined with morphinization, chloroforming, or soporific agents.[2]

Electric Analgesia and Sleep in Wireless Circuits.[3]—In 1909 a new variety of electric current was used—one produced by a Vreeland oscillator.[4] Rabbits and dogs were subjected to the effects of this current and a certain degree of analgesia and sleep was produced. In one rabbit the tissues of the back of the chest were even cut through and the bones of the spinal column scraped with a knife, without causing any apparent reaction to pain. But in dogs we could not produce any analgesia for operative purposes without using a current so strong that it caused excessive muscular rigidity and endangered life. The more interesting feature of the effects of this pulsating current was in regard to sleep. A dog was put into a closed wired circuit of this current. The animal remained stretched out on its side, in a condition of muscular relaxation, during a period of 3 hours, when one of the electrodes accidentally became disconnected. The animal, however, continued in a condition of somnolence for ½ hour thereafter, despite the continued disconnection of one electrode in this circuit. A pin was thrust through its skin and the animal arose to its feet. We repeated similar experiments of unipolar connection with the working current of the oscillator, and similar results were obtained. We then disconnected both electrodes, and still the dog remained on its side in a drowsy condition upon the table, awaking only when shaken vigorously.

While the animal remained in a drowsy condition the oscillator was in operation. The oscillator's important features in relation to this sleep were not the working current supplied by the apparatus, this current not being used then, but the two field coils and rapid electric oscillations in the vacuum tube of the apparatus made for the purpose of supplying the working current. The magnetic flux and the arc in the

Pathology and Physiology of the American Medical Association, St. Louis, Mo., June, 1910.

[2] Robinovitch: "Electric Anesthesia in Laboratory Surgery Successfully Applied During a Period of Three Years. Demonstration on an Animal and Clinical Application, Presentation of Patients," *J. Ment. Path.*, 1909, No. 4; also, "Presentation of Instruments: Motor-interrupter Supplying a Current of Frequent Interruption for Electric Anesthesia," *J. Ment. Path.*, 1909, *8*, No. 4.

[3] *Med. Rec.*, Dec., 1910.

[4] Robinovitch: "Physiological Effects of a New Variety of Electric Current," *J. Ment. Path.*, 1909, *8*, No. 4; *Med. Rec.*, Dec. 11, 1909, 1009.

vacuum tube caused displacement currents in the air, as is shown in the myogram studies.

In our experiments the continuance of electric sleep in dogs by means of displacement currents was practised after the animals had been subjected to the effects of the pulsating current conducted through a closed wired circuit during periods of from 2 to 3 hours. We are not in a position to affirm that this sleep could be obtained in all dogs without the preliminary effect of the pulsating current in a wired circuit. But myograms obtained demonstrate the decided effect of displacement currents on living tissues; these studies seem to indicate that, where we failed to produce sleep with displacement currents at our disposal, it was because these currents were not sufficiently strong for the purpose.

In these experiments the muscle-nerve preparation is in a damp chamber, covered with a glass globe; the nerve lies across two non-polarizable electrodes; these electrodes are filled with a saturated solution of zinc sulphate, and wires connect them with binding posts on the disk of the damp chamber.

Conclusions.—Living beings and muscle-nerve preparations react to displacement currents. A muscle-nerve preparation may react to currents that an ordinary telephone receiver does not detect. A muscle-nerve preparation seems to be a sensitive detector of displacement currents.

An electromagnetic flux of an ordinary portable small-sized primary coil with a ribbon vibrator in operation causes muscle-nerve reaction in circuits with gaps of from 3 to 5 centimeters. A larger electromagnetic flux (core 10 inches long, 1 inch in diameter, primary coil six layers of wire, diameter 12/10 mm., with condenser on primary) causes marked reaction by unipolar methods. It is possible to produce effects on animal and living tissue by means of unipolar and wireless methods. The question of producing sleep in man in paths of displacement currents requires further study.

In our studies of wireless effects of displacement currents on living tissue, positive results have also been obtained without grounding the muscle-nerve preparations and even when everything connected with the experiment was insulated on a platform. This proved that reactions could be obtained by reason of free displacement currents in the air.[1]

Electric Analgesia, and Electric Resuscitation after Heart Failure Under Chloroform or Electrocution.[2]—By the use of electric currents it is possible to resuscitate subjects in a condition of apparent death caused

[1] *Med. Rec.*, Aug. 13, 1910.

[2] "Electric Anesthesia and Electric Resuscitation After Heart Failure under Chloroform or Electrocution." Am. Med. Assn., June, 1910. The part on resuscitation was published in the *J. Am. Med. Assn.*, Feb. 18, 1911, *56*, 478-481.

by chloroform, ether, morphin, electrocution, etc. The first important researches into resuscitation of electrocuted subjects were made at about the same time by Battelli [1] in Europe and R. H. Cunningham in this country.[2] Both authors used enormous currents for causing single electric shocks with which they attempted to restore life after ventricular tremulation had set in. Battelli used 4,800 and 2,400 volts respectively, of alternating currents (amperage not stated). The means was not practical because one shock caused with such high voltage was all the heart could stand; a second shock killed the animal definitely.

Leduc and Rouxeau [3] tried to resuscitate animals by means of direct interrupted currents of low tension, but they committed their predecessors' error of including the animal's head in the circuit. Besides, they used the lethal current for producing the shocks. The method was useless in cases of dogs.

Exclusion of the Head.—While experimenting on the cerebral circulation during electric epilepsy,[4] we saw, through a trephined opening in the skull, that every electric shock caused profound anemia of the brain at the time of the closure of the circuit. This led us to exclude the animal's head from the circuit during the rhythmic excitations, in order to exclude the medulla oblongata with the cardiac and respiratory centers, and to avoid any further anemia of these centers during apparent death, while the electric rhythmic excitations were being practiced. We also reduced the current to minimal doses for the first rhythmic excitations, because we found that useful cardiac and respiratory excitability was rapidly exhausted within the few minutes of apparent death. The maximum potential at the end of the resuscitation did not exceed 120 volts. Even this is too high voltage: in dogs it causes marked vagus stimulation, so that the heart beats are very slow during a long period of time after resuscitation, and the wave form of the beat does not resemble the normal form. In ordinarily severe cases, 70 volts is a good maximum potential.[5]

[1] Battelli and Prevost: "La mort par les courants électriques: courant alternatif à bas voltage et à haute tension," *J. d. Physiol. et de Path. gén.*, May, 1899.

[2] Cunningham: "The Cause of Death from Industrial Electric Currents," *N. Y. Med. J.*, 1899, *70*.

[3] Quoted by Robinovitch, in "Sommeil électrique, épilepsie électrique et électrocution," *Thèse,* Paris, 1906.

[4] Robinovitch: "General and Cerebral Blood Pressure During an Attack of Electric Epilepsy," *J. Ment. Pathol.*, 1907, *8*, No. 3.

[5] Robinovitch: "Method of Resuscitating Animals in a Condition of Cardiac and Respiratory Syncope Caused by Chloroform," *J. Ment. Path.*, 1907, *8*, No. 3. "Method of Resuscitating Electrocuted Animals," *ibid.;* "Méthod de rappeller à la vie des animaux en syncope chloroformique et des animaux en mort apparente causée par l'électrocution. Effets différents de différents courants électriques. Importance d'exclusion du circuit électrique de la tête de l'animal

The method of resuscitation consists in causing artificial blood pressure and respirations by means of rhythmic electric excitations, until normal function is restored.

Kind of Current Used.—Our choice of electric current is the one we use for causing electric sleep and analgesia: a direct current, interrupted from 6,000 to 8,000 times per minute, period 1/10. Next in value is a direct current interrupted from 25,000 to 40,000 times per minute with a triple interrupter.[1] The last choice, and the one that we do not recommend if the first two can be had, is an induction current obtained with our special model of induction coil, an ordinary Dubois-Reymond coil, the special feature of which is the diameter of the wire of the coil, 1.2 mm. for the primary and 0.6 mm. for the secondary coil.[2] In cases of grave forms of apparent death, currents supplied by coils with fine wire will kill the animal.[3] Induction currents are alternating currents, the wave form of the current running above and below the base line. The physiologic effects of anodal and cathodal stimulations are distinctly different; the anodal stimulations are particularly dangerous in pulmonary and cardiac areas when the current is obtained from a secondary coil the wire of which is finer than 0.6 mm. Alternating and direct currents are deadly to cellular life, especially during apparent death.[4] But, if nothing else can be had, rhythmic excitations may be practiced with these currents, rather than make no attempt to save life.

Procedure.—The dog's back is shaved in two places—on the chest covering the pulmonary area and the back over the loins. The negative electrode is applied under the chest, the upper border reaching to the root of the neck. It is dangerous to use the positive pole under the chest. The positive electrode is applied over the loins. The electrodes measure 12 by 25 cm. for dogs of large size. They are made of zinc and are covered with a thick layer of absorbent cotton wet in a salt solution, 7 : 1000. In man the chest electrode measures 25 by 30 cm.

Chloroforming is performed intensively, admitting little or no air

pendant les excitations rythmiques,'' *Compt. rend. Soc. de Biol.*, Feb. 1, 1908; ''De l'emploi des courants électriques pour le rappel à la vie, dans les cas de mort apparente causée par le chloroforme ou par l'électrocution. Nécessité d'exclure du circuit la tête, pendant les excitations rythmiques. Expériences pratiquées sur le chien. Application clinique,'' *Bull. Soc. Clin. de Méd. ment.*, Nov., 1908; ''Resuscitation of Subjects in a Condition of Apparent Death,'' etc., *J. Ment. Path.*, 1909, *8*, No. 4.

[1] Robinovitch: ''Triple Interrupter of Direct Currents for Resuscitation. Portable Model for Ambulance Service,'' *J. Ment. Path.*, 1909, *8*, No. 4.

[2] Robinovitch: ''Bobine à induction pour rappel à la vie, etc.,'' *Bull. Soc. Clin. d. Méd. ment.*, Nov., 1908; ''Induction Coil for Purposes of Resuscitation,'' *J. Ment. Path.*, 1909, *8*, No. 4.

[3] Robinovitch: Thesis, *loc. cit.*

[4] Robinovitch: ''Different Effects of Various Electric Currents for Purposes of Resuscitation, etc.'' *J. Ment. Path.*, 1909, *8*, No. 4.

and causing arrest of respiration and heart beats as quickly as possible. When breathing is no longer registered by the pneumograph and the manometer does not register any blood pressure, the chloroforming is discontinued at once. An assistant holds the animal's tongue with a tongue forceps, cleanses the mouth of mucus, and pulls the tongue outward to allow free access of air during the rhythmic excitations.

The instrumentation with the preferred current is the same as that used for electric sleep. The operator now opens the switch of the cathode line and turns on a current of some 20 to 25 volts by means of the potentiometer. The circuit is then closed by means of the switch for a fraction of a second. A deep inspiratory movement takes place. The mouth opens, the flabby, lifeless tongue that was lying on the roof of the mouth (the animal is on its back) contracts and is drawn inward; the fore paws are thrust upward with marked force; the posterior limbs are extended; the diaphragm is pushed downward and all the respiratory muscles enter into play. The chest is fully expanded and the pneumograph registers an ample artificial inspiration. The manometer may also register an artificial blood pressure; but in cases of severe cardiac syncope the first few rhythmic excitations cause respiratory reaction without artificial blood pressure. The operator breaks the circuit by opening the switch. This is followed by a deep expiratory movement, and all the muscles that entered into play to cause the artificial inspiration are now again flabby and lifeless; the expanded chest collapses and the pneumograph registers an ample expiration; the anterior paws fall one on each side of the body, the tongue falls to the roof of the mouth, lifeless, the mouth closes and the whole body is again lifeless and relaxed. The switch is kept open for a period of from ½ to 1 second, according to the gravity of the case. If the first voltage used causes an ample respiratory reaction and the manometer shows a momentary rise of blood pressure, the succeeding rhythmic excitation is caused with the same voltage, but, as a general rule, it is necessary to increase the current to 30 volts or more; the excitations are now practiced with the increased current, the aim being to obtain ample respiratory reaction and blood pressure with this minimal voltage within the shortest possible time, because useful cardiac excitability is quickly exhausted during apparent death. It is generally necessary to increase the current to 35, 40, 50, 60, and 70 volts within the course of 3 or more minutes of apparent death; the excitations are being practiced while the voltage is being increased. In favorable cases ample respiratory reaction and artificial blood pressure are soon established, then accompanied by feeble spontaneous respiratory and cardiac reactions; these soon increase in amplitude; they are alternated with ample artificial reactions if necessary, taking care not to encroach on the spontaneous heart beats and respirations, but rather to precede or to follow them. The operator

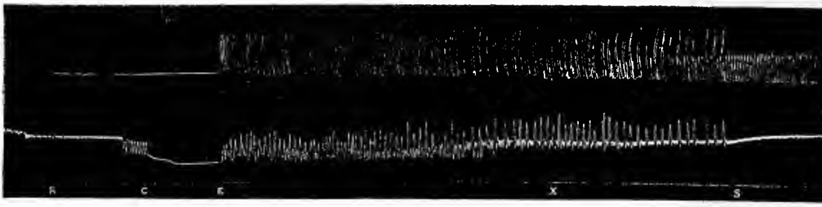


Fig. 272.—Tracing No. 1. Made During Usual Form of Apparent Death Caused by Intensive Chloroforming in a Dog. Upper tracing, respiration; second tracing, blood-pressure in carotid artery; third tracing, time; two lines indicate one second, during cardiac failure only. In rest of tracing: one line indicates one second. R, respiratory syncope; C, cardiac syncope; E, commencement of electric rhythmic excitations (direct current interrupted 8,000 times per minute, period 1–10); gradual increasing current from 20 to 65 volts. The ample respiratory and cardiac reactions are artificial, caused by the rhythmic excitations; then the small spontaneous heart-beats appear and alternate with the ample artificial ones. The cross shows where the first small spontaneous respiration appeared; ample artificial respirations alternate with the small spontaneous ones. S, synchronous respirations and heart-beats; final resuscitation.

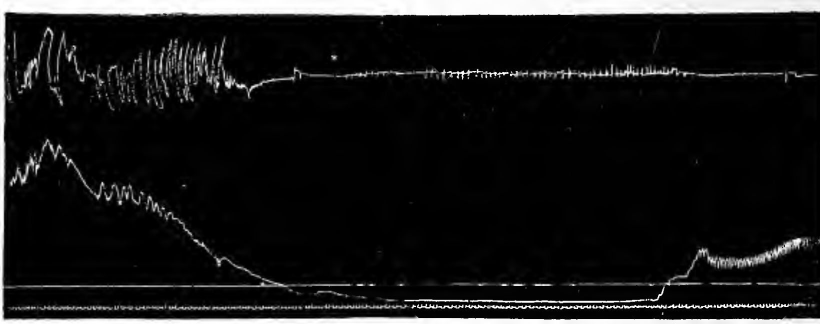


Fig. 273.—Tracing No. 2. Primary Cardiac Syncope in Dog. Intensive chloroforming. Upper line, respiration; second line, blood pressure in carotid artery; third line, signal; fourth line, time, one second. Tracing reduced one-half. Imitation of method used by surgeons (Sylvester method): small respiratory reaction caused by limited current of 8 volts (6,000 interruptions per minute, period 1–10). S, cardiac syncope, respirations continuing; R, rhythmic excitations; C, commencement of spontaneous cardiac beats; D, spontaneous respiration does not appear; commencement of descent of blood pressure, ending in death of animal.

judges by the spontaneous cardiac and respiratory reactions when it is advisable to discontinue the rhythmic excitations. If they are discontinued too soon, death may set in after resuscitation, because in chloroform poisoning the blood is asphyxiated and dark; the feeble respirations and heart beats may not be sufficient to cause useful oxygenation of the blood. But once ample spontaneous reactions are established, the carotid artery is tied, the wound is closed, and the animal lives without showing any ill effects. We have kept such dogs during a period of one year and longer after resuscitation; they were in excellent condition.

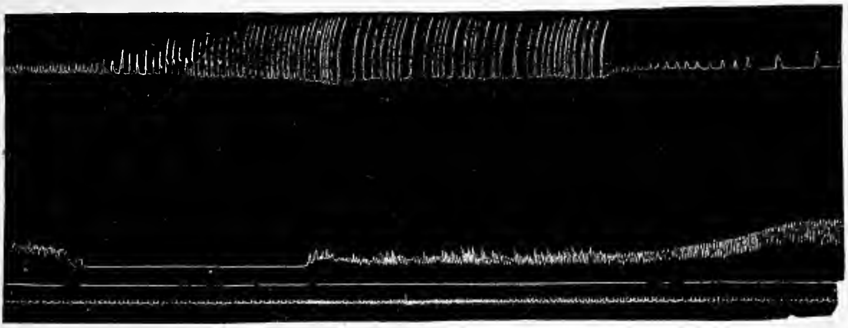


Fig. 274.—Tracing No. 3. Primary Cardiac Syncope in Dog. Intensive chloroforming. Upper line, respiration; second line, blood pressure in carotid artery; third line, signal; fourth line, time, one second. Tracing reduced one-half. S, cardiac syncope, respiration continuing; E, commencement of the rhythmic excitations with induction current, wire of secondary coil 6–10 mm. in diameter; gradually increasing current causes gradually increasing amplitude of artificial respirations; C, commencement of ample artificial heart beats; small heart beats are spontaneous and alternate with artificial ones; R, spontaneous respirations and final recovery.

Limitations.—The period of apparent death is short; four minutes (including the time of the rhythmic excitations) is a long time, and 5 minutes is an exceedingly long period. But, once resuscitated, the animal lives and shows no after-effects.

In chloroform poisoning death may take place in various ways: By respiratory arrest and ensuing cardiac failure, which is the usual form in man; by primary cardiac failure, which is a rare form in dogs, but is quite familiar to surgeons in the case of human beings; and by simultaneous cardiac and respiratory arrest. In the majority of cases, in human beings as well as in dogs, death sets in by respiratory paralysis followed by cardiac failure.

Figure 272 shows the usual form of apparent death from chloroform poisoning and the mode of resuscitation by electric rhythmic excitations with a gradually increasing current. The amperage cannot be read in these experiments because the closures are of too short duration, but there are generally between 4 and 40 milliamperes of current used.

This amperage was obtained in experiments on dogs sacrificed for this purpose.

Figure 273 shows primary cardiac syncope in a dog during chloroforming; imitation of the Sylvester method of resuscitation: feeble current causing the delayed and feeble cardiac and respiratory reaction that ends in death.

Figure 274 shows primary cardiac syncope in a dog during chloroforming; resuscitation was practiced by gradually increasing the current. The result was recovery. Electrocuted dogs are resuscitated less easily than are chloroformed dogs. It is especially difficult to resuscitate when ventricular tremulation sets in.

All experimenters on this subject agree that artificial respiration and the Sylvester method are useless when ventricular tremulation sets in.[1] Our method seems to give the best results known to-day for practical application, because it produces ample artificial blood pressure as well as respiration.

Application in Accidental Electrocution.—According to personal information given us by practical electricians both in Europe and this country, death does not always take place instantaneously in accidental electrocution with moderate industrial currents. The workingman generally touches the "live" wire with his hand or foot; contact is generally "bad," but it is sufficient to cause cardiac and respiratory paresis, from which the patient may die within from a few minutes to one-half hour after the accident. These are facts observed in daily accidents, regardless of some experimenters' claim that all is well if the patient's heart beats and he breathes when taken out of the circuit.

The blood is asphyxiated and dark, after the slightest shock; a few rhythmic electric excitations will help to whip up the circulation and respiration, if the excitations are practiced immediately following the accident or as soon as possible—before the patient is removed to a hospital. Without this help, the patient may die when he is brought into the ward—some half hour after the accident. The blood remains asphyxiated even after resuscitation. This asphyxia may continue during many hours.

Application in Surgery.—Direct and indirect cardiac massage has claimed its victims of chloroform poisoning in surgical work.[2] Crile's method of resuscitation is admirable as regards the range of time during which the heart's action may be restored. Unfortunately, it presents physiologic limitations; attempted resuscitation after a period of 7 minutes (in man), counting from the time of cardiac arrest, becomes

[1] Rodenwaldt, Ernest: "Ueber Verletzungen durch elektrische Starkstroeme vomgerichtsaerzlichen Standpunkte," *Vrtljschr. f. gericht. Med.* (3), *37*, 1.

[2] White, Charles S.: "The Rôle of Heart Massage in Surgery," *J. Surg. Gynec. and Obstet.*, Oct., 1909.

useless, because the anemia of the brain during this time is fatal to the life of the brain cells; the restoring of heart action becomes useless from the point of view of restoration of life.

The method has the great advantage of simplicity; it does not necessitate opening the carotid artery and injecting a pint or so of solutions into the heart; it does not necessitate opening the trachea. The method may be applied immediately when the first sign of cardiac or respiratory failure appears. Before an operation is commenced the electrodes may be put in their proper places under the patient; the chest electrode, 25 by 30 cm., the loin electrode, 12 by 25 cm. The apparatus and chosen electric source should be in readiness before the operation is commenced.

The tracing shows that it is possible to resuscitate dogs after respiratory and cardiac functions are no longer registered during a given period of time. It should not be assumed, however, that resuscitation is easy in all grave cases. There are no two subjects alike in physical vitality. For practical application in surgery the safest method is to commence rhythmic electric excitations at the first sign of respiratory or cardiac failure. The surgeon does not wait until both the respiration and the heart have failed. In a series of experiments on dogs we commenced the rhythmic excitations a few seconds after respiratory syncope set in—in imitation of what a surgeon would do if he had a patient showing signs of syncope caused by chloroform or ether. Resuscitation was easy and complete in these experiments after a few rhythmic excitations. Resuscitation is more difficult, of course, when heart failure dominates in the accident.

Considered in its proper light, the method should really serve as a preventive measure against grave forms of syncope, because a few rhythmic excitations, practiced in time, promptly oxygenate the blood by reason of the ample respiratory and cardiac reactions.

Clinical Application.—In November, 1908, we had occasion to revive a patient in a condition of profound syncope caused by chronic morphin poisoning. She was in Magnan's service, Ste. Anne Asylum, Paris. Magnan had revived her after she had had a first attack of syncope. A second attack set in within a few minutes; his assistants attempted to revive her by applying the Sylvester method and rhythmic traction of the tongue; this proved useless during a period of 20 minutes. The patient's face became "blue" from asphyxia. As is known, in morphin poisoning the respiratory center is paralyzed first, and heart failure follows, as is the case in ordinary asphyxia. The patient's respirations were about 3 or 4 per minute; the pulse was hardly perceptible, and death seemed to be imminent.

We applied electric rhythmic excitations; the patient revived definitely after a period of from 25 to 30 seconds.[1]

[1] Robinovitch: "Resuscitation of a Woman in Profound Syncope Caused by Chronic Morphin Poisoning," *J. Ment. Path.*, 1909, *8*, No. 4.

CHAPTER XVII

MENTAL INFLUENCE AND HYPNOSIS IN ANESTHESIA

PART I

MENTAL INFLUENCE IN ANESTHESIA

James J. Walsh, M.D.

Hypnotism: Anesthesia in Hypnotic States; Chemical Anesthetics and Hypnotism; Advantages of Hypnotism in Anesthesia; Hypnotism and Child-birth; Hypnotism in Minor Operations; Disadvantages of Hypnotism; Charlatanism and Hypnotism.

Suggestion: Suggestion Instead of Hypnotism; Psychic Influences and Surgical Anesthesia; Local Anesthesia and Mental Influence; Mental Influence as a Valuable Auxiliary; Deep Breathing and Concentration of Mind; Preliminary Medication and Mental Influence.

HYPNOTISM

Anesthesia in Hypnotic States.—When hypnotism developed in the first half of the nineteenth century, its influence on the production of insensibility to pain was noted, and attempts were made to employ it to lessen the awful tortures of surgical operations in the pre-anesthetic days. About 1840 some cases of surgical anesthesia by hypnotism were reported, and there was a discussion on the subject before the Medico-Chirurgical Society of London. In 1843 Elliottson wrote a work well known to persons interested in the influence of mind on body, entitled "Numerous Cases of Surgical Operations Without Pain in the Mesmeric State." Elliottson's treatise, however, attracted very little attention in England. There was profound distrust of procedures of this kind, which had been thoroughly discredited by Mesmer a little earlier in the century, and which, at that time, were usually called Mesmerism. By 1846, however, so much had been accomplished that Sir John Forbes, a thoroughly conservative English medical authority, wrote in his *Review* for October: "Indeed, we hesitate not to assert that the testimony is now of so varied and extensive a kind, so strong, and, in a certain proportion of cases, so seemingly unexceptionable, as to authorize us—nay, honestly to compel us—to recommend that an immediate and complete trial of the practice be made in surgical cases."

Chemical Anesthetics and Hypnotism.—It was on December 17, 1846, that the news of the employment of ether for anesthetic purposes reached England. On December 18 the discovery was announced in the *Medical Gazette.* Nothing can better show how much attention hypnotism for anesthesia had come to occupy than the heading under which the anouncement of ether as an anesthetic was made. It was "Animal Magnetism Superseded." On December 19 Lister operated on a patient under ether, and then all attention was given to that subject. As has been pointed out by Hack Tuke, it was soon seen that many sensory phenomena which had been noted under hypnosis for surgical purposes, such as calling out as if in pain, sensitiveness, moaning, wincing as if from tenderness, and the like, were not, as many had supposed them to be when they occurred in Mesmeric patients, proofs of imposture or of inability to control their feelings in spite of their wish to do so, or of suppressed suffering, but only curious psychic manifestations that might well occur in conjunction with a state of complete painlessness. It is easy to understand, however, how, in the progress of chemical anesthesia and the discovery of chloroform as an anesthetic by Simpson, hypnotism no longer attracted attention. Furthermore, Elliottson unfortunately allowed himself, somewhat as did Luys in Paris, to be deceived by some of his subjects. Later this was discovered, and he was compelled to resign as hospital attendant.

Elliottson's work, however, attracted the attention of Esdaile in India, who found, on attempting to lessen pain by means of Elliottson's procedures, that he could actually produce complete analgesia. This led him into a series of observations, from which he discovered that he could perform all sorts of operations on his Hindu patients after preliminary hypnotism, without any manifestation of pain, and he succeeded in performing painless operations in many hundreds of cases. He had, of course, a particularly favorable field. His patients were devoted to him and had the greatest confidence in his hypnotic and surgical powers. They trusted him absolutely. The Orientals have certain mystical tendencies that predispose them to such concentration of mind as keeps external sensations from annoying them, and they proved especially susceptible to hypnotic suggestions. As a consequence, even the most serious operations—amputations, the removal of stone from the bladder, and even grave abdominal operations—were performed under hypnosis without pain, and without any unfortunate effects. Two hundred recorded operations, consisting of the removal of large tumors weighing from 10 to 103 pounds, are the best evidence of this.

Case Illustration.—The description of one of Esdaile's cases as recorded by Bramwell[1] shows how much can be done in this way under favorable conditions. The patient was a peasant suffering from a tumor in the antromaxillare. The tumor had pushed up the orbit of the eye, filled up the nose, passed into the throat, and caused an enlargement of the glands of the neck. In the hypnotic condition the patient permitted one of the most severe and protracted operations in surgery. Esdaile describes the operation as follows: "I put a long knife in at the corner of his mouth, and brought the point out over the cheek bone, dividing the parts between; from this I pushed it through the skin at the inner corner of the eye, and dissected the cheek bone to the nose. The pressure of the tumor had caused absorption of the anterior walls of the antrum, and, on pressing my fingers between it and the bone, it burst, and a shocking rush of blood and matter followed. The tumor extended as far as my fingers could reach under the orbit and the cheek bone, and passed into the gullet—having destroyed the bones and partition of the nose. No one touched the man, and I turned his head in any position I desired, without resistance, and there it remained until I wished to move it again; when the blood accumulated, I bent his head forward, and it ran from his mouth as if from a spout. The man never moved nor showed any signs of life, except an occasional indistinct moan; but when I threw back his head, and passed my fingers into his throat to detach the mass in that direction, the stream of blood was directed into his windpipe, and some instinctive effort became necessary for existence; he therefore coughed and leaned forward to get rid of the blood, and I suppose that he then awoke. The operation was finished, and he was laid on the floor to have his face sewed up, and while this was being done he, for the first time, opened his eyes."

Bramwell, commenting on the case, says: "The patient afterward informed Esdaile that he did not know he had coughed and was quite unconscious up to the termination of the operation." The dressings were removed 2 days afterward, when it was found that the wounds had healed by first intention. The recovery was satisfactory. Such a mode of anesthesia would seem eminently desirable to those who know how troublesome are operations of this nature upon the face, necessitating, as they do, the continuous administration of the anesthetic, and involving the practical impossibility of securing healing by first intention, because of the manipulation necessary for the administration of the anesthetic. It is interesting to note that Esdaile's assistant had first tried to hypnotize the patient and had failed. Esdaile succeeded in bringing about profound hypnosis only after half an hour of very patient labor.

Other cases not unlike this are reported by Bramwell, and there is a series of well-authenticated cases from Braid and Bramwell. It is evi-

[1] "Hypnotism, Its History, Practice and Theory," by J. Milne Bramwell, London, 1906.

dent that, under certain circumstances and for special patients, hypnotism may prove a valuable auxiliary, and the thought of its usefulness in this regard should not be put aside as visionary until we have had much more experience.

Advantages of Hypnotism in Anesthesia.—Bramwell is an enthusiast in the matter, and undoubtedly views the subject much more favorably than do many others. It must not be forgotten, however, that in science negative observations are of little value compared with positive observations. Bramwell has succeeded in securing results; if others cannot, it may very well be because of lack of confidence in themselves, lack of faith on the part of their patients, defect of technique, and want of persistency. Bramwell has summarized some of the advantages of hypnosis as an anesthetic as follows:

(1) When once deep hypnosis with anesthesia has been obtained, it can immediately be reinduced at any time.

(2) No repetition of any hypnotic process is necessary; the verbal order to go to sleep is sufficient.

(3) The hypnotizer's presence is not essential. The patient can be put *en rapport* with the operator by written order, or by other means previously suggested during hypnosis.

(4) No abstinence from food or other preparation is necessary.

(5) Nervous apprehension can be removed by suggestion.

(6) Hypnosis is pleasant and absolutely devoid of danger.

(7) It can be maintained indefinitely and terminated immediately at will.

(8) The patient can be placed in any position without risk—an important point in operations on the mouth and throat—and will alter that position at the command of the operator. Gags and other retentive apparatus are unnecessary.

(9) Analgesia alone can be suggested, and the patient left sensitive to other impressions—an advantage in throat operations.

(10) In labor cases the influence of the voluntary muscles can be increased or diminished by suggestion.

(11) There is no tendency to sickness during or after operation—a distinct gain in abdominal cases.

(12) Pain after operation or during subsequent dressing can be entirely prevented.

(13) The rapidity of the healing process, possibly as the result of the absence of pain, is frequently very marked.

Hypnotism and Child-birth.—In a certain number of cases hypnotism has been used successfully for the relief or even complete suppression of pains of child-birth. A number of observers, among whom are Schrenck-Notzing and a number of French observers, have reported cases in which even the pains of severe labor were thus relieved. There is no doubt that the mind can greatly influence the course of labor. It has often been noted that when a patient has expected a particular physician in whom she has confidence, and for some reason another comes in his stead, the labor, which may have been progressing normally or even rapidly, becomes sluggish or its progress ceases entirely. It has been said that insufficient contractions of the uterus and accessory muscles can be stimulated by suggestion, while excessive muscular contractions can be diminished in this way. Fianton has even claimed that he can successfully excite premature labor by suggestion. Undoubtedly mental influence means much in these cases. Probably the persuasion that a definite time should be the occasion for birth may save a woman from the retention of the child *in utero* for a month beyond the normal time, while this delay may be occasioned by a wrong persuasion in the matter. Certainly the use of suggestion to save woman from many of the troubles of the puerperium should not be neglected.

Hypnotism in Minor Operations.—Many others have employed hypnotism for the production of insensibility to pain during minor surgical operations. As we have said, it was overshadowed by the newer anesthetic methods. Some devotees of hypnotism, however, have continued to practice surgical anesthesia by hypnotic methods.

Disadvantages of Hypnotism.—It should be borne in mind that there are many drawbacks to this method of inducing anesthesia. Surgical anesthesia requires deep hypnosis. Only a limited number of individuals, probably not more than one in ten (if that many), can be brought into such deep hypnosis as will allow of cutting operations without pain. This is true particularly if the operations are prolonged. The length of the hypnotic state is not always well under control of the operator. Occasionally patients come out of the hypnotic state during the course of an operation; they are then liable to suffer more than if this method had not been employed and to be somewhat uncontrollable. Besides, there are psychic disadvantages. Occasionally patients have suffered very much afterward, as if somehow the suppressed pain produced an exaggerated reaction. Occasionally too deep suggestion has left a curiously susceptible condition, and patients have suffered more in the after-treatment than would otherwise have been the case.

As a rule, a number of séances of hypnotism must be held, in order that the operator may be assured that he can produce a condition of hypnosis sufficiently profound for surgical purposes. This has many disadvantages. A sort of hypnotic habit has been developed in some people, manifesting itself during convalescence, so that almost any unusual incident would recall the hypnotic state. As a consequence of all these disadvantages, hypnotism has never been generally used for surgical anesthesia. There is no doubt, however, that in a great many persons hypnotism can be employed to secure almost complete anesthesia for shorter surgical operations. The pulling of teeth, the opening of a boil or even a carbuncle, the dilatation of a sinus, the removal of a wart or of a small mole, or even of a wen, may be accomplished in the hypnotic state. The hypnotism in these cases is not something special to the operator, but is due to the confidence that the patient has in him, so that, at his persuasion, the mind becomes concentrated on a single thought, with the senses dulled except the sense of hearing, and that receives only the impressions that the operator desires to give. Hypnotism is not a mysterious process, but a state that can be induced in susceptible persons by anyone who has the confidence of the subject and sufficient assurance in his own power to accomplish it to make the patient accept his declaration.

Charlatanism and Hypnotism.—Undoubtedly some of the minor operations that are done by wandering advertising physicians who remove teeth or open boils or abscesses without pain are accomplished in a state resembling, if not identical with, hypnotism. In country places particularly people are likely to have an exaggerated sense of the wondrous powers of men who claim to have the faculty of producing insensibility to pain by rubbing something over the part that is to be affected by the operation. They become so much occupied with this thought, and with the positive assurance given them of the painlessness of the operation, that they feel very little or no pain. The wonderful "pain killer" that has been applied is then sold to them, but it practically always fails to produce similar results to those first experienced when its maker is not present and producing a very definite mental effect.

SUGGESTION

Suggestion Instead of Hypnotism.—In recent years hypnotism has fallen into disrepute once more, and its dangers have come to be emphasized. These are mainly connected with frequently repeated hypnotic séances. Many who are interested in the influence of mind on body have come to realize, however, that most of the effects that can be secured through hypnotism can, with equal patience and persistence, and with the confidence of the physician and the trust of the patient, be obtained by suggestion in the waking state. It is probable that this would never be true for complete anesthesia such as would permit the performance of a serious surgical operation. There is no doubt, however, that the operator's mind can to a great degree influence the susceptibility to pain, and so predispose the patient's mind and preoccupy his attention that the solicitude before operation is greatly lessened and the preliminary stage of excitement during inhalation anesthesia is practically obliterated. This is not of trifling importance, for it greatly diminishes the amount of the anesthetic necessary to produce complete insensibility to pain. It must not be forgotten that the mortality after operations in our time is distinctly increased by the after-effects of the anesthetic, and that the less of the agent that is given the better the outlook. A careful application of suggestion, then, as an auxiliary, may not only save the patient worry and the lowering of resistive vitality, but may tend at least to be actually life-saving.

Psychic Influences and Surgical Anesthesia.—The principles of mental influence in the production of absolute anesthesia and hyperesthetic conditions have a valuable application in surgical anesthesia. If the patient's mind is properly prepared, if his confidence is secured, if solicitude is removed, if anticipation is blunted, then much less of an anesthetic is needed to bring the patient into insensibility to pain than would otherwise be the case. A terrified, excitable patient requires a large amount of an anesthetic that must be administered in heavy, continuous doses, and, even with that, often does not exhibit complete relaxation and absolute insensibility. It is extremely important, then, that patients be assured as much as possible with regard both to the operation and the anesthetic itself. They should not be allowed to be in or near operating rooms where there is any manifestation of pain on the part of the preceding patient, nor in contact with those who are coming out of the anesthetic, nor near those who are exhibiting any lack of control during the early administration of the anesthetic. Surgeons should bear this in mind, and not discuss subjects which in this excitable stage may unduly impress and perhaps terrify the patients about to be anesthetized. As far as possible the anesthetist should not be a stranger to them, or, if a stranger, should be introduced under circumstances that impress them with the idea that the going under anesthesia will be easy and that there will be absolutely no reason for solicitude during its course.

Anyone who has seen a man gain the full confidence of patients and take pains to reassure them, telling them soothingly to concentrate their attention on deep breathing, and controlling quietly the first sign of excitement, and bring them fully under an anesthetic without any difficulty and with only a few drops of the anesthetic material, will realize how important the patient's state of mind is in anesthesia. It has been suggested that the patient should be asked to put the hands together quietly across the chest, and that, whenever there is a tendency to separate them, the suggestion should be given to keep them together. The constantly repeated suggestion of keeping the hands together and breathing deeply, if given quietly, so occupies the patient's attention that the excitable stage of anesthesia often passes over unnoticed, or with only the beginning of movements of the muscles controlled at once by gentle contrary suggestion.

Classes of Patients Where Psychic Influences Are Most Useful.—This method is particularly important for patients who are nervous, excitable, and inclined to be terrified over the operation. Unless negroes have complete confidence in the operator and the anesthetist, there is almost sure to be a disturbing excited stage. On the other hand, there are men who have the confidence of such patients and are able to bring them under the anesthetic influence without any difficulty. The same thing is true of children. Some one whom the child knows and trusts implicitly, but who is not likely to grow excited or to show, even by the slightest sign in voice or action, that they are worried, is a great help in bringing the child under anesthesia. The stroking of the child's hands by this person, and repeated suggestions to breathe deeply, to keep the hands together and not to move the feet, will usually bring the little patient under the anesthetic without any difficuly. This represents a real mental influence due to suggestion, and it is of great value. It can be adapted to various patients so as to produce the best possible effects. In its absence there may be trouble and excitement, and force may have to be employed; the patient, in such an event, is not so well disposed to resist the influence of the shock of the operation. With it everything goes smoothly, and a waste of precious vitality, often needed for the strain of the operation, is spared.

Local Anesthesia and Mental Influence.—The varying phases of interest in local anesthesia illustrate very well how large a rôle mental influence plays in these conditions. Some surgeons can perform almost any operation under local anesthesia without complaint on the part of the patient. Others, who employ much more of the nerve-obtunding drugs, are unable to accomplish anything like the same amount of surgical intervention, even this being accompanied by rather serious complaints on the part of the patient. Many a young physician who has seen an experienced surgeon perform a rather serious operation by means of infiltration anesthesia has gone home impressed with the idea that he could surely do a much simpler operation in the same way. He has been inclined to think that the chemical agent used was the most important portion of the anesthesia. He may have found, however, that his patient complained very bitterly. Often such an experience has been enough to make him give up the idea of using local anesthesia. What he needed to realize, however, was that the patient was not so deeply influenced by him as by the more experienced surgeon, and that, as a consequence, even the slight pain produced, owing to nervous irritability, became exaggerated after a time, giving rise to the patient's bitter complaints.

Importance of Personality of the Anesthetist.—The surgeons who have reported success with local anesthesia have been men of a special personality capable of attracting the confidence of patients, and of making them feel absolutely sure of their physician's assurance that there was to be no pain. Schleich did much, some fifteen years ago, to develop local anesthesia by infiltration methods. Numbers of physicians who visited him thought they possessed his full secret when they had learned his technique and secured his formulæ. Many of them found, however, that, while Schleich's patients seemed to suffer no pain even from serious operations, their patients often suffered pain from even trifling surgical intervention. Everywhere that local anesthesia was being employed at that time the personality of the operator was the most interesting feature of the work. The mental element was an essential factor in the insensibility to pain. In this country our local anesthetists have been of the same class.

Mental Influence as a Valuable Auxiliary.—No matter what the form of anesthesia, it is an extremely helpful auxiliary to have the mind favorably disposed toward it, and the patient properly assured and confident of the successful issue of both the anesthetic and the operation. Undoubtedly many of the adjuncts of various kinds that have been introduced, and that for a time were efficient in producing anesthesia without excitement in conjunction with ether and chloroform, have owed their success more to the influence on the patient's mind than to their own efficiency. They have come and gone, acquiring reputations and then losing them, as remedies of all kinds have done which affected the mind, because they were given with a strong suggestion that they would produce a definite effect, and this effect was manifested as a consequence of the suggestion. Certain it is that almost anything given the patient with the promise that it will make the taking of the anesthetic easier and will do away with its worst effects will greatly lessen the stage of preliminary excitement. Patients who have heard much of the awful choking and suffocating sensation produced by an anesthetic, and who dwell on the thought, do not succumb to its effects very readily, and more of the anesthetic is generally required to bring them under its influence. Physicians, as a rule, go under anesthesia badly for this reason. Suggestion works both favorably and unfavorably, according to its significance.

Deep Breathing and Concentration of Mind.—Hack Tuke, in his "Influence of the Mind on the Body," [1] records some stories of anesthesia produced by the thought on the part of the patient that he or she was inhaling an anesthetic. Such experiences are not uncommon. Every anesthetist is likely to have had patients who began to manifest symptoms of disturbance of consciousness at least, if by chance the in-

[1] Philadelphia, 1889.

haler without any anesthetic was placed over their mouths and they were told to breathe deeply. Deep, rapid breathing will of itself produce certain changes in the blood which bring about a certain amount of analgesia; and, if patients are told to do it, and have emphasized for them its effect upon their pain sense, it is rather easy to open boils or abscesses with the production of very little pain. It is probable that in all cases it is of advantage to properly compose the patient's mind and begin the anesthesia by deep breathing through the inhaler before any anesthetic is put on it. A few deep breaths, with the concentration of mind on the breathing, and some soothing words, will usually put a patient in a better disposition to take the anesthetic without excitement than any procedure even more complex than this.

Preliminary Medication and Mental Influence.—Certain substances, opium, for instance, when used with discretion, seem to predispose the patient to take an anesthetic without excitement and with much better control. If given an hour before the administration of an anesthetic, even a small dose will, especially in conjunction with a proper reassurance of the patient, produce a state of mind in which the anesthetic will be taken without difficulty. In nervous, excitable persons some such treatment is advisable for the sake of its good effects. Sometimes bromids taken for several days will produce a more placid state of mind than would otherwise be the case. These drugs, however, will not replace the personal element of strong mental influence. Experience has demonstrated that patients of the most varied ages, types, and temperaments go under an anesthetic without difficulty in the hands of a skilled anesthetist, while one without skill required help and produced rather serious stages of excitement in exactly the same classes of patients. This personal influence is largely an individual matter, but, if the influence of the mind in the induction of anesthesia is properly recognized, it is probable that much of its valuable help can be secured by anyone who deliberately tries to employ it as an auxiliary.

PART II

HYPNOSIS IN ANESTHESIA

H. W. Frink, M.D.

Hypnosis: The Different Degrees of Hypnosis and Some of the Phenomena Accompanying Them; Factors Which Influence Suggestibility; The Attitude of the Hypnotist; Methods of Inducing the State of Hypnosis; The Induction of Anesthesia.

The Different Degrees of Hypnosis and Some of the Phenomena Accompanying Them.—Every person is in some degree susceptible to suggestion, but hypnosis cannot be induced in everyone, nor can all hypnotizable persons be influenced to the same extent. Three degrees of influence or stages of hypnosis are described by Forel, while other writers make as many as seven or eight. Forel's classification, which seems to be the simplest and most practical of any, is as follows:

(1) Somnolence, or Drowsiness.—The subject influenced only to this degree experiences more or less lazy or sleepy feelings. He can open his eyes, however; is perfectly conscious of all that goes on; and, by making an effort, he can resist any or all of the hypnotist's suggestions.

(2) Hypotaxis, Charme, or Light Sleep.—Here the subject cannot open his eyes. He is aware of all that takes place, but certain suggestions given by the hypnotist cannot be resisted. Thus, when he receives the suggestion that his arm is stiff, it becomes so, and he is unable to bend it. If he is told that one of his limbs is paralyzed he cannot move it, or, if told to clap his hands together or to perform any like movements, and then given the suggestion that he cannot stop these movements, he is unable to do so. In this stage some sensory phenomena, such as feelings of weight in the limbs, or of itching or tickling in the skin, etc., may be produced. A touch of a pencil, for instance, is felt to be hot, cold, or painful, according to the suggestion given. Some degree of hypesthesia and, occasionally, visual or auditory hallucinations may be successfully suggested. Though the subject is quiet and appears to be asleep, there is no amnesia, and upon "awaking" he remembers everything that has taken place.

(3) Somnambulism, or Deep Sleep.—This degree of hypnosis is characterized by the presence of amnesia for everything that occurs during the period of trance. In deep somnambulism suggestibility is very great. Subjects, while *en rapport,* believe everything the hypnotist tells them, almost any conceivable effect upon the voluntary muscles can be produced, and even involuntary motor or secretory mechanisms may be influenced (e. g., sneezing, defecation, perspiration, menstruation, etc.). All sorts of hallucinations, illusions, and delusions are produced. Thus a good subject will accept suggestions that he is a great orator, a baby, or even an inanimate object, and he will act the part in a most striking manner.

Hyperesthesia, paresthesia, or anesthesia of any of the senses may be induced. Though, in response to the hypnotist's command, the subject will carry out the most complicated actions, if left alone he appears to be sound asleep, and orders, shouts, slaps, or pinches from a third person have no apparent effect upon him either in stimulating him to any activity or in arousing him from his trance. Nevertheless the word "awake," whispered by the hypnotist, will at any time promptly terminate the sleep. Suggestions during the trance may be so given as to have their effect either directly carried over into the waking state or produced after an interval of waking, at a given time or in response to a given signal (post-hypnotic suggestion). Many persons after having once been deeply hypnotized are quite susceptible in the waking state, to the suggestions of the hypnotist, and various motor and sensory phenomena, even to surgical anesthesia, may be induced while the subject appears in all other respects to be entirely in his usual state of mind.

The three stages of hypnosis here described show no sharp demarcation from one another, and this or any other classification is purely arbitrary. There is little similarity to the stages of chloroform or ether anesthesia, for a subject may pass immediately into somnambulism without going through the first or second stages of influence, or, in other cases, in spite of the most prolonged and painstaking effort on the part of the hypnotist, amnesia and the other phenomena of the third stage cannot be produced. Generally speaking, surgical anesthesia is possible only in the third stage. Though a certain diminution of pain sensibility may be produced in the second stage, complete anesthesia is rare, and cutting operations are seldom possible. To practically all somnambules one can successfully suggest that the prick of a pin will be painless, but it is quite a different matter to cause complete insensibility to the cut of knife and scissors. In very suggestible subjects absolute anesthesia can be obtained, and, either during the trance or post-hypnotically, really extensive surgical operations may be performed without the slightest discomfort to the patient; but such instances are uncommon, and in not a few somnambules surgical anesthesia is an impossibility, while upon others only minor operations are possible.

Whether or not somnambulism may be induced in a given subject depends in no small degree upon the skill of the hypnotist, but to a greater extent upon the suggestibility of the subject. Out of one hundred and nineteen cases, Vogt obtained somnambulism ninety-nine times, hypotaxis eighteen times, and somnolence twice. This percentage of somnambules is very high, and for the average hypnotist to equal this record by half would be no small task. Different operators influence to some extent from 80 to 98 per cent of their subjects, but not more than 10 per cent of those influenced could be rendered surgically anesthetic.

Factors Which Influence Suggestibility.—Of the general factors which influence suggestibility age is the most important. Children under four or five years of age usually cannot be hypnotized, but from the 6th to the 16th year nearly all children are very readily influenced, and a large percentage of them can be made somnambulistic. After sixteen suggestibility diminishes very gradually up to about the forty-fifth year and then more rapidly. As a rule, old people are very hard to influence or are practically insusceptible. Sex and nationality have very little influence upon suggestibility. Health is an important factor, and, speaking in general, well people are more easy to hypnotize than sick ones. This is especially true of mental health, and the neurasthenic, psychasthenic, and hysterical usually are resistant subjects. Idiots, low-grade imbeciles, and most of the insane cannot be hypnotized at all. Most writers believe that intelligent and educated people are more readily influenced than the ignorant and stupid. People accustomed to obedience, such as soldiers, servants, etc., seem to be more susceptible than those who are wont to command.

It must be emphasized that there are no means of determining beforehand whether a person may or may not be hypnotized readily, and the statements here made as to suggestibility in general are subject to a great number of individual contradictions. Subjects who present no evident difference in respect to age, education, temperament, intelligence, etc., show great and inexplicable differences in suggestibility. Thus one occasionally finds children who are quite unresponsive, while, on the other hand, a subject who, according to all expectations, should be difficult to hypnotize turns out to be extremely suggestible. A case in point is that of a woman of about fifty years of age whom I saw in consultation with J. H. Richards. Because of her age and the fact that for twelve years she had suffered from phobias and various sorts of hysterical manifestations, I thought that she would prove a very poor subject. As a matter of fact, Dr. Richards induced deep sleep at the first attempt, and at a later date W. C. Cramp operated upon her for ingrowing toenail under hypnotic anesthesia.

The Attitude of the Hypnotist.—It was quite the custom among many of the early hypnotists, as well as some of the later ones, to create, by the use of passes, magnets, and mirrors, or by the assumption of various peculiarities of voice and manner, an impression in the mind of the subject that the hypnotist either had at his command some mysterious forces or was the possessor of peculiar and almost superhuman strength of will. Though, doubtless, such methods might occasionally impress credulous individuals in a way favorable to the induction of hypnosis, yet, in many more cases, an air of mystery is apt to antagonize the subject and to create a feeling of fear or distrust which makes hypnotization difficult or even impossible. On this account it is now generally considered an essential part of the technique of hypnotizing for the operator to explain to his subject that there is no magic connected with hypnotism, that it is a condition of mind into which nearly all normal people are capable of passing, and that its successful induction in no way depends upon the operator's possessing a strong will or the subject a weak one; but merely upon the willingness and ability of the two persons to coöperate in carrying out a technique that can be learned by almost anyone. The subject is further assured that hypnosis will not, as is popularly supposed, "weaken his will" or render him responsive to commands or requests which, in his natural state, would be strongly objectionable to him.

In inducing hypnosis or the giving of suggestions, some hypnotists use a loud, commanding tone, and, so to speak, bully their subjects into the trance. Others, as does the writer, speak in a perfectly natural, quiet conversational tone and avoid any assumption of authority. Either method is effective, and ordinarily an operator succeeds best with the one more natural to him.

Methods of Inducing the State of Hypnosis.—A very simple but not particularly efficient method is that mentioned by James. "Leave the subject seated by himself, telling him that if he close his eyes and relax his muscles, and, as far possible, think of vacancy, in a few minutes he will 'go off.' On returning in ten minutes, you may find him effectually hypnotized."

The method of hypnotizing employed by Bramwell is the same, practically, as that used by Liebeaut, Bernheim, and many others. It has, perhaps, the most general use of any. Bramwell does not attempt to hypnotize his subject at the first sitting, but devotes this time to making the patient's acquaintance and ascertaining his attitude toward hypnotism. At the same time he endeavors to remove any erroneous ideas the patient may have, and he refuses to make any attempt to hypnotize until his patient is convinced of the desirability and safety of the procedure. At the next meeting Bramwell addresses his patient as follows: "Presently I shall ask you to look at my eyes for a few seconds, when probably your eyelids will become heavy and you will feel impelled to close them. Should this not happen, I shall ask you to shut them, and to keep them closed until I tell you to open them. I shall then make certain passes and suggestions, but I do not wish you to pay much attention to what I am saying or doing, and, above all, you are not to attempt to analyze your sensations. Your best plan will be to create some drowsy mental picture and to fix your attention on that. You must not expect to go to sleep. A certain number of hypnotized persons pass into a condition more or less closely resembling sleep; few do so at the first sitting, however, and you must only expect to feel drowsy and heavy."

After having given these instructions, he places the patient in a comfortable chair, and darkens the room. Bramwell continues: "I request the patient to look at my eyes, at the same time bringing my face slightly above and about ten inches from his. The patient's eyes sometimes close almost immediately. Should they not do so, I continue to look steadily at him and make suggestions. These are twofold: the patient's attention is directed to the sensations he is probably experiencing, and others which I wish him to feel are suggested. Thus: 'Your eyes are heavy, the lids are beginning to quiver, the eyes are filling with water. You begin to feel drowsy; your limbs are becoming heavy; you are finding it more and more difficult to keep your eyes open, etc.' Sometimes this produces the desired result; the eyes close and the first stage of hypnosis is induced. If this does not take place, I direct the patient to close his eyes, and make passes over the head and face, either with or without contact, repeating meanwhile appropriate verbal suggestions. This is continued for half an hour."

The following method is the one generally employed by the writer. It is a combination of the methods of Vogt and Forel. Its chief advantage is that it gives ample opportunity for "training" the subject.

The patient is seated in an easy-chair or reclines upon a couch. I then tell him to relax his muscles and to make himself as quiet and comfortable as possible. By lifting his hand and letting it drop, I test the muscular relaxation and do not proceed until it is quite complete. Then, holding my fingers a short distance above the patient's head and in such a position that he cannot see them without straining his eyes upward, I ask him to look at them for a few moments and then to close his eyes. I then press with one of my fingers well up in the middle line of the patient's forehead and direct him to keep his eyes closed, but to roll his eyeballs upward as if to look at the spot where I am pressing. I then say something to this effect: "You have noticed, probably, that your eyes have begun to feel a little tired and strained. While you keep your eyes rolled up, you will doubtless find that they tend to become more and more tired, that the lids begin to feel heavy, and, as you keep looking up, I think you will notice that it is harder for you to open your eyes than usual—the lids have a tendency to stick together." Then, after lightly stroking the patient's lids and brow for a moment with my other hand, I say: "Now try to open your eyes slowly, and see if I am not right."

In employing this technique, the hypnotist takes advantage of a physiological fact which is unknown to most patients. When the subject strongly stimulates the third nerve in the effort of straining the eyeballs upward with the eyelids closed, it is practically impossible for him to open his eyes without looking down. On this account if, as the majority of people do, the subject follows directions exactly, and tries to open his eyes while his eyeballs are rolled up, he suddenly discovers that he cannot do so, and, unable to assign any other cause for this occurrence, he attributes it to the hypnotist's suggestions. This apparently brilliant beginning impresses the subject and makes him think that all further suggestions will succeed equally well. Thus half the battle is won. It is not necessary to test him with his eyeballs lowered; one merely says: "Yes, your eyelids stick fast together; you cannot open them; the harder you try to open your eyes the tighter they stick; this is the beginning of sleep," etc.

In case the subject fails to follow directions and succeeds in opening his eyes, I betray no disappointment, but say expectantly, "What did you notice? Your eyes did not open easily" or something of the kind, and, in this way, try to lead the subject into admitting that he felt something. As soon as I have gained an admission, such as that the eyelids "stick a little," that he felt lazy about opening them, or something of the kind, I have him close his eyes again and repeat the procedure, adding: "This time your eyelids will stick harder. You may notice that you are becoming lazy and absent-minded, and consequently adverse to making any effort," etc. In this way I endeavor to increase by suggestion whatever the patient admits he felt and, at the same time, to introduce new suggestions. I continue to repeat the operation, and, when I see that the subject, at each repetition, meets with greater and greater difficulty in opening his eyes, I become more definite in suggesting, until, finally, I can say positively: "Your eyes now stick fast together; you cannot open them at all." While giving the above suggestions, I, at the same time, throw out occasional hints to the effect that a lazy, drowsy feeling is coming over the subject, and that he is beginning to go to sleep.

This description of beginning the séance will, I trust, make clear the general scheme of this method of hypnotization, a consideration of which now follows.

Introduce as Early as Possible Several Lines of Suggestion.—In doing this the hypnotist should avoid making definite statements that such and such phenomena will appear, but should seek to bring about the beginning of the desired effects by hinting, verbally and otherwise, at their probable occurrence. The four lines of suggestion most conveniently followed are: Inability to open the eyes, advent of drowsiness or sleep, involuntary rigidity of an arm, and heaviness of a hand.

To create an expectation of drowsiness, I tell the subject, before attempting to hypnotize him, that it is a scientific fact that, if anyone pretends to be in a rage, he will actually feel a little angry; if he kneels as if to pray, he tends to feel devout; and, in the same way, if the subject will assume a quiet and comfortable position, close his eyes, and relax his muscles as if he were asleep, he may expect to feel drowsy.

The method of suggesting inability to open the eyes has been indicated. In suggesting rigidity of the arm, the limb is held as in Figure 275, with elbow and wrist hyperextended. I then bend his wrist very slightly back and forth until I feel a little resistance in either the flexors or extensors. Here I immediately bend the wrist in the direction necessary to oppose this resistance. This gives the subject the impression that the muscles of his arm are becoming tense and introduces the line of suggestion desired. To suggest heaviness of the hand, I lift the patient's hand and then drop it. If his muscles are well relaxed, the hand falls heavily, and it is easy for him to be made to believe that it really feels heavier than usual. I assist the impression by taking hold of his wrist as if to lift it, and then letting it slip from my fingers as if it were very heavy.

Push the Suggestion That Works Best Until Some Definite Effect Is Produced Which the Subject Cannot Resist.—When, either from what the subject says in response to my hints or from what I observe (for instance, I may see that the subject lifts his hand with difficulty or I may

Fig. 275.—Suggesting Rigidity of the Arm.

feel that the muscles of his arm contract), I conclude that one or another line of suggestion is beginning to produce some effect; I direct my suggestions toward increasing this one effect. The more my suggestions work, the more positive I become in suggesting until I can say with conviction that the effect I am seeking *is* produced and that the subject cannot raise his hand, bend his arm, or open his eyes, as the case may be. I am always careful never to commit myself to a definite assertion unless I am sure that the subject already feels or will immediately feel what I tell him. In this way I avoid the danger of his thinking that this or that suggestion has failed with him.

When One Phenomenon Has Been Successfully Suggested, Employ It in Producing New Ones.—Up to a certain point each suggestion successfully given increases the subject's suggestibility and makes him more ready to accept new suggestions. Also, a new suggestion is more acceptable if it can be represented as the result of or dependent upon some already induced phenomenon. Consequently, if I succeed in producing irresistible heaviness of the subject's hand, I suggest that his efforts to lift it have made him very tired and sleepy, that the feeling of weight is extending from his hand all over his body, that even his

Fig. 276.—Beginning of Sleep by Frink's Method.

head is affected so that it becomes heavy and drowsy, and he finds himself going off to sleep. Or, if I have made his arm stiff, one way of putting him to sleep is by telling him that his arm is being drawn to his head as if by a magnet, that the closer his arm comes to his head the more sleepy he becomes, and that by the time his arm touches his head he will be sound asleep.

Endeavor to Get the Subject into the Third Stage of Hypnosis as Soon as Possible, but Terminate the Séance Rather Than Give Non-effective Suggestions.—When I find that a subject immediately accepts my suggestions and that everything I tell him promptly produces the desired effect, I keep on until I have him soundly asleep and have induced automatic movements, anesthesia, and other phenomena of the third stage. But in cases where the séance proceeds less smoothly it is necessary to be very cautious in suggesting, for, if one attempts too much at one sitting and gives suggestions that do not take effect immediately, the subject gets the impression that these suggestions will continue to be unsuccessful. Such an impression is difficult to remove, and operates as a barrier against further progress in that particular direction. On this account I content myself with what results I can obtain from perfectly safe suggesting and terminate the sitting as soon as I

Fig. 277.—Beginning of Sleep by Frink's Method.

find myself on dangerous ground. To do this one need only say to the subject: "You are waking up now," or, "When I have finished counting ten, you will be perfectly wide awake."

After Each Sitting Ascertain Exactly What the Subject Experienced and Plan the Suggestions to Be Given at the Next Sitting on the Basis of This Information.—When the subject awakes, I ask him to describe in detail everything he experienced, and lead him on with appropriate questions if necessary. In this way I learn the extent and nature of the effect that each of my suggestions had upon him, and at the next séance I follow up those that promise well, and avoid the ones that are ineffective. At the same time, if the subject's nervousness, curiosity or some misconception has interfered with his going to sleep, this will be disclosed and can be dealt with. In addition, any undesirable auto-suggestions that may have formed are brought to light, and may be overcome before they can do any harm. It will be found that some patients will feel a certain sort of pride if they have been resistant to suggestion. One may then call their attention to that fact, show them that the ability to resist need cause them no conceit, and thus prevent further trouble from such a source. With some patients it may be noticed that, though by suggestion an arm may be made perfectly rigid, yet as soon as the hypnotist says "You cannot bend your arm," the reverse of the desired result is obtained and the limb is promptly bent. These are persons who resent what they consider an attempt to deprive them of the "freedom of the will," and in dealing with them it is better to give such suggestions as "You will feel unwilling to bend your arm; the effort is a disagreeable one," etc., until when it is perfectly clear that the subject has attempted to bend his arm, but without success, one can then say, "You cannot do it."

At Subsequent Séances Continue the Subjects Training Until the Different Phenomena of the Third Stage May Be Induced Readily or the Impossibility of Their Induction is Demonstrated.—Subjects who are influenced only slightly in the first or second séance may often be made quite susceptible by careful training. An effect once produced on a given subject can always be reproduced without difficulty, so that at one séance it requires only a few moments to bring about the same degree of hypnotization that existed in the preceding one. At each sitting, therefore, the hypnotist can begin where he left off at the preceding one, and continue by pushing those lines of suggestion which appear promising. Whatever that subject admits of having felt at the preceding sitting, the hypnotist endeavors to increase by further suggestions, and whenever any definite phenomenon is successfully induced it is employed in furthering some partly successful line of suggestion or in introducing a new one. In this way, by carefully analyzing the results of previous sittings and proceeding cautiously, one may change slight hypotaxis to complete hypotaxis, and then, by gradually suggesting amnesia, convert this stage, in turn, into somnambulism. For instance, when a subject tells me that during a sitting he felt drowsy, lazy, and absent-minded, I suggest at the early part of the next séance that he feels so lazy and absent-minded as to pay little attention to what I am saying. Later in the séance I tell him that he has been so inattentive, because of lazy and drowsy feelings, that when he awakes, he will experience some difficulty in recalling all that I have said to him. If, at the close of the séance, I find that my suggestions have had the desired effect, then, at the next meeting, I suggest still greater drowsiness and inattention, and greater consequent difficulty in remembering in the waking state what has occurred. At subsequent sittings I continue in the same way until complete amnesia is produced. If, in five or six sittings, deep hypotaxis has not been produced, it is generally certain that surgical anesthesia is impossible, and therefore further attempts are practically useless.

In any case where operation is contemplated, the hypnotist should arrange to see the patient at least half a dozen times before the date of operation.

The Induction of Anesthesia.—In hypnotizing with a view toward surgical anesthesia, it is best not to run the risk of failure by beginning

FIG. 278.—INDUCTION OF ANESTHESIA.

to suggest anesthesia too soon. One should first get the subject into a state of somnambulism, or, if this cannot be done, into as deep hypotaxis as possible. Then one may begin by closing the subject's hand and producing rigidity of the whole arm. The subject is then told that the contraction of the hand and arm muscles begins to impede the circulation in his hand, in consequence of which he will probably become aware of a feeling of numbness in that region. He is then informed that in order to test this numbness the hypnotist will prick the back of the hand with a pin and that the pin will feel less sharp than usual. Instead of using a pin, however, the hypnotist touches the subject's hand with a sharpened match or a toothpick. If this works well, and the subject seems to believe that a pin has been used, greater diminution of sensibility is then suggested, and a real pin is then employed, though very lightly. The hypnotist continues in the same manner, suggesting increasing hypalgesia, and applying the pin with more and more force until even a vigorous thrust causes the subject no pain. After this it is well to suggest that not only is the pin thrust entirely painless, but that it is not felt at all—that is, that the part is both analgesic and anesthetic —"perfectly numb and dead, like a piece of rubber."

When anesthesia or analgesia has been successfully suggested in one part of the body, it is always easy to reproduce it in any other part, and for so doing the preliminary suggestion of rigidity or other phenomena is unnecessary.

In any case where an operation is contemplated the hypnotist should assure himself that he has the subject well under control, that anesthesia can be produced both promptly and certainly, and that it is sufficiently deep. The depth of anesthesia should be put to rather severe tests, such as thrusting pins into the finger tips (with due care to avoid infection) or by touching the cornea after having suggested insensibility of that part. Before the operation, appropriate suggestions should be given with a view toward relieving the patient's mind of any anxiety or dread in regard to it and its consequences. The whole matter should be treated rather lightly, as if there could be nothing to fear and everything was sure to go smoothly.

At the time of operation the patient may be placed upon the table and hypnotized there, but it is preferable to induce the hypnosis in an adjoining room and either let the patient walk or be carried to the table while in the hypnotic state. In any case, for the patient to see a great display of knives, scissors, and other instruments is decidedly undesirable. During the operation the hypnotist should remain with the patient, and from time to time suggest that he continue to sleep quietly, that the field of operation is entirely without sensation, and that everything is going on nicely. The operating surgeons had best avoid references to cuts, blood, and other matters which might tend to have a disquieting effect upon the patient, who, though apparently in profound slumber, is not entirely unsusceptible to external influences. When the operation is finished, before awaking the patient, it is well to suggest that even in the waking state his wounds will cause him no pain and that the necessary dressings will give rise to no discomfort.[1]

[1] For other considerations of hypnotic therapeutics, see Tuke: "Treatment by Hypnotism and Suggestion," 5th ed., London, 1907; Ford: "Hypnotism and Psychotherapy"; Hilzer: "Hypnosis and Suggestion"; Bernheim: "Suggestive Therapeutics"; Moll: "Hypnotism"; Quackenbos: "Hypnotic Therapeutics in Theory and Practice."

CHAPTER XVIII

THERAPEUTIC USES OF INHALATION ANESTHETICS

Anesthetic Treatment for Special Conditions: In Renal and Biliary Colic; In Acute Pain or Shock; In the Passage of Renal or Biliary Calculi; In Extreme Irritability of the Central Nervous System; Convulsions of Infancy and Childhood; Puerperal Eclampsia; In Anemic Convulsions; Convulsions and Seizures Depending Upon Poisoning, and Cerebral Diseases; Use in Diagnosis; Insomnia or Extreme Restlessness; Acute Mania; Nitrous Oxid and Oxygen; Some Miscellaneous Applications of Ethyl Chlorid.

Other Uses of Agents Employed in the Administration of Anesthetics: Ether in the Treatment of Infections; Ether Irrigation of the Abdomen.

ANESTHETIC TREATMENT FOR SPECIAL CONDITIONS

Anesthesia has been used sporadically and, in some few instances and localities, regularly for special conditions or for diseases not yielding to surgical operations.

In Renal and Biliary Colic.—In renal and biliary colic and for similar acutely painful seizures it has been used with great success. Now that the analgesic stage of all anesthetics, especially of nitrous oxid and oxygen, is more clearly recognized, it is probable that anesthesia will be used more frequently than ever before for conditions just stated and for similar conditions. A patient in an acute seizure of renal colic, who might seriously object to being anesthetized to the surgical stage, would embrace the opportunity of the analgesic stage of any anesthetic.

In Acute Pain or Shock.—In cases of acute pain or shock it is used for temporary relief, not with the idea of curing, but simply to afford time for recovery to take place without pain. When anesthetics are given for the analgesic qualities alone they should be employed only under the direct supervision of a physician. If cyanosis or unconsciousness appear, the agent should be withdrawn, to be reapplied again solely for the relief of pain.

In the Passage of Renal or Biliary Calculi.—In the passage of renal or biliary calculi, chloroform or ether by the drop method on gauze or a handkerchief affords speedy relief; also in the crises of locomotor ataxia.

In Extreme Irritability of the Central Nervous System.—Wherever extreme irritability of the central nervous system exists, as in tetanus, strychnin poisoning, or convulsive affections, chloroform to the second stage will easily relieve suffering without affecting the consciousness. Hewitt records one case of a child kept more or less under the influence of chloroform for thirteen days, one hundred ounces being used. It is necessary to administer the anesthetic only to the point where muscular spasm subsides, when it is discontinued. The anesthetic is to be reapplied only when tetanic spasm is imminent. If the rigidity is continuous the administration must be maintained until signs of the rigidity disappear.

It is unnecessary to state that, except in the presence of urgent indications, these agents should not take the place of morphin or opium. When, despite the use of morphin or opium, acute pain persists, chloroform or ether may be administered for short periods to supplement the action of these drugs.

Convulsions of Infancy and Childhood.—Convulsions of infancy and childhood are easily and safely treated with pulmonary anesthetics, administered to the analgesic stage. Ethyl chlorid is preferred, because its analgesic stage is longer than that of any other inhalation anesthetic, and because it is the preferable anesthetic for children, in the opinion of many anesthetists.

Puerperal Eclampsia.—Chloroform has been used for a number of years for *puerperal eclampsia.* Care must be taken, however, if the patient is cyanosed. In these cases ether is the safest drug.

In Anemic Convulsions, Convulsions and Seizures Depending Upon Poisoning, and Cerebral Diseases.—In anemic convulsions, convulsions and seizures depending upon poisoning, and cerebral diseases it is better to use nitrous oxid and oxygen, with a nasal inhaler, for the analgesic effect than to use chloroform or ether, especially chloroform, inasmuch as these latter drugs in themselves sometimes, under certain conditions, induce serious after-effects.

Use in Diagnosis.—General anesthesia is frequently employed to produce muscular relaxation where diagnosis of certain conditions is doubtful. The selection of the anesthetic in these instances would depend upon the conditions already stated. Unless contraindicated, nitrous oxid and oxygen is the best agent for such conditions as "hysterical contractions," phantom tumors, and malingering.

Insomnia or Extreme Restlessness.—In insomnia or extreme restlessness morphin and similar drugs are often ineffectual. The patient may be in such a condition that the usual measures necessary to produce a quiet state, such as warm baths, massage, etc., cannot be used except to very great disadvantage. Under these circumstances it is perfectly justifiable to produce anesthesia and to inaugurate the necessary remedial procedures. Mortimer[1] treated a vigorous man who had had no sleep for many days and nights in spite of various hypnotics. The anesthetic was administered, and the patient remained asleep for four hours. By giving a little more anesthetic at longer intervals the patient remained asleep for two hours longer. The rest of the night he remained quiet instead of wandering about. The next morning he was rational, had a bath, and ate a good breakfast. He slept most of the day and the following night, awakening quite recovered on the second morning.

Acute Mania.—In cases of acute mania, either temporary or recurrent, if the condition is apparently dependent upon no perceptible or

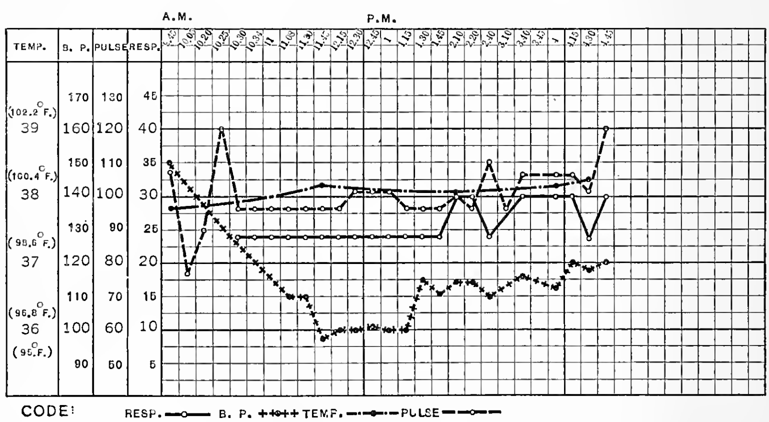


Fig. 279.—Anesthesia in a Case of Acute Mania.

organic lesion, it would seem, theoretically at least, that general anesthesia would,—in connection with other remedies before, during, and after,—tend to lessen or shorten the usual period in which the patient may have to be confined.

Anesthetics may be given with less danger for therapeutical purposes than when surgical interference is necessary.

The first case, as far as we are aware, in which an anesthetic was given for the definite purpose of attempting to affect favorably the brain cells without injuring the body occurred at the instigation of one of us (J. T. G.) in March, 1912, Dr. Swepson J. Brooks and Dr. T. Drysdale Buchanan associated. The case was one of mania of ten or twelve years' standing. It is given in full to show that a patient may be

[1] Mortimer, J. D.: *Brit. Med. J.*, Jan. 7, 1899.

successfully and easily anesthetized for a number of hours without complications or shock resulting therefrom. The case is suggestive of great possibilities in psychiatry, and is given here primarily for that reason.

The patient was in full surgical anesthesia at 10 o'clock, and the anesthetic was discontinued at 4:30 P. M., the patient being practically under the anesthetic for six and one-half hours. The result was entirely negative, as far as affecting the patient's condition favorably. It was satisfactory from an anesthetic standpoint. The patient came out of the anesthesia, and was entirely rational, with absolutely no unpleasant symptoms of any kind. The temperature, pulse, respiration, and blood pressure were taken at regular intervals, and the chart (Fig. 279) shows the result. The narcosis was started with one-quarter of a grain of morphin with 1/150th grain of atropin at 9 o'clock. The pulmonary anesthesia was commenced with chloroform at 9:55 by the drop method,

Hour	Temp.	Pulse	Resp.	B.P.	Sleep	Stim.	Medicine	Nourishment	Remarks
A.M. 8.—							(Enema): Saline Glucose ℥i O. i (per Hypo): Morph. Sulph. gr. $\frac{1}{4}$ Atrop. gr. $\frac{1}{150}$		
9.30									Heart normal on examination.
9.55	99.2	108		150					Chloroform administered (drop).
10.05		76							
10.15									Ether administered (drop).
10.20		90							
10.25		120							Oxygen & Ether administered (vapor).
10.30		96	24						
10.34		96	24						
11.—		96	24						
11.08		96	24	110					
11.20									Slight snore—lid reflex —pupil slightly dil. —eyeballs rolling.
11.30		96	24	110					
11.45	99.8	96	24	98					Slight perspiration—breathing easy.
									Pt. warm but not perspiring.
12.15		96	24	100					
12.30		102	24	100					Slight perspiration—eyeballs rolling.
12.45		102	24	100$\frac{1}{4}$					do.
P.M. 1.—		102	24	100					do.
1.15		96	24	100					do
1.30		96	24	115					do.
1.45		96	24	112					
2.10		102	30	114					
2.20		96	30	114					
2.40		112	24	112					
3.10		96					(Enema): Olive Oil		
3.40		108	30	116					Massage—Alcohol rub.
3.45									Catheterized—℥ix
4.00	99.8	108	30	114					
4.15		108	30	120					Slight perspiration.
4.30	100	102	24	118					Ether discontinued.
4.45		120	30	120					
									Amt. Ether used ℥ix

and was gradually changed to ether by the drop method. At 10 o'clock the patient was in full surgical anesthesia, and at 10:25 oxygen and ether by the vapor method were substituted. This was continued to the end.

In acute mania or other mental condition the alimentary canal should be thoroughly evacuated, and when the patient is under the anesthetic lecithin, olive oil, and saline should be continuously administered with the idea of having enough lecithin absorbed to affect the brain cells favorably. The patient should be given enough morphin toward the close of the pulmonary anesthetic to continue sleep, so that he will awake in as nearly a natural manner as possible. The table on the preceding page and chart (Fig. 279) show the result of this anesthesia.

Nitrous Oxid and Oxygen.—Under the influence of nitrous oxid with 20 per cent oxygen, Klikowitsch [1] found in the majority of healthy individuals accelerated cardiac contractions, diminished pulse waves, rarer and deeper inspirations. In cases of weakened heart action an unfavorable influence upon the heart not only failed to occur, but a favorable effect was actually demonstrable. The cardiac contractions, while somewhat diminished in number, were increased in efficiency. For these reasons, as well as on account of the beneficial influence on attacks of angina pectoris, on vomiting and cough of reflex origin, Klikowitsch employed nitrous oxid for therapeutic purposes.

Some Miscellaneous Applications of Ethyl Chlorid.[2]—To Differentiate Between a Neuralgia of Central and One of Peripheral Origin.—The theory is that if the lesion be central no interference along the course of a centripetal nerve will alter its manifestation; while if the trouble is with terminal nerves, when communication between the periphery and the centers is cut off, all pain will disappear.

The method is to freeze the tissues between the apparent lesion and the spinal canal or cranium either by freezing, as done for local anesthesia, or by "reinforced freezing," i. e., by injecting a quantity of distilled water beneath the skin over the part to be frozen or directly into the tissue until an appreciable bulging is produced, and then directing the spray of ethyl chlorid on this spot. The water will become ice, and the deeper tissues will be frozen or thoroughly chilled. "Coin" freezing is accomplished by placing a coin of suitable size and wet with water on the skin and spraying ethyl chlorid on it, when "a congelation" less severe than reinforced freezing, more severe than ordinary cutaneous congelation and one more accurately localized is obtained.

To Differentiate Neuritis from Neuralgia.—"Neuralgia of an accessible nerve treated by freezing near its point of exit and failing to yield to repeated applications of the spray is not a veritable neuralgia, but a neuritis or a complicated neuralgia."

[1] Quoted by Brunn: "Die Allgemeine Narkose," 1913, 325.

[2] Abrams: *Am. Med. Surg. Bull.*, Dec. 15, 1895, 1487-1490.

As a Means of Localizing Pain.—If the area of pain is large, or there are many painful points, the pain will not cease until the exact spot of origin is frozen. In this way Abrams has discovered out of many cicatrices the one causing pain, a small neuroma, and a carious tooth not otherwise suspected.

To Differentiate Many Neuralgic Affections of the Head and Thoracic and Abdominal Parietes from Visceral Diseases.—For this freezing is usually necessary along the intercostal nerves at their exit from the vertebræ. In this way symptoms that have been or could be interpreted as disease of some viscus have been referred to their true origin.

OTHER USES OF AGENTS EMPLOYED IN THE ADMINISTRATION OF ANESTHETICS

Reference (Chapter II, p. 91) has been made to the use of various agents which have been found, from laboratory experimentation and clinical experience, to modify the action of inhalation anesthetics.

Reference will be found in Chapter XV, p. 598, to the use of ether as an antidote to the various agents employed for purposes of spinal analgesia.

Ether in the Treatment of Infections.—We come now to the consideration of ether in the treatment of various infections. While this may be said to be apart from the subject of anesthesia, it has a practical bearing with which the anesthetist should be familiar.

Souligoux[1] has habitually and successfully employed ether in the treatment of peritoneal infections. He was led to this in 1891 by the following observation: In his service as an interne, with Leport, he was in charge of a man, both of whose legs had been crushed by a heavily loaded truck. The legs were reduced to a mass with crushed bones, which protruded from the midst of the large wounds, and there seemed nothing left but a double amputation at the thigh, to which the patient refused to submit. Souligoux carefully cleansed the wounds and poured in a liberal supply of ether, after which the two legs were put up in plaster. To his extreme astonishment, no infection occurred, and the patient's legs were preserved. He believed this to be due to the ether, which is very volatile and which had penetrated into all the corners and irregularities of the wounds, thus permitting their disinfection. Since that time he has washed all wounds with ether, and employs ether also for all superficial infections, lymphangitis, erysipelas, etc.

Mode of Application.—The mode of application is as follows: In

[1] Souligoux: "Sur l'emploi de l'ether dans les infections," *Bull. et Mém. Soc. de Chir. de Paris,* Feb. 25, 1913, No. 7, 293.

a case of lymphangitis of the arm, for example, the limb is carefully washed with water and soap, as if to prepare for operation. After the skin has been wiped dry the entire affected region is wrapped in bandages, on which a liberal supply of ether is poured. The part is then wrapped in oiled silk, which is held in place with straps, which are tightened at the two extremities of the dressing, so that the ether can only evaporate slowly, and, to guard still further against evaporation, the limb is surrounded with a thick layer of non-absorbent cotton.

Results Obtained.—The results obtained with this treatment are excellent, according to Souligoux, who has been able to obtain many cures in cases of grave infections. Ether has been employed by him in this manner in several hundreds of cases, always with commendable results.

Ether Irrigation of the Abdomen.—Since 1891 he has introduced ether into the peritoneal cavity of guinea-pigs without harm. He did not venture to experiment in this way upon man, however, until 1912. This was done under the following conditions: In July he was called to see a patient who for eight days had suffered from intestinal obstruction, with entire arrest of feces and gas, and stercoral vomiting. On the sixth day a laparotomy was performed for making an artificial anus. The iliac incisions were followed by the escape of gas and fecal matter from the abdomen, showing the existence of a perforation of the intestine, which required closure. Median laparotomy was performed. The abdomen was filled with fecal matter and gas; the bloated coils were covered with false membranes, and, after a prolonged search, a perforation was found on the cecum, the size of a quarter. This was closed. Regarding the patient as doomed, remembering his experience with ether in 1891, and being aware of Morestin's frequent employment of ether in abdominal operations, Souligoux poured ether into the abdomen, upon the coils, into the small pelvis,—in other words, applying a thorough irrigation of the abdomen with ether. After careful wiping two drains were placed, one toward the small pelvis, the other toward the upper portion of the abdomen.

To the great surprise of Souligoux, the patient made a good recovery, and he has since made free use of ether, with excellent results, in all abdominal interventions associated with pus.

Marcille, according to Souligoux, followed the same procedure in surgical cases, as a routine method. The following is a summary of his observations.

Clinic Cases.—(1) Six patients, operated upon, with peritoneal infection, through ruptured tubal pregnancies. In each instance the peritoneum of the small pelvis and the affected coils of intestine were wiped off with ether-soaked bandages. He obtained six cures.

(2) Seventeen patients, operated upon, with strangulated hernia.

In each instance the coil was washed with ether. All the patients heard from were cured.

(3) Three patients, operated upon, with abdominal wounds and contusions. (a) Contusion, at 9 A. M. Operation, at 10 P. M. A perforated coil, turbid fluid in peritoneal cavity, found. Copious ether irrigation. Drainage. Cure. (b) Knife wound of abdomen, operated upon in third hour. A divided coil, a small perforation of another coil, two wounds of mesentery, found. Copious ether irrigation. Drainage. Cure. (c) Case of frightful abdominal traumatism, the individual being practically cut in two, the wound extending from Scarpa's triangle on the right side to the left iliac fossa. Repair of the numerous vascular and visceral wounds. Irrigation with ether. Death during the night.

(4) Three cases of general peritonitis, operated upon. Ether; free drainage. Two cures; one death.

(5) Infarct of entire large intestine and two meters of small gut, all contained in an enormous eventration. Operation. Part of these coils were gangrenous; stercoral abscesses had formed. Resection of the entire mass contained in the eventration, involving the entire large intestine as far as the iliac flexure, and two meters of the small intestine. Free ether irrigation. Reëstablishment of intestinal functions; gas and stools. Good pulse next morning. Death from syncope after thirty-six hours.

(6) Rupture of stomach, through ulcer. General peritonitis, with large amount of purulent fluid, false membranes in intestine found upon operation. Suture of the perforation. Free ether irrigation. Drainage. Cure.

(7) Compound fracture of forearm bones. Badly soiled wound. Washed with ether, and sutured without drainage. Healed by primary union.

OBSERVATIONS.—It appears, from the sum-total of these observations: (1) That irrigation of the peritoneal cavity with ether is in no way injurious. In all the cases where Souligoux employed it he noted that the coils of intestine became pink, and contracted under the action of the ether; (2) that this irrigation seemed to have a powerful action as a disinfectant of the peritoneum.

In the discussion of Souligoux's paper Cunéo stated that ether dressings, according to the technique of Souligoux, had been employed by him in cases of lesion of the extremities, usually lesions of an inflammatory character, such as panaris, phlegmons, etc. Excellent results were obtained by this method. On the other hand, the idea of pouring ether into the peritoneum did not appeal to him. The observations of Souligoux did not seem to him to be demonstrative, and the cures appeared to be especially referable to the timeliness of the intervention. The suppression of the cause of complications was a factor in the success. The question of drainage he regarded as secondary in itself. He had become convinced of this by obtaining a considerable proportion of cures in general peritonitis of appendicular origin, through the simple ablation of the appendix, and closure, without drainage. There is nothing, in his opinion, to permit the claim that in the observations of Souligoux the cure was due to the irrigation of the peritoneum with ether.

Souligoux, in replying to the remarks of Cunéo, said the latter had not well understood the observations described. He reiterated some of the details of the case of obstruction of eight days' standing. The perforation, he said, may be assumed to have coincided with the severe pain which was felt at this time. There was an inundation of fecal matter and gas in the abdomen. He had had so little confidence himself in the recovery of the patient that when he saw her in the evening he believed he had made a mistake in the room, and left without speaking to her. On learning of his mistake he returned, finding the woman in fairly good condition. He was unable to believe that her recovery was entirely independent of the ether. He was convinced, from his observations, that ether is not only harmless, but may be very useful in the treatment of peritoneal infections.

CHAPTER XIX

THE MEDICO-LEGAL STATUS OF THE ANESTHETIST

JOHN W. H. CRIM

INTRODUCTION: Police Power; The Medical Profession Established; Contest Between the Schools of Medicine; The Status of the Physician.

THE PHYSICIAN'S LIABILITY: Ethical Liability of the Physician; The Civil Liability of the Physician; Malpractice; Liability of the Specialist; The Criminal Liability of the Physician; Gross Ignorance or Negligence; Statutory Liability.

INTRODUCTION

An examination of the vast number of decisions of the higher courts of the several States of the United States discloses the fact that the discovery and use of anesthetics [1] by the medical profession have had little or no effect upon the well-established principles of medical jurisprudence, and the profession of the anesthetist, of inestimable importance to the medical profession, and consequently to society in general, has found no place either in our courts or legislatures. At the outset it may be said that only those having qualifications of a physician [2] or dentist should be permitted to administer anesthetics; that it should be made a penal offense in every State for any person other than a legally qualified medical or dental practitioner to administer either a general or local anesthetic or a drug for the purpose of produc-

[1] That which produces insensibility to pain: *State v. Baldwin, 36* Kan., 1.

[2] The term "physician" is here used in a broad sense, including all who are lawfully engaged in the practice of medicine: *Harrison v. State, 102* Ala., 170.

At one time the term "physician" was employed in contradistinction to that of "surgeon," but the modern use of the term includes those who perform surgery as well: *Alison v. Haydon, 4* Bing., 619; *Wetherel v. Marion County, 28* Iowa, 22; *Little v. Sliker, 33* N. J. L., 507; *Matter of Hunter, 60* N. C., 447.

The term "Physician and Surgeon" is not limited to any one school of practitioners: *Raynor v. State, 62* Wis., 289.

Osteopaths hardly come within this classification, unless they have pursued successfully an accepted course of study in medicine. For statutory definitions of above terms, see Public Health Law New York, *1909*.

ing a state of unconsciousness during any medical, surgical, or dental operation. Dentists should be permitted to administer such anesthetics, general and local, as are necessary in the practice of dental or oral surgery and medicine, and should not be permitted to give either a local or general anesthetic in other medical or surgical operations or during childbirth. To determine the fundamental responsibility of an anesthetist, one must look to the general principles of law which apply to the physician in the ordinary practice of his profession, with this exception: the practitioner holding himself out to the public as an anesthetist is properly considered a specialist, and is therefore held to a commensurately higher degree of skill and learning, in so far as the administration of anesthetics is concerned, than the ordinary practitioner.[1] It will therefore suffice, for the purposes of this chapter, to indicate the general principles which define the duties of the physician with regard to his ethical, civil, and criminal responsibility, and to dis-

[1] In this place it is appropriate to insert a summary of views relative to the training and status of the anesthetist.

Hellman (*N. Y. Med. J.*, *95*, No. 22, 1146) considers that no one without a medical training can ever become an expert anesthetist, and that nurses, sisters of mercy, and others should be excluded from general anesthetic work. The administration of anesthetics is legally medical practice, and as such may be handled only by graduate physicians in New York.

However, we may point out that instruction in the practical administration of anesthetics should be a requisite part of the regular medical and dental courses. On the training required by the anesthetist, see the discussion in *J. Am. Med. Assn.*, *52*, No. 20, 1614-5; and on the teaching of anesthetics, see an earlier paper, *ibid.*, *51*, No. 14, 1167.

Chipman (*Va. Med. Semi-Mon.*, *15*, No. 12, 278) discusses the general significance of the term ''anesthetist.'' In the ''paid anesthetist system,'' the anesthetist gives all anesthetics, in private cases receiving remuneration from the patient, directly or indirectly, while with ward cases he either administers himself or has an interne give the anesthetic under his direction, and for these cases he receives no compensation. This system, Chipman maintains, is a long-delayed need. He considers that the trained anesthetist should play a very large part in reducing the death rate to a minimum.

''The Trained Anesthetist'' has been discussed by Porter. (*Lancet-Clinic*, *103*, No. 25, 641.) He thinks that the administration of anesthetics should only be done by the trained man and that he should be an expert. He goes on to say: ''Surgeons should insist upon having a trained anesthetist for all operations. . . . The anesthetist's work is the equal of any other special line of work.''

Abernethy (*Southern Med. J.*, *3*, No. 8, 489) has treated of the anesthetist as a specialist. In the administration of a general anesthetic the exercise of judgment and skill is necessary, and this can only be obtained through special study and experience. As much care should be exercised in the administration as in the performance of an operation; and the anesthetist should have, and does have in properly regulated cases, as much responsibility as the surgeon.

On the general practitioner as an anesthetist, see Moriarta: *J. Am. Med. Assn.*, *53*, No. 10, 768; and, on the professional anesthetist, consult Metzenbaum: *Ohio State Med. J.*, *6*, No. 3, 124.

cuss, in appropriate places, the legislation and decisions pertaining to the administration of anesthetics by physicians, surgeons, anesthetists, and dentists.

Police Power.—The application of the principles of law to the relations between physician and patient has its source in the right of society to prescribe rules of human conduct which conduce to the general welfare, that is, the police power inherent in sovereignty; accordingly, it is to the police power of a State [1] that society looks for protection from ignorance, superstititon, and quackery in the medical profession. The limitation upon legislatures in enacting statutes for the purpose of regulating the practice of medicine is measured by the extent of the police power; and, conceding that the protection of public health is of vital importance in modern government, a most casual examination of the early legislation, or the want thereof, reveals the inadequacy, as it were, of the ancient forms of government in this respect. For example, we are told that, under the Roman civil law and the English common law, the right to practice medicine and surgery was free to all persons.[2] It is therefore not surprising to learn that the barber [3] and the priest [4] were relied upon to "heal the ill." Speculation upon the inadequacy of a government which permitted such a condition receives additional interest in the fact that the barber and priest could not sue and recover for their services—a cardinal privilege of the twentieth century practitioner, not only from the standpoint of sustenance, but because a judgment in his favor for services rendered is an estoppel to a civil action against him for malpractice; conversely, proof of malpractice is a defense to an action for professional services.[5] Custom precluded the practitioner from making a specific charge for his services, and required him to accept whatever compensation, or *honorarium,* as it was then called, his patient chose to pay. The inevitable result of the conditions fostered by these customs prompted Parliament to pass a statute during the reign of Henry V. (1422), which, under a penalty of both fine and imprisonment, prohibited anyone "using the mysterie of physyck unless he hath studied in some university and is at least a bachelor of science."

The Medical Profession Established.—Following this legislation by

[1] See *Com. v. Gibson,* 7 Pa. Dist. Rep., 386; *Com. v. Finn,* 11 Pa. Sup. Ct., 620; *Matter of Campbell's Registration, 197* Pa., 581; *Dent v. W. Va., 129* U. S., 114; *Reetz v. Mich., 188* U. S., 505.

[2] *Denton v. State, 21* Neb., 445; *State v. Morrill,* 7 Ohio Dec., 52; *State v. Carey, 4* Wash., 424.

[3] *Allison v. Haydon, 4* Bing., 619. On the low state of surgery in the Middle Ages, see Kottelmann: "Gesundheitspflege in Mittelalter," 1890, 216.

[4] Baas: "Geschichte der Medicin," 204; von Raumer: "Hohenstaufen," *6,* 438; Fort: "History of Medical Economy During the Middle Ages," 1883, chaps. xiii and xviii.

[5] *Abbott v. Mayfield, 8* Kan. App., 387.

Parliament, the practice of medicine savored of a profession; but it was not until Parliament enacted the well-known act of Henry VIII.,[1] which denounced the medical profession as "ignorant persons who could tell no letters on the book, common artificers, smiths, weavers, and women, who took upon themselves great cures, partly using sorcery and witchcraft, and partly applying very noxious medicines to the disease," that it became a well-defined and established profession. With this cloak of legislative protection thrown around it, the profession at once attained a higher standard; medical schools were organized and various systems of medicine came into existence.

Contest Between the Schools of Medicine.—The greater amount of subsequent legislation in both England and America, between 1550 and 1890, grew out of the jealousy existing between the followers of such schools as Allopathy and Homeopathy. It is indeed a curious commentary on the history of the medical profession that the enmity between the several schools and systems, growing out of the efforts of one to fortify itself by legislation at the expense of loss of privilege to the other, was reflected in the legislature of the State of New York during the latter half of the nineteenth century, when, in its efforts to appease the warring schools, it enacted laws so liberal that the doors of the medical profession were opened to ignorant, and even fraudulent, empirics—a condition which happily has been remedied by more recent legislation.

The Status of the Physician.—The legal status of a physician is frequently compared to that of the lawyer, but there is one important element which differentiates the two professions and should be constantly borne in mind in any comparison; the lawyer is an officer of the Court, and, because of this relation, the Court has summary power to inquire into his professional conduct in connection with any case; whereas the physician is under no such restraint, and the medical societies, which have been organized for the purpose of protecting the public against imposters, frequently find this power so limited that it often becomes necessary for the public to resort to the legislature for protection. The status of a physician in this country was ably described by the late Justice Field, in delivering the opinion of the Supreme Court of the United States affirming the constitutionality of the legislation prescribing the qualifications of one to practice medicine:[2] "Few professions require more careful preparation by one who seeks to enter it than that of medicine. It has to deal with all those subtle and mysterious influences upon which health and life depend, and requires not only a knowledge of the properties of vegetable and

[1] *3* Henry VIII., c. 11; *14* and *15* Henry VIII. 5; *5* Car., 1.

[2] *Dent v. West Virginia, 129* U. S., 114, affirming *25* W. Va., 1. For the medical practice laws of all States, see "American Medical Directory," 3rd ed., 1912.

mineral substances, but of the human body in all its complicated parts, and their relation to each other, as well as their influence upon the mind. The physician must be able to detect readily the presence of disease, and prescribe appropriate remedies for its recovery. Everyone may have occasion to consult him, but comparatively few can judge of the qualifications of learning and skill which he possesses. Reliance must be placed upon the assurance given by his license, issued by an authority competent to judge in that respect, that he possesses the requisite qualifications. Due consideration, therefore, for the protection of society may well induce the State to exclude from practice those who have not such a license or who are found upon examination not to be fully qualified. The same reasons which control in imposing conditions, upon compliance with which the physician is allowed to practice in the first instance, may call for further conditions as new modes of treating disease are discovered, or more thorough acquaintance is obtained of the remedial properties of vegetable and mineral substances, or a more accurate knowledge is acquired of the human system and of the agencies by which it is affected. It would not be deemed a matter for serious discussion that a knowledge of the new acquisitions of the profession, as it, from time to time, advances in its attainments for the relief of the sick and suffering, should be required for continuance in its practice, but for the earnestness with which the plaintiff in error insists that, by being compelled to obtain the certificate required, and prevented from continuing in his practice without it, he is deprived of his right and estate in his profession without due process of law. We perceive nothing in the statute which indicates an intention of the legislature to deprive one of any of his rights."

The wisdom underlying the statutes requiring a general education as a prerequisite, supplemented by special study at accredited medical schools, as qualifications precedent to the application for the license to practice medicine, cannot be questioned. The legislation of the several States of the United States in this respect has been approved by the courts in holding those statutes constitutional which prohibit the practice of medicine and surgery by unlicensed persons.[1] On the other hand, when the licentiate has conformed to these reasonable requirements, it follows that it is the better part of wisdom to rely on his integrity[2] and desire to succeed in the application of his knowledge, skill, and judgment, thereby characterizing his profession with little restraint in the fields of experiment and investigation; for to limit the

[1] *Blalock v. State, 112* Ga., 338; *O'Conner v. State, 46* Neb., 157; *State v. Mylod, 20* R. I., 632; *State v. Van Doran, 109* N. C., 864; *Hale v. State, 58* Ohio St., 676; *State v. Carey, 4* Wash., 424.

[2] That a State may require good character on the part of the licentiate: *Hawker v. New York, 170* U. S., 189.

latitude, as it were, of his independence of thought, obviously would be tantamount to impeding progress in both the art and science of medicine. By the same token, it is impossible to prescribe a fixed rule of responsibility on the part of the practitioner, inasmuch as the circumstances and conditions surrounding cases vary, and accordingly all conclusions with respect to a physician's liability must be drawn from the facts underlying each particular case. It is upon this theory that the courts have held that the defendant cannot successfully meet the charge of malpractice by showing his methods were successful in similar cases.[1]

THE PHYSICIAN'S LIABILITY

Ethical Liability of the Physician.—While the privilege which permits the lips of the physician to remain sealed and to hold inviolate the relations between physician and patient has its foundation in the civil responsibility of the physician to inform himself of the habits, tendencies, circumstances, and history of the patient,[2] it is to that higher law, the ethics of the medical profession, that society must ultimately

[1] *Baker v. Hancock, 63* N. E., 323; *64* N. E., 38; but see *Stern v. Laning, 106* La., 738.

[2] Communications from a patient to his physician were not privileged at common law: *Rex v. Gibbons,* L. C. and P., *97*; *Broad v. Pitt,* 3 C. and P., 518; *Goddard v. Gardner, 28* Conn., 172; *Barnes v. Harris, 7* Cush. Mass., 577; *People v. Stout, 3* Park. Crim. N. Y., 670; *Kendall v. Grey, 2* Hilt. N. Y., 300; but on considerations of public policy: *Lissak v. Crocker, 119* Cal., 442; *Kling v. Kansas City, 27* Mo. App., 231; *Hoyt v. Hoyt, 112* N. Y., 493.

Statutes have been enacted in most jurisdictions prohibiting the disclosure, against the will of the patient, of information acquired by physicians in their professional capacity: *Conn. Mut. L. Ins. Co. v. Union Trust Co., 112* U. S., 250; *Dreier v. Cont. L. Ins. Co., 24* Fed. Rep., 670; *Shafer v. Eau Claire, 105* Wis., 239; *Wells v. N. E. Mut. L. Ins. Co., 187* Pa St., 166; *Davis v. Supreme Lodge,* etc., *165* N. Y., 159; *Territory v. Corbett, 3* Mont., 50; *Blair v. Chicago,* etc., *89* Mo., 334, 383; *Cooley v. Foltz, 85* Mich., 47; *Nelson v. Niederland Co., 110* Iowa, 600; *Bower v. Bower, 142* Ind., 194; and *Colo. Fuel Co. v. Cummings, 8* Colo. App., 541. In the case of *Robinson v. Supreme Commandery,* U. C. G. C. of W., *79* N. Y. S., 13, it was stated that *Code Civ. Proc.,* 834, provides that physicians shall not be allowed to disclose information acquired in attending a patient in a professional capacity. An Indiana statute provides that a physician shall be incompetent to testify, over his patient's objections, as to any knowledge acquired by him in treating such patient: *Aspy v. Botkin, 66* N. E., 462. Utah Rev. St., 3414, provides that a physician cannot, without the consent of his patient, be examined in a civil action as to any information acquired in attending the patient which was necessary to enable him to prescribe for the patient. In order that such statutes may apply, it is necessary that the relation of physician and patient should exist or at least that conditions are such that the patient is impressed with the belief that it does: *People v. Koerner, 154* N. Y., 355; *Clarke v. State, 8* Kan. App., 782.

look for protection rather than to legislatures and courts. The sanctity of the relations between physician and patient has ever been held with a most profound appreciation throughout the history of the medical profession; and in this respect the comprehensive ethical code attributed to Hippocrates admits of no amendment.

The Civil Liability of the Physician.—In defining the necessary qualifications on the part of the practitioner, the courts have held, without exception, that one holding himself out to the public as a general practitioner of medicine and surgery must possess and exercise the average degree of skill and learning possessed by members of the profession practicing in similar localities,[1] in the light of the present state of medical science.[2] The physician is not infallible, and, except by express agreement, in accepting a case, does not guarantee a cure.[3] The reasonable and ordinary care, skill, and diligence demanded by this rule, are those which are commonly practiced by physicians and surgeons in the same, or similar, localities and in the same general line of practice in similar cases. The degree of care, skill, and diligence varies in different communities [4] and in different cases. The opportunity for observing the latest approved methods of treatment, and the facilities for obtaining drugs and appliances, are material in determining the responsibility on the part of the practitioner; hence, it will be seen that the above rule exacts higher degrees of care, skill, and diligence on the part of the city practitioner, than is demanded of the practitioner in the more remote communities.

[1] *Pike v. Honsinger, 155* N. Y., 201; *Eislein v. Palmer, 7* Ohio Dec., 365; *Lawson v. Comnaway, 37* W. Va., 159; *Nelson v. Harrington, 72* Wis., 591; *Mullin v. Flanders, 73* Vt., 95; *Jackson v. Burnham, 20* Colo., 532; and *Force v. Gregory, 63* Conn., 167.

Not in "his locality": *Whitesell v. Hill, 101* Iowa, 629; *Burk v. Foster, 24 Ky. Law Rep.*, 791; *114* Ky., 20. Cf. *53* Neb., 28; 92 N. Y. S., 1063; and *37* W. Va., 159, wherein "his community" is specified. In *Wohlert v. Seibert, 23* Pa. Super. Ct., 213, the comparative distinction is "the skill . . . ordinarily possessed by the average of members of the profession in good standing."

[2] *Baker v. Hancock, 63* N. E., 323; *29* Ind. App., 456; *64* N. E., 38; *Thomas v. Dabblemont, 67* N. E., 463; *31* Ind. App., 146; *Dunbauld v. Thompson, 80* N. W., 324; *109* Iowa, 199; *Forrell v. Ellis, 105* N. W., 993; *129* Iowa, 614; *Gillette v. Tucker, 65* N. E., 865; *67* Ohio St., 106; *93* Am. St. Rep., 639; *Bigney v. Fischer, 59* A., 72; *26* R. I., 402; and *Eislein v. Palmer, 7* Ohio, Dec., 365. On the implied undertaking of a physician, see also *Rich v. Pierpont, 3* F. and F., 35; *Pettigrew v. Lewis, 46* Kan., 78; *Small v. Howard,* 128 Mass., 131; *Pike v. Honsinger, 155* N. Y., 203; *McCandless v. McWha, 22* Pa. St., 261. In the last case it was stated that the care, skill, and diligence exercised must be that of "thoroughly educated" physicians, but it was evidently not intended to impose a higher standard of care than that usually required. See *Smothers v. Hanks, 34* Iowa, 286.

[3] *Ewing v. Goode, 78* F., 442; *Dye v. Corbin, 59* W. Va., 266.

[4] *Whitesell v. Hill, 70* N. W., 750.

Malpractice.—The failure on the part of the practitioner to exercise "the average degree of skill and learning possessed by members of the profession practicing in similar localities, in the light of the present state of medical science," resulting in injury to the patient, is malpractice, and renders the practitioner liable for the injuries resulting therefrom.[1] However, a mere error in judgment does not constitute malpractice, unless such error is inconsistent with the degree of skill which it is the duty of a physician to possess. In a leading case the Court has said:[2] "The law relating to malpractice is simple and well settled, although not always easy of application. A physician and surgeon, by taking charge of a case, impliedly represents that he possesses, and the law places upon him the duty of possessing, that reasonable degree of learning and skill that is ordinarily possessed by physicians and surgeons in the same or similar locality where he practices, and which is ordinarily regarded by those conversant with the employment as necessary to qualify him to engage in the business of practicing medicine and surgery. Upon consenting to treat a patient, it becomes his duty to use reasonable care and diligence in the exercise of his skill and the application of his learning to accomplish the purpose for which he was employed. He is under the further obligation to use his best judgment in exercising his skill and applying his knowledge. The law holds him liable for an injury to his patient resulting from want of the requisite knowledge and skill, or the omission to exercise reasonable care, or the failure to use his best judgment. The rule in relation to learning and skill does not require the surgeon to possess that extraordinary learning and skill which belong only to few men of rare endowments, but such as are possessed by the average number of the medical profession in good standing. Still he is bound to keep abreast with the times, and a departure from approved methods in general use, if it injures the patient, will render him liable, however good his intentions may have been."

The failure on the part of the patient to follow the reasonable and necessary instructions of the physician relieves him of responsibility.[3] Similarly, a physician is under no legal obligation to accept a case against his will; but, having accepted, he cannot withdraw without

[1] But a mere want of due care and skill gives no right of action when no injury has resulted: *Ewing v. Goode, 78* Fed. Rep., 442; *Cayford v. Wilbur, 86* Me., 414; *Rowe v. Lent, 42* N. Y., 483; *Fowler v. Sergeant, 1* Gant. Cas. Pa., 355.

[2] *Pike v. Honsinger, 155* N. Y., 201. On a physician's liability for errors of judgment, see also *Carpenter v. Blaker, 50* N. Y., 696; *Heath v. Glisan, 3* Or., 64; *McKee v. Allen, 94* Ill., App., 147. As to what constitutes negligence or malpractice, see *Sullivan v. McGraw, 118* Mich., 39; *Keller v. Lewis, 65* Ark., 578.

[3] *Geiselman v. Scott, 25* Ohio St., 86; *Becker v. Janinski, 27* Abb. Cas. N. Y., 45; *Haire v. Reese, 7* Phila., 138; *Haering v. Spicer, 92* Ill. App., 449; *DuBois v. Decker, 130* N. Y., 325. For contributory negligence on the part of patient: *Haering v. Spicer, 92* Ill. App., 449.

giving reasonable notice,[1] and the fact that his services are gratuitous does not relieve him of the responsibility to exercise reasonable and ordinary care, skill, and diligence. He is civilly responsible for the want of skill and negligence on the part of his partners, agents, apprentices, and assistants,[2] and, while he incurs no liability in the failure to effect a cure,[3] in case he doubts his competency in a particular case it is both his legal and moral duty to recommend the employment of another physician.[4] The physician is under an implied obligation, when he undertakes a case, to bring to his assistance such obtainable remedies and appliances as discovery and experience have found to be most proper and beneficial, and which are therefore sanctioned by use in such cases;[5] but the mere fact that the instrument used is unusual is not sufficient to show a want of care and skill.[6] The practitioner is chargeable with a knowledge of the probable consequences of an injury or of negligence or unskilfulness;[7] he is bound also to know the natural and probable results of the remedy he uses;[8] and, in order to be relieved from liability on the ground that his course was pursued through an error of judgment, he must keep within recognized and approved methods, and cannot depart from the known rule and usage of the profession to ramble in the fields of investigation and experiment.[9] Finally, it should not be overlooked that it is the duty of the physician to inform himself of those habits, tendencies, and circumstances of the pa-

[1] On the liability of a physician for failure to attend a patient, see *Dale v. Lumber Co., 48* Ark., 188; *Mucci v. Houghton, 89* Iowa, 608; *Barbour v. Martin, 62* Me., 536; *Gerken v. Plimpton, 70* N. Y. S., 793; *62* App. Div., 35; *Lathrope v. Flood, 63* Pac., 1007.

On the physician's right to determine the frequency of his visits to a patient, see *51* L. R. A., 298.

[2] *Tish v. Welker, 5* Ohio Dec., 725; *Wilkins v. Ferrell, 10* Texas Giv. App., 231.

[3] Physicians are not insurers of successful or beneficial results: *Ewing v. Goode, 78* Fed. Rep., 442; *Styles v. Tyler, 64* Conn., 432; *Tish v. Welker, 7* Ohio N. P., 472; *McKee v. Allen, 94* Ill. App., 147; *English v. Free, 205* Pa., 624.

[4] See *Mallen v. Boynton, 132* Mass., 443.

[5] *Stevenson v. Gelsthorpe, 10* Mont., 563; *McCandless v. McWha, 22* Pa., 261.

[6] *Alder v. Buckley, 1* Swan Tenn., 69; *Prichard v. Moore, 75* Ill. App., 553.

It has been ruled in Missouri (*Vanhooser v. Berghoof, 90* Mo., 487) that whether or not the practitioner in substituting other appliances for those which had been properly tested and were *commonly* used was guilty of a want of the requisite degree of care and skill is a question for the jury. This decision is of particular interest to the anesthetist, since the development of anesthetic apparatus is progressive, and the introduction of novel appliances is largely due to individual effort and experience.

[7] *Gerken v. Plimpton, 62* N. Y. App. Div., 35; *Dubois v. Decker, 130* N. Y., 325.

[8] *Bogle v. Winslow, 5* Phila., 136; *20 Leg. Int.*, 46.

[9] *Slater v. Baker, 2* Wils. C. Pl., 359; *Jackson v. Burnham, 20* Colo., 532; *Tefft v. Wilcox, 6* Kan., 46; *Branner v. Stormont, 9* Kan., 51; *Patten v. Wiggin, 51* Me., 594; *Hesse v. Knippel, 1* Mich. N. P., 109; *Pike v. Honsinger, 155* N. Y., 203.

tient which are necessary and relevant in the prudent management of the case.

Liability of the Specialist.—If the specialist professes to belong to a particular school of practitioners,[1] he must measure up to the standard of that school,[2] for "the law implies that surgeons and physicians, in the treatment of all cases they undertake, should exercise reasonable care and diligence, and should give attention proportionate to the delicacy of the operation and case."

It is upon this theory that if a physician holds himself out as having special knowledge and skill, "he is bound to bring to the discharge of his duty to a patient employing him as such specialist not merely the average degree of skill possessed by general practitioners, but that special degree of skill and knowledge possessed by physicians who are specialists in such cases, in the light of the present state of scientific knowledge,[3] for, obviously, to measure the liability of a specialist by the standard appliable to the ordinary family physician, would open the door of the medical profession to quackery and permit consequent fraud upon the public.

In defining the responsibilities of a specialist, a Court[4] has well said: "The question when a physician becomes a specialist is not one of law, but one of fact primarily for his own determination; but, when he holds himself out as a specialist, it becomes his duty to use that degree of skill which such a practitioner of necessity should possess."

The reasoning in this opinion is not predicated upon any new theory, nor in its application is it peculiar to the relations between physician and patient, for it is a well-established principle of law that, "in all those employments where peculiar skill is requisite, the one who offers his services is understood as holding himself out to the public as possessing the degree of skill commonly possessed by others in the same employment."

With respect to the degree of skill required by anesthetists, the decisions pertaining to specialists[5] fortify the conclusion that the anesthetist should be held to that degree of care, skill, and knowledge ordinarily possessed by practitioners in good standing devoting *special* attention and study to the administration of anesthetics. As a rule, the surgeon is responsible to the family, while the anesthetist is responsible to the surgeon; but if the anesthetist has been specially called in by

[1] *Force v. Gregory, 63* Conn., 167; *Bowman v. Woods, 1* Greene Iowa, 441; *Corsi v. Maretzek, 4* E. D. Smith, N. Y., 1; *Williams v. Poppleton, 3* Or., 131; *Hesse v. Knippel, 1* Mich. N. P., 109.

[2] *Martin v. Courtney, 77* N. W., 813.

[3] *Baker v. Hancock, 63* N. E., 323; *64* N. E., 38; *29* Ind. App., 456.

[4] *Baker v. Hancock, 63* N. E., 323.

[5] *Feeney v. Spalding, 89* Me., Ill; *McMurdock v. Kimberlin, 23* Mo. App. 523; *Stern v. Lanng, 106* La., 738.

the patient or the practitioner, he is on the same footing as the surgeon.

The Criminal Liability of the Physician.—The criminal liability on the part of a physician, for the purposes of this discussion, may be summarized in the following propositions:

(1) Where the practitioner wilfully adopts procedure liable to jeopardize the life or health of the patient.[1]

(2) Where the practitioner wilfully omits to adopt the procedure necessary in safeguarding the life or health of the patient.[2]

(3) Where injury to the patient results from gross ignorance or negligence on the part of the physician.

(4) Where the practitioner is guilty of conduct prohibited by statute.

No application of the above propositions to procedure on the part of the practitioner can be made without due regard to the principle of law that one is presumed to intend the natural, necessary, and probable consequence of his acts.

Gross Ignorance or Negligence.—The liability on the part of the practitioner growing out of gross ignorance or negligence is of serious concern to the anesthetist in view of the occasional deaths which occur during and immediately subsequent to an anesthetization.

It is a monument to the honor of the American medical profession that so few cases have grown out of the liability of the practitioner for death resulting from gross ignorance or negligence in the administration of anesthetics that the law in this country cannot be said to be clearly defined.

In general it may be said that the law presumes that the practitioner has used due care and skill, and accordingly the burden of proof is on him who alleges gross ignorance or negligence.[3] This presumption requires the plaintiff in civil actions to prove his case by a preponderance of evidence and in criminal cases beyond a reasonable doubt.

The few American decisions read in the light of the English law

[1] For a discussion of the question, "Has the Physician Ever the Right to Terminate Life?" see *55 Albany Law J.*, 136; and Haeckel: *"Wonders of Life,"* 1905, 116.

[2] Where the death of a person results from the criminal negligence of the practitioner in the treatment of a case, the latter is guilty of manslaughter: *State v. Reynolds, 42* Kan., 320; *Hyatt v. Adams, 16* Mich., 198; *State v. Gile, 8* Wash., 12. The real question upon which criminal liability depends is whether there was criminal negligence, which is hardly a matter of degree. On the facts constituting criminal negligence, see *State v. Hardister, 38* Ark., 605; *Com. v. Pierce, 138* Mass., 165; *Rex v. Long, 4* C. and P., 398; *Webb's case, 2 Lewin C. C.*, 196; and *Reg. v. Chamberlain, 10* Cox C. C., 486.

[3] *Pettigrew v. Lewis, 25* Pac. R., 458; *Feeney v. Spalding, 80* Me., Ill.; *Peck v. Hutchinson, 55* N. W., 511; *Wohlert v. Siebert, 23* Pa. Super., 214; *Georgia Northern Ry Co. v. Ingram, 40* S. E., 708.

indicate that the courts, in ascertaining the responsibility of the practitioner when death has resulted from the administration of anesthetics, consider three classes of facts, viz.: (1) the necessity of the operation; (2) the competency of the operator; (3) whether the wound or injury would have proved mortal without the operation.

Among the pertinent inquiries which arise in determining gross ignorance or negligence under this classification of facts are the kind and fitness [1] and quality of the anesthetic administered, the method of administration followed, the consent [2] of the patient to its administration, the peculiar condition or temperament of the patient, if necessary and relevant, and the circumstances permitting of their acquirement,[3] skill in the use of instruments, and proper qualifications [4] of and instructions to those in immediate charge of the patient as to the use of medicines,[5] a disregard of which by the practitioner, if found gross, renders him criminally responsible. Hence, it will be seen that criminal malpractice in this respect differs from civil malpractice only in degree. In defining criminal malpractice in a leading case, the Court said:[6]

"Criminal negligence exists where the physician or surgeon, or person assuming to act as such, exhibits gross lack of competency, or gross inattention, or criminal indifference to the patient's safety, and this may arise from his gross ignorance of the science of medicine or surgery and of the effects of the remedies employed, through his gross negligence in the application and selection of remedies and his lack of proper skill in the use of instruments, or through his failure to give proper instructions to the patient as to the use of the medicines."

It is important to mention here that it has been held by the Supreme Court of Vermont that a physician administering an anesthetic is not liable for not protesting against an operation not favored.[7]

Statutory Liability.—To determine the statutory liability on the part of the practitioner, it is necessary to examine the statutes of the several States. As indicated above, they have their origin in the police power of the State. Other than those statutes which prohibit the per-

[1] *Bogle v. Winslow, 5* Phila. Reports, 136.

[2] *Mohr v. Williams, 95* Minn., 261. Actions have been brought in England for alleged anesthetization without consent. In these cases, the patient and anesthetist, who was also the operator, were alone together; but they failed on the grounds that anesthetization by force was impossible and that there was collateral evidence of consent.

For discussion of consent from an English anesthetist's point of view, see J. D. Mortimer: "Anesthesia and Analgesia," 1911, 255.

[3] *Lewis v. Dwinel, 84,* Me., 497; *Logan v. Field, 75* Mo. App., 594.

[4] For qualifications of a trained nurse, see Art. 12, *Public Health Law,* State of New York, 1909.

[5] *Hampton v. State, 50* Fla., 55.

[6] *Hampton v. State, 39* Southern R., 424.

[7] *75* Atl. Rept., 641.

formance of illegal operations [1] and the treatment of a patient by a physician under the influence of intoxicants, with the exception of Ohio, which prohibits the administration of anesthetics except in the presence of a third party who must be a competent witness,[2] none of the States has passed statutes directly affecting the anesthetist. An anesthetic should not be administered without the presence of an assistant or a third person, except in cases of emergency; and, in the absence of a professional assistant, the operator must assume the entire responsibility. If, however, the assistant is duly licensed, the responsibility is assumed by both.

Finally, it may be said that, in the administration of anesthetics, whether by physician, surgeon, dentist, anesthetist, or other professional assistant, the practitioner should at all times exercise the highest degree of caution, for it is not only difficult to determine the proximate cause of death in cases where an anesthetic has been used, but women, particularly young women, are likely to have erotic sensations while under its influence, and thus an added responsibility may be brought to the practitioner in defending his good character and fidelity of purpose.[3]

[1] No one may give an anesthetic for an illegal operation.

[2] "Whoever uses upon another an anesthetic, unless at its administration, and during the whole time the person is wholly or partly under the direct influence of it, there is present a third person competent to be a witness, shall be fined not more than Twenty-five Dollars nor less than Five Dollars" (Laning's "Rev. Stat.," 10685).

[3] Sexual intercourse with a woman while she is *unconscious* has been held to be against the will of the woman and without her consent so as to constitute rape: *Com. v. Burke, 105* Mass., 377; *Com. v. Childs, 2* Pgh., 398; *Lewis v. State, 30* Ala., 54; *Shirwin v. People, 69* Ill., 55. An attempt to administer chloroform to a woman for the purpose of having sexual intercourse with her while she is under its influence is an attempt to rape: *Milton v. State, 24* Texas App., 284.

As to chloroform as a means of facilitating crime, see *Proc. N. Y. Med. Leg. Soc.*, 1872, 298-317; cf. also *Rogers v. State, 33* Ind., 543.

However, in an interesting pamphlet by Stephen Rogers on chloroform (Harper and Bros., New York, 1877), it is argued with much force that for the purposes of attack chloroform cannot be effectively used. See also: *3* Whart. and *St. Med. J.*, 245, 594; and Wharton's "Criminal Law," 1896, *1*, 527. But cf. *Ford v. State, 41* Tex. Crim., 270; *State v. Greene, 2* Ohio Dec., 255; *2 West. L. Month.*, 185.

For cases of conviction for rape committed on a woman under the influence of ether, see *State v. Green, 3* Whart. and *St. Med. J.*, 597; and *Com. v. Beale, ibid.*, 245, 596, 612.

On alleged murder by inhalation of chloroform to sleeping unconscious victim, see Fairchild: *Medico-Legal J., 24,* 19, 34.

For a discussion of the question, "Can Chloroform Be Used by Inhalation to Commit Murder, Robbery or other Crime on an Unconscious Victim," Bell: *Medico-Legal J., 24,* 28.

On "The Medico-Legal Questions Arising in the Case of Patrick," Bell: *Medico-Legal J., 22,* 494, 529.

CHAPTER XX

A LIST OF ANESTHETICS[1]

Including General Anesthetics, Local Anesthetics, and Anesthetic Mixtures, Both Past and Present, With Synonyms

While local anesthetics may be regarded as nothing more than strong hypnotics, so far as possible anesthetics have been carefully discriminated from hypnotics. However, hypnotics employed as adjuvants have been included.

Anesthetic sequences are not included, except in exceptional cases, as, for example, those not referred to elsewhere in the text of this work. Such substances as atropin, phenylacetyl, homatropin, ortho-chlor-cocain, meta-nitro-cocain, vanillin, piperonal, etc., which have little or no pronounced anesthetic action, or whose anesthetic action is obscure, and which have never been employed in practice for the production of anesthesia or whose effects have never been the cause of complaint among workmen in industries, are not considered. While the effects of some of the many dental anesthetics may be due, at least in part, to the results of pressure, yet the authors have adhered to the plan of presenting a full and complete list of these. The preparations termed "eye drops" have been, in general, omitted.

A. C. E. Mixture.—A mixture of A(lcohol), C(hloroform), and E(ther), intended for a safer and quicker anesthetic than either ingredient alone. The theoretical neutralization of the bad effects of the one anesthetic by the good effects of the others and an intensifying of the anesthetic qualities have not been realized in practice.

[1] In the *Am. Drug. and Pharm. Rec.*, Feb. 13 and 27, and Mar. 13, 1911, one of the authors (C. B.) published "A List of Anesthetics"; but a number of omissions occurred in this very brief paper, and the insertions necessitated for completion of the list, together with fuller descriptive matter and bibliographical data, are included here. The plan has been to present a complete list of all anesthetics, both past and present; consequently, by no means all mentioned are in use or on the market. A number of preparations which include anesthetics in their composition are given.

The authors are indebted to a number of manufacturers for information concerning their products; but, wherever possible, the information presented has been taken from the literature. We are especially grateful to Dr. Robert H. Ferguson for helpful suggestions.

Mixtures began with Pitha to be used in 1861 (*Wiener med. Woch.*, 1861, *25* and *26*). In England, George Hartley is said to have used them and to have introduced the alcohol before 1864. He proposed the A. C. E. Mixture, now commonly known, which is often referred to as the L. M. & C. S. (London Med. and Chir. Soc.) Mixture, since this society investigated and recommended it in 1864 (*Med.-Chir. Trans.*, London Med. and Chir. Soc., *47*, 341, 342). As defined by them it consists of:

Alcohol (sp. gr., 0.838),	1 part;
Chloroform (sp. gr., 1.497),	2 parts; and
Ether (sp. gr., 0735),	3 parts.
Mix.	

For other combinations of alcohol, chloroform and ether, see *Martindale's Mixture, Reyné's Anesthetic Mixture, Billroth's Mixture, Nussbaum's Mixture, Richardson's Mixture, Vienna General Hospital Mixture,* and *Vienna Anesthetic.*

Acetaldehyd.—Poggiale found aldehyd to be a prompt and energetic anesthetic, but Simpson stated that it produced irritation and dyspnea.

Francis and Fortescue-Brickdale ("The Chemical Basis of Pharmacology," 1908, 107) state that in acetaldehyd "the anesthetic properties are more marked (than in formaldehyd), and still more pronounced in its polymeric form paraldehyd, which is not so toxic as metaldehyd." See *Paraldehyd.*

Acetic Ether.—See *Ethyl Acetate.*

Acetoform.—Acetoform is a brand name for *acetone-chloroform. Acetoform dusting-powder* consists of acetoform 1 part and boric acid 47 parts. See *Chloretone* and *Methaform.*

Acetone.—Acetone (Dimethylketone; Dimethylketal; Ketopropane; Methylacetyl; Pyroacetic Ether), $CH_3.CO.CH_3$, produces intoxication and sleep; it is, however, less powerful in action than ethyl ether or chloroform, and is less toxic than ethyl alcohol. It possesses anesthetic properties. See *Propion.*

Acetone-Chloroform.—See *Chloretone* and *Methaform.*

Acetylene.—One per cent of acetylene in air is said to produce narcosis with failure of heart and respiration. Lauder Brunton has indicated that the characteristic action of aliphatic hydrocarbons, such as acetylene, ethylene, propylene, butylene, amylene, etc., is on the nerve centers, tending to produce first excitement and then narcosis; they act on the sensory side. On the other hand, the aromatic hydrocarbons (see *Benzene,* e. g.) act mainly on the motor side, producing convulsions and paralysis. On these points, see Francis and Fortescue-Brickdale: "The Chemical Basis of Pharmacology," 1908, 45.

On the toxicology of acetylene, see Rosemann: *Arch. f. exper. Path. u. Pharmakol.,* 1895, *36*; Moissan: *Compt. rend., 121*; Mosso and Ottolengui: *Rend. della R. Accad. dei Lincei,* 1896; and Oliver: *Brit. Med. J.,* 1898, *1.*

Acetylene Dichlorid.—See *Dioform.*

Acetylene Tetrachlorid.—See *Tetrachlorethane.*

Acidum Amidobenzoicum Æthylatum.—See *Anesthesin.*

Acoin or Acoine (Di-para-anisyl-monophenetyl-guanidin hydrochlorid: "Acoine C",

$$C \begin{cases} NH < \_\_\_\_ > OCH_3 . HCl \\ : N < \_\_\_\_ > OC_2H_5 \\ NH < \_\_\_\_ > OCH_3 \end{cases}$$

). A local (dental and ophthalmic) anesthetic, also used in Schleich's infiltration anesthesia.

Acoin is the collective name of the alkyloxy-phenyl-guanidin group of which the hydrochlorid of di-para-anisyl-monophenetyl-guanidin is clinically especially important. Acoine is obtained in the form of a white powder which fuses at 176° F. It is readily soluble in alcohol, and water at 63° F. will dissolve 6 per cent of its weight of acoin. Its solutions are said to be powerful antiseptics and a solution of 0.02 per cent in a nutritive medium will prevent the development of anthrax spores. A 1 per cent solution will not decompose for a long time *if kept in a dark place,* but should be kept in non-soluble glass. Strong solutions of acoin have corrosive properties and consequently are not adapted for subcutaneous or endermal application; a 1 per cent solution or one which is even less concentrated accomplishes anesthesia, and it is said that it can be used without bad results, either immediate or remote.

On the anesthetic properties and applications of acoin, see the following:

Trolldenier: *Therap. Monatsh.,* 1898, No. 1, 36.
Guibert: *Clin. Ophthal.,* 1899, No. 17.
Darier: *Clin. Ophthal.,* 1899, No. 12.
Hirsch: *Archiv f. Augenheil., 42,* No. 3.
Randolph: *Ophthal. Rec.,* Aug., 1899.
Carter: *Lancet,* Oct. 21, 1899.
Braun: Kocher's "Enzyklopädie der Chir.," 1900.
Trolldenier: *Z. f. Thiermedicin,* 1901, 80.
Stasinski: *Therap. der Gegenwart,* 1901, No. 5.
Senn, Schw.: *Vrtljschr. f. Zahnheil., 10,* No. 4.
Etievant: *La Provence Méd.,* Lyon, July 14, 1900.
Nipperdey: *Deut. Monatschr. f. Zahnheil.,* Nov. 20, 1902.
Spindler: *Wratsch. Gaz.,* 1902, No. 14.
Daconto: *Deut. Z. f. Chir., 69,* 457.
Bab: *Wiener Zahnärztl. Monatsh.,* 1902.

On acoin in combination with cocain ("Acoincocain") as a local anesthetic, see:

Darier: "Leçons de thérapeutique oculaire," Paris, 1902.
Kraus: *Münch. med. Woch.*, 1903, 1459.

On acoin for purposes of dental surgery, see:
Bab: *Jour. f. Zahnheilkunde,* 1903, No. 1.
Simon: *Dental Cosmos,* Jan., 1904.
Krakowski: *Subowpatschebny Wjestnik,* 1901, No. 8.

Acoincocain.—See *Acoin.*

Acoin Oil.—This is a one per cent solution of acoin base in peanut oil and is used principally in eye diseases.

Acoinöl.—This does not contain acoin hydrochlorid, but 1 per cent of acoin base.

Adralgin.—An anesthetic for dental and surgical practice containing thymol, cocain, and adrenalin (epinephrin) in physiological salt solution. This preparation is marketed by a Swiss firm in ampules.

Adralgin Chirurgicum.—This contains in 2 c. c. 0.015 gm. thymol-cocain compound and 0.0001 gm. adrenalin.

Adralgin Dentale.—This contains 0.01 thymol-cocain compound and 0.000051 gm. adrenalin.

Adrenalin and Cocain Tablets.—Each hypodermic tablet contains cocain hydrochlorid 0.01 gm. (1/6 grain) and adrenalin, as borate, 0.0002 gm. (1/300 grain).

Esch (*Arch. f. exp. Path. u. Pharm., 64,* 84) reported that the addition of adrenalin to novocain, alypin, and especially cocain intensified their local narcotic action.

Adrenalin-Kokain-Tabletten.—These small cylindrical tablets contain 0.0002 gm. adrenalin and 0.01 gm. cocain hydrochlorid; they are used in dentistry.

Adricain.—This is a dental anesthetic tablet containing adrin 1/100 gr. and cocain hydrochlorid 1/10 gr., marketed by a Philadelphia firm.

Adrin and Cocain Tablets.—Tablets of epinephrin and cocain. (For dental practice.) Each tablet contains adrin, 0.00065 gm. (1/100 gr.) and cocain hydrochlorid, 0.016 gm. (¼ gr.).

Æther Anæstheticus Aranii.—In the chlorination of ethyl chlorid isomers are obtained, and these are also produced in the manufacture of chloral. A variable mixture of the middle members of the series is Liquor Anæstheticus. Another similar mixture, containing the less chlorinated bodies, is the Æther Anæstheticus Aranii, which boils between + 64° and + 100° C. The composition of Aran's ether has been given as $\begin{matrix} CCl_3 \\ CHCl_2 \end{matrix}$ (sp. gr., 1.55—1.60; b. p., + 130° *circa*); but its composition is very variable and it has been considered unsafe as an anesthetic. It is not used at present. See Lyman's "Artificial Anæsthesia and Anesthetics," 204.

Æther Anæstheticus König.—A local anesthetic composed of alcohol-free ether, 1 part, with 4 parts of rhigolene or petroleum ether.

Æther Anæstheticus Wiggers.—This anesthetic contains the more highly chlorinated products referred to under Æther Anæstheticus Aranii, and boils between + 100° and + 140° C. See *Ethyl Chlorid Polychlorated.*

Æther Chloratus.—See *Ethyl Chlorid.*

Ætho-Methyl.—A mixture of ethyl and methyl chlorids, prepared by a Mayence firm. See *Pharm. Ztg., 47,* 916.

Æthoxycaffein.—Used with sodium salicylate (Ceola). Æthoxycaffeine ($C_8H_9.OC_2H_5.N_4O_2$) is obtained by heating monobrom-caffein with an excess of alcoholic potassium hydroxid. It forms white or colorless crystals, melting at + 140° C., and soluble in hot alcohol and in ethyl ether. The solubility is increased by sodium salicylate.

Æthylenum Chloratum.—See *Ethylene Chlorid.*

Æthylium Amidobenzoicum.—An anesthetic.

Æthylium Aminobenzoicum.—See *Anesthesin.*

Æthyloform.—A mixture of ethyl bromid, ethyl chlorid, and methyl chlorid.

Air.—In 1867 an American dentist advertised that he "now takes teeth out painlessly by merely causing the patient to inhale the constituents of the atmosphere—oxygen and hydrogen (!)—chemically combined." (*Chem. News, 16,* 26.) Nitrous oxid was undoubtedly referred to.

Alcohol Phenicum.—See *Carbolic Acid.*

Alcool Trichloramidoethylique.—See *Chloralformamid.*

Allocain.—This is a mixture of novocain and alypin (*q. v.*), recommended, in combination with synthetic suprarenin and thymol, as a local anesthetic in tooth extraction by Proskauer (*Z. Zahnheilk.,* 1911, No. 17).

Flury (*Z. angew. Chem., 26,* No. 35, 242) describes allocain as a mixture of novocain, alypin and adrenalin.

Alvatunder.—A local anesthetic said to contain 1 gm. cocain hydrochlorid, 3 drops of liquid phenol, 3 drops of decolorized tincture of iodin, 10 gm. glycerin, and water to 100 gm.

Alypin.—Alypin is 2-benzoxy-2-dimethyl-amino-methyl-1-dimethyl-amino-butane hydrochlorid, $CH_3.CH_2.C(C_6H_5COO)(CH_2N(CH_3)_2).CH_2N(CH_3)_2.HCl = C_{16}H_{26}O_2N_2.HCl$. It is closely related to Stovain (*q. v.*).

By the action of dichloracetone, $CH_2Cl.CO.CH_2Cl$, on ethyl-magnesium bromid dissolved in ether and decomposition by water of the magnesium compound formed, ethyl-dichlorhydrin, $CH_2Cl.C(C_2H_5)(OH.)CH_2Cl$, is obtained. From this, by the action of dimethylamin, ethyl-tetramethyl-diamino-propanol is produced. This product is treated with benzoyl chlorid and the benzoyl-ethyl-tetramethyl-diamino-propanol is neutralized with hydrochloric acid to form the chlorid.

Alypin is a white crystalline powder, melting at + 169° C. (336.2° F.), hygroscopic and extremely soluble in water. Its solutions are neutral and are not rendered turbid on addition of sodium bicarbonate in moderate quantities, and may be sterilized by boiling for a period not exceeding five minutes, without decomposition. It is easily soluble in alcohol. It has a markedly bitter taste.

It should be protected from the air in well-stoppered containers. Two and four per cent solutions are quite stable, but weaker solutions are likely to become mouldy.

Addition of potassium iodid test solution to the aqueous solution (1-100) produces a white precipitate; potassium dichromate test solution produces a yellow crystalline precipitate soluble in hydrochloric acid; potassium permanganate test solution produces a violet crystalline precipitate, which turns brown on standing. If 0.1 gm. alypin be mixed with 1 c. c. sulphuric acid and warmed to + 100° C. (212° F.) for five minutes and then 2 c. c. water carefully added, the odor of benzoic-ethyl-ester is developed; on cooling, crystals separate out, which are dissolved on adding 2 c. c. alcohol. If alypin is dried at + 100° C. (212° F.), the loss should not exceed 1.5 per cent.

Actions and Uses.—It is a local anesthetic, claimed to be equal to cocain, but not a mydriatic; it is said not to produce disturbance of accommodation and to be less toxic than cocain. It has been highly recommended in ophthalmic practice, and is said to be safe and efficient in nose, throat, and ear work, general surgery (spinal analgesia, infiltration anesthesia), and dentistry. Internally it acts as a sedative. With regard to the manner of use, the strengths of solutions employed are about the same as those of cocain. Sterilization may be effected by boiling the required amount of water for ten minutes in a small flask or test-tube stoppered with cotton; alypin is then added and the boiling continued over a small flame for another minute. The solutions should be freshly prepared. Alypin is compatible with alkaline solutions and with suprarenal preparations. According to Schleich, the addition of alypin to cocain in infiltration anesthesia permits of larger quantities of fluid being used, the solutions proposed by him being as follows: (1) Cocain, 0.1; alypin, 0.1; sodium chlorid, 0.2; and distilled water, 100. (2) Cocain, 0.05; alypin, 0.05; sodium chlorid, 0.2; distilled water, 100. (3) Cocain, 0.01; alypin, 0.01; sodium chlorid, 0.2; distilled water, 100.

DOSAGE.—Externally in the form of a 10 per cent. solution; hypodermically in 1 to 4 per cent solutions; for the eye in 1 to 2 per cent solutions. As much as 5 c. c. of a 3 per cent solution was well tolerated in one case.

Alypin Tablets, 3 1/3 grains. Each tablet contains 0.22 gm. (3 1/3 grains) of alypin.

Alypin Tablets, 1⅛ grains. Each tablet contains 0.073 gm. (1⅛ grains) of alypin.

Alypin Tablets, ¾ grain. Each tablet contains 0.048 gm. (¾ grain) of alypin.

Alypin Tablets, 1/3 grain. Each tablet contains 0.022 gm. (1/3 grain) of alypin.

For further particulars concerning alypin, which has been widely tested therapeutically, consult the following literature, chronologically arranged:

Impens: *Deut. med. Woch.,* 1905, 1154.
Seifert: *Ibid.,* 1905, No. 34.
Stotzer: *Ibid.,* 1905, No. 36.
von Kraus: *Ibid.,* 1905, No. 49, 1966.
Peckert: *Deut. Zahnärztliche Woch.,* 1905, No. 43, 721.
Braun: *Deut. med. Woch.,* 1905, No. 42, 1669.
Jakobsohn: *Woch. f. Therapie und Hygiene des Auges,* 1905, No. 52.
Gebb: *Aerztl. Rundsch.,* 1905, No. 39.
Geth: *Dissert. Giessen,* 1905.
Seeligsohn: *Deut. med. Woch.,* 1905, No. 35.
Stephenson: *Ophthalmoscope,* Nov., 1905.
von Sicherer: *Ophthal. Klinik,* 1905, No. 16.
Neustätter: *Münch. med. Woch.,* 1905, No. 42, 2015.
Ohm: *Woch. f. Therapie und Hygiene des Auges,* 1905, No. 6, 41.
Köllner: *Berl. klin. Woch.,* 1905, No. 43.
Landolt: *Woch. f. Therapie und Hygiene des Auges, 9,* No. 16, 122.
Kauffmann: *Aerztl. Rundsc.,* 1906, No. 9, 97.
Steindorff: "Sammelreferat und eigene Beobachtungen," 1906.
Sendral: *Revue de Thérap.,* 1906, No. 9, 297.
Massi: *Boll. del Osped. oftalmico di Roma,* 1906, No. 1.
Kirchner: *Ophthalmol. Klinik,* 1906, No. 7.
Kraus: *Münch. med. Woch.,* 1906, No. 29, 1443.
Truc: *Revue Générale d'Ophthalmol.,* Mar. 31, 1906.
Darier: *Clin. Ophthal.,* 1906, No. 4.
Kuoli: *Westnik oftalmologie,* 1906, No. 6; *Petersburger med. Woch.,* 1906, Revue No. 8, 25.
Weil: *Allg. med. Centr.-Ztg.,* 1905, No. 36.
Haass: *Woch. f. Therapie und Hygiene des Auges,* 1906, No. 50.
Zimmermann: *Klin. Monats. f. Augenheilk.,* 1906, No. 9.
Wibo: *J. Méd. de Bruxelles,* 1906, No. 4.

Koll: *Z. f. ärztliche Fortbildung,* 1906, No. 6.
Castresana: *Siglo médico,* May 16, 1906.
Cohen: *J. Am. Med. Assn.,* July 28, 1906.
Fischer: *Gyógyászat,* 1906, No. 7.
Baumgarten: *Wien. klin. Rundsc.,* 1906, No. 36, 676.
Finder: *Berl. klin. Woch.,* 1906, No. 5, 130.
Sternberg: *Aerztl. Rundsc.,* 1905, No. 38.
Katz: *Deut. med. Woch.,* 1906, No. 36.
Joubeline: *Russkij Wratsch.,* December 31, 1905; *Revue de Thérap.,* 1906, No. 4, 131.
Ruprecht: *Monatssch. f. Ohrenheil.,* 1906, No. 6.
Dold: *Korrespond. des württemberg. ärztl. Landesvereins,* 1906, No. 26.
Anten: *Scapel,* 1906, No. 50.
Venus: *Wiener klin. Rundsc.,* 1906, No. 51.
Raoult-Pillement: *Archiv Internat. de Laryng.,* Sept., 1906.
Freudenthal: *Critic and Guide,* May-June, 1906.
Borszeky: *Orvosi Hetilap,* 1906, No. 25.
Gilles: *Zahnärztl. Rundsc.,* 1906, Nos. 22 and 23.
Phillips: *Laryngoscope,* July, 1906.
Dehogues: *L'Odontologie,* 1906, No. 5.
Lohnstein: *Deut. med. Woch.,* 1906, No. 13, 504.
Chevallier: *Münch. med. Woch.,* 1906, No. 14, 683; *Klin.-therap. Woch.,* 1906, No. 12, 282.
Mahler: *Deut. zahnärztl. Woch.,* 1906, No. 127.
Tauszk: *Wiener med. Ztg.,* 1906, No. 12.
Cooper: *Denver Med. Times,* Nov., 1906.
Wanietschek: *Prager med. Woch.,* 1906, No. 50; *Allg. med. Centr.-Ztg.,* 1907, No. 38, 582.
Laufer: *Reichs-Medizinal-Anzeiger,* 1907, No. 17.
Borbely: *Pester med.-chir. Presse,* 1907, No. 31.
Shulebin: *Mitteil. der militär-med. Akad.,* St. Petersburg, 1907, 176.
Bürkner: *Berl. klin. Woch.,* 1907, 389.
Ruprecht: *Monats. f. Ohrenheil.,* 1907, No. 6.
Spira: *Die Heilkunde,* 1907, No. 9.
Kurzwelly: *Beitr. z. klin. Chir.,* 1907, No. 3.
Meyer: *N. Y. Med. J.,* Apr. 27, 1907.
Dittmer: *Monatsh. f. praktische Tierheilk.,* 1907, No. 5.
Frank: *Am. J. Ophthal.,* Nov., 1907.
DuFour: *Va. Med. Semi-Month.,* Jan. 24, 1908.
Lewis: *J. Am. Med. Assn.,* May 9, 1908.
Bremerman: *Surg. Gynec. and Obstet.,* Nov., 1908.
Winslow: *Hosp. Bull. of Univ. Md.,* Jan. 15, 1908.

Gwathmey: *Va. Med. Semi-Month.*, Nov. 13, 1908.
Zaun: *Milwaukee Med. J.*, June, 1909.
Green: *Brit. Med. J.*, July 24, 1909.
Lokey: *Atlanta J.-Rec. of Med.*, July, 1909.
Littlejohn: *Yale Med. J.*, Oct.-Nov., 1909.
Knight: "Diseases of the Nose, Throat, and Ear," 2nd ed., 1909.
Keyes: "Diseases of the Genito-Urinary Organs," 1910.
Senator: *Münch. med. Woch.*, 1910, No. 10, 524.
Bruck: *Merck's Reports*, 1909, 169.
Hamm: *Deut. med. Woch.*, 1910, No. 25, 1198.
Bubenhofer: *Münch. med. Woch.*, 1909, No. 42.
Fleissig: *Med. Klinik*, 1910, No. 5.
Eisert: *Zahnärztl. Rundsc.*, 1910, No. 30.
Peters: *Deut. zahnärzt. Woch.*, 1910, No. 10.
Fischer: *Deut. med. Woch.*, 1910, No. 38, 1759.
Barringer: *Fol. urolog.*, Mar., 1910.
Goldschmidt: *Münch. med. Woch.*, 1910, No. 43, 2241.
Voigt: *Berl. klin. Woch.*, 1910, No. 46, 2113.
Garasch: *Wratsch*, 1911, No. 32.
Ritter: *Med. Klinik*, 1912, 1236.
Ruprecht: *Monatsh. f. Ohrenheilkunde u. Laryngo-Rhinologie*, 1911, No. 2.

Alypin-Gleitmittel.—Tragacanth, 13 gm.; glycerin, 36 gm.; mercury oxycyanid, 1 gm.; distilled water, 370 gm.; and alypin, 21 gm. Used for anesthetization of the urethra by means of Utzmann's unguent injector.

Alypin Nitrate.—Alypin (*q. v.*) is incompatible with silver nitrate; it is therefore not well adapted for anesthetizing mucous membranes to which silver nitrate is afterward to be applied, since it may to some extent neutralize the effect of the latter through chemical decomposition. Alypin nitrate is said to overcome this difficulty, and it is therefore recommended in such cases. Its chemical characters, solubility, and strength of solutions are said to correspond essentially to those of alypin. It is a white powder, fusing at + 159° C., and soluble in water, chloroform, and alcohol.

Alypinoids.—Tablets containing alypin and suprarenin, for use in dentistry.

Alypin-Tabletten.—0.02-0.2 gm. alypin, with or without suprarenin borate. See *Dolonephran*.

American Painless Dentists' Anesthetic.—This dental anesthetic is said to contain nitroglycerin, cocain hydrochlorid, morphin hydrochlorid, listerin, and water.

Amidin.—See *Holocain Hydrochlorid*.

Aminobenzoic Acid Ethyl Ester (Para-).—See *Anesthesin.*

Aminobenzoic Acid Isobutyl Ester.—See *Cycloform.*

Aminobenzoyldiethylaminoethanolum Hydrochloricum (Para-).—See *Novocain.*

Aminocinnamic Acid Alkamine Esters.—These are stated (Meister Lucius and Brüning: *German Patent* 187,593) to have several times the local anesthetic power of those of aminobenzoic acid.

Aminocinnamic ethyl ester is said to have met with little success commercially.

Ampules Solution Atoxyl, 10 per cent, with Novocain, 1 per cent (*Sterilized*).—Each 100 c. c. contain: atoxyl, 10 gm., and novocain, 1 gm. (each fluid ounce contains: atoxyl, 48 gm., and novocain, 4 8/10 gm., dissolved in distilled water.

Amydricain.—A local anesthetic.

Amyl Chlorid.—Richardson (*Sci. Am. Suppl.,* No. 515, 8227) gave the physiological properties of this compound as follows: Odor of vapor slightly pungent. Quantity of fluid required for complete anesthesia, 6 to 8 fluid drachms. Required charge of air, 10 per cent. Action slow, with very slight rigidity in second stage. Anesthesia extremely profound and prolonged. Animal temperature much reduced. Recovery rapid when it commences. Vomiting frequent. The great peculiarity in the action of amyl chlorid is in the reduction of animal temperature. In one instance recorded by Richardson, in a rabbit, the temperature fell from + 103° F. to + 82° F., yet perfect recovery, in warm air, followed. According to the same authority, the anesthesia is too slow and profound for ordinary practice, but might be valuable for reduction of high febrile temperatures. After death, cardiac action is long persistent; the blood is fluid, but of natural color on both sides. The red corpuscles are shrunken and elongated, with truncated ends, some stellate. The brain is left bloodless and of purest white.

Amyl chlorid was introduced by B. W. Richardson in 1869.

Amyl Hydrid.—This compound, introduced as an anesthetic by J. Bigelow and B. W. Richardson in 1867, has, according to the latter (*Sci. Am. Suppl.,* No. 515, 8227), the following physiological properties: Vapor odorless and free from pungency. Quantity of fluid required, 6 to 12 fluid drachms for complete anesthesia. Required charge of air by vapor, 40 per cent. Anesthesia is very rapid, being profound in two minutes, with a short period of spasmodic movements. Recovery is very rapid, without vomiting, and the temperature of the body is unchanged. According to Richardson, the anesthetic action is extremely rapid, but dangerous, probably from the insolubility of the vapor in the blood. The heart is easily paralyzed, but irritability of the voluntary muscles is long retained.

See *Hydramyl* and *Pentene.*

On death from the inhalation of a mixture of ether and amyl hydrid, see Hardie, *Lancet,* April, 1875.

Amyl Nitrite (Isoamyl Nitrite).—Amyl nitrite was first brought into notice by Guthrie in 1859, and was made the subject of investigation by Richardson in 1863-5 and 1870; by Rutherford, Gamage, and Brunton in 1869; by Wood in 1871, by Landendorf in 1874, by Bourneville in 1875, and at various times by a number of other investigators.

Richardson states that amyl nitrite is absorbed by the bodies of animals, however introduced. The effects of the compound are most conspicuous upon the motor apparatus of the body, especially upon the vascular motor apparatus. Its effects upon the power of sensation are not as early apparent; hence it is often considered to be devoid of anesthetic properties. Consciousness, however, may disappear before death from its use.

Brunton believed that amyl nitrite diminished the blood pressure by a local effect upon the walls of the smaller arteries. Wood demonstrated that amyl nitrite diminished motor energy and reflex excitability.

Amyl nitrite is well known for its supposed efficacy as an antidote to chloroform in cases of impending death during the inhalation of the vapor of the anesthetic. A mixture of amyl nitrite and chloroform has been experimented with, in the hope of thus procuring a greater degree of safety than with chloroform alone (see *Med. Rec.,* Oct. 5, 1878). See *Chloramyl.*

Amylene (Beta-isoamylene; trimethylethylene; valerene; pentene).—This highly inflammable compound was proposed as an anesthetic by John Snow in 1856; it has been used as a dental anesthetic, but great caution is necessary. See *Trimethylethylene* and *Pental.*

Amylene was found to produce a loss of sensibility without causing complete coma or stupor. Although Snow introduced it as a substitute for chloroform, it was found not to be so safe an agent. See *Med. Times and Gaz.,* Apr. 4, 1857, 332; Apr. 18, 1857, 381; and Aug. 8, 1857, 133. The French Academy of Medicine formally condemned amylene as a dangerous anesthetic soon after its introduction.

Richardson (*Sci. Am. Suppl.,* No. 515, 8227) stated that the "odor of its vapor, like wood spirit, was not pungent. Quantity of fluid required for complete anesthesia, 4 to 8 fluid drachms. Required charge of air by vapor, 15 per cent. Anesthesia rapidly produced, with short but sharp second or spasmodic stage. Consciousness sometimes apparently retained during insensibility, as in somnambulism. Recovery rapid, with freedom generally from all after-effect. Vomiting extremely rare." Richardson stated, however, that the anesthetic value of amylene was doubtful. It caused two deaths in 238 administrations between Nov., 1856, and July, 1857. "Sudden failure of cardiac motion is the source of danger from amylene."

It may be mentioned here that Mering introduced amylene hydrate as a hypnotic in 1887.

On amylene anesthesia, see also Livon: *Compt. rend. Soc. de Biol.,* 1903, *55,* 143.

Amylenechloral.—This alcoholate, formed by the combination of chloral and amylene hydrate, is Di-methyl-ethyl-carbinol-chloral,

$$CCl_3.CH.OH.O.C(CH_3)_2.C_2H_5.$$

It is colorless and possesses a density of 1.24; its odor is camphor-like and the taste is slightly caustic. It is insoluble in cold water, but is miscible to any desired extent with alcohol, ethyl ether, acetone, and fatty oils.

Fuchs and Koch (*Münch. med. Woch.,* 1898, No. 37, 1175) investigated the properties of amylenechloral, finding it to be productive of certain sleep, deeper than that induced by chloral hydrate, when administered subcutaneously or per os in dogs. It appeared to be equivalent to other hypnotics, such as paraldehyd, amylene hydrate, etc., and for this reason is included here.

Amylocain.—A local anesthetic.

Anemogenol.—A dental anesthetic containing novocain and suprarenin.

Anemorenin.—This preparation consists of 5 c. c. of a 1 per cent solution of suprarenal extract, and another solution containing per c. c. 0.003 gm. of tropacocain hydrochlorid and 0.002 gm. of sodium chlorid. The solutions are mixed before use. Möller describes "anemorenin" as specially adapted for dental purposes. See Möller: *Zahnärztl. Rundschau,* 1902, No. 532, 9353.

Anesthesin.—This local anesthetic, ethyl-para-amido-benzoate, NH_2-$C_6H_4.COOC_2H_5$, was first prepared in 1890 by Ritsert, and was introduced as a substitute for cocain. It is obtained by the reduction of ethyl-para-nitro-benzoate by means of zinc and hydrochloric acid, and forms a fine white crystalline powder melting at + 90-91° C., and is easily pulverized. It is almost insoluble in cold water, difficultly soluble in hot water, but readily soluble in ethyl ether, alcohol, benzene, and fatty oils. It dissolves in almond oil to the extent of 2 per cent, in olive oil to 3 per cent, and those oleaginous anesthesin solutions are said to be sterilizable without decomposition. Anesthesin is decomposed into para-amido-benzoic acid and alcohol on long-continued boiling with water or on warming it with dilute solutions of the alkalies.

Anesthesin was investigated from a pharmacological standpoint by Kobert and Binz (*Berl. klin. Woch.,* 1902, No. 17). Experiments on animals determined that there was no danger from the use of anesthesin in therapeutic doses. Clinical trials led to the same conclusion. In physiological activity anesthesin is on a parallel with orthoform (*q. v.*); it is said to be equally effective, but free from irritant action and toxicity. It is said to quickly render insensible to painful operations sensitive nerves with which it comes in contact, and to subdue pain with the same certainty as orthoform. The most delicate tissues are said to tolerate anesthesin without the slightest symptom of irritation. The anesthetic action resembles that of cocain, but is purely local; it does not penetrate the mucous membranes. In consequence of its insolubility, anesthesin cannot be used by hypodermic injection. See *Cocainol.*

Some of the extensive literature on anesthesin follows:

von Noorden: "On Ethyl-para-amido-benzoate as a Local Anæsthetic," *Berl. klin. Woch.,* 1902, No. 17.

Dunbar: "Contribution to Local Anæsthesia with Ethyl-para-amido-benzoate," *Deut. med. Woch.,* 1902, Nos. 10, 20, and 22.

Lengemann: "Anæsthesin in the Treatment of Wounds," *Centr. f. Chir.,* 1902, No. 22.

Kassel: "Employment of Anæsthesin," *Therap. Monatsh.,* July, 1902, 386.

Rammstedt: "On the Employment of Anæsthesin Hydrochlorate (Ritsert) for Local Anæsthesia," *Centr. f. Chir.,* 192, No. 38.

Schaeffer-Struckert: "Dr. E. Ritsert's Anæsthesin; Its Employment in Dentistry," *Vort. a. d. Kongr. Zahnärz. in Münch.,* Aug. 5, 1902.

Hartmann: "Employment of Anæsthesin in Surgical Practice," *Therap. der Gegenwart,* Oct., 1902, No. 10.

Spiess: "Anæsthesin, a New Local Anæsthetic, from the Point of View of the Remedial Action of Anæsthesin," *Münch. med. Woch.,* 1902, No. 39, 1611.

Geyer: "Practical Experiences with Cocainol Preparations," *Reichs-Med.-Anz.,* Nov., 1902, No. 23.

Scherer: "A Report on Four Cases Treated with Anæsthesin," *Med. and Surg. Mon.,* Nov., 1902, No. 11.

Glas: "Anæsthesin Treatment in Laryngeal Cavities." Read in the Session of the Vienna Laryngological Society, December 3, 1902, (Ref.: *Wiener klin. Woch.,* Jan., 1903, No. 1.)

Earp: "A Report of Cases in Which Good Results Were Partly or Wholly Due to Anæsthesin," *Cincin. Lancet Clin.,* Dec. 13, 1902; Merck's *Archives,* 1903, 27.

Chevalier: "Anæsthesin," *Rev. d. Therap.,* Dec., 1902, No. 24, 835.

Kennel: "Anæsthesin (Dr. Ritsert), A Therapeutical Trial," *Berl. klin. Woch.,* Dec., 1902, No. 52, 1218.

Pollatschek: "Contribution to the Treatment of Laryngeal Tuberculosis," *Magyar Orvosok Lapja,* Jan., 1903, No. 1.

Henius: "Anæsthesin in the Treatment of Erysipelas," *Therap. d. Gegenwart,* Jan., 1903; Merck's *Archives,* 1903, 99.

Maramaldi: "Anæsthesin," *Giornale inter. delle scienze-medische,* Jan. 31, 1903, No. 2.

Duhot: "Anæsthesin: Its Applications in Urology and Dermo-syphilography," *Ann. d. l. Policlin. Central. de Brux.,* Feb., 1903, No. 2.

Courtade: "Anæsthesin in Rhino-laryngology," *Rev. d. Therap.,* March 1, 1903; *Alle. Wiener med. Zeit.,* March, 1903, No. 12; *Nouveaux remédes,* 1903, No. 4, 73.

Duplan: "Contribution to the Study of Anæsthesin," *Inaugural-Dissertation,* Paris, March 25, 1903.

Lorand: "Contribution to the Pathology and Therapeutics of the 'Pruritus vulvæ' of Diabetes," *La Policlinique, Brüssel,* March 15, 1903.

Kobert: "Anæsthesin as a Dental Anæsthetic," *Pharm. Zeitung,* 1903, No. 41, 413.

Haug: "Anæsthesin in the Treatment of Inflammations of the Aural Passages and for Local Anæsthesia in Paracentesis," *Archiv f. Ohrenheilk.,* 1903, *58,* Nos. 3 and 4, 267.

Lengemann: *Wiener med. Presse,* 1903, 1010.

Hoenigschmied: *Die Heilkunde,* 1904, No. 2.

Imhofer: *Prager med. Woch.,* 1904, Nos. 4 and 5.

Reinburg: *Bull. gén. de thérap.,* Feb. 23, 1904.

Duhot: *Ann. d. l. Policlin. Central. de Brux.,* 1904, No. 2.

Viollet: *Gaz. d. Hôp.,* 1904, Nos. 23 and 25.

Freudenthal: *Med.-Pharm. Critic and Guide,* 1904, No. 3.

Scherer: *Med. and Surg. Mon.,* 1904, No. 5.

Lotheissen: *Wiener klin. Rundsc.,* 1904, No. 44.

Kuhnt: *Deut. med. Woch.,* 1905, No. 34.

Baccarani: *Soc. Med.-chir. di Modena,* Seduta del 7 aprile, 1905;

Baumgarten: *Budapesti Orvosi Ujság,* 1905, No. 13.

Rasp: *Excerpta Medica,* 1905, No. 5.

Finder: *Berl. klin. Woch.,* 1905, No. 8.

Reiss: *Therap. d. Gegenwart,* 1905, No. 10.

Kassel: *Z. für Ohrenheilk.,* 1905, No. 1.

Vohsen: *Berl. klin. Woch.,* 1905, No. 40.

Saxtorph-Stein: *Hospitalstidende,* 1905, No. 34 and 35 (Ref *Deutsche Med.-Zeit.,* 1906, No. 24).

Choronshitzky: *Monats. f. Ohrenheil.,* 1905, No. 1.

Klingmüller: *Deutsche med. Woch.,* 1905, No. 29.

Lublinski: *Berl. klin. Woch.,* 1906, No. 52.

Freund: *Therap. d. Gegenwart,* 1906, No. 6.

Reissner: *Deutsche zahnärtzl. Zeit.,* 1906, No. 123.

Drucker: *Budapesti Orvosi Ujság,* 1907, No. 15.

Avellis: *Münch. med. Woch.,* 1907, No. 11.

Bruhn: *Therap. Neuheiten,* 1908, No. 2.

Hoffman: *Münch. med. Woch.,* 1908, No. 14.

Payr: *Med. Klinik,* 1908, No. 18.

Frese: *Med. Klinik,* 1908, No. 16.

Karabinski: *Aerztlicher Central-Anzeiger,* 1909, No. 17.

Ritter-Bier: Vortrag auf der 38. Verhandlungen der deutschen Gesellschaft für Chirurgie, 13-17 April, 1909. *Allg. med. Central-Ztg.,* 1909, No. 21.

Pinner and Siegert: *Berl. klin. Woch.,* 1909, No. 22.

Fackelmann: *Allg. med. Central-Ztg.,* 1911, No. 3, 32.

Anæsthesin Solubile (Dr. Ritsert).—According to *Pharm.-Ztg., 47,* 460, this is a form of Ritsert's anesthesin marketed by a Frankfort firm.

Anæsthesin Bormelin.—Bormelin containing 10 per cent anesthesin.

Anæsthesinum Solubile.—See *Subcutin.*

Anæsthesinum Sulfophenylicum.—See *Subcutin.*

Anesthol.—A liquid of red color, ethereal odor, and bitter taste, used as a local anesthetic in dental practice in Germany.

Anesthetic Mixture (Reynés).—This consists of chloroform, 2 parts; ether and absolute alcohol, 1 part each. Coblentz: "The Newer Remedies," 4th ed., 12; *Gehe's Codex,* Nov., 1910, 21.

Anæsthetica Tabletten.—A German dental anesthetic for injection into the gums, containing atropin sulphate, 0.0003 gm.; morphin hydrochlorid, 0.005 gm.; cocain hydrochlorid, 0.01 gm.; potassium ortho-oxy-chinolin-sulphonate, 0.0007 gm.; and sodium chlorid, 0.014 gm. One to two tablets are dissolved in 2 to 4 c. c. of water.

Anæstheticum.—A dental anesthetic, said to be a 10 per cent solution of cocain in phenyl acetate.

Anæstheticum (Edison's).—This contains chloral, 30 parts; alcohol, 110 parts; chloroform, 90 parts; camphor, 60 parts; oil of cloves, 59 parts; oil of peppermint, 59 parts; ethyl ether, 50 parts; salicylic acid, 5 parts; amyl nitrite, 3 parts; and morphin sulphate, 2 parts (Coblentz: "The Newer Remedies," 4th ed., 12).

Anæstheticum Bottwini.—A mixture of 3 parts by weight each of menthol and crystalline phenol, with 1 part of cocain hydrochlorid.

Anæstheticum Gray.—See *Gray's Anæstheticum.*

Anæstheticum Witte.—A dental local anesthetic, consisting of a solution of methylbenzoylecgonin hydrochlorid and hydroiodid in solution in sterilized physiological salt solution containing iodin and phenol.

Anæsthin and Anæsthol (Speier).—A mixture of five parts of ethyl chlorid and 1 part of methyl chlorid. Employed as a local anesthetic by spraying. See *Z. angew. Chem.,* 1901, 261.

Anæsthol Katz.—A local anesthetic containing methyl chlorid and ethyl chlorid.

Anæsthol (W. Meyer); **Weidig's Anæsthol; Anesthol.**—Schleich ("Schmerzlose Operationen," II Aufl., Berlin, 1897) endeavored to improve general anesthesia by starting from a physical instead of from a chemical basis. Without ignoring any of the important points in administration, he attempted to adapt the boiling point of the narcotic to the temperature of the body. As is well known, chloroform possesses a boiling point considerably above the body temperature, while ethyl ether boils somewhat below the same. In consequence thereof, Schleich reasoned that chloroform, when administered by inhalation for the production of narcosis, is absorbed by the blood in larger amount than is really necessary for the purpose. Furthermore, since it is eliminated by the organism gradually, it overtaxes all the parenchymatous organs, injuring, as a result thereof, their cells. On the other hand, ether is vaporized so rapidly when inhaled that it will not enter the blood if the alveoli do not first become overfilled with carbon dioxid, producing primary cyanosis and dyspnea. To quote Willy Meyer (*Med. Rec.*, Aug. 15, 1908): "It is with the onset of this cyanotic condition, it seems, that the narcotic effect of the ether begins. Although the elimination of ether almost keeps pace with its absorption, the slight excess that remains in the blood is sufficient to affect the brain and produce unconsciousness. The greatly accelerated rhythm of breathing, which increases the amount of oxygen inhaled, facilitates the elimination of carbon dioxid by the laws of diffusion of gases involved in normal respiration." It follows from this reasoning that the essential condition for the regular elimination of ether in a state of vapor is an absolutely intact lung—one able, if required, to perform an abnormal amount of work.

In view of the preceding, Schleich sought a safer narcotic which would not tax the parenchymatous organs or the lung tissue, and one possessing a boiling point corresponding to the body temperature, in order that the amount eliminated during expiration should be about equal to that absorbed during inspiration. He finally selected a combination of chloroform, ether, and petroleum ether (benzin), the latter being added for the purpose of diminishing the toxic effects of chloroform upon the system. Schleich employed three mixtures (see Schleich: "Anæsthetics").

Notwithstanding the position taken by Dawbarn (*Atlanta Med. Surg. J.*, Sept. and Oct., 1897) and others, it is a fact that in practice mixtures have proved to be safer than ether or chloroform alone (on this point see Meyer: *J. Am. Med. Assn.*, Feb. 28, 1903). English anesthetists have, for instance, experienced great success with A. C. E. mixture (*q. v.*), and it has also been reported from Vienna that Vienna mixture (*q. v.*) possesses great safety. Schleich maintained that such anesthetic mixtures were chemical solutions, not mixtures, possessing a boiling point differing from that of any of the components. Ellis ("Anæsthesia with Mixed Vapors," London, 1866) had earlier found that, when London Medical and Chirurgical Mixture A. (alcohol, 1 part;

chloroform, 2 parts; and ether, 3 parts) was evaporated, during the six or seven minutes required for the evaporation of two grams of the liquid, the vapor of ether, almost exclusively, was given off during the first minute, the vapor of chloroform predominated during the next three minutes, and the evaporation of alcohol occupied the last three minutes.

H. P. Weidig, of Newark, N. J., found, on analyzing Schleich's anesthetic mixtures, that "they contain a permanent nucleus—a chemical combination of chloroform and ether, according to their molecular weight" (Meyer: *J. Am. Med. Assn.,* Feb. 28, 1903). Meyer reports that 43.25 parts of pure chloroform by volume and 56.75 parts of absolute ether by volume, mixed together, "enter into chemical combination" (see "M. S."), forming "a stable molecular solution," which resists fractionation to the last, and which has an evaporating point of its own. According to Weidig (see Meyer, *Loc. cit.*), Schleich's mixtures contain "this fixed molecular solution of chloroform and ether ("M. S.") plus 36 to 53 per cent (in volume) of free ether, plus petrolic ether, the latter most probably not in chemical combination." Meyer therefore concluded that patients subjected to general anesthesia by means of Schleich's mixtures inhale in the beginning of the narcosis ether plus "M. S." plus petrolic ether. After the ether and petrolic ether have evaporated the narcosis continues with "M. S." Meyer considered Schleich's principle of improving general anesthesia on a physical basis to be correct, but was obliged to abandon the use of his mixture, in view of the findings of Meltzer (*N. Y. Med. Rec.,* 1898, 607; Aug. 15, 1908), whose experiments showed that petrolic ether had no narcotizing power and produced paralysis of the respiratory muscles if administered in large amount.

After numerous experiments during 1897 and 1898, Weidig and Meyer tried ethyl chlorid as a substitute for petrolic ether, and found that a mixture of 18 per cent by volume of ethyl chlorid plus 82 per cent by volume of "M. S." possessed a boiling point of + 100.4° F. (+ 38° C.), that 17 per cent by volume of ethyl chlorid plus 83 per cent by volume of "M. S." had a boiling point of + 104° F. (+ 40° C.), and that 16 per cent by volume plus 84 per cent of "M. S." had a boiling point of + 107.6° F. (+ 42° C.). Meyer proposed that only the second mixture be used, namely, that containing 83 per cent by volume of "M. S." plus 17 per cent by volume of ethyl chlorid, and he used this new mixture, which was termed "anesthol" or "anæsthol," for the first time on October 15, 1898, in an interval operation for appendicitis. Meyer has stated (*Med. Rec.,* Aug. 15, 1908) that the combination was trade-marked "anesthol" by the manufacturers much against his will, but it is not patented, and has been marketed also under the name "anæsthol."

Anesthol is a clear, transparent liquid of very agreeable odor, possessing a density of 1.045 and a boiling point of + 104° F. (+ 40° C.). "It is," to quote Meyer, "a chemical combination of ethyl chlorid and M. S., not a mixture; for, on evaporating 1,000 c. c. of anesthol for five hours at a uniform temperature of + 104° F., 22 c. c. (2.2 per cent by volume), with a specific gravity of 1.262, were left. . . . This fact proves that up to the last moment a 'solution of components' discharges, and does not leave a final residual chloroform, . . . as is the case in Schleich's mixtures (Weidig)." Weidig found, upon analysis, that anesthol contains 17 per cent of ethyl chlorid, 35.89 per cent of chloroform, and 47.10 per cent of ether (method of analysis not stated in Meyer's communications). *"Gehe's Codex"* (Nov., 1910, 22) gives the composition of "anæsthol Meyer" as: 17 per cent ethyl chlorid, 31.7 per cent ether, and 51.5 per cent chloroform. In the same place "anesthol" is described as a mixture of chloroform, 43.25; ether, 56.75; and ethyl chlorid, 20.5. Schleich later adopted the combination recommended by Meyer, substituting ethyl chlorid for petrolic ether; he again proposed three different mixtures, which, to quote Meyer, "is not practical."

Meyer (*Med. Rec.,* Aug. 15, 1908) stated that he had used anesthol in his hospital and private work for ten years, and that it was also extensively employed by his colleagues at the German Hospital, New York. Early in the fall of 1899 they introduced the rule of giving a hypodermic of morphin about one hour prior to the administration of the general anesthetic. "We have used the chloroform, ether, and ethyl chlorid mixture in many thousands of cases, . . . and consider it, when preceded by a hypodermic of morphin, the least dangerous of all anesthetics thus far known, especially in the hands of comparatively inexperienced anesthetists, and this not only as regards the safety of the patient while on the operating table, but principally as to the after-effects of the anesthetic (Meyer)."

On anesthol, see the following papers: Meyer: *J. Am. Med. Assn.,* Feb. 28, 1903; Meyer: *Münch. med. Woch.,* 1903, 1221; Katz: *Deut. med. Woch.,* 1903, 431; Förster: *Centr. f. Gynäkol.,* 1903, No. 24; *Klin.-therap. Woch.,* 1903, No. 32; Heger: *Pharm. Post, 42,* 373; see also, *Pharm. Ztg., 48,* 544; Meyer: *Med. Rec.,* Aug. 15, 1908.

Rosenthaler (*Archiv der Pharmazie,* Berlin, 1906, 244, 24) found that chloroform and ethyl ether, both at + 15.2° C., mixed in the proportion of their molecular weights, increased in temperature to + 30.2° C. Mme. and H. Marcelet (*Bull. Sci. Pharmacol.,* Nov., 1912, 676) also referred to the disengagement of heat observed on mixing chloroform and ether, and they investigated the effects on mixing the two liquids in varying proportions, using chloroform which had been carefully freed from alcohol. With a mixture of 25 c. c. of each liquid, the temperature rose from an initial of + 16.55° to + 30.3° C.

Whether the evolution of heat noted upon mixing ether and chloroform is due to solution or reaction, the above mentioned authors did not attempt to explain. With the view of throwing some light upon this question, in so far as it pertained to the contention of Weidig (*loc. cit.*) that 43.25 parts of chloroform and 56.75 parts of absolute ether by volume, mixed together, "enter into chemical combination," Baskerville,[1] assisted by Neidle, made an experimental investigation of the rise of temperature when chloroform and ethyl ether are mixed.

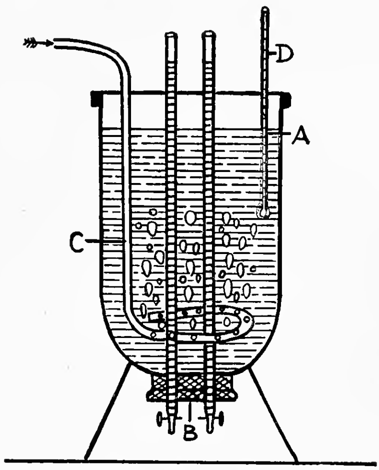


Fig. 280.—Apparatus Used by Baskerville and Neidle. A, an inverted bell-jar; B, a rubber-stopper supporting the bath of water and containing two burettes, one for ether and the other for chloroform; C, an arrangement for agitating the bath by means of compressed air; D, a thermometer.

The ethyl ether used in the experiments performed by Baskerville and Neidle was "anhydrous ether"; but it contained about 0.1 per cent water and 0.8 per cent ethyl alcohol. Such a grade was used because an ether containing minimum quantities of water and alcohol was desired. The chloroform used was "chloroform, U. S. P." (anesthetic chloroform); it contained approximately 1 per cent of 95 per cent ethyl alcohol.

In the first experiments both the chloroform and ether were taken at + 15.2° C., in order to repeat the work of Rosenthaler. The apparatus is shown in Figure 280. As the working temperature was below the room temperature which obtained, this was maintained by adding ice to the water bath. On account of the greater volatility of the ether, in most of the experiments the chloroform was run out from the constant temperature bath first, and then the ether was added to the vessel containing the measured amount of chloroform. A small conical vessel with rather a narrow neck was used for mixing.

Results.—From the results presented in Table I (see p. 707) it will be seen that the maximum rise in temperature is obtained in the case of the molecular mixture.

The investigation of Philip (*Z. physikal. Chem.*, 1897, *24*, 18) on the dielectric properties of this molecular mixture indicated that it might be an individual chemical compound. However, Baskerville and Neidle found that, on boiling, it behaved like a mixture, and not like a compound; that is, it begins boiling, when fractionated, near the

[1] Charles Baskerville: "An Investigation of 'M. S.'"

TABLE I

Per Cent of Chloroform			Temperature of mixture in degrees C.
1. By volume	2. By weight	3. Molecular	
11.1	20.4	13.9	23.7
20.0	34.1	24.4	26.9
33.3	50.9	39.2	30.6
42.8	60.9	49.1	32.5
50.0	67.5	56.3	32.4
55.6	72.2	61.7	31.9
60.0	75.6	65.9	31.4
63.6	78.4	69.3	31.0
66.6	80.6	72.1	30.1
69.2	82.3	74.4	29.5
72.7	84.7	77.5	29.0
80.0	89.2	83.7	26.9
88.9	94.3	91.2	23.7

boiling point of ethyl ether, and gradually rises to the boiling point of chloroform. This indicated that the heat developed when ethyl ether and chloroform are mixed was largely, if not entirely, heat of solution, and that the molecular mixture gave the greatest increase in temperature was accidental. This conclusion, based upon the observations recorded above, is hardly supported by the work of Baskerville and Singer, which indicates that there is a compound of Et_2O and $CHCl_3$ existing in equilibrium with the components of the solution (see Baskerville and Singer, *infra*).

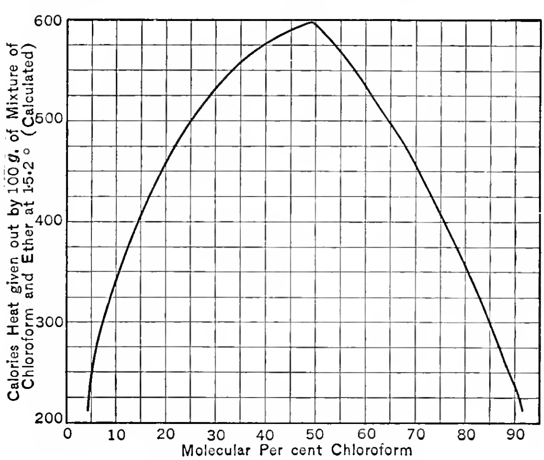


Fig. 281.—Graph Showing the Heat Generated by Mixing Ether and Chloroform.

In Table II are given the calculated heats given out by 100 gm. of the various mixtures, on the assumption that the specific heats are additive. This assumption is justified by the small coefficient of contraction even in the case of maximum contraction. If the heat generated by mixing ether and chloroform were mainly attributable to the formation of a molecular compound, the heat in mixture 4 should be nearly three times that in mixture 1, for three times as much of the compound could be formed. In the graph representing these quantities of heat (Fig. 281), a break is observed at the molecular mixture, which may be explained by the large difference between the specific heats of ether and chloroform.

In Table III are the calculated quantities of heat produced on adding successively increasing quantities of chloroform to 100 gm. of ether.

Georgiewsky (*J. Russ. Phys.-Chem. Soc.*, 1902, *34*, ii, 565) gives the coefficient of contraction between ether and chloroform as 1.4 per cent at temperatures between + 20° and + 22° C. Baskerville and Neidle found the coefficient of contraction at + 30° C. to be 1.5 per cent.

$$\text{Ether} — d\frac{30°}{4°} = 0.70305$$

$$\text{Chloroform} — d\frac{30°}{4°} = 1.4658$$

$$\text{Molecular mixture} — d\frac{30°}{4°} = 1.0514$$

TABLE II

	Molecular per cent chloroform	Calories given out by 100 gm. of mixture
1	13.9	392
2	24.4	494
3	39.2	577
4	49.1	**598**
5	56.3	552
6	61.7	523
7	65.9	492
8	69.3	467
9	72.1	432
10	74.4	407
11	77.5	383
12	83.7	310
13	91.2	213

TABLE III

	Grams of $CHCl_3$ added to 100 gm. of ether	Heat generated in calories
1	25.6	492
2	51.7	750
3	103.7	1175
4	155.8	1529
5	208.6	1704
6	259.7	1881
7	309.8	2016
8	363.0	2162
9	415.5	2227

In the experiments performed by Baskerville and Singer "M. S." was investigated along different lines from those described above, in order to ascertain whether ether and chloroform, mixed in the proportions stated by Meyer (*loc. cit.*), form a "stable molecular solution."

	Density of residual solution at + 23.5° C.
After the evaporation of 50 c.c.	1.0788
" " " " 100 "	1.1010
" " " " 150 "	1.1134
" " " " 200 "	1.1325
" " " " 250 "	1.1469
" " " " 300 "	1.1640
" " " " 350 "	1.1866

The ethyl ether used possessed a density of 0.7113 at + 23.5° C.; the chloroform, a density of 1.4786 at + 23.5° C.; and the "molecular solution," a specific gravity of 1.0645 at +23.5° C. In the preparation of the "molecular solution," upon mixing the ether and chloroform, considerable heat was developed, as noted by Baskerville and Neidle. Five hundred c. c. of this solution were placed in a gas absorption bottle, and a regular current of compressed air, previously purified, was passed through, the current being about the same as that used in the Gwathmey method of vapor anesthesia. The vapors were conducted through a glass worm condenser and a train of Wolff bottles, surrounded by ice, but very little of the evaporated solution could be condensed. The density of the residual solution was then determined after the evaporation, at room temperature, by means of the aforesaid air current, of each 50 c. c. The results obtained from duplicate experiments were as given in the table above.

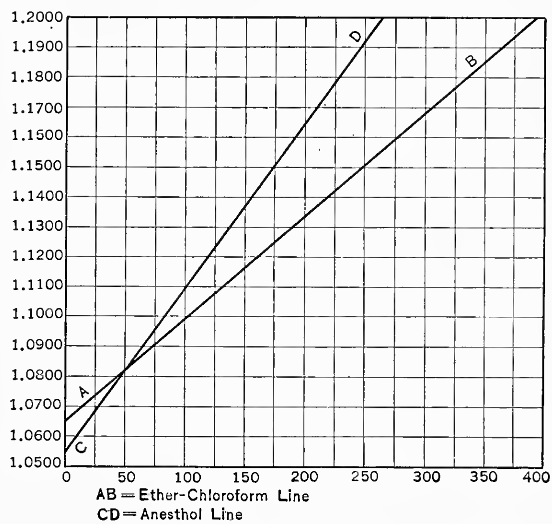


FIG. 282.—GRAPH SHOWING DENSITIES OF RESIDUES.

The remaining 150 c. c. were then removed from the gas absorption bottle, and evaporated down to 25 c. c. This residue possessed a density of 1.3075 at + 23.5° C.

It will be seen from these results that the components of the solution do not come off in order under the described conditions; but the chloroform and ether are evaporated together, although the ether comes off in much greater quantity. The solution itself, of course, is not a chemical compound, but the results indicate that a compound of chloroform and ether exists. As Meyer observed, a "solution of components" is evaporated, and residual chloroform does not remain.

In Figure 282 the results obtained on "M. S." are shown by line A B.

Similar experiments were performed with "Dr. Weidig's Anæsthol," claimed to be a stable "chemical union" of 35.89 per cent chloroform, 17 per cent ethyl chlorid, and 47.10 per cent ethyl ether. The anesthol possessed a density of 1.0538 at + 23.5° C. Using 400 c. c., and operating as in the case of "M. S.," the following results were obtained:

	Density of residual solution at + 23.5° C.
After the evaporation of 50 c .c.	1.0815
" " " " 100 "	1.1076
" " " " 150 "	1.1344
" " " " 200 "	1.1625
" " " " 250 "	1.1913
The last 25 c. c. possessed a density of	1.2590

In Figure 282 the results obtained on anesthol are shown by line C D. In the case of anesthol the lines of distillate and residue are both straight and nearly parallel.

Undoubtedly anesthol contains a compound of chloroform and ether in equilibrium with the components of the solution.

Anæsthyl (Anestyle).—A mixture of 1 part methyl chlorid and 5 parts ethyl chlorid, for the production of anesthesia by freezing in dental operations.

Anæsthyle.—See *Anæsthol* (W. Meyer).

Anæstiform (Oppenheimer).—Cocain hydrochlorid and renaglandin in distilled extract of witch hazel, containing, in addition, the sulphates of sodium and ammonium (Coblentz: "The Newer Remedies," 4th ed., 12). According to Heger (*Pharm. Post.*, *42*, 373), anæstiform is a solution of renaglandin, cocain hydrochlorid, and sodium sulphate in albumin.

Anæzol.—An antiseptic local anesthetic containing, in solution, thymol, menthol, alcohol, benzoic acid, carbolic acid, oils of wintergreen and eucalyptus, glycerin, boric acid, indigo, and 1 per cent cocain.

Analgos (Stephan).—A dental local anesthetic consisting of a mixture of thymol, menthol, phenol, aspirin, and sodium chlorid, each 1 gm. with 0.5 of cocain hydrochlorid, dissolved in 95 gm. of diluted alcohol.

Andolin.—A cocain-free local anesthetic. See Mayer, *Monatsh. f. prakt. Dermatol.*, 1907, *45*, 603. It is said to consist of 0.5 gm. eucain B, 0.75 gm. stovain, 0.008 gm. suprarenin hydrochlorid and physiological salt solution to make 100 gm. Andolin is marketed by a Berlin concern, being sold in sealed tubes containing 2 c. c. for dental practice. See *Pharm. Ztg., 53,* 161.

Anesin or Aneson.—An aqueous solution of 1 per cent acetone-chloroform (see *Chloretone* and *Methaform*); a local anesthetic, and also substitute for cocain in infiltration anesthesia and in Oberst's regionary anesthesia.

On the chemistry of Anesin, see Cohn: *Pharm. Zentralhalle, 40,* 33; and Vamossy: *Apoth.-Ztg., 12,* 608.

On the application of Aneson, see the following contributions:

Vamossy: *Ungar. med. Presse,* 1897, No. 21; *Deut. med. Woch.,* 1897, No. 36.

Sternberg: *Klin.-therapeut. Woch.,* 1898, No. 39, 1398.

Rubinstein: *Med.-Ztg.,* 1898, No. 33.

Hanzel: *Wien. klin. Woch.,* 1898, 1123.

Mosbacher: *Münch. med. Woch.,* 1899, No. 3, 81.

Impens: *Arch. intern. de Pharmacodymie,* 1901, *8,* 77.

Anesthaine.—This is a local anesthetic, "each fluid ounce of which contains 5 gm. of stovain with synergistic antiseptics in a sterile and ready-to-use solution."

Anesthia.—See *Anæsthesin.*

Anesthesin Sulphophenate, or Sulphophenalylate or Sulphocarbolate.—See *Subcutin.*

Anesthol (Meyer).—See *Anæsthol* (W. Meyer).

Anesthol (Weidig).—See *Anæsthol* (W. Meyer).

Anesthone-Creme.—Adrenalin hydrochlorid, 1:20,000; paramido-ethyl benzoate, 10 per cent, with a salve (bland oleaginous) base.

Anesthone-tape.—Gauze which has been treated with a solution of adrenalin hydrochlorid (1:20,000) and 5 per cent of paramido-ethyl benzoate.

Anestile (*Anesthyl*).—A local anesthetic containing methyl chlorid, 1 part, and ethyl chlorid, 5 parts. This preparation, formerly known as anestyle-bengué, is a mixture of ethyl and methyl chlorids. See *Z. angew. Chem.,* 1901, 261.

Anestol.—This is an anesthetic balm intended for local application in neuralgia, headache, etc. It is said to consist essentially of menthol and methylsalicylate in a readily penetrating ointment base.

Anestyle.—See *Anæsthol.*

Anestyle-bengue.—See *Anestile.*

Anodyne.—See *Ethyl Chlorid.*

Anodynone.—This is a trade name for *Ethyl Chlorid* (*q. v.*).

Antemesin.—This is a fanciful designation for capsules containing 1–1.2 grs. of anesthesin (*q. v.*); it is used as an anodyne in gastric ulcer, dyspepsia, etc.

Antidolorin.—A "purified" ethyl chlorid, used as a local as well as an inhalation anesthetic.

Antipyrin (*Dimethyloxyquinizin*).—To quote Heineck ("General and Local Anesthesia," 1900, 79): "Antipyrin is valuable to obtain anesthesia of the urinary bladder. Its anesthetic power is less than that of cocain, but it has the advantage of being less toxic."

Using as a test object one of the lower legs of a frog immersed in 5 c. c. of the solution to be tested, and determining the concentration necessary to produce complete numbness in 30 minutes, Bela von Issekutz (*Arch. ges. Physiol., 145*, 448) found that 2.5 per cent cocain, 3.2 per cent eucain-B, 6 per cent novocain, and 5 per cent antipyrin produced numbness. Employed together, antipyrin increased the action of cocain 46 per cent, of eucain-B 39 per cent, and of novocain 19 per cent.

The employment of antipyrin as a local anesthetic has been discussed in the following reports:

Brick: "De l'action calmante de l'antipyrin chez les prostatiques," *Semaine méd.*, 1894, 128.

Heinze: "Experimentelle Untersuchungen über Infiltrationsanästhesie," *Virchows Archiv*, 1898, 153.

Kocher: (Antipyrin-cocain solutions) "Operationslehre," 4th ed., 202.

Lydston: "Antipyrin as a Local Anæsthetic," *J. of Cutaneous and Genito-urinary Diseases*, May, 1898.

Pousson: "Analgésie vesicale par l'antipyrin," *J. de Méd. de Bordeaux*, May 19, 1895.

Vigneron: "Analgésie vesicale par l'antipyrin," *Ann. des Maladies des Org. génito-urin.*, 1894, 348.

Antivom.—Anesthesin tablets, used in nervous dyspepsia, seasickness, etc., and in chloroform narcosis.

Apinol (*Apinolum*).—Apinol is a product obtained in the destructive distillation of the wood of *pinus palustris* and *pinus australis*. It is claimed to consist mainly of lævomenthon, $C_{10}H_{18}O$.

Apinol is obtained from the products of destructive distillation of pine wood. After the removal of turpentine and other low boiling constituents by distillation, the portion boiling between + 182.2°–193.3° C. (360°–380° F.) is collected and purified.

It is a clear amber-colored oil with an odor resembling that of the pine, having a specific gravity of 0.946 and an approximate boiling point of + 182.2° C. (360° F.). It is neutral in reaction.

Actions and Uses.—Apinol is said to be an antiseptic, local anesthetic, and expectorant.

It is said to be useful when applied externally to wounds, burns, ulcers, and denuded surfaces for the relief of pain and promotion of healing.

Apotheker Maier's Radikal-Anästhetikum.—See *Radikal-Anästhetikum.*

Arabic Acid Salts with Anesthetic Bases.—Erhardt, in German Patent of May 22, 1908, No. 211,800, claims a process for manufacturing salts of arabic acid with anesthetic bases, consisting in acting with pure arabic acid on cocain, tropacocain, stovain, novocain, and analogous compounds.

Erhardt (*Arch. Intern. Pharmacodyn., 21,* 237) stated that the arabinates of cocain produced fewer toxic symptoms than the chlorids. The arabinate anesthesia lasts two to four times longer than that due to chlorids; the mucilaginous elements of the arabinates render the anesthetizing bases less irritant, and, according to Erhardt, a higher grade of anesthesia can be produced than with the chlorids.

Aran's Anæsthetic Ether.—See *Æther Anæstheticus Aranii.*

Arnold's Dental Anodyne or Local Anæsthetic.—Acetic acid is neutralized with ammonium carbonate, and the mixture is saturated with salicylic acid. The whole is then filtered and treated with cocain hydrochlorid (Eng. Pat., 1887, No. 7061).

Barker's Anesthetic.—Arthur E. Barker, of London, recommended the following formula for the anesthetic solution in infiltration anesthesia:

Eucain, 1 part by weight; sodium chlorid, 8 parts by weight; water, 1,000 parts by weight.

Heineck's "General and Local Anæsthetics," 1900, 115.

Benesol.—A local anesthetic used in dental surgery and containing eucain-B, cocain hydrochlorid, phenol, menthol, eucalyptol, and amyl nitrite, in solution in sterilized distilled water. On this local dental anesthetic, see Heger: *Pharm. Post, 42,* 373.

Bengué's Mentholdragées.—These are said to contain menthol and sodium borate, with 0.001 gm. cocain.

Benzcain.—Guaiacol benzoate, or benzyl ester; a local anesthetic.

Benzene (Benzol).—John Snow, in 1848, found that benzene is an indifferent anesthetic with severe after-effects. Simpson (1848) found that benzol is capable of producing anesthesia by inhalation, but "ringing and noises in the head are excessive." It was also tried by T. Nunneley in 1849.

The inhalation of benzol vapor was found to produce narcotic effects, but with some symptoms indicative of a noxious action on the brain and spinal cord (Stone: *Med. Gaz.,* 1848, *41,* 1077). It may be mentioned that liquid benzol is said to act as a narcotic ("Anilin und Anilinfarben," 1864, 13). Richardson (*Sci. Am. Suppl.,* No. 515, Nov. 14, 1885, 8227) reported that benzol vapor is heavy and disagreeable to breathe; that the action is determinate, but slow; and that the anesthetic value is very indifferent, and the after-effects severe and prolonged. Benzene is said to produce slight paresis of the voluntary muscles, but its principal action is on the higher cerebral centers, producing lethargy and somnolence. Later a kind of "intention tremor" occurs in the voluntary muscles. Naphthalene is less toxic than benzene, and pyrrol, furfurane, and thiophene resemble benzene to a certain extent in their physiological action.

On the influence of benzene on the organism, see *Arch. Hygiene,* 1911, *75,* 1-119. "Benzine" is less toxic than benzene. See *Carbon Tetrachlorid.*

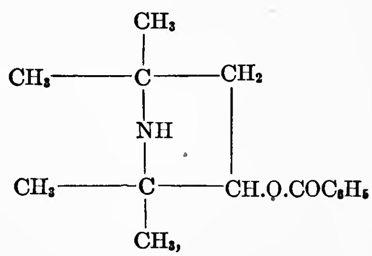
Benzenoform.—See *Carbon Tetrachlorid.*

Benzineroid.—See *Carbon Tetrachlorid.*

Benzinoform.—See *Carbon Tetrachlorid.*

Benzoylaminœthanol.—The hydrochlorid forms long, slightly soluble needles, melting at + 125° C. It possesses anesthetic properties.

Benzoyl-beta-hydroxy-tetramethyl-pyrrolidin.



This has, it is said, a powerful local anesthetic action; it is also said to be less toxic than beta-eucain (Francis and Fortescue-Brickdale: "The Chemical Basis of Pharmacology," 1908, 309).

Benzoyl-ethyl-dimethylaminopropanol-hydrochlorid.—See *Stovain.*

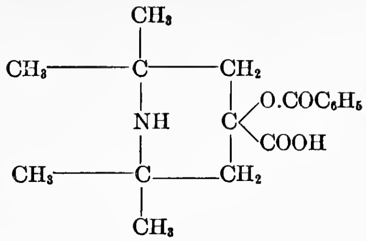
Benzol Peroxid.—This compound, $C_6H_5 — CO.O_2.CO — C_6H_5$, consists of white crystals fusing at + 103.5° C., and freely soluble in alcohol, ether and carbon disulphid, more sparingly in water and fatty oils. It is odorless and keeps well.

Loewenhart (*Therap. Monatsh.,* 1905, No. 8, 426; *Bull. de Pharm du Sud-Est,* 1905, No. 10, 569) recommended benzoyl peroxid as a useful antiseptic. From his observations, when applied locally as a powder and in the form of a solution, it does not produce symptoms of irritation, but causes a mild anesthetic effect.

Benzoylpseudotropein.—See *Tropacocain.*

Benzoyl-triacetone-alkamin-carboxyl.

A local anesthetic, which has not, to our knowledge, been marketed.



Benzoyl-tropein.—A local anesthetic. It is described as a soluble compound in silky needles.

Filehne (*Berl. klin. Woch.*, 1887, 7) found that benzoyl-tropein is a powerful local anesthetic. He also reported that other benzoyl compounds are local anesthetics. According to Filehne, benzoyl methyl triacetonalkamin is the most powerful, benzoyl quinin is next, and benzoyl morphin is the least.

Benzoyl Vinyl Diacetonalkamin.—See *Eucain-B.*

Benzyl-morphin.—See *Peronin.*

Beta-benzoyloxy-beta-3:4-methylenedioxyphenylethyldimethylamin.—This compound is an example of local anesthetic alkamin ester derived from secondary alcohols and containing only two carbon atoms between the acyl and amino groups. It is built on an adrenin skeleton, and is said by Jowett and Pyman (*Proc. of 7th Internat. Cong. of Applied Chem.*, Section IVa, 1) to have very considerable local anesthetic action.

Betacain.—See *Eucain-B.*

Beta-ethyletramethyldiaminoglycerin Benzoyl Monochlorid.—Said to be of value as a local anesthetic.

Beta-eucain.—See *Eucain-B.*

Beta-gamma-dibenzoyloxy-dimethyl-propylamin.—This compound is an example of local anesthetic alkamin ester derived from secondary alcohols and containing only two carbon atoms between the acyl and amino groups. See Jowett and Pyman: *Proc. of the 7th Internat. Cong. of Appl. Chem.*, Section IVa, 1.

Billroth's Mixture A. C. E.—Alcohol, 1 part; chloroform, 3 parts; and ether, 1 part. Mix. See Hewitt: "Anæsthetics and Their Administration," 3rd ed., 467.

According to Buxton (p. 292), Billroth's mixture may be considered an alcohol-chloroform mixture of 20 per cent alcohol. It is said by the same authority to have no advantage over the "1 in 10 mixture." Terrier and Peraire ("Petit manuel d'anesthésie chirurgical," 1894, 179-80) give the following formula: Chloroform, 100 gm.; alcohol, 30 gm.; and ether, 30 gm. "This anesthetic mixture is used in the surgical clinics at Vienna by Billroth, Albert, Mosetig, Moorhof, etc." The formula given by Terrier and Peraire was communicated to Lermoyez, who assisted at many practical anesthesias in Vienna, by Eiselberh, the assistant to Billroth.

Blue Light.—E. C. Titus has reported that blue light possesses anesthetic properties. In his experiments he employed a series of glass rods about 1/8 inch in diameter, placed side by side and tied together to form a flexible mat. The glass used was cobalt blue, so that no red rays would be transmitted. When the glass-rod mat was placed upon the part to be anesthetized, and a tungsten lamp was brought thereover as closely as possible, in about twenty minutes the part became insensitive, so that superficial and even deep incisions were not felt.

Bonain or Bonainsche Mixture.—This consists of equal parts of crystalline menthol, cocain hydrochlorid, and pure carbolic acid, with or without 1 per cent adrenalin.

Boro-chloretone.—A mixture of boric acid, 3 parts, and chloretone, 1 part, used as an antiseptic anesthetic, especially as a dusting powder in painful wounds.

Borsain.—This anesthetic, according to Rabow (*Chem.-Ztg.,* 1912, No. 23, 206), consists of pure carbolic acid, menthol, and cocain hydrochlorid, aa. On its use, see Mource: *La clinique,* 1911, No. 6.

Brandwundenöl.—A colorless and odorless oil with an addition of cocain or eucain.

Braun's Solutions for Anesthesia.—I. Cocain hydrochlorid, 0.1; physiological salt solution, 100.0; 1 per cent suprarenin solution, 5 drops. II. Cocain hydrochlorid, 0.1; physiological salt solution, 50.0; 1 per cent suprarenin solution, 5 drops. III. Cocain hydrochlorid, 0.05; physiological salt solution, 10.0; 1 per cent suprarenin solution, 10 drops. IV. Cocain hydrochlorid, 0.05; physiological salt solution, 5.0; 1 per cent suprarenin solution, 10 drops.

Braun's Suprarenin Tablets.—These contain 0.00013 gm. suprarenin borate, 0.01 gm. cocain hydrochlorid, and 0.009 gm. sodium chlorid. They are used for the production of local anesthesia, particularly in dental surgery.

Brenzcain.—Pyrocatechin-methyl-benzyl ester, or guaiacolbenzyl ester,

$$C_6H_4.\left\langle\begin{matrix}OCH_3\\OCH_2.C_6H_5,\end{matrix}\right.$$

forms colorless crystals, soluble in alcohol, ether, and vasogen, and fusing at + 62° C.

The irritant action of guaiacol on the mucous membranes suggested the desirability of the existence of a preparation which might possess all the advantageous properties of guaiacol without its disadvantages. Brenzcain seemed to satisfy this requirement, and was accordingly used by Marcus for the induction of local anesthesia by means of cataphoresis (*Deut. med. Woch.*, 1897, No. 10; *Bericht über die Verhandlung des Central-Vereins Deutscher Zahnärzte,* 1897, 409).

See *Cocain Hydriodid.*

Brenz (Pyro) **Catechin Methyl-benzyl Ether.**—See *Brenzcain.*

Bromal.—Tribromacetaldehyd hydrated, $CBr_3.CH(OH)_2$, causes irritation of the respiratory passages in animals; larger doses produce dyspnea and cyanosis; still larger doses cause anesthesia, but not hypnosis.

On the anesthetic properties of Bromal, see Steinauer: *Virchow's Archiv f. path. Anat. u. Phys.,* May 19, 1870.

Bromic Ether.—See *Ethyl Bromid.*

Bromoform (Tri-bromo-methane; Formyl tribromid).—When pure this compound is a colorless liquid solidifying at + 8° C. and boiling with slight decomposition under ordinary pressure at + 151° C. It possesses a specific gravity of 2.902 at + 15° C., but with 1 per cent of ethyl alcohol present the density is 2.885 at + 15° C. The ordinary preparation deteriorates rapidly.

Bromoform of the *Deutsches Arzneibuch* V. contains 4 per cent alcohol, and has the density 2.829–2.833. It boils at + 148–150° C., and has a solidification point of + 5–6° C. Feist and Garner (*Arch. Pharm., 249,* 458) made experiments with bromoform carefully purified, and bromoform to which was added 4 per cent ethyl alcohol; they found the density to be 2.6354, the boiling point to be + 146.25° C., and the solidification point to be + 4° C.

As early as 1849 Nunneley and Schuchard proposed bromoform as a general anesthetic. The later experiences of anesthetists have shown, however, that, although bromoform produces a rapid narcosis when inhaled, its use is attended with great danger. On bromoform poisoning, consult Gerson: *Aerztl. Sachverst.-Ztg.,* 1910; *Zentr. f. d. ges. Therap.,* 1910, 447.

Brucin.—Brucin in 5 per cent solution was, at one time, employed as a local anesthetic, but it was abandoned because it did not give uniform results; it was not readily absorbed, and had none of the advantages of cocain. See Heineck: "General and Local Anesthetics," 1900, 78.

On the physiological action of brucin, see Mays: *Therap. Gaz.,* June, 1885. On the employment of a 5 per cent solution of brucin for the production of local anesthesia, see *Therap. Gaz.,* 1886, 173.

Bünte and Moral's Local Anesthetic.—Bünte and Moral (*Deut. Monats. f. Zahnheilk.,* 1910, No. 2) proposed the two following solutions for local anesthesia in dental practice:

	I	II
Novocain..............	1.50................	0.50
Sodium Chlorid	0.92................	0.92
Thymol.................	0.02................	0.02
Distilled water..........ad	100.00................	100.00

Solution I is for adults and solution II for children. One drop of suprarenin (1:1,000) should be added to each c. c. before use.

Butyl-chloral Hydrate (Trichlorbutylidene glycol).—Proposed by Liebreich in 1870 as a remedy for trigeminal neuralgia. In medicinal doses it produces deep sleep with cranial analgesia.

Butyl Chlorid.—This compound was introduced as an anesthetic by B. W. Richardson in 1869. He reported (*Sci. Am. Suppl.,* No. 515, 8227) that its physiological properties are practically identical with those of amyl chlorid (*q. v.*), and that its anesthetic value is practically the same as for amyl chlorid. The committee of the British Medical Association stated that, when butyl chlorid was administered to rabbits, it affected respiration, although not very rapidly.

Butyl Hydrid.—This compound, introduced by B. W. Richardson in 1867, was found by him to have the same physiological properties as amyl hydrid (*q. v.*), but the action was more rapidly developed. As regards its anesthetic value, this was found to be the same as for amyl hydrid, but, being a gas, it was found to be less practical for administration (see Richardson: *Sci. Am. Suppl.,* Nov. 14, 1885, No. 515, 8227).

Calcium Guaiacol Sulphonate.—See *Guaiacyl.*

Camphor Phenylated (Camphora carbolisata; Phenol Camphor).—A local anesthetic, used chiefly in dental practice.

For the physical properties of phenol camphor, consult Lemberger, *Therapie die Gegenwart,* 1906, No. 5; *Przeglad lekarski,* 1906, No. 23; and *Pharm. Ztg.,* 1906, No. 38.

Camphorated Salol.—See *Salol Camphor.*

Canadol.—A very light petroleum ether ("light ligroin") of the specific gravity 0.650–0.700; a local anesthetic used by spraying.

Caprylic Hydrid.—The experiments of Richardson upon animals showed that this compound produced a long period of preliminary excitement, accompanied by vomiting. Anesthesia thus induced was very evanescent.

Carbolic Acid.—Phenol has found use as a local anesthetic. Like creosote, phenol is popularly employed to inhibit toothache; indeed, it seems that all phenols containing at least one free hydroxyl group are anesthetic. However, their use is very limited, owing to their caustic action. Moreover, carbolic acid does not penetrate deeply.

Barwell (*Archiv. Internat. de Laryng.,* 1907, No. 3) described a solution containing carbolic acid, 10 parts by weight; lactic acid, 50 parts by weight; and formaldehyd, 7 parts by weight, for the treatment of tuberculous laryngitis. It was said to have an anesthetic as well as a curative effect.

On carbolic acid as a local anesthetic, consult the following contributions:

Bericht d. K. K. Krankenanstalt Rudolphstiftung in Wien, 1876, 293.

Bill: *Am. J. Med. Sci.,* Oct., 1870.

Caspari: *Z. klin. Med.,* 1883, 537.

Pirri: *Lancet,* Sept. 19, 1867.

Rae: *Am. J. Med. Sci.,* 1870, 573.

Richardson: *Deut. med. Woch.,* 1891, 1161.

Smith: *Med. Rec.,* 1872.

Walser: *Mitteilungen des Vereins der Ärzte Steiermarks,* 1896, No. 4.

Van der Weyde: *Phila. Med. Surg. Rec.,* Aug., 1868.

Carbon Dioxid.—A mixture of limestone and vinegar was used by the Romans as a local anesthetic (Pliny); Hickman proposed, in 1828, that it be used for inhalation (for a full account of Hickman's work, see pp. 5-7); and it was used by Snow in 1848.

B. W. Richardson used carbon dioxid as an anesthetic in 1852, and it had been also tried by Nunneley three years earlier. Richardson (*Sci. Am. Suppl.,* No. 515, 8227) found that air containing 25 per cent of carbon dioxid produced rapid insensibility; that the insensibility was deep, with convulsive action, asphyxia, and reduction of temperature. He pointed out that its anesthetic action had not been investigated fully, but that death probably resulted from asphyxia, with the respiration failing primarily and the muscular irritability becoming rapidly exhausted; the after-effects of recovery were stated to be neither very prolonged nor severe from deep anesthesia. Ozanam used a mixture of 75 parts of carbon dioxid with 25 parts of air in an operation upon a young man for the removal of an abscess.

Malan (*Gazzetta degli espedali e delle cliniche,* 1910, No. 105) used solid carbon dioxid to produce anesthesia by cold; he found the anesthesia sufficient and deeper than that produced by ethyl chlorid. Gottheil (*J. Surg., 22,* 7; *N. Y. Med. J.,* July 3, 1909) used solid carbon dioxid as an anesthetic cauterant. See also:

Serano-Nouell: *Monatsh. f. prakt. Dermatol., 50,* No. 7.

Pusey: *Monatsh. f. prakt. Dermatol., 51,* No. 7.

Macleod: *Brit. Med. J.,* 1910, No. 2561, 254.

Fabry and Zweig: *Münch. med. Woch.,* 1910, No. 13.

Klotz: *Berl. klin. Woch.,* 1910, No. 48.

On the inhalation of a mixture of carbon dioxid and oxygen as an auxiliary to chloroform anesthesia, see Levi: *Rivista critica di clinica medica,* 1910, 465; Crescenzi: *Klin.-therap. Woch.,* 1910, No. 40, 960; Marchetti: *Ibid.,* 961.

Carbon Disulphid.—Although Nunneley introduced carbon disulphid for complete anesthesia in 1849, it has only found employment as a local anesthetic. Simpson found carbon disulphid to be a rapid and powerful anesthetic, but disadvantageous. It was also tried by Harold Thanlow in 1850, B. W. Richardson in 1868, Hermann, Miller, Serre, and others.

On the physiological action of carbon disulphid, see the following:

Delpech: "Mémoire sur les accidents que developpe chez les ouvrières en caoutchouc du sulfure de carbone en vapeur," Paris, 1865. For a discussion of the investigations of Delpech, see *Chem. News,* 1863, 216; Bernhardt: *Ber. klin. Woch.,* 1866, No. 32; Husemann: *Jahresber.,* 1872, 495; Vermorel: "Le sulfure de carbone, ses propriétés, sa fabrication, moyens pratiques de verifier sa purité," Tours, 1886.

Richardson (*Sci. Am. Suppl.,* No. 515, Nov. 14, 1885, 8227) reported that, when perfectly pure, carbon disulphid is of a pleasant ethereal odor, and free from pungency; that the quantity required for anesthesia was 4 to 8 fluid drachms; that the quantity of vapor in air was 10 per cent; that anesthesia was very rapid, being produced in from three to five minutes with a brief spasmodic stage; that recovery was rapid and complete, with few bad effects; and that the reduction of body temperature under deep anesthesia was 2° F. He stated then (1885) that its anesthetic value was yet undetermined, but that from experiments on inferior animals it seemed to be safe. To quote Richardson, "Death in the vapor is gradual, the circulation outliving the respiration. In one animal, a dog, author observed life return, spontaneously, after respiration had ceased for seven minutes."

Workmen in caoutchouc factories, wherein carbon disulphid is employed as a solvent, sometimes develop toxic phenomena, as headache, giddiness, deafness, amaurosis, and occasionally paraplegia. It would seem to be demonstrated that carbon disulphid is a powerful poison, the direct action being narcotic.

It may be mentioned here that the xanthates have a similar action to carbon disulphid, and it is said that a general narcosis can be effected in man by them; this is as one would expect since the xanthates are readily decomposed into alcohol and carbon disulphid.

Carbon Monoxid.—Nunneley proposed carbon monoxid as an anesthetic in 1849. Snow, Herapath, and Richardson experimented with it in 1852. Although dangerous to the human economy, it was used on lower animals by Richardson. He reported that 5 per cent of carbon monoxid in air caused rapid anesthesia, with convulsive action, and a fall of temperature at 2° F. under deep narcotism. The gas is a cumulative poison.

Carbon Tetrachlorid.—A. Sansom and Protheroe Smith (*B. and F. Med. Chir. Rev.,* 1867, 551) introduced "chloro-carbon" for inhalation in 1867; however, it has been but little used for this purpose, although it has been employed as a local anesthetic.

Richardson (*Sci. Am. Suppl.,* No. 515, 8227) stated that the quantity of carbon tetrachlorid required for complete anesthesia was 4 to 8 fluid drachms; that the required change of air by vapor was 5 to 10 per cent; that the anesthesia was very slow and prolonged when induced, and that the convulsive stage was long and acute. He reported that its anesthetic value was indifferent, the action being too slow and the recovery too prolonged; the temperature was found to be reduced 4° F. during deep anesthesia. See, also, Simpson: *Med. Times and Gaz.*, Dec., 1865; *Lancet*, June, 1867.

Carbon tetrachlorid is said to act much more slowly and persistently than chloroform. It is usually stated to be a more powerful heart depressant (Simpson, *loc. cit.*), but Cushny describes it as only half as powerful as chloroform. Marshall found that the differences in action between carbon tetrachlorid and chloroform were mainly due to its physical characteristics. It is, however, more toxic and more irritating to the mucous membrane of the trachea and bronchi. It has been used by hairdressers to clean the hair, and a case of accidental poisoning owing to the inhalation of the vapor is recorded in the *Lancet*, 1907, 1, 1725; this case very nearly had a fatal termination. There is record of a fatal case in Paris.

According to the investigations of Lehmann (*Chem.-Ztg.*, 1906, No. 29, 330), the anesthetic action of benzin (see *Benzene*) is quantitatively greater than that of carbon tetrachlorid.

On the physiological action of carbon tetrachlorid, see the following:

Andrews: *Chicago Med. Exam.*, Dec., 1867.

Bianchini: *Stazione Sperimentale Agraria Italiana*, 1904, 171.

Freyss: *Chem.-Ztg.*, 1903, 1137.

Haller: *Bericht über die Weltausstellung im Paris*, 1900.

Morel: *Compt. rend.*, *1877*, 1460.

Regnauld: *Ibid.*, 1885, 1146.

Schwartz: "Handbuch zur Erkennung, Beurteilung und verhutung der Feuers- und Explosionsgefahr chemisch-technischer Stoffe und Betriebsanlagen," 1902, 284.

Caustica.—A, White: Arsenic acid, 0.001, morphin hydrochlorid, 0.0005; and cocain hydrochlorid, 0.0005. C, Black: Cobalt, 0.003; morphin hydrochlorid, 0.0005; and cocain hydrochlorid, 0.0005. For application in teeth cavities.

C. E. Mixture.—An anesthetic mixture of 2 parts of chloroform and 3 parts of ethyl ether. Schäfer and Scharlieb (*Trans. Roy. Soc. Edinburgh, 41,* ii, No. 12) have shown that C. E. Mixture is based upon the wholly fallacious theory that alcohol in the A. C. E. Mixture is merely a menstruum, and that ethyl ether in the C. E. Mixture exerts a stimulating action on the circulation.

Ceratum Odontalgicum.—This toothache paste is composed of wax, chloral hydrate, camphor, and thymol; it is also known as *dontocerat.*

Chelen or **Chelene.**—A "purified" ethyl chlorid. See *Kelene.*

Chevanne's Local Anesthetic.—The following anesthetic has been proposed by Chevanne for mucous surfaces without cocain: Phenol, 30 gr.; menthol, 30 gr.; quinin hydrochlorid, 24 gr.; and adrenalin, 1/12th gr. See *Pharm. J., 32,* 820. Chevanne states that this solution has no caustic action and that it is better than urea-quinin solution (*Klin.-therap. Woch.,* 1910, No. 50, 1253; *Rev. Hebd. de Laryng.,* 1910, 305).

Chloræthoform.—Chloroform containing 0.25 per cent of ethyl chlorid. See *Chem. and Drug.,* 1904, 1289.

Chloral (Chloral Hydrate).—Forne stated that the administration of chloral hydrate in connection with the inhalation of chloroform produced an effect upon the patient which very closely resembled the effects produced by the combined use of morphin and chloroform. In a discussion of this affirmation before the Chirurgical Society of Paris, Dolbeau and Demarquay insisted upon the dangers attending such a combination. Kappeler made trial of the combination of chloral hydrate with ether; though rather less disagreeable than the association of morphin with ether, there was very little to recommend this mode of inducing anesthesia. On a case of death from the effects of chloral and ether, see Morton and Lewis: *Am. J. Med. Sci.,* Oct., 1876, 415.

This narcotic may produce complete surgical anesthesia. It was used intravenously for a short period in the middle of the last century, and major operations have been performed under its influence. The dosage had, however, to be too high for the complete safety of the patient. Chloral hydrate was found by Delbet and Dupont (*Rev. de Chir.,* June 10, 1910; *Klin.-therap. Woch.,* 1910, 682) to possess advantages over even scopolamin for commencing chloroform anesthesia. They reported on 850 cases of chloroform anesthesia in which chloral hydrate was employed.

On chloral hydrate as a veterinary anesthetic, see Rehse: *Monatsh. f. prakt. Tierheilk., 21,* 413; *Berl. tierärztl. Woch.,* 1911, 77.

Chloral-acetone Chloroform (Chloran).—It has been said that the use of acetone-chloroform (see *Chloretone* and *Methaform*) as a hypnotic and local anesthetic is somewhat limited, owing to its insolubility in water, dilute alcohol, and its burning taste (Coblentz: "The Newer Remedies," 4th ed., 33). It has been found that molecular quantities of chloral hydrate or chloral and acetone-chloroform condense, affording a compound which is said to be soluble to the extent of 1 per cent in cold water, very soluble in weak water-alcohol solutions, and free from burning taste. The combination possesses the following formula:

$$(CH_3)_2C\begin{cases}CCl_3\\O.CH(OH).CCl_3\end{cases}$$

It forms fine feathery needles, melting at + 65° C., and having a camphoraceous odor. It is said to be a prompt hypnotic and to have local anesthetic properties. Chloral-acetone chloroform is manufactured by a Swiss firm.

Chloralamid.—See *Chloralformamid.*

Chloralformamid.—This compound, $CCl_3CH(OH).CONH_2$, also known as "chloralamid" and "formamidated chloral," is said to be an uninjurious hypnotic and analgesic; its action is less harmful than that of chloral, but it has less hypnotic power. Chloralformamid forms lustrous, colorless crystals, melting at + 114–115° C. It is decomposed at higher temperatures and by warm solvents. It slowly dissolves in 20 parts of water, and, at + 25° C., in 1.3 parts of alcohol.

Chloralimid.—Trichlorethylidenimid, $CCl_3.CH{:}NH$, is prepared from chloral-ammonia by means of heat or from hydrated chloral by ammonium acetate. It forms colorless crystals which are tasteless and odorless; it possesses a melting point of + 155° C., and is readily soluble in alcohol, ethyl ether, chloroform, and oils, but is only sparingly soluble in water. Chloralimid is employed both as a hypnotic and an analgesic.

Chloral-menthol (Mentholated Chloral).—This preparation has been used as a local anesthetic in facial and other neuralgias.

Chloral-orthoform.—Amido-oxybenzoic esters combined with chloral have been found to act as local anesthetics and antiseptics.

Chloral-orthoform occurs in yellow crusts, sparingly soluble in water, but readily soluble in warm alcohol and in ethyl ether. When it is warmed with diluted inorganic acids, chloral is produced.

Chloralose.—Chloralose (Alphachloralose; anhydroglucochloral) forms colorless crystals, possessing a bitter, disagreeable taste, and having the composition $C_8H_{11}Cl_3O_6$. It is soluble in alcohol and in 200 parts of water; it melts at + 185° C. Chloralose is known chiefly as a hypnotic, but Kshishkovskii (*Zentr. Physiol., 25,* 8) found that when it was injected intravenously (0.07 per kg.) it produced in ruminants, in 15 to 20 minutes, a deep sleep, which lasted from 5 to 6 hours, with no ill effects. The anesthetic action was especially good in sheep (5 experiments), but not so satisfactory in rabbits and cats (4 experiments). When administered *per os* or *per rectum,* it was found to be less effective.

Chloramyl.—Chloroform, one pound, mixed with 2 drachms of amyl nitrite (*q. v.*).

Chlorbutane.—This compound has been employed for producing total anesthesia. See *Butyl Chlorid.*

Chlorbutanol.—See *Chloretone* and *Methaform.*

Chlorbutol.—A synonym for *Chloretone* (*q. v.*).

Chlorethyl.—See *Ethyl Chlorid.*

Chlorethylidene.—See *Ethylidene Chlorid.*

Chlorethylene Chlorid.—See *Ethylene* (*Monochloro-chlorid*).

Chloreton or **Chloretone** (Acetone chloroform; chlorbutanol; "Aneson"; "Anesin").—This preparation is the tertiary trichlorbutyl alcohol [$HO.C(CH_3)_2CCl_3$], and is used as a local anesthetic and internal hypnotic. It forms white acicular crystals possessing a taste resembling that of camphor. It dissolves sparingly in water, but more freely in alcohol and glycerin. Acetone chloroform was discovered in 1881 by Willgerodt, and its solution (see *Anesin*) is said to produce no local irritation and no toxic symptoms. Because of the insolubility of chloretone in ordinary aqueous liquids or exudates, the local anesthetic effect develops very slowly, and consequently the substance cannot be compared with cocain hydrochlorid for rapidity of action. The manufacturers do not lay any stress whatsoever upon the effect of chloretone as a rapid-acting local anesthetic, but do commend it very highly as a sedative and hypnotic (Kossa, in 1893, found acetone-chloroform to have anesthetic and narcotic properties), and also for its power of preventing the growth of bacteria or fungi. A practical objection to the use of chloretone is that the toxic and therapeutic doses are too nearly alike, but it may be employed in small doses to produce local anesthesia.

See *Anesin;* but on crystalline acetone-chloroform, a 1 per cent water solution of which constitutes anesin, see the following:

Willgerodt: *Ber.,* 1881, 2455; Willgerodt and Gemeser: *J. prakt. Chem.,* (2), *37,* 362.

Houghton and Albrich: *J. Am. Med. Assn.,* 1899, 77

Lyon: *Pharm. J.,* 1901, No. 1609, 521.

Cappelletti: *Riforma medica,* 1901, Nos. 277 and 278.

Wheder: *Lancet,* 1903, No. 4148, 615.

Fawcitt: *Ibid.,* 1903, No. 4149, 687.

Bickle: *Therap. Gaz.,* Oct., 1902.

Wynter: *Lancet,* 1907, No. 4361, 879.

Fiocre: *Presse méd.,* 1907, No. 58, 460.

De Boter: *Rev. Barcelonesa d. enferm. de oido,* 1907, No. 9.

Martinet: *Therap. Monatsh.,* 1908, 115.

Wargnier: *Thèse de Lille,* 1908.

Leyden: *Med. Klinik,* 1910, No. 52.

Friedeberg: *Deut. med. Woch.,* 1910, 9.

Jenny-Berne: *Therapie der Gegenwart,* Aug., 1911, *13,* No. 8.

Welsh: *Lancet,* 1911, No. 4582.

See *Methaform.*

Chloriden.—See *Ethylidene Chlorid.*

Chlorocarbon.—See *Carbon Tetrachlorid.*

Chloroform.—See Chapter VII.

Chloroform-Acetic Acid.—Fournier (*Compt. rend., 53,* 1066) used a mixture of chloroform and glacial acetic acid as a local anesthetic.

Chloroform-Ether-Menthol.—This spray for local anesthesia consists of chloroform, 10 parts; ethyl ether, 15 parts; and menthol, 1 part. The local anesthesia produced thereby is said to last from two to six minutes.

Chloroformium Albuminatum.—See *Chloroformium Gelatinosum.*

Chloroformium Colloidale.—See *Desalgin.*

Chloroformium Gelatinosum.—Prepared from a mixture of equal parts of fresh albumen and chloroform; used for applying chloroform locally.

Chloromethane.—See *Methyl Chlorid.*

Chloryl (Coryl).—A local anesthetic mixture consisting of methyl and ethyl chlorids; it is said to be milder in action than ethyl chlorid. Chloryl has also been used externally.

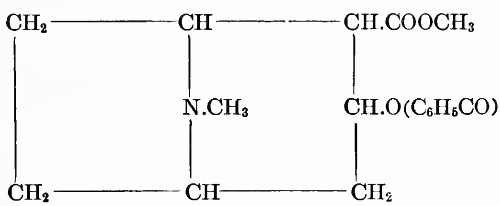
Chloryl Anesthetic.—An "absolute ethyl chlorid" of Scottish manufacture.

Cloran.—See *Chloral-Acetone Choloroform.*

Cocadrenal.—A sterilized solution of adrenalin hydrochlorid and cocain, used as a local anesthetic.

Cocæthylin (Ethyl-benzoylecgonin).—A local anesthetic, like cocain in action, but milder.

Cocain.—The constitution of benzoyl-ecgonin-methyl-ester is expressed by the formula:



It is well known as a producer of local anesthesia (Schraff, 1862), which is by far its most important physiological attribute from a practical standpoint. Not only pain but all sensations are affected; for example, taste is abolished upon the application of cocain to the mucous membrane of the mouth, and heat and cold are not felt. This local anesthetic action appears to be dependent upon the structure of the ecgonin nucleus, and upon the presence and relative positions of the two substituting groups, the alkyl and benzoyl radicals. Of these factors, the presence of the benzoyl group seems to be the most important. The anesthetic property of cocain has been shown to be associated with its functions as an alkalamin ester.

For an investigation of its recommended substitutes, see, among others, Le Brocq: *Pharm. J., 82,* 673; *Brit. Med. J.,* Mar. 27, 1909, 783. On the results of a clinical study of cocain, stovain, tropacocain, novocain, eucain, etc. (*q. v.*), see Piquand and Dreyfus: *J. physiol. path. gén., 12,* 70. On the comparative toxicity and pharmacological action of cocain, stovain, anesthesin, novocain, alypin, and eucain-B, as determined by Chevalier and his students, see *Bull. sci. pharmacolog., 16,* 518; cf. also Šenator: *Münch. med. Woch.,* 1910, No. 10, 524.

On the distinction between cocain and its substitutes, see Scherbatschev: *Apoth.-Ztg., 27,* 441.

For a report of an investigation relating to combinations of cocain with other local anesthetics, see Leo Zorn: *Z. f. exper. Path. u. Therap., 12,* 529.

Cocain-Aluminum Citrate.—This product of a patented process is employed as an astringent and local anesthetic; it is a compound of 1 molecule of aluminum citrate with 1 molecule of cocain.

Cocain and Adrenalin Ointment.—An ointment said to contain cocain hydrochlorid, 2 per cent; solution of adrenalin chlorid, 17 per cent; hydrous wool fat, 25 per cent; white petrolatum sufficient to make 100 per cent. Put up in collapsible tubes for application to the eye.

Cocain Arabinate.—This salt was introduced by Erhardt as a *succedaneum* for the hydrochlorid, especially for lumbar anesthesia. It is said to be absorbed much more slowly and it is reported that its anesthetic effect lasts three times as long as that of the hydrochlorid; moreover it has been recorded that it scarcely disturbs the nervous system.

Cocain-Ethyl (or Methyl) **Chlorid.**—In Eng. Pat. 10,594, 1897, the claim is made for the production of local anesthetics by means of solutions of cocain in liquids boiling below + 30° C.

Cocain Benzoate; Cocain Borate; Cocain Formate.—Employed as local anesthetics. Cocain borate (68.7 per cent cocain) solutions are more permanent than those of the hydrochlorid.

Cocain Hydriodid.—Marcus (*Ber. über Verhandlung Central-Vereins. Deut. Zahnärzte,* 1897, 409) proposed the employment of "cocainæ hydroiodidas" in dental surgery as a substitute for cocain hydrochlorid as a means of producing electro-anesthesia. See, also, Mewes: *Elektrochem. Z.,* 1897, No. 3, 49.

Cocain Hydrobromid; Cocain Hydrochlorid.—Employed as local anesthetics.

Cocain Lactate.—A dental anesthetic. It is a thick, white liquid, soluble in water and alcohol.

Cocain Nitrate; Cocain Oleate.—Employed as local anesthetics. Cocain oleate is a 5, 10, 15, 25, or 50 per cent solution of cocain in oleic acid, soluble in alcohol and oils.

Cocain Phenate (Phenol-Cocain; Cocain Carbolate; Cocain Phenylate).—Veasey (*Med. News,* 1893, 345) states that cocain phenate in a 2 per cent solution in alcohol and water acts excellently as a local anesthetic, while it does not produce the unpleasant secondary effects caused by cocain hydrochlorid. It also possesses an antiseptic action.

Cocainum Phenylicum Merck-Oefele.—A honey-yellow mass of butter-like consistency with crystals distributed throughout; it is insoluble in water, and is slightly soluble in alcohol and ether. It possesses the composition $C_{17}H_{21}NO_4.C_6H_5OH$. It is used as a local anesthetic in dental operations.

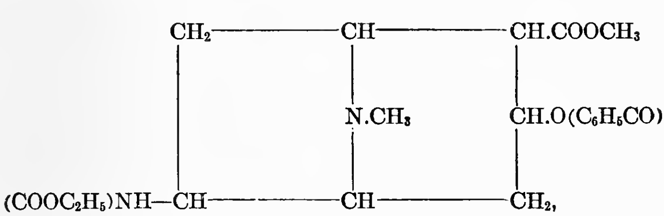
Cocainum Phenylicum Poisnot.—A mixture of 2 parts of cocain, 1 part of phenol, 20 parts arachis oil, and 40 parts paraffin oil, supplied in 1-gm. tubes.

Cocainum Phenylicum Vian.—A mixture of phenol with cocain hydrochlorid.

Cocain Spray.—Cocain hydrochlorid, 0.12 part; menthol, 0.24 part; oil of eucalyptus, 0.3 part; camphor, 0.48 part; and 28.5 parts of a mixture of 2.5 parts of Peru balsam with 100 parts of rectified petroleum.

Cocain Tartrate.—A local anesthetic, the uses and dosage of which are the same as for cocain hydrochlorid. It is a white, crystalline powder, soluble in water and alcohol.

Cocain-Urethane.—By the action of chlorformic ester on the amido-derivative of cocain, Cocain-Urethane,



is produced. This is said to be a strong anesthetic, acting on the liver in a characteristic manner and giving rise to toxic symptoms.

Cocainol.—A Berlin firm has placed various forms of this external remedy on the market; these all contain anesthesin (Ritsert's), but no cocain. Among the forms are: Cocainol-menthol drops, cocainol tablets, and cocainol drops. The latter contain 0.2 gm. of anesthesin each. Hemostatic cocainol bougies contain 10 per cent of anesthesin and 0.0001 gm. of suprarenin; there are also listed cocainol bismuth tablets, cocainol quinin tablets, cocainol condurango tablets, and cocainol sanoform dusting powder. See *Pharm. Ztg.*, *47*, 916.

Cocainolbalsam, Schmerzstillender.—This salve contains vaselin, menthol, methyl salicylate, and anesthesin.

Cocainol-Crême.—This contains anesthesin, aluminum beta-naphtholdisulphonate, zinc acetate and thymol (*Chem. Centr.*, 1909, ii, 1584). According to *Gehe's Codex* (Nov., 1910, 311), sanovagin (cocainol-crême) is "a combination product of anesthesin with B-naphtholsulphonate of aluminum-zinc acetate, methyl di-iodosalicylate, mercury oxycyanid, and thymol." It is used in the treatment of genito-urinary diseases, especially those of the female organs.

Cocainol-Lösungen.—Sterilized solutions of 0.7 per cent subcutin dissolved in water.

Cocainum Arabinicum.—Employed in lumbar anesthesia. See *Gummitropakokain.*

Co-Capsulin.—This anesthetic and hemostatic contains alcohol, 2 per cent; cocain, 0.5 per cent; and supracapsulin, 1:2000.

Codrenin.—Two forms of this preparation, which is used as a local anesthetic and hemostatic in dentistry, are offered, of different strengths, in ounce bottles, namely:

"A"—Each fluid ounce contains:	
Cocain hydrochlorid (2 per cent)	9 1/5 grs.
Adrenalin chlorid (1:15,000)	1/36 gr.
Chloretone	2 1/4 grs.
"B"—Each fluid ounce contains:	
Cocain hydrochlorid (1 per cent)	4 3/5 grs.
Adrenalin chlorid (1:5,000)	1/12 gr.
Chloretone	2 1/4 grs.

The chloretone is said to be added not because of any local anesthetic effect, but specifically to prevent the growth of fungus. For this purpose it is said to have been found to be most efficient, more so, in fact, than all of the preservatives known in solutions of the alkaloids or similar substances employed hypodermatically.

Cold.—On the production of local anesthesia by means of refrigeration or cold, see the following contributions:

Arnott: "On Cold as a Means of Producing Local Insensibility," *Lancet,* 1848, *2,* 98, 287.

Bailly: "Nouveau procédé de réfrigération locale par le chlorure de méthyle," *Gaz. hebd.,* 1888, No. 5.

Baudouin: "Chlorure d'éthyle comme anesthésique locale," *Progrès méd.,* 1892.

Berger: "Bromäthyl als Lokalanästheticum," *Breslauer ärztl. Z.,* 1883, No. 8.

Bernard: "Anesthésie locale par le sulfure de carbone," *Gaz. méd.,* 1874, 27.

Bigelow: *Gaz. hebd.,* 1866, No. 23.

Bloch. "Om Indskränkning i Anvendelse af Inhalationsanästhesi," *Nordiskt med. Arkiv,* 1899, No. 33; *Bibliothek for Laeger,* 1898.

Boeri and Silvestro: "Sur la mode de se comporter des différentes sensibilités sous l'action des divers agents," *Archiv. Ital. d. Biol., 31,* 460.

Braatz: "Zur Lokalanästhesie," *Zentralbl. f. Chir.*, 1895, No. 26.

Bumm: "Über lokale Anästhesierung," *Wiener Klinik*, 1886.

Cardenal: "Une découverte de Dr. Letamendi sur l'anesthésie locale," *Archiv. d. physiol. norm. et pathol.*, 1875, *5*, 769.

Debove: "Traitement de la sciatique par la congélation," *Société méd. des hôp.*, Aug., 1884.

Delcominète: *Gaz. des hôp.*, 1866, No. 45.

Ehrmann: "Äthylchlorid als Lokalanästheticum in der Dermatotherapie," *Wiener med. Woch.*, 1892, No. 26.

Feiber: "Chlormethyl als lokales Anästheticum," *Berl. klin. Woch.*, 1889, No. 5.

Fratscher: "Kontinuierliche und langsame Nervenreizung," *Jena. Z. f. Naturkunde, 11*, 481.

Galeczowski: "De l'anesthésie locale dans la chirurgie oculaire," *Rec. d'ophthal.*, 1876, 93.

Ganz: "Über Äthychlorid," *Therap. Monatsh.*, 1893, 113.

Gendre: Einfluss der Temperatur auf einige tierisch-elektr. Erscheinungen," *Pflügers Archiv, 34*, 422.

Giraldès: "Anesthésie chirurgicale," in "Nouveau dictionnaire de médecine et de chirurgie," Paris, 1865.

Girard: "Zur Erleichterung der Lokalanästhesie," *Zentralbl. f. Chir.*, 1874, No. 2.

Grützner: "Über verschiedene Arten der Nervenerregung," *Pflügers Archiv, 17*, 215.

Guérard: *Gaz. des hôp.*, 1854, 88.

von Hacker: "Zur lokalen Anästhesie," *Wiener klin. Woch.*, 1893.

Hattyasi: "Versuche mit Äthylchlorid," *Pester med. Chir. Presse*, 1892, No. 22.

Heinzmann: "Über die Wirkung allmählicher Anderungen thermischer Reize," *Pflügers Archiv, 6*, 222.

Herzog: *Neue Zeitung für Medizin*, 1850.

Husemann: *Virchow-Hirsch Jahre.*, 1866, *1*, 344; 1867, *1*, 501.

Illich: *Med. Ztg. Russlands*, 1852, No. 55, and 1853, No. 15.

Kümmell: "Über Narkose und lokale Anästhesie," *Festschr. z. 80 jähr. Stiftung. des ärztl Vereins*, Hamburg, Leipzig, 1896.

Lauenstein: "Die lokale Anästhesie durch Äther," *Zentralbl. f. Chir.*, 1880, 497.

von Lesser: "Demonstration zur lokalen Anästhesierung," *Deut. Chir.*, 1881.

Letamendi: "Un pas vers la résolution du problème de l'anesthésie locale," Barcelona, 1895.

Létang: "Note sur un nouveau procédé d'anesthésie locale," *Thèse*, Paris, 1894.

Num: *Lancet*, Aug., 1850.

Redard: "Chloräthyl als Lokalanästheticum," *La sem. méd.,* 1891, 133.

Richardson: *Med. Times,* 1866.

Richardson and Greenhalgh: *Med. Times,* 1866.

Richet: "Anesthésie localisée," *Gaz. des Hôp.,* 1854, 251, 263, 267; *Bull. de la Soc. de Chir., 4,* 519.

Rosenthal: "Experimentelle und praktische Beiträge zur Einwirkung der Lokalanästhesie auf das Nervensystem," *Osterr. Z. f. Heilkunde,* 1867, 373.

Rossbach: "Eine neue Anästhesierungsmethode des Kehlkopfs," *Wiener med. Presse,* 1880, No. 40.

Rottenstein: *Tageblatt d. Versammlung deut. Natur. u. Ärzte in Frankfurt a. M.,* 1867, 43.

Scheller: "Reines Äthylchlorid als örtliches Anästheticum und Antineuralgicum," *Deut. Monats. f. Zahnheil.,* 1891, No. 5.

Simonin: *Gaz. Méd. de Paris,* 1866, No. 11.

Terillon: "Anesthésie locale et générale produite par le bromure d'éthyle," *Gaz. Méd. de Paris,* 1880, No. 22.

Velpeau: *Bull. de l'Académie de Méd., 15,* 85.

Warren: "Surgical Observations," Boston, 1867.

Wells, Spencer: *Med. Times,* 1866.

Wiesendenger: "Flüssige Kohlensäure als Lokalanästheticum," *J. f. Zahnheilk.,* 1891, No. 21.

Wittmeyer: "Über Anästhesie," *Deut. Klinik,* 1852, No. 19.

Compound Anesthetic Ether.—A mixture of equal parts of absolute ether and amyl hydrid (rhigolene) (Richardson, 1868).

Richardson (*Sci. Am. Suppl.,* No. 516, 8240) states that this mixture possesses a density of 0.672 and boils at + 90° F. He found that it is pleasant to breathe and that it is a rapidly acting anesthetic, but that it is dangerous, causing death in the lower animals, suddenly, from cardiac paralysis. "It is not recommendable as a general anesthetic, and has once been a cause of death in man. For producing local anesthesia from cold in the form of a spray it is good and is generally employed" (1885).

Compressed Lozenges Orthoform, 1 grain.—Each lozenge contains orthoform (*q. v.*), 0.065 gm. (1 grain).

Compressed Tablets Anesthesin, 2½ grains.—Each tablet contains anesthesin (*q. v.*), 0.162 gm. (2½ grains).

Conephrin.—A solution containing cocain and paranephrin, used as a local anesthetic.

Corona.—This is a local anesthetic, put on the market by a Leipzig firm, claimed to consist of a solution of less than 1 per cent of cocain in distilled water, with the addition of picric acid, nitric acid, oils of wintergreen, thyme, mentha arvensis, and eucalyptus, and benzoic and boric acids. It is employed in painless dentistry. It is stated in *Gehe's Codex* (Nov., 1910, 88) that "corona" contains, besides cocain, nitric acid, picric acid, potassium hydroxid, oils of gaultheria, baptisia, thyme, mentha arvensis and eucalyptus, benzoic acid and boric acid, in water solution.

Coryl.—See *Chloryl.*

Coryloform.—An anesthetic mixture containing ethyl chlorid, methyl chlorid, and ethyl bromid. See *Pharm. Ztg., 53,* 817.

Coumarin.—Ellinger (*Archiv exper. Pathol. Pharmakol.,* 1908, Suppl.) found that in frogs injections of 0.02 to 0.05 gm. of coumarin, the anhydrid of coumaric acid, caused deep anesthesia of the nervous centers in the brain and spinal cord, extending to the vagus and the respiratory center, while the vasomotor center was not paralyzed and the functions were not demonstrably altered. In rabbits injections of 0.15 to 0.2 gm. per kg. body weight produced deep anesthesia lasting about 10 minutes. He concluded that coumarin was a harmless anesthetic when properly administered, and that it was not a dangerous cardiac poison as claimed by Köhler (*Zentr. f. d. med. Wissenschaft.,* 1875, 867 and 881). Cianci (*Giornale Internaz. delle Sci. med.,* 1908, Nov.) ascribed to coumarin an action resembling that of camphor.

Crême Déhné.—A salve of the following formula:

Extr. Hamamel. destill.	30.0
Acidi borici Anesthesin. } āā	5.0
Ad. Lanæ c. aqua	55.0
Camphor. Essent. Heliotrop. Essent. Rosemar. } āā	1.0

Creosote.—Used in dentistry, as a local anesthetic. See *Carbolic Acid.*

Cycloform.—This compound is the isobutyl ester of para-amido-benzoic acid; it is a white crystalline powder, melting at + 65° C., sparingly soluble in water, but readily soluble in alcohol and ether.

Impens (*Therap. d. Gegenwart,* 1910, No. 8) showed that cycloform has the advantage that it dissolves in water only to the amount of 0.022 per cent; this sparing solubility leads to an entirely local action and prevents symptoms due to absorption. Impens found the anesthetic action of cycloform to be very great.

On cycloform, see also:

Krecke: *Münch. med. Woch.,* 1910, 2447.

Most: *Heilkunde,* 1910.

Strauss: *Münch. med. Woch.,* 1910, No. 50, 2643.

Wyss: *Archiv f. Verdauungs-Krankheiten, 16,* No. 4.

Werner: *Münch. med. Woch.*, 1910, No. 38, 2004.
Zeller: *Med. Klinik*, 1910, No. 45, 1748.
Bircher: *Idem*, 1911, No. 6, 223.
Rosenberg: *Deut. med. Woch.*, 1911, No. 9, 409.

Cycloform appears from these reports to be non-irritant, prompt and intense in anesthetic action.

Cyclorenal.—A combination of cycloform, adrenalin, balsam Peru, and coryfin, made in Berlin, in the form of salves and suppositories for the treatment of rectal diseases. See Kretschmer: *Berl. klin. Woch.*, 1911, *48*, 2168. Rabow (*Chem. Ztg.*, 1912, No. 21, 190) states that cyclorenal is a local anesthetic.

Dentesthin.—A dental local anesthetic containing in 1 c. c. of a physiological salt solution 0.005 gm. cocain hydrochlorid, 0.015 gm. novocain, and 0.05 gm. of synthetic suprarenin. See *Pharm. Zentralh.*, *51*, 1126.

Dentalon or Dentalone.—This dental local anesthetic is a combination of chloretone (*q. v.*) and several essential oils, and is used specifically in the treatment of exposed nerves and decaying teeth. It has been found to be a very practical and satisfactory obtundent.

Each fluid ounce of dentalone contains approximately:

Oil Cloves	300 min.
Oil Birch	12 min.
Oil Cinnamon	50 min.
Chloretone	175 min.

The label bears the information that dentalone is an admixture of the oils of cloves, cassia, and gaultheria, containing in solution 30 per cent of their weight of chloretone; that is 175 gr. of chloretone, and Oils of Cloves, Gaultheria, and Cassia (*q. v.*), to each fluid ounce.

Dentola.—This contains cocain, 1; potassium bromid, 10; glycerin, 200; and water, 200. It is used in dentistry.

Dentorol.—"Eugenol-para-chloro-chlorphenol-Menthol." It is used in dentistry.

Desalgin.—Schleich (*Therap. d. Gegenwart*, 1909, *1*, 138) succeeded in combining chloroform with an albumin and in procuring a definite compound with a fairly constant percentage of about 25 per cent of chloroform in the dry state. This preparation is a gray, amorphous, fine powder; it represents "colloidal chloroform" in a solid state, and may find application in anesthesia.

Dialkylaminoalkyl 3:4-Diaminobenzoates.—According to Einhorn (German Patent 194,365), these compounds have considerable local anesthetic properties.

Dibromethane.—See *Ethylene Bromid.*

Dichlorethane.—This ester, $CH_3.CHCl_2$, is said to have a similar action to chloroform.

Dichlormethane.—See *Methylene Chlorid.*

Dichlorpropane.—According to Brissemoret and Chevalier (*Compt. rend., 148,* 731), 2, 2—Dichlorpropane, $CH_3C(Cl_2).CH_3$, is a fugitive anesthetic not to be considered the superior of ethyl chlorid.

Diethylaminoethyl Benzoate.—This dialkylaminoethyl benzoate, described by Schering (German Patent 175,080), has been stated to have local anesthetic properties.

Dimethylacetal (Ethylidene dimethyl ether), $CH_3CH(OCH_3)_2$.—An anesthetic used in the place of, or with, chloroform. It is prepared from aldehyd, methyl alcohol, and glacial acetic acid by the action of heat. It forms a colorless liquid, soluble in water, alcohol, ether, and chloroform; the specific gravity is 0.879 at 0° C. and the boiling point + 62° to 63° C. See *von Mering's Mixture.*

Dioform.—Dioform, or acetylene dichlorid, is a colorless fluid with an odor resembling that of ethyl chlorid and chloroform. Its graphic formula is $\begin{matrix} CH\ Cl \\ \| \\ CH\ Cl \end{matrix}$ (symmetrical 1.2-dichlorethylene). Its specific gravity is 1.29 and it boils at about + 55° C.

Villinger (*Archiv f. klin. Chir.,* 1907, No. 3; *Zentr. f. Chir.,* 1907, No. 44, 1282; *Odontol. Blätter,* 1907, No. 17, 327) conducted some experiments with dioform on dogs with the view of ascertaining whether the narcotic action resembled that of chloroform. He produced narcosis lasting 10 minutes to 2 hours, and gave doses up to 125 gm. without observing any threatening symptoms. Sleep set in within 6 to 10 minutes, and was preceded by only a short stage of excitation. The reflexes were completely abolished during sleep, while the strength and frequency of the pulse remained constant. The urine remained almost normal, so that there was no reason to suspect inflammation of the kidneys. The trials made by Villinger on human subjects also gave satisfactory results. 15 to 25 gm. of dioform were used; after about a minute, slight excitation was observed; after 3 minutes more, sleep ensued, to become deep sleep 5 minutes after the beginning of the anesthesia. Pulse and respiration remained good, the patients awakened quickly, there was but slight tendency to vomit, and no albumin was found in the urine. However, systematic clinical study is required before acetylene dichlorid should be used as a substitute for chloroform.

Dionin.—Dionin (ethyl-morphin hydrochlorid) is a white, somewhat bitter powder fusing at + 123°–125° C.; it is soluble in seven parts of water, one and one-half parts of alcohol, and twenty parts of syrup; it is insoluble in chloroform and ethyl ether. Dionin is precipitated from its solutions by most of the alkaloidal reagents.

Dionin has been reported upon by a number of observers; it would seem that it shares the analgesic and hypnotic properties of morphin without producing the nausea, constipation, and other disagreeable after-effects of that alkaloid. However, it acts even more powerfully upon the respiratory centers than does morphin. According to *The Dispensatory of the United States of America,* 19th ed., 1473, it is, nevertheless, less decisive in its action than is morphin, so that in cases of severe pain morphin will bring relief after the failure of dionin.

A 5 per cent solution of dionin has been used by ophthalmologists; it occasions immediate irritation and swelling of the conjunctiva, followed, in a short time, by a rapid subsidence of the swelling and a condition of analgesia and anesthesia.

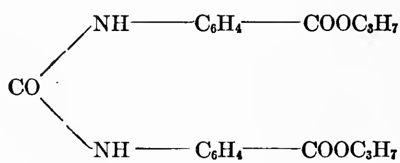
The employment of dionin in local anesthesia has been discussed by the following authors:

Graefe: "Das Dionin in der Augenheilkunde," *Deut. med. Woch.,* 1900, *Therap. Beil.,* No. 2.

Wolffberg: "Die Dioninophthalmie und ihre Bedeutung," *Therap. Monatsh.,* May, 1900.

Di-para-anisyl-monophenetyl-guanidin hydrochlorid.—See *Acoin.*

Dipropesin.—This seems (*Apoth.-Ztg.,* 1908, 786; *Vierteljahr. f. prak. Pharm.,* 1908, 305; *Pharm. Ztg., 53,* 817) to be a derivative of urea, containing two molecules of propesin (*q. v.*) bound together by a CO group:



Dipropesin is described as a white crystalline powder melting at + 171-172° C., tasteless and soluble in alcohol, but insoluble in water. It is said to develop its anesthetic action only in alkaline media, and to be therefore of use as an internal sedative in intestinal affections.

Kluger (*Therap. Monats.,* 1909, 76) published clinical reports on the use of dipropesin. He stated that dipropesin has no anesthetic effect until propesin (*q. v.*) is liberated in the alkaline body fluids.

Dolonephran.—An anesthetic of German manufacture, said to contain alypin (*q. v.*), suprarenin, and sodium chlorid.

Dolorant Tablets.—Each of these tablets of Swiss preparation is said to contain 0.0001 gm. of adrenalin, 0.01 gm. of cocain, 0.002 gm. of sodium chlorid. When dissolved in water, the solution is used in the painless extraction of teeth.

Dolorant Tabletten.—Each tablet contains 0.00001 gm. adrenalin, 0.01 gm. cocain, and 0.00499 gm. sodium chlorid. One to four tablets are dissolved in 1-4 c. c. of water for use in the production of local anesthesia in dentistry (*Gehe's Codex,* Nov., 1910, 100).

Dolorifuge.—A mixture of creosote, 1; chloroform, 1; and ethyl acetate, 2. It is used in dentistry.

Dontocerat.—See *Ceratum Odontalgicum.*

Dutch Liquid; Elayl Chlorid.—See *Ethylene Chlorid.*

Dysphagin.—No I. Tablets containing cocain, menthol, anesthesin, sodium biborate, and aromatics; No. II. The same, but without cocain; No. III. Anesthesin, citric acid, tannin, and aluminum acetate.

Dysphagin is used in the treatment of angina and throat affections.

Elayl Chlorid.—See *Ethylene Chlorid.*

Electric Analgesia.—On Electric Analgesia and Sleep, see Chapter XVI.

Enophthalmin.—The hydrochlorid of oxytouyl-methyl-vinyl-di-acetonalkamin, slightly soluble in water. Used, in 2 per cent solution, as an anesthetic in ophthalmology.

Ensemin.—A solution of about 1 per cent cocain, containing, in addition, adrenalin and chloretone. Used as a dental anesthetic.

Epicain.—A solution containing cocain hydrochlorid and epinin (dihydroxyphenylethylmethylamin), marketed also as tabloid ophthalmic epicain.

Erhardt's Solutions.—These are solutions for lumbar anesthesia, consisting of salts of arabic acid with certain anesthetic bases, as cocain, tropacocain, stovain, novocain, etc. See German Patent 211,800 of 1908; and also Erhardt: *Woch. f. Tierheilkunde,* 1908, Nos. 27 and 28; *Münch. med. Woch.,* 1908, Nos. 19 and 26.

Epsom Salts.—A saturated solution of magnesium sulphate has been employed as a dental local anesthetic; it is said to be very satisfactory. See *Magnesium Salts.*

Erythrophlein Hydrochlorid, Erythrophlœinum Hydrochloricum (Erythrophleinæ Hydrochloras).—This salt of an alkaloid from the bark of Erythrophlœum guinense, Don. (sassy bark), is used as a local anesthetic in eye practice in 0.05 to 0.25 per cent solutions. It forms a yellowish-white amorphous powder, soluble in water and alcohol. Its solutions are not stable. On the physiological action of Erythrophlein Hydrochlorid, see Harnack: *Berl. klin. Woch.,* 1895, 759. On its employment as a local anesthetic, see the following papers:

Brandt: "Versuche mit Erythrophlaein bei Odontalgie," *Therap. Monatsh.,* June, 1888.

Guttmann: "Versuche mit Erythrophlaein," *Berl. klin. Woch.,* 1888, No. 13.

Hirschfeld: "Ueber Erythrophlaein," *ibid.,* 1888, No. 11.

Karewski: "Ueber die praktische Verwendbarkeit der Erythrophlaein-anästhesie," *ibid.,* 1888, No. 11.

Koller: "Erythrophlaein," *Wiener klin. Woch.*, 1888, No. 6.

Lewin: "Ueber das Hayagift und das Erythrophlaein," *Berl. klin. Woch.*, 1888, No. 9; *Virchows Archiv, 111*, 575; "Bemerkungen zu Liebreichs Arbeit über Erythrophlaein," *Berl. klin. Woch.*, 1888, No. 9.

Liebreich: "Erythrophlaein," *Therap. Monatsh.*, March, 1888; "Ueber die Wirkung der N-Cassa Rinde und des Erythrophlaein," *Berl. klin. Woch.*, 1888, No. 9; "Haya und Erythrophlaein," *ibid.*, 1888, No. 16.

Lipp: "Wirkungen des Erythrophlaein," *Wiener klin. Woch.*, 1888, No. 11, 12.

Loewenhardt: "Zur praktischen Verwertung des Erythrophlaein," *Berl. klin. Woch.*, 1888, No. 10.

Onodi: "Versuche mit Erythrophlaein," *Med. Zentr.*, 1888, No. 12.

von Reuss: "Ueber Erythrophlaein," *Internat. klin. Rundschau*, 1888, No. 9.

Schöler: "Bemerkungen über Erythrophlaein," *Berl. klin. Woch.*, 1888, No. 10.

Tweedy: "Erythrophlaeine," *Lancet*, 1888, 249.

Ethene.—Olefiant Gas was proposed as an anesthetic by Nunneley in 1849. B. W. Richardson investigated it in 1865; he reported later (*Sci. Am. Suppl.*, No. 515, Nov. 14, 1885, 8228) that it was a good anesthetic, but inconvenient at that time on account of its being a gas. He found that the respiration ceased before the circulation. Anesthesia was found to be rapidly produced with a 10 to 15 per cent charge of air by gas, with a short spasmodic stage; recovery was rapid, without bad effects.

Ether.—See *Ethyl Ether*, Chapter V.

Ether-Menthol-Chloroform.—This anesthetic spray is composed of ether, 15 parts; chloroform, 10 parts; and menthol, 1 part.

Ethidene Dichlorid.—See *Ethylidene Chlorid.*

Ethyl Acetate (Acetic Ether; "Vinegar Naphtha").—This compound has been used as an external anesthetic.

Acetic Ether U. S. P. consists of about 90 per cent by weight of $CH_3CO.OC_2H_5$ and about 10 per cent of ethyl alcohol containing a little water. It is soluble in about 9 parts of water at $+ 25°$ C., but is miscible in all proportions with alcohol and ether.

H. C. Wood found ethyl acetate to be capable of being used as an anesthetic, but to be too slow in its action for practical purposes. Its action on the system is probably very similar to that of ethyl ether; but, since it is less volatile, it is less rapidly absorbed and eliminated, and therefore is much less prompt and is fugacious. Kappeler recorded cases in which ethyl acetate was administered to man. Tracy was opposed to its use, and Sigmund and Bouisson found it less agreeable and efficient than ether.

Ethyl Alcohol.—Alcohol was used by Horvath (*Gaz. des Hôpitaux,* Sept. 10, 1878) for the production of local anesthesia. It had been used previously by surgeons to produce immunity from pain in operation, and Lynk (*Cin. Lancet and Observer,* May, 1876) stated that he had long employed it as an anesthetic. Turnbull (1879) recommended inhalation of dilute alcohol.

Ethyl Aminobenzoate (Æthylis Amino-Benzoas; Paramidobenzoic Acid Ethyl Ester).—Ethyl aminobenzoate, $C_6H_4.NH_2.COO(C_2H_5)$ 1:4, is the ethyl ester of paraminobenzoic acid, $C_6H_4.NH_2.COOH$, 1:4.

Paranitrobenzoic acid is obtained by the oxidation of paranitrotoluene, and this may be ethylized by the action of sulphuric acid and alcohol, and the ester so obtained reduced to paramidobenzoic acid ethyl ester by the action of nascent hydrogen, or the acid may first be reduced and subsequently converted into the ethyl ester. It is a white, crystalline powder, easily reduced to impalpability, melting at + 90° to + 91° C. (194° to 195.8° F.); odorless and tasteless, but producing a sensation of numbness when placed on the tongue; almost insoluble in cold and difficultly soluble in hot water; soluble in six parts of alcohol, in ether, benzene, and to the amount of 2 to 3 per cent in fatty oils. In oil solutions it may be sterilized without decomposition, but by prolonged boiling or by warming with dilute alkalies it is split up into alcohol and paramidobenzoic acid.

It should form clear, colorless, and neutral solutions in alcohol or ether; after acidification with nitric acid, it should not give a precipitate with silver nitrate. Its solution in dilute hydrochloric acid (1 to 10) is not affected by hydrogen sulphid. If a few drops of sodium nitrate solution are added to the slightly acidulated water solution followed by some alkaline beta-naphthol solution, a cherry red coloration of bluish shade is produced, which changes to orange on further addition of hydrochloric acid. It is decomposed by prolonged heating with water, and is incompatible with alkalies and their carbonates.

Ethyl aminobenzoate was introduced as a substitute for cocain and is a local anesthetic, similar in its action to orthoform and said to be equally effective, but free from irritant action and toxicity. The anesthetic action, like that of the related compound orthoform (*q. v.*), resembles that of cocain, but is purely local, does not penetrate the mucous membranes, and, in consequence of its insolubility, the compound cannot be used by hypodermic injection. In consequence of its insolubility, also, the anesthetic effect is more prolonged than that of cocain.

It is said to be useful for the relief of pain in various forms of gastralgia, in ulcer and cancer of the stomach, and is applied locally in rhinologic and laryngeal affections, urethritis, etc.; it is also employed for anesthetizing wounded surfaces, burns, ulcerations, and painful affections of the skin. It is more effective in cases where the skin is broken.

Dosage.—Internally, 0.3 to 0.5 gm. (5 to 8 grains), in pastilles. Externally it is applied as a dusting powder, either pure or diluted. It may be applied in ointment or in the form of suppositories. See *Anesthesin.*

Ethylbenzoylecgonin.—A local anesthetic.

Ethyl Bromid (Monobromethane; Hydrobromic or Bromic Ether).—By many, ethyl bromid is considered to be an efficient and safe inhalation and local anesthetic. T. Nunneley, who introduced ethyl bromid as an anesthetic in 1849, considered it to be one of the best of anesthetics, in which view Richardson (*Sci. Am. Suppl.,* No. 515, 8228) concurred. The latter pointed out, in 1885, that the objections to its use were its cost and instability; that no deaths from it had occurred in the human subject, and that in death induced by it in the lower animals the respiration and circulation failed together. He stated that the quantity required for complete anesthesia was 1 to 6 fluid drachms, and that the required charge of air by vapor was 5 to 10 per cent. Its action was found to be rapid and effective, with scarcely any second or spasmodic stage; recovery from deep narcotism was obtained in four to five minutes, without bad effects; and during full anesthesia the animal temperature was reduced 2° F. M. Robin studied the use of ethyl bromid in 1850, and Richardson in 1870.

On the physiological action of ethyl bromid, see Cole: *Brit. Med. J.,* June 20, 1903, 1421; and Webster: *Bio-Chemical J.,* 1906, *1,* 328.

Ethyl bromid is only slightly toxic, but causes more irritation of the respiratory passages than ethyl chlorid. The narcosis produced by means of it is said to differ from that of choloroform in that it sets in more rapidly and ceases more quickly. Subsequently the patient may have general mild depression. Pain is abolished before consciousness. The respiration is paralyzed at about the same time as the reflexes, so that the zone of safety is very narrow.

From the third statistical record compiled by the Central Society of German Dentists (see Lipschitz: *Deut. Monats. f. Zahnheilk.,* 1905, No. 11, 683), it is seen that 5,973 administrations of chloroform, *14,921 of ethyl bromid,* and 1,509 of ethyl chlorid involved no fatal case. The mortality due to the administration of these three narcotics was expressed as follows:

Ethyl Bromid	1 : 112,001
Ethyl Chlorid	0 : 2,583
Chloroform	1 : 35,342

It is undoubtedly true that some of the evil effects formerly observed with ethyl bromid anesthesia are attributable to unreliable commercial preparations, but several deaths have occurred when a pure article was given. For prolonged anesthesia ethyl bromid is not suitable, owing to the fact that, after long-continued inhalation, unpleasant effects may result, and in addition the preparation loses its power if administered for a long time. It has been found to answer satisfactorily in short operations, as in dental surgery (Roth: *Prager med. Woch.*, 1906, No. 21); and, as indicated by Merck (*Ann. Rep., 20*, 22), its use may be recommended in cases where there is a desire to avoid the use of cocain and adrenalin. Roth concluded that ethyl bromid is an anesthetic which brings about unconsciousness and complete anesthesia in a very short time, enabling a brief surgical operation to be completed without hurry, and without fear of ill effects either accompanying or following the anesthesia. He considered that it is very easy of application, in any place, and without the necessity for complicated apparatus.

Chloroform anesthesia is said to be advantageously commenced by giving ethyl bromid, since the latter effects a more rapid abolition of consciousness.

Breitbach (*Deut. med. Woch.*, 1911, 374) stated that ethyl bromid is free from danger when carefully used, and declares that it is effective for all dental operations.

On the avoidance of the possibility of delayed intoxication after ethyl bromid anesthesia, see Mounier: *Münch. med. Woch.*, 1911, 1150; he states that the age of the patient and the presence of digestive disturbances should be especially considered.

Ethyl bromid must, however, be looked upon as a dangerous agent in inexperienced hands.

Dosage: 3 c. c. to 12 c. c. (45 minims to 3 fluid drams) are sufficient to induce anesthesia. It should be administered rapidly, with little or no air. The administration requires from 20 to 40 seconds; the anesthesia lasts about two minutes. The dose for children should not exceed 1 c. c. per year of age.

It should be protected from the light, and a bottle or tube once opened should be used at once, as it deteriorates rapidly. (To be preserved carefully in a small, opaque bottle containing not more than 50 c. c.: "Pharm. Helvetica," edit. 4.) It should not be confounded with ethylene bromid (*q. v.*), which is said to be very poisonous. The sp. gr. of ethylene bromid is 2.179, while that of ethyl bromid is about 1.45.

For further information relating to the employment of ethyl bromid for the production of anesthesia the reader is referred to the following literature:

Abonyi: "Das Bromäthyl in der zahnärztlichen Praxis," *Verh. d. X. Internat. med. Kongr. zu Berlin*, 1890, *5* Abt. 14, 66. "Ueber Narkotika mit besondere Berucksichtigung des Bromäthyls," *Wiener Klinik*, 1891, No. 1; *Zentralbl. f. Chir.*, 1891, 319.

Asch: "Über Bromäthyl," *Therap. Monatsheft,* 1887, 54.

von Baracz: "Beobachtungen über die Bromäthylnarkose in der chirurigischen Praxis auf Grund, von 200 mit diesem Mittel ausgeführten Narkosen," *Wiener klin. Woch.,* 1892, No. 26, 383. "Über die Bromäthylnarkose auf Grund, von 200 eigenen Beobachtungen," *Nowy lekarskie,* 1891, No. 6; *Zentralbl. f. Chir.,* 1892, 640.

von Bardeleben: "Todesfall in Bromäthylnarkose" (Identisch mit dem von A. Koehler beschriebenen), Anlage 2 der gurltschen Statistik, *Verh. d. XXIII. Deut. Chirurgenkongr.,* 1894, Teil ii, 24.

Billroth: "Todesfall in der Bromäthylnarkose" (Identisch mit dem von Gleich veröffentlichten Fall. Im Bericht fälschlicherweise der Billroth-Mischung zugeschrieben). Anlage 4 zu Gurltschen Statistik. *Verh. d. XXI. Deut. Chirurgenkongr.,* 1892, Teil ii, 325.

Blumm: "Stickstoffoxydul oder Bromäthyl als Anästhetikum," *Deut. Monats. f. Zahnheilk.,* 1889, 25. "Diskussion zu Hamecher" (Polemisch gegen A. Witzel: "Bromäthyl ist kein Herzgift"), *Verh. d. LXII Vers. deuts. Naturf. u. Ärzte zu Heidelberg,* 1889, 673.

Boennecken: "Bericht über narkosen mit Aether bromatus," Anlage 4 der Gurltschen Statistik. *Verh. d. XXIII. Deut. Chirurgenkongr.,* 1904, Teil ii, 31.

Bonomeu u. Mazza: "Über die physiologische Wirkung des Bromoform, des Bromäthyl und des Bromäthylen," *Selbstbericht Zentralbl. f. Chir.,* 1884, 593.

Bosscha: "Die Bromäthylnarkose," "Haar gescheedenis en haar toepassing in de chirurgie." *Nederl. Tijdschr. v. Geneeskunde,* 1894, 2, No. 24. *Zentralbl. f. Chir.,* 1895, 277.

Bourneville et Olliver: "Recherches sur l'action physiologique et therapeutique du bromure d'éthyle dans l'épilepsie et l'hysterie," *Gaz. méd. de Paris,* 13, 173; *Progrès méd.,* 1880 et 1881; *Deut. Med.,* 1880, 349 u. 1881, 271.

Boyals: "De l'emploi du bromure d'éthyle comme anesthésique pour l'opération des végétations adénoides du pharynx nasal chez l'enfant." *Thèse,* Paris, 1890.

Breitbach: "Die Bromäthylnarkose, praktische Erfahrungen mit 15,032 Bromäthylnarkosen." *XVI. Internat. Med. Kongr. in Budapest,* 1909; Separat bei Fr. Tittel Nachf., Dresden, 1911.

Bruns: "30 Bromäthylnarkosen," Anlage 9 zu Gurltschen Statistik. *Verh. d. XXI. Deut. Chirurgenkongr.,* 1892, Teil ii, 330. "54 Bromäthylnarkosen," Anlarge 3 der Gurltschen Statistik, *Verh. d. XXII. Deut. Chirurgenkongr.,* 1893, Teil ii, 26.

Busch: "47 Bromäthylnarkosen," Anlage 4 der Gurltschen Statistik, *Verh. d. XXII. Deut. Chirurgenkongr.,* 1893, Teil ii, 26.

Calmettes et Lubet: Barbon, "Nouveau procédé pour opérer les végétations adénoides," *Gaz. hebd.,* Paris, 1890, 399.

Chaigneau: "Études comparatives des divers agents anesthésiques employés dans les accouchements naturels." *Thèse*, Paris, 1890.

Challand: "Bromäthyl kupiert hysterische Anfälle," *Correspond. f. schweizer Aerzte*, 1882, 649.

Chisholm: "Bromid of Ethyl, the Most Perfect Anesthetic for Short, Painful Surgical Operations," 1883; *Auszug aus dieser Broschüre in J. British dent. Association*, April, 1883. See *Zentralbl. f. Chir.*, 1883, 313.

Chudovszky: "Morphium, Atropin, Bromäthyl, Sauerstoff, Chloroformnarkose," *Ungaris. Chirurgenkong.*, 1911; *Zentralbl. für Chir.*, 1912, 469.

Clover: "Bromid of Ethyl as an Anesthetic," *Brit. Med. J.*, 1880, i, 586.

Cohn, C.: "Die Entstehung des Knoblauchgeruches bei Anwendung des Bromäthers," *Monats. f. Zahnheilk.*, 1891, *9*, 107. "Die Zersetzung des Bromäthers," *Monats. f. Zahnheilk.*, 1891, *9*, 292.

Cohn, E.: "Ueber Anästhesierung Kreissender," *Deut. med. Woch.*, 1886, No. 16, 268.

Cole: "The Physiological Action of Ethyl Bromide and Somnoform," *Brit. Med. J.*, 1903, i, 1421.

Desguinn: "Les nouveaux anesthésiques, le bromure d'éthyle." *Archiv med. Belge*, 1880, 277.

Dischl: "Le bromure d'éthyle comme anesthésique," *Pittsburgh Med. Rev.*, etc., 1887, 360; *loc. cit., Zit. nach L. Fraenkel.*

Drakin: "Zur Frage von der Anästhesie durch Bromäthyl in der Zahnchirurgie," *Nowosti tierapii*, 1889, No. 38, 202, *bei v. Ziemacki, loc. cit.*, 730.

Dreser: "Zur Pharmakologie des Bromäthyls," *Arch. f. exper. Path. u. Pharmak.*, 1895, *36*, 285.

Dubrowin: "Ein Todesfall bei gemischter Narkose," *Chir. Ann.*, 1895, 342; *Zentralbl. f. Chir.*, 1895, 1011.

Ducasse: "Essai sur l'emploi du bromure d'éthyle dans les accouchements naturels simples," *Thèse*, Paris, 1883.

Duval: "Des l'anesthésie générale par les inhalations de bromure d'éthyle," *Thèse*, Paris, 1880.

Ebermann: "Ueber kombinierte Bromäthyl-Chloroform-Narkose." *Wratsch*, 1898, Nos. 30-31. *Zentralbl. f. Chir.*, 1898, 1095.

Eschricht: "Die Bromäthylnarkose," *Deut. med. Woch.*, 1899, No. 31, 626. "Bemerkungen über Bromäthylnarkosen," *Deut. Monats. f. Zahnheilk.*, 1889, 299.

Falk: "Nebenwirkungen und Intoxikationen bei der Anwendung neuerer Arzneimittel," 2 *Bromäthyl. therap. Monats.*, 1890, 463.

Fessler: "Narkosen mit Bromäther, Aether bromatus." *Monats. f. Zahnheilk.*, 1891, *9*, 179. *Münch. med. Woch.*, 1890, 25.

Fischer: "Bromäthylnarkose," *Nordisk Tidskrift for Terapie, 1,* 111. *Zentralbl. f. Chir.,* 1903, 1109.

du Fougeray: "Note sur l'action du chloroforme administré à très petites doses après le bromure d'éthyle, etc." *Ann. des Malad. de l'Oreille, 22,* 308; *Zentralbl. f. Chir.,* 1897, 317.

Fraenkel: "Contribution à l'étude du bromure d'éthyle comme anesthésique général," *Thèse,* Paris, 1894.

Garin: "Die Bromäthylnarkose bei Zahnextraktion," *Wratsch,* 1900, No. 31. *Zentralbl. f. Chir.,* 1900, 1307.

Geza Dieballa: "Ueber die quantitative Wirksamket verschiedener Stoffe der Alkohol—und Chloroformgruppe auf das Froschherz," *Archiv f. exper. Path.,* 1894, *34,* 137.

Gilles: "Ueber Bromäthylnarkose," *Deut. Monats. f. Zahnheilk.,* 1889, 271, 347; "Beschreibung einer Bromäthernarkose nebst weiteren Bemerkungen zur Bromäthernakose," *Deut. Monats. f. Zahnheilk.,* 1891, *9, 4,* "Ueber Bromäthylnarkose," *Berl. klin. Woch.,* 1892, Nos. 8-9, 166, 195.

Givel: "De l'emploi du bromure d'éthyle dans les accouchements naturels," *Diss.,* Berne, 1881.

Gleich: "Ueber Bromäthylnarkosen," *Wiener klin. Woch.,* 1891, 1002; "Ein Todesfall nach Bromäthylnarkose," *Wiener klin. Woch.,* 1892, No. 11, 167.

Grunert: "Die Gefährlichkeit des Bromäthers ist 200mal so gross als die des Stickoxyduls," Diskussionsbem., *Gesellsch. f. Natur. u. Heilk. zu Dresden,* 30 März, 1912. *Münch. med Woch.,* 1912, 1404.

Günzberg: "Ueber Bromäthyl," *Med. Kalenderj,* 1891. Ref. bei v. Ziemacki, *loc. cit.,* 731.

Gurlt: "Zur Narkotisierungsstatistik," *Verh. d. XXIV Deut. Chirurgenkongr.,* 1895, Teil ii, 460.

von Hacker: "25 Bromäthylnarkosen, Anlage 12 zu Gurlts. Statistik." *Verh. d. XXI. Deut. Chirurgenkongr.,* 1892, Teil ii, 331.

Häckermann: "Ueber die Anwendung des Bromäthyls zur Narkose Kreissender," *Gesellsch. f. Geburtsh. u. Gynäk. zu Berlin,* 1883; *Zentralbl. f. Gynäkol.,* 1883, 546.

Härdy: "Bromäthylnarkose in der Zahnheilkunde," *Schweiz. Vierteljahrs. f. Zahnheilk.,* 1898.

Haffter: "Die Bromäthylnarkose," *Correspondenz-Blatt f. Schweizer Aerzte,* 1890, 106, 143.

Hagedorn: "Zirka 100 Bromäthylnarkosen, Anlage 13 zu Gurlts. Statistik." *Verh. d. XXI. Deut. Chirurgenkongr.,* 1892, Teil ii, 332.

Hahn: "Die Narkose der Chirurgie und Zahnheilkund," *Diss.,* 1896.

Hammecher: "Ueber Bromäthylnarkosen," *Deut. Monats. f. Zahnheilk.,* 1889, 7. *Verh. d. LXII. Vers. deut. Naturuf. u. Aerzte zu Heidelberg,* 1889, 668; *Korrespond. f. Zahnärzte,* 1889, 343.

Hartmann et Bourbon: "Le bromure d'éthyle comme anesthésique général," *Rev. de Chir.*, 1893, *13*, 701.

Haslebacher: "Experimentelle Beobachtungen über die Nachwirkungen bei der Bromäthyl. und Chloräthylnarkose," *Diss.*, Berne, 1901.

Heitmüller: "Empfehlung des Bromäthers," *Diskussionsbem. Gesellsch. f. Natur. u. Heilk. zu Dresden*, 30 März, 1912. *Münch. med. Woch.*, 1912, 1403.

Hennicke: "Vergleichende Untersuchungen über die Gefährlichkeit der gebräuchlichten Inhalationsanästhetika," *Diss.*, Bonn, 1895.

Hoddes: "Ueber Bromäthernarkosen," *Diss.*, Freiburg i. B., 1892.

Holländer: "Das Bromäthyl in der zahnärztlichen Praxis," *Verh. d. X. Internat. med. Kongr. zu Berlin*, 1890, *5*, 14, 57.

Jendritza: "Ein Fall von Bromäthylintoxikation," *Therap. Monats.*, 1892, 152.

Kappeler: "Beiträge zur Lehre von dem Anästheticis," *Arch. f. klin. Chir.*, 1888, *37*, 364; *Bromäthyl*, 376.

Kocher: "Über kombinierte Chloroform-Äther-Narkose," Nachtrag: "Bromäthyl-Äther-Narkose." *Korrespondenz-Blatt. f. Schweizer Ärzte*, 1890, 590. "Chirurgische Operationslehre," 1902. Empfehlung der Bromäthyl-Äther-Narkose.

Köhler: "Zur Bromäthylnarkose," *Freie Verein. d. Chir. Berlins*, *2*, 1893; *Deut. med. Woch.*, 1894, *Vereinsbeilage*, 7; *Zentralbl. f. Chir.*, 1894, 41.

Kölliker: "Über die Anwendung der Bromäthylnarkose in der chirurgischen Praxis," *Zentralbl. f. Chir.*, 1891, 385.

Krecke: "Beitrag zur Narkotisierungsfrage," *Münch. med. Woch.*, 1894, 806. Bromäthyl.

Kretschmann: "Anwendung des Bromäthyls in der Ohrenkeilkunde," *Archiv f. Ohrenheilk.*, 1889. "Bericht über neuere Mittel in der Ohrenheilkunde," *Archiv f. Ohrenh.*, 1889.

Langgaard: "Über Bromäthyl," *Therap. Monat.*, 1887, 62.

Lanz: "Bemerkung zu der Mitteilung von Dr. Otto Zuckerkandl, Uber eine Modifikation des Chloroformiernes," *Zentralbl. f. Chir.*, 1891, 969, Bromäthyl, 972.

Larisch: "1263 Bromäthylnarkosen," *Diss.*, Breslau, 1899.

Laury: "872 Bromäthylnarkosen, Anlage 24 zu Gurlts. Statistik." *Verh. d. XXI. Deut. Chir.*, 1892, Teil ii, 350.

Lebert: "Des accouchements sans douleur ou de l'analgésie obstétricale par le bromure d'éthyle," *Rev. méd. de l'Est*, 1882. *Deut. Med.*, 1882, 250; *Archiv de Tocol.*, 1882. Ref. bei Givel, *1*.

Lepmann: "Experimentelle und klinische Untersuchungen zur Frage der Bromäthernarkosen," Berlin, 1895.

Lesin: "Über die gemischte Bromäthyl-Chloroform-Narkose," *V. Kongr. Ärzte*, St. Petersburg, 1894. *Zentralbl. f. Chir.*, 1894, 982.

Levis: "The New Anesthetic, The Bromid of Ethyl," *Phila. Med. Times,* 1880, 188. Virchow-Hirsch: *Jahresber.,* 1880, 454.

Lewin: "Nebenwirkungen der Arzneimittel," Berlin, 1893.

Löhers: Über den Einfluss des Bromäthyls auf Atmung und Kreislauf," *Diss.,* Berlin, 1890. "Sitzung der Physiol. Gesellsch. zu Berlin," 9. Mai, 1890, *Zit. Nach Kocher.* (Kaninchenversuche mit Bromäthylnarkose.)

Löwenstein: "Empfehlung des Bromäthers für kurzdaurende Narkosen." *Verein. westd. Hals. Ohrenärzte zu Köln,* April, 1912, *21. Med. Klinik,* 1912, 1406.

Lucas-Championnière: "Diskussionsbem. über Bromäthyl bei Kreissenden." *Bull. de la Soc. de Chir.,* 1880, 320; Virchow-Hirsch, 1880, *1,* 454.

Lustig: "Über die Anwendung und Wirkung der Anästhetika und Narkotika bei Kindern," *Verh. d. XXIX. Jahresver. d. zentral. Deuts. Zahnärzte,* 1890. *Vgl. deut. Monats. f. Zahnheilk.,* 1891, 355. Auch über die Diskussion, s. bei v. Ziemacki, *loc. cit.,* 374-376.

Magill: "A New and Rapid Method of Anesthesia," *N. Y. Med. Rec.,* 1893, 21; Okt: *Zentralbl. f. Chir.* 1894, 750; *Internat. Med. Rec.,* 1894; Okt: *Zentralbl. f. Chir.,* 1895, 658.

Malherbe: "De l'anesthésie au bromure d'éthyle dans la position de Rose pour les petites opérations pratiquées sur les voies respiratoires supérieures," *Rev. hebd. de Laryngol., d'Etol. et de Rhinol.,* 1900, Nr. 26. *Zentralbl. f. Chir.,* 1901, 662.

Mittenzweig: "Über tödliche Nachwirkung der Bromäthylnarkose," *Zeitschr. f. Med.,* 1890, *3,* 40.

Mittenzweig und Stahn: "Experimenteller Beitrag zur Vergiftung durch Bromäthyl," *Zeitschr. f. Med.,* 1890, *3,* 373.

Montgomery: *Am. J. of Obstet.,* 1885, 561. Ref. bei Haffter, *loc. cit.,* 110. "Bromäthyl in der Geburtshilfe."

Moses: *Vereinig. west. Hals- u. Ohrenärzte zu Köln,* Apr., 1912, 21, "Bromäthylnarkose der Chloräthylnarkose gleichwertig für Tonsillotomien," *Med. Klinik,* 1912, 1685.

Müller, B.: "Uber Fettmetamorphose in den inneren parenchymatösen lebenswichtigen Organen nach einfachen und Mischnarkosen," *Arch. f. klin. Chir.,* 1905, *75,* 896.

Müller, B.: "Über die Anwendung des Bromäthyls in der Geburtshilfe," *Berl. klin. Woch.,* 1883, 673.

Napalkow: "Zur Frage der kombinierten Bromäthyl-Chloroform-Narkose," *Chir.,* Aug., 1902; *Zentralbl. f. Chir.,* 1903, 263.

Norton: "Bromide of Ethyl as an Anesthetic," *Brit. Med. J.,* 1880, *2,* 535; "New Forms of Anesthetics," *Brit. Med. Assn.,* 1865. Nunneley: *Brit. Med. J.,* 1865, *2,* 192.

Österlen: "Bromäthyl," *Korrespond. f. Zahnärzte,* 1889.

Pauschinger: "Bromäthyl," *Münchener med. Woch.*, 1887. Nr. 30, 568.

Petsch: "Das Bromäthyl und seine Verwendung als Anästhetikum," *Deut. Monats. f. Zahnheilk.*, 1888, 471.

Phillips: "Ethylbromid in Ophthalmic Surgery," *Phil. Med. and Surg. Rep.*, Feb. 5, 1887, 177.

Pomeranzew: "Charakteristik des Bromäthyls in bezug auf die Gefar seine Anwendung als Anästhetikum," *Chirurgia,* Russisch, 1897, S. 1. *Zentralbl. f. Chir.*, 1897, 462.

Rabuteau: *Compt. rend. de la Soc. de Biol.*, 1876, *28*, 49; M. Fraenkel: *Loc. cit.* "Recherches sur les propriétés physiologiques et la mode de l'administration de l'éther bromhydrique," *Compt. rendu. de l'Acad. des Sciences,* 1876, *33*, 1294; Virchow-Hirsch: *Jahresber.*, 1876, i, 415; Fraenkel: *Loc. cit.* "Recherches sur les propriétés physiologiques et la mode d'élimination de l'éther bromhydrique," *Gaz. des Hôp.*, 1877, 50. "Recherches sur les propriétés physiologiques et la mode d'élimination du bromure d'éthyle; usage de cet éther; son action sur la germination et la végétation," *Mém. communiqué à la Soc. de Biol. Gaz. méd. de Paris,* 1880, 334, 385 et 411; Virchow-Hirsch: *Jahresber.*, 1880, i, 455.

Regli: "Eperimentelle Beiträge zur Kenntnis der Wirkung des Bromäthyls auf Herz und Nieren," *Diss.*, Berne, 1892.

Reich: "Über Bromäther und kombinierte (sukzessive) Bromäther-Chloroform-Narkose," *Wiener med. Woch.*, 1893, No. 23 u. 28, 993, 1046, 1090, 1141, 1178 u. 1224.

Rein: "Über die Mischnarkose von Bromäthyl und Chloroform," *Chirurgie 5*, 530; *Zentralbl. f. Chir.*, 1900, 638.

Richelot: "Bromäthyl-Chloroform-Narkose," *Bull. de l'Acad. de Méd.*, 1902, *47*, 179.

Ritter: "478 Bromäthylnarkosen," Anlage 30 zu gurlts. Statistik. *Verh. f. XXI. Deut. Chirurgenkongr.*, 1892, Teil ii, 355. "406 Bromäthylnarkosen," Anlage 12 zu Gurlts. Statistik. *Verh. d. XXII. Deut. Chirurgenkongr.*, 1893, Teil ii, 38. "Bericht über weitere 335 Bromäthylnarkosen," Anlage 29 der Gurltschen Statistik. *Verh. XXIV. Deut. Chirurgenkongr.*, 1895, Teil ii, 519. "Bericht über 1365 Bromäthylnarkosen," Anlage 21 der Gurltschen Statistik. *Verh. d. XXIII. Deut. Chirurgenkongr.*, 1894, Teil ii, 54.

Roberts: "Case of Death Occurring During the Administration of Bromid of Ethyl," *Phila. Med. Times,* July 17, 1880. *Zentralbl. f. Chir.*, 1880, 639.

Robin: "Note sur un nouvel agent anesthésique, l'éther bromhydrique," *Compt. rendu. de l'Acad. des Sci.*, Paris, 1851, *32*, 649.

Rose: "Diskussion über Bromäthylnarkose," *Gesell. f. Geburtsh. u. Gynäkol. zu Berlin,* 1883; *Zentralbl. f. Gynäkol.*, 1883, 546.

Roth: "Über Brom-Äther-Narkose," *Prager med. Woch.*, 1906, No. 21; *Zentralbl. f. Chir.*, 1907, 1048.

Salzer: "Einige Worte über Narkose im Dienste der Zahnheilkunde," *Pest. med.-chir. Presse*, 1893, No. 22; *Zentralbl. f. Chir.*, 1893, 853.

Schede: "149 Bromäthylnarkosen," Anlage 31 zu Gurlts. Statistik. *Verh. d. XXI. Deut. Chirurgenkongr.*, 1892, Teil ii, 360.

Scheps: "Das Bromäthyl und seine Verwendbarkeit bei zahnärztlichen Operationen," *Diss.*, Breslau, 1887.

Schneider: "Über das Wesen der Narkose im allgemeinen, mit besonderer Berücksichtigung der Bromäthernarkose," *Deut. Monat. f. Zahnheilk.*, 1890, *8*, 170 u. 217; von Ziemacki: *Arch. f. klin. Chir.*, 1891, *42*, 732. "Das Bromäthyl in der zahnärztlichen Praxis," *Verh. d. X. Internat. med. Kongr. zu Berlin*, 1890, Bd. *5*, Abt. 14, 66. Vgl. *Deut. Monat. f. Zahnheilk.*, 1890, Nos. 8-10.

Schroeder: "Ein neuer Betäubungsapparat für Bromäther," *Monats. f. Zahnheilk.*, 1891, *9*, 513.

Schwartzkoph: "Erfahrungen mit Bromäthylnarkosen," Diskussionsbemerkung. *Deut. Monats. f. Zahnheilk.*, 1889, 350.

Segond: "Sur l'anesthésie combinée avec le bromure d'éthyle et le chloroforme," *Bull. et Mém. de la Soc. de Chir. de Paris, 20*, 39; *Zentralbl. f. Chir.*, 1895, 659.

Sims: "The Bromid of Ethyl as an Anesthetic," *N. Y. Med. Rec.*, 1880, 361; Virchow-Hirsch: *Jahresber.*, 1880, *50*, 454; *Vgl. auch Zentralbl. f. Chir.*, 1880, 714; *N. Y. Med. J.*, 1880, *32*, 176. *Zentralbl. f. Chir.*, 1880, 714.

Sowers: "Ethyl Bromid, or Hydrobromic Ether; Cases Operated on under Its Influence," *Phila. Med. and Sur. Rep.*, 1880, 92; Virchow-Hirsch: *Jahresber.*, 1880, 454.

Sternfeld: "Über Bromäthyl und seine Verwendung in der ärztlichen Praxis," *Münch. med. Woch.*, 1890, No. 1415, 251, 267.

Szuman: "Das Bromäthyl und die Bromäthyl-narkose," *Therap. Monats.*, 1888, 155 u. 226; *Zentralbl. f. Chir.*, 1888. "Über Bromäthyl und die Gefahren der Bromäthylennarkose," *Gaz. Lekarska*, 1890, No. 36; *Zentralbl. f. Chir.*, 1890, 1024.

Terrier: "Sur l'anesthésie combinée par le bromure d'éthyle et le chloroforme," *Bull. et Mém. de la Soc. de Chir. de Paris, 20*, 400. *Zentralbl. f. Chir.*, 1895, 658.

Terrier et Peraire: "Manuel de l'anesthésie chirurgicale," Paris, 1894.

Terrillon: "Anesthésie locale et générale par le bromure d'éthyle," *Compt. rendu*, 1880, *91*, 1170. Virchow-Hirsch: *Jahresbericht*, 1880, *1*, 454-455; *Gaz. méd. de Paris*, 1880, No. 22; *Zentralbl. f. Chir.*, 1880, 500. "De l'anesthésie générale par le bromure d'éthyle," *Bull. Gén de* *thérap.*, 1880, 300; *loc. cit.*, *Bull. de la Soc. de Chir.*, 1880, 316 et 320. "Diskussion über Bromäthyl," *Soc. de Chir. de Paris; Bull de Thérap.*, 1881, 337.

Thiem: "Diskussionsbemerkung betreffend Bromäthyl-narkose," *Verh. d. XIX. Deut. Chirurgenkongr.*, 1890, Teil i, 14.

Tschunichin: "Bromäthyl in der geburtschilflichen Praxis," *Wratsch*, 1885, No. 30; von Ziemacki: *Loc. cit.*, 730.

Turnbull: "Advantages and Accidents of Artificial Anesthesia," Phila., 1879. Virchow-Hirsch: *Jahresber.*, 1880, *1*, 454. "Artificial Anesthesia, A Manual of Anesthetic Agents, and Their Employment in the Treatment of Disease." Philadelphia, 1891, P. Blakiston's Son & Company.

Vajna: "Bromäthylmaske," Anlage 18 zu Gurlts. Statistik. *Verh. d. XXII. Deut. Chirurgenkongr.*, 1893, Teil ii, 43.

Veit: "Bromäthyl bei Kreissenden," *Diskussion in der Gesellsch. f. Geburtsh. u. Gynäk. zu Berlin*, 1883; *Zentralbl. f. Gynäk.*, 1883, 547.

Villeneuve: "Sur l'anesthésie combinée par le bromure d'éthyle et le chloroforme," *Bull. et Mém. de la Soc. de Chir. de Paris*, *20*, 418; *Zentralbl. f. Chir.*, 1895, 659.

Vutzeys: *Bull. de l'Acad. roy. de Belgique*, 1876; Zit. nach M. Fraenkel, *loc. cit.*, 9.

Walkhoff: "Todesfall durch Bromäther," *Monats. f. Zahnheilk.*, 1891, *9*, 517.

Wessler: "Skandinavisk Tidskrift för Tandläkara, 1889," Edition 4. von Ziemacki: *Loc. cit.*, 734 (41 Bromäthylnarkosen mit durchschnittlich 5 g.).

Wiedemann: "Über das Hydrobromäthyl als Anästhetikum am Kreissbett," *St. Petersburger med. Woch.*, 1883.

Wietland: "Die Narkosen im Basler Kinderspital," *Correspondenz-Blatt f. schweizer Ärzte*, 1894, 564 u. 597.

Wilcox: "Bromide of Ethyl as an Anesthetic," *Annals of Surg.*, 1891, No. 4; *Zentralbl. f. Chir.*, 1891, 1000.

Willemer: "64 Bromäthylnarkosen," Anlage 37 zu Gurlts. Statistik. *Verh. d. XXI. Deut. Chirurgenkongr.*, 1892, Teil ii, 365.

Williams: "Bromide of Ethyl as an Anæsthetic for Short Operations and as a Percursor to the Administration of Ether," *Brit. Med. J.*, 1882, *1*, 402.

Witzel, A. "Über den Gebrauch des Schlafgases in der zahnärztlichen Praxis" (Gefährlichkeit des Bromäthyls: vgl. 10). *Deut. Zahnheilkunde in Vorträgen*, 1889, Nos. 5-6, Hagen i. W., H. Riesel & Co.

Witzel, J.: "Bericht über 465 Bromäthernarkosen," *Monats. f. Zahnheilk.*, 1891, *9*, 421.

Witzel, O.: "Wie sollen wirk Narkotisieren," *Münch. med. Woch.*, 1902, 1903.

Wood: "The Physiological Action of Ethyl-Chlorid and Ethyl-Bromid," *Phil. Med. Times,* 1880, 370; Virchow-Hirsch: *Jahresber.,* 1880, *1.* 455.

v. Ziemacki: "Bromäthyl in der Chirurgie," *Arch. f. klin. Chir.,* 1891, *42,* 717.

Zimmer: "Mahnung zur Vorsicht mit Bromäther auf Grund zweier nich näher mitgeteilter Todesfälle in Berlin," Diskussionsbemerkung. *Monats. f. Zahnheilk.,* 1891, *9,* 518.

Ethyl Chlorid.—Monochlorethane is well known as an anesthetic (Heyfelder, 1848; Nunneley, 1849; Snow and Richardson, 1852.) See Chapter VI.

See *Kelene, Antidolorin, Loco-Dolor,* and *Ethylol.*

Ethyl Chlorid Bengue.—A purified ethyl chlorid.

Ethyl Chlorid C. P.—A "chemically pure" ethyl chlorid, for both local and general anesthesia.

Ethyl Chlorid Polychlorated.—This mixture of chlorinated ethyl chlorids, principally tri-, tetra-, and penta-chlorethane, is also known as "Wiggers' anesthetic ether" and as "polychlorated hydrochloric ether."

Ethyl Ether.—See Chapter V.

Ethyl ether (1 ounce) containing camphor (4 drachms) was used as a local anesthetic quite extensively about 1875.

Ethyl Ether-Chloroform Mixtures.—On the production of narcosis with a mixture of 1 volume of chloroform and 5 to 6 volumes of ethyl ether, see Kionka: *Jahreskurse f. ärztl. Fortbildung,* 1910, No. 8, 3.

Ethyl Formate.—Byasson experimented upon the lower animals with formic ether. He supposed that it was decomposed in the blood into alcohol and alkaline formates. Inhalation of its vapor lowered the temperature as much as 3.5° C., caused muscular relaxation and anesthesia, with some degree of asphyxia. Its effects resembled those produced by chloral hydrate rather than the effects of an ether. Upon the human subject, the use of 6 or 8 grams only caused drowsiness, without any other symptom.

Ethyl Hydrid.—Richardson (*Sci. Am. Suppl.,* No. 515, 8228) stated that the physiological action of this gas was generally the same as for amyl hydrid (*q. v.*); and that its anesthetic value was also practically the same, but less manageable, owing to its being a gas. It was Richardson who introduced ethyl hydrid in 1867.

Ethyl Iodid.—Hydriodic ether (mono-iodoethane) decomposes quite rapidly even in diffused daylight, the light liberating iodin which colors the ether; the decomposition is very slow in the dark, and may be rendered still slower by the addition of a very dilute solution of soda. It may also be kept in contact with a small amount of mercury. Ethyl iodid has been considered unsuitable for clinical purposes, owing to its unpleasant taste and its volatility (b. p., + 70-75° C.). It acts like chloroform, but anesthesia comes on slowly and is more permanent.

On the physiological action of ethyl iodid, see Webster: *Bio-Chem. J.*, 1906, *1*, 328.

Ethyl Nitrate.—Simpson (1848) found that "nitric ether" was a rapid and powerful anesthetic, but the subsequent headaches and disagreeable after-effects were of so serious a nature as to condemn it. Fifty or sixty drops were inhaled.

Ethly Nitrite.—"Nitrous ether" was tried by the Committee of the British Medical Association, which reported that it produced "great excitement and convulsions, almost immediately followed by cessation of respiration."

Ethyl-o-Anisidin Formate.—Found by Goldschmidt (*Chem. Ztg.*, *25*, 329) to be a strong local anesthetic. Goldschmidt (Eng. Pat. 9792, 1898) has also claimed the manufacture of compounds of orthoformic ester with o- and p-phenetidin and anisidin, for use as anesthetics.

Ethylene Chlorid.—S-Dichlorethane, $CH_2Cl.CH_2Cl$ ("dutch liquid"; elayl chlorid), has been employed as a general anesthetic instead of chloroform, especially in ophthalmic surgery. Its anesthetic action was first studied by Simpson in 1846, Snow in 1848, Clover in 1848, and Richardson in 1851. The latter (*Sci. Am. Suppl.*, No. 515, 8228) regarded it as a good anesthetic, very much like chloroform in its action, although less rapid. He pointed out that the vapor was pleasant to inhale; that the quantity required for complete anesthesia was 2 to 8 fluid drachms; that the required amount of air by vapor was 5 to 10 per cent; that the stages were induced slowly, with a rather long spasmodic period; and that recovery was slow, with, in rare cases, vomiting. It "deserves more experimental study."

Macleve (*Chem. News*, *41*, 154) used a mixture of ethylene chlorid and nitrous oxid. Reichert (*Phila. Med. Times*, *11*, 518) found that ethylene chlorid (?) caused anesthesia with the usual stages, and that, like chloroform, it depressed the heart and steadily lowered arterial pressure.

The ethylene chlorid on the market is a colorless, oily liquid, which possesses a density of 1.265 at + 15° C., and a boiling point of + 83° C.; it has a pleasant odor and sweet taste, but the vapor is irritating; it is soluble in alcohol, ether, chloroform, and slightly soluble in water. It is said to have a similar action to chloroform, and to have found extensive use as a chloroform substitute.

See Wallace: *Brit. Med. J.*, 1910, 1288.

Ethylene (Monochloro-) Chlorid.—This anesthetic, called also monochlorethylene chlorid, monochlorinated dutch liquid, and vinyl trichlorid, has been said to be superior to chloroform and ethylene chlorid. The preparation now on the market is prepared from vinyl chlorid by the action of antimony pentachlorid; it is a colorless liquid with a pleasant odor, boiling at + 114° C., and having a density of 1.458 at + 9° C. Taube (*Am. J. Pharm.*, 1880, 603; 1881, 119) showed the availability of monochlorethylidene and monochlorethylene chlorids as anesthetics.

Ethylene Dibromid.—S-Dibromethane ($CH_2Br.CH_2Br$) is a colorless, volatile, emulsifiable liquid, possessing a chloroform-like odor. The density of the product on the market is 2.189 at + 15° C., and it boils at + 129-131° C. It is miscible in all proportions with alcohol, but is insoluble in water. Ethylene dibromid is a cardiac poison and its anesthetic action is slight. Scherbatscheff (*Arch. exp. Path. u. Pharm.*, 1902, 47) found that ethylene bromid is not a true anesthetic in lower animals. It is probable that some of the evil effects produced in the early use of *ethyl bromid* (*q. v.*) were due to the presence of ethylene bromid in the preparations then in use.

Ethylidene Chlorid (Chlorinated muriatic ether; a-dichlorethane; ethidene bichlorid; chloridene; Aran's ether).—This compound is used instead of chloroform for minor operations, producing rapid narcosis of short duration. Ethylidene chlorid was apparently first used by Snow (see *"On Anesthetics,"* p. 23) in 1851. Richardson states (*Sci. Am. Suppl.*, No. 515, 8228) that "Snow, who introduced this anesthetic, and who was seized with his first fatal attack while writing upon it, told me he estimated its value as equal to chloroform, an estimate which has been sustained by later experience. The anesthetic has, however, more than once proved fatal, apparently from failure of the circulation, although in my own experiments with it on lower animals I once restored a rabbit to life by artificial respiration seven minutes after the natural respiration had ceased." Richardson found the vapor of "ethene dichlorid" pleasant to breathe; that the quantity required for complete anesthesia was 2 to 8 drachms; and the required charge of air by vapor was from 5 to 10 per cent. Anesthesia was found to be produced rather more rapidly than by chloroform, with the second or spasmodic stage sometimes acute; but recovery was easy, with no important after-effects, and vomiting was a less frequent accompaniment than after chloroform.

Binz (*Med. Times and Gaz.*, 1879, 1) produced human anesthesia by means of ethylidene chlorid and thought it increased the force of circulation; but Reeve ("New Remedies," 1880, 334) found that it lowers arterial pressure, although it does not suddenly paralyze the heart. See, also, Clover: *Brit. Med. J.*, May 29, 1880, 797; and *Comm. Rep., idem,* Jan. 4, 1879.

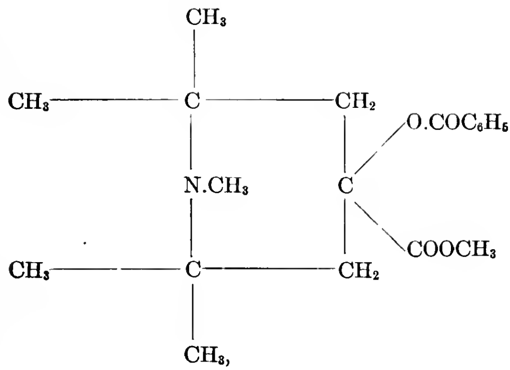
The ethylidene chlorid on the market is a colorless, oily liquid, possessing the odor and taste of chloroform; it has a density of 1.178 at

+ 15° C., and boils at + 58-60° C. That used by Richardson possessed a density of 1.174 and a boiling point of + 64° C.; it was undoubtedly lacking in purity, and it would be of value to thoroughly study the physiological action of this compound, using the pure preparation.

See *Æther Anæstheticus Aranii.*

Ethylol.—A purified ethyl chlorid of German manufacture.

Eucain-A.—"Alpha-eucain" is the hydrochlorid of benzoyl-n-methyl-tetramethyl-gamma-oxypiperidin carboxylic methyl ester, $C_{19}H_{27}NO_4.HCl.H_2O$. It was also termed eucainæ hydrochloras, since eucain-A



(or alpha-eucain), is properly the base, of which eucain-A, so-called, is the hydrochlorid. The preparation on the market in 1896 formed colorless crystals and was soluble in about 10 parts of water. Its solution was sterilizable by boiling

The base eucain-A is constitutionally closely allied to cocain, and, like the latter, is a local anesthetic; it is, however, cheaper than cocain. Gaetono Vinci (*Berl. klin. Woch.,* 1896, No. 27) found that, in the case of the eye, anesthesia resulted in 2 to 5 minutes after the application of a 2 per cent water solution, while its influence lasted from 10 to 15 minutes. Its application was said to cause neither mydriasis nor paresis of accommodation—it did not act on the pupil or contract the arterioles—but to produce a slight hyperemia of the mucous membrane.

A number of writers have expressed themselves on the properties of eucain-A, namely:

Kiesel: *Zahnärztl. Rundschau,* 1896, No. 196.
Wolff: *Zahnärztl. Woch.,* 1896, No. 472.
Berger: *Rev. de thérap. méd. chir.,* 1896, 355.
Vollert: *Münch. med. Woch.,* 1896, Nos. 22 and 37.
Görl: *Therap. Monatsh.,* 1896, No. 7, 378.
Deneffe: *Le Scalpel,* Sept. 13, 1896, No. 11.

Fuller: *Internat. J. of Surg.*, 1896, No. 9.
Forster: *Langsdale's Lancet,* August, 1896.
de Mets: *Belg. méd.*, 1896, No. 43.
Legueu: *Presse médicale,* 1896, No. 88.
Vinci: *Virchows Archiv, 145,* 78; *Therap. Monatsh.*, 1896, 330.
Carter: *Pharm. J.*, 1896, No. 1360.
Zwillinger: *Pest. med. chir. Presse,* 1896, Nos. 44 and 45.
Best: *Deut. med. Woch.*, Sept. 3, 1896, 573.
Vogt: *Bull. Gén. de Thérap.*, 1897, 112.
Bocquillon: *J. méd.*, Paris, 1897, No. 37.
Reclus: *La France Méd.*, 1897, No. 8.

These journal contributors seemed to be favorably impressed with eucain-A on the whole and regarded it as a suitable substitute for cocain, although Vollert, Zwillinger, and Best drew attention to the irritating action, which was so considerable that even a 1 per cent solution caused a sensation of pain and burning. Vollert (*loc. cit.*), as well as Wüstefeld (*Münch. med. Woch.*, 1896, No. 51), also observed that mydriasis and accommodation were affected, but not in the same degree as by cocain; they also objected to the destructive action on the epithelium of the cornea and conjunctiva. Deneffe noticed that eucain-A hardened the tissue to such an extent as to make it difficult to introduce a suture needle through it.

In 1897 there were two varieties of eucain on the market, viz.: *Eucain-A* and *Eucain-B* (*q. v.*). Schmitt (*"Nouveaux remèdes,"* 1897, 353) pointed out that eucain-B was superior to eucain-A, inasmuch as it was 2 to 3 times less toxic. Eucain-A was, in 1897, prescribed in the form of an ointment for producing anesthesia on mucous membranes, and in painful wounds, and for itching piles, *pruritus ani,* and *pruritus pudendorum* (*Therap. Monatsh.*, 1897, No. 2, 127); and the majority of the clinical observations published during this year related to eucain-A, while it was ascertained that eucain-B was particularly suitable for ophthalmic operations.

For experimental data relating to the physiological action of eucain, as compared with that of cocain, consult the following contributions on the subject:

Pouchet: *Nouveaux remèdes,* 1897, 169; *J. de méd. de Paris,* 1897, No. 10.
Von Eecke: *Belgique méd.*, 1897, No. 790.
Charteris: *Brit. Med. J.*, 1897, No. 1891.
Noel: *Sem. méd.*, 1897, No. 26, 210.
Vinci: *Virchows Archiv,* 1897, No. 2, 145.
Schmitt: *Nouveaux remèdes,* 1897, No. 12, 353.
Hobday: *Brit. Med. J.*, 1897, No. 1901.
Legrand: *Nouveaux remèdes,* 1897, 161.

On the therapeutic application of eucain-A, see Reclus-Hernette: *Nouveaux remèdes,* 1897, 172.

On the employment of eucain-A in surgery, see the following papers:

Horne: *Brit. Med. J.,* Nov. 27, 1897.

Hernette: *Thèse,* Paris, 1897.

Legrand: *Nouveaux remèdes,* 1897, 161.

Jarrow: *Med. Rec.,* 1897, 49.

Legueu and Lihou: *Presse méd.,* 1897, No. 15, 80.

Lohmann: *Therap. Monatsh.,* 1897, 427.

Legueu and Lehuell: *Gaz. des Hôp.,* 1897, No. 19, 20.

Heinze: *Virchows Archiv,* 1898, 466.

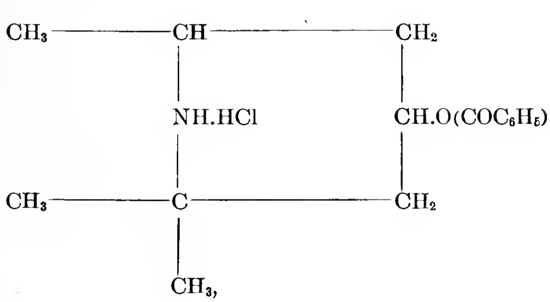
Reclus: *Therap. Woch.,* 1897, No. 8, 191.

Hackenbruch: *"Oertliche Schmerzlosigheit bei Operationen,"* Wiesbaden, 1897.

Spencer: *Univ. Med. Mag.,* Nov., 1896; *Med. and Surg. Rep.,* Nov. 28, 1896.

These contributions, together with many others on the bearing of eucain in ophthalmic surgery, rhino-laryngology, and otology, dental surgery, and in the treatment of urethral diseases, showed that eucain-A, or rather the eucains, are endowed with considerable anesthetic power. Eucain-A was objected to, especially by ophthalmic surgeons, particularly because it produced a slight irritation on the mucous membrane; and it may be said that it was practically discontinued on the introduction of eucain-B (*q. v.*). Moreover, eucain-A is more toxic than eucain-B in the proportion of about four to one.

Eucain-B.—"Beta-eucain," beta-eucain hydrochlorate, 2, 6, 6-trimethyl-4-benzoxy-piperidin hydrochlorid, or benzoyl-vinyl-diacetone-alkamin hydrochlorid.



or $C_5H_6.C_7H_5O_2.CH_3.NH(CH_3)_2HCl$, is a white crystalline powder possessing the following solubilities at ordinary temperatures:

In water	3.5 per cent.
In alcohol	3.5 " "
In chloroform	15.0 " "
In glycerin	2.0 " "

One part of beta-eucain hydrochlorid is soluble in 5 parts each of anilin and alcohol, and is insoluble in olive oil and paraffin oil alone, or in ethyl ether in material amounts. Suspensions with lanolin and the heavy mineral oils may be prepared by first mixing the salt with 4 to 5 parts of hot water. It fuses with decomposition at + 268° C.

Benzoyl-vinyl-diacetone-alkamine was proposed by Vinci as a local anesthetic in 1897; it is an alkaloid related to *Tropacocain* (*q. v.*) Vinci termed it eucain-B (beta-eucain), while the earlier preparation, which is decidedly of less value, had been designated eucain-A (*q. v.*). This nomenclature, as shown by Marcinowski, gave rise to some confusion and error; but, since eucain-A is now off the market, this need no longer exist. The free base, the proper eucain-B, is, like cocain and eucain-A, almost insoluble in water; but it combines with acids to form soluble salts, of which that with hydrochloric acid has been most employed. It is for this reason that beta-eucain hydrochlorid has been commonly referred to as eucain-B or beta-eucain. The preparation has displaced eucain-A, and is employed as a local anesthetic in dentistry and ophthalmic practice, and, like cocain, is mixed with ethyl chlorid for inducing local anesthesia by spraying or plugging.

Schmitt (*Nouveaux remèdes,* 1897, 353) stated that eucain-B is superior to eucain-A, since it is 2 to 3 times less poisonous, and it has been pointed out that it is less toxic than eucain-A, in the proportion of one to four (Francis and Fortescue-Brickdale's "The Chemical Basis of Pharmacology," 1908, 307). It has been stated that it is somewhat painful to inject, and that it dilates the blood vessels, and so promotes bleeding—disadvantages which may be overcome by injecting beta-eucain in normal saline at body temperature, or by mixing some adrenalin solution with the preparation.

As mentioned under eucain-A, it was ascertained that eucain-B is particularly adapted for ophthalmic operations in 1897 (see Darier: *La Clinique ophthalmol.,* 1897, 210; Dolganoff: *Wratsch,* 1896, No. 51; Mayrard: *Indian. Med. Gaz.,* 1897, 44; Silex: *Therap. Monatsh.,* June, 1897; and Sweet: *Am. Therap.,* 1897, No. 8). In 1898 its utility had not received general recognition, although a number of physicians spoke in its favor, and it was given as an opinion by several recognized medical authorities that cocain was a more satisfactory anesthetic. Reclus (*Semaine méd.,* 1898, No. 18, 193), supported by Legrand (*Nouveaux remèdes,* 1898, No. 11, 251) recognized the main disadvantages of eucain-B, as compared with cocain, in the fact that its anesthetic action was observed to be a little feebler, and that in consequence of its vasodilatory properties it produced hemorrhages, besides causing pain when injected; and Wohlgemuth (*Deut. med. Ztg.,* 1898, No. 33, 337) pointed out that the view that eucain-B was less toxic than cocain was based upon a delusion. Consequently, many looked upon eucain-B as by no means a complete substitute for cocain, and only regarded tropacocain as such. In the next year, however, we find Bardet, Bolognesi, and Touchard (*Nouveaux remèdes,* 1899, No. 3, 49) employing eucain-B, like cocain, mixed with ethyl chlorid for inducing local anesthesia by spraying or plugging, although the results of this method were hardly so favorable as those obtained with cocain-ethyl chlorid. In this year Porter (*Brit. Med. J.,* 1899, No. 2010, 84) recorded a case in which the injection of eucain into the prepuce, preparatory to circumcision, gave rise to an extensive edema of the penis and, ultimately, suppuration at the site of injection. Experiences of this kind seemed to indicate that cocain and eucain were by no means identical in their action, and that they were only partially equivalent.

In 1900 Lohmann recommended eucain-B as a substitute for cocain in Schleich's method of infiltration (*Therap. Monatsh.,* 1900, No. 9, 478). In the opinion of Engelmann (*Münch. med. Woch.,* 1900, No. 44, 1532), however, eucain-B was not available as a substitute for cocain in Bier's method of cocainizing the spinal cord, since it did not in this respect possess any advantage over cocain.

In 1901 Gray (*Lancet,* 1901, No. 4045) published new methods of applying eucain-B; he employed the compound in combination with cocain for local anesthesia in the ear, nose, and throat. In opposition to the view of Engelmann, expressed the previous year, Fink (*Prager med. Woch.,* 1901, April 11 and 18) recommended eucanization of the spinal cord by Bier's method in those cases in which cardiac, pulmonary, and renal complications, or the age and feebleness of the patient, precluded the narcosis by chloroform. It was at this time that beta-eucain acetate (*q. v.*) began to be used.

More recently eucain-B has been used with successful results in the treatment of sciatica by Lange (*Münch. med. Woch.,* 1904, No. 52), and by Opitz (*Klin.-therap. Woch.,* 1907, No. 14) and Gallatia (*Gynäkol. Rundschau,* 1907, No. 21).

H. Braun, in his text-book on local anesthesia, published in Leipzig in 1905, pays many tributes to the properties of eucain-B. He points out that he and Heinze have shown that it is entirely equal in effect to cocain when endermically administered, and that there is no pain or specific irritation from the injection even when 10 per cent solutions, made with the aid of heat, are employed. Even 0.005 per cent solutions effect a distinct diminution of sensibility, and eucain anesthesia is slightly less persistent than cocain anesthesia under like conditions, although a 1.5 per cent beta-eucain solution has about the same effect as a 1 per cent cocain solution in the duration of the anesthesia. No damage, we are told, is done to the tissues by the injection of an osmotically indifferent and moderately concentrated beta-eucain solution. Braun also states that the local anesthetic properties of beta-eucain solutions are, in general, equal to those of a cocain solution of slightly less concentration; its diffusive action is somewhat less, but it can be increased by making the solution stronger. Dolbeau, Schmidt, Dumont, and Legrand found that the fatal dose of beta-eucain was 3 to 3¾ times greater than that of cocain; Braun's experiments gave similar results for equal concentrations, but he could not agree with Dolbeau when he stated that, on intravenous injection, beta-eucain was as poisonous as cocain. He found that there was an important difference in favor of beta-eucain under these circumstances. Braun stated that the literature contains no records of poisoning by beta-eucain, except in the cases in which it was employed for lumbar anesthesia. He thought, however, that these ill effects after lumbar injection were undoubtedly chiefly due to the actual contact effects of the injected fluid on the central nervous system, and that they were not due at all to absorption phenomena.

On eucain-B in infiltration analgesia, see Houghton: *J. Roy. Army Med. Corps,* April, 1905; Tinker: *J. Am. Med. Assn.,* Feb. 11, 1905; and Parker: *Chicago Med. Rec.,* April 15, 1905.

On eucain-B in local anesthesia, see Link: *Indiana Med. J.,* June, 1905; *Harrison, Va., Hosp. Bull.,* Oct. 15, 1904; Hildebrandt: *Berl. klin. Woch.,* May 1, 1905; Marquis and Kraft: *J. Am. Med. Assn.,* April 22, 1905; Tuller: *Dental Cosmos,* April, 1903; Connell: *Ann. of Surg.,* Dec., 1903; Witherspoon: *Interstate Med. J.,* July, 1903.

The literature relating to eucain-B is quite extensive and cannot be included here in its entirety. Suffice it to say in conclusion that it is recorded as a local anesthetic which has been favorably reported upon in more than one hundred journal contributions; that it is said to possess the same analgesic power as cocain, but is only one-fourth as toxic; that it does not affect the heart or the nervous system, not causing local irritation or general intoxication; that it is devoid of the stimulating powers which render cocain, particularly when used in the nose and throat, so seductive a drug; and that its solutions are permanent and undergo no change when boiled.

Dusterbehn (*Apoth.-Ztg., 26,* 22) found that, when eucain-B is heated at + 100° C. with 10 times as much sulphuric acid, benzoic acid splits off; in the case of eucain-A, however, methyl benzoate is formed. The *Deut. Arzne.* states the contrary.

On reactions for differentiating between alpha and beta-eucain, see Saporetti: *Boll. chim. farm., 48,* 479. The deportment of these compounds with various reagents is given and discussed, and novocain, nirvanin, alypin, and cocain are also considered.

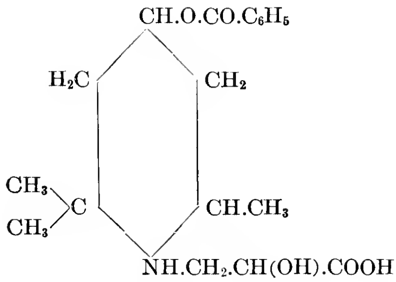
Eucain Acetate.—In 1901 eucain acetate ($C_{15}H_{21}NO_2.C_2H_4O_2$) was recommended in the place of beta-eucain hydrochlorid, being said to surpass the latter as regards solubility.

Cohn (*Med. Woch.,* 1901; No. 36; *Therap. Monatsh.,* 1901, No. 11,

595) employed eucain acetate in the form of a 2 per cent water solution, and produced, with the application of as little as 4 or 5 drops, complete anesthesia, which set in within 3 minutes and lasted for 10 to 15 minutes, so as to be available for the extraction of foreign bodies, the galvano-cauterization of corneal ulcers and pterygia, and the performance of minor operations on the lacrymal apparatus and the conjunctiva. Eucain acetate therefore appeared to be well adapted for minor operations on the eye—an anesthetic not likely to fail except in cases where portions of the anterior half of the bulbus were *per se* congested with blood and irritated.

Eucain acetate solutions were said to be capable of boiling without danger of decomposition. This salt of eucain is, however, no longer on the market.

Eucain Lactate.—Beta-eucain lactate (2, 6, 6-trimethyl-4-benzoxypiperidin lactate; benzoylvinyldiacetone-alkalamin lactate) has the following composition:



It is a white crystalline powder, fusing at about + 152° C. and possessing the following solubility at the ordinary temperature:

In water	22 per cent.
In alcohol	11 " "
In chloroform	20 " "
In glycerin	5 " "

The water solution is feebly alkaline to litmus. One part of eucain lactate is said to be soluble in 5 parts each of anilin and alcohol, and it may be dissolved in paraffin oil by the aid of chloroform. It is said to be insoluble in olive oil and paraffin oil alone, and not to be soluble in ethyl ether in material amounts. Suspensions in lanolin and the heavy mineral oils may be prepared by first mixing the salt in 4 or 5 parts of hot water.

Beta-eucain lactate is prepared according to the process claimed in U. S. Patent 657,880 of Sept. 11, 1900. It is said to have all the properties of *Beta-eucain Hydrochlorid* (*q. v.*), but to possess the advantage of being over six times as soluble in water.

Langgaard (*Therap. Monatsh.*, 1904, No. 8, 416) advocated the employment of eucain lactate for local anesthesia, since he found it to be non-irritant, to induce neither hyperemia nor local anemia, and to cause no shrinkage. He stated that it is appropriately applied in the form of the following solutions:

In ophthalmic surgery..............	2 to 3	per cent. solutions.
In dental surgery..................	2 to 3	" " "
In anesthesia by infiltration.........	0.12 ——	" " "
In regionary anesthesia.............	2 to 5	" " "
Surgery of nose, throat and ear......	10 to 15	" " "

According to Langgaard, solutions of a concentration of less than 1 per cent should have added thereto 0.8 per cent of sodium chlorid, 0.6 per cent of which should be added to 1 to 2 per cent solutions of eucain lactate. Katz (*ibid.*, 1904, No. 8, 419) was the first to treat diseases of the throat, nose, and ear with the aid of this preparation, whereby he obtained very satisfactory results. Braun, in his text-book on local anesthesia referred to above, stated that eucain lactate has the same anesthetic effect as the hydrochlorid, and is equally free from irritative properties. He recommended that it be used instead of beta-eucain when a readily soluble salt of eucain is desired.

On the use of eucain lactate in eye, nose, ear, and throat work, see the following:

Ellis: *Cal. State J. of Med.*, May, 1905; Harris and Wilson: *Laryngoscope*, June, 1905; Meyer: *Therap. Monatsh.*, May, 1905.

On its use in ano-rectal surgery, see Pennington: *J. Am. Med. Assn.*, April 8, 1905; and *Am. Med.*, July 29, 1905.

Eucain-snuffpowder.—Lactose with 2 to 3 per cent of eucain hydrochlorid, also with an addition of 0.01 per cent of adrenalin.

Eucalyptus Extract.—This has been used as a local anesthetic in dental operations.

Eucapren.—A local anesthetic solution of suprarenalin (1 in 5,000) containing 1 per cent of beta-eucain lactate.

Eucarenalin.—An anesthetic consisting of a 1 per cent solution of beta-eucain lactate in 1 to 2,000 of suprarenalin. This preparation was made for the English market, but the name is now discontinued. See *Eucapren.*

Eudont.—Two separate liquids: One a solution of oil of cloves, camphor, alcohol, and chloroform; and the other a mixture of tincture of iodin, glycerin, and tincture of opium. Eudont is employed in dentistry.

Eudrenin.—This is a solution of eucain hydrochlorid, intended for dental local anesthesia, the local anesthetic effect of which is said to be augmented and prolonged by the addition of adrenalin chlorid, this latter compound having the power of contracting the capillaries and thus preventing the distribution of the eucain hydrochlorid throughout the system.

Eudrenin is offered to the trade in 1 c. c. ampules for hypodermic injection, and possesses the following composition:

Beta-eucain hydrochlorid....................	0.25 per cent.
Adrenalin chlorid...........................	1:10,000.

Both compounds are dissolved in physiologic salt solution, 1 c. c. Each ampule therefore contains beta-eucain hydrochlorid, 0.0025 gm.; adrenalin chlorid, 0.0001 gm.; and physiologic salt solution, q. s. See *Beta-eucain Hydrochlorid.*

Eugallol.—Ehrmann (*Therap. Monatsh.,* 1910, No. 5, 230) used Eugallol (pyrogallol monacetate) in an aqueous or oily dilution in the treatment of chronic proliferating catarrh, etc., and called the remedy a "caustic anesthetic" or a "caustic mucous membrane anesthetic," in opposition to the anesthesia of purely peripheral neurotic origin produced by cocain, and to the local anesthesia produced by cold.

Eugenol (Eugenic acid; carpophyllic acid; para-oxy-meta-methoxy-allyl-benzene).—Used in dentistry as a local anesthetic. An old-fashioned remedy for toothache consisted in filling the cavity with a clove, which owes its anesthetic properties to eugenol. Like all the phenols, eugenol acts on nerve endings. Eugenol was recommended by Redman (Holländer-Schneidermühl's "Handbuch der zahnärztl. Heilmittellehre," 1890, 149) as an anesthetic suitable for sensitive dentine. It was reported upon by Wittel, Scheuer, and Richter (*J. f. Zahnheilkunde,* 1902, No. 12, 115), and Hertwig (*ibid.*) praised eugenol as an excellent antiseptic and anesthetic for sensitive dentine and for the pulp.

On Eugenol as an anesthetic, see Cohn: *Pharm. Centralh., 40,* 33.

Eugenol Acetamid.—This compound,

$$C_6H_3.C_3H_5.OCH_3.OCH_2.CONH_2,$$

is used in the form of a fine powder in the place of cocain as a local anesthetic on mucous surfaces. It forms glossy scales, fusing at + 110° C.

On this preparation, see Cohn: *Pharm. Centralh., 40,* 33.

Eugenol-alcohol.—On this preparation as a local anesthetic, see Cohn: *Pharm. Centralh., 40,* 33.

Eugenol Esters of the Aminobenzoic Acids.—Riedel, in German Patent 203,093, of Nov. 7, 1907, claims the substitution for the heretofore employed anesthetics, carbolic acid, eugenol, creosote, and other phenol derivatives, of the eugenol esters of the aminobenzoic acids, in the application of arsenic trioxid as a tooth nerve devitalizer.

Euphorin.—See *Phenyl-urethane.*

Eupnema (Eupneuma).—This remedy for asthma contains 1 part of anesthesin and 2 parts of subcutin in 100.

Euroform Paste.—This dental anodyne and wound packing consists of orthoform 1 dram, europhen 1½ drams, petronol 2½ drams. and white petrolatum 2½ drams.

Euscopol.—A "chemically pure, inactive *Scopolamin Hydrobromid* (*q. v.*), free from foreign bases." It forms colorless crystals, melting at + 180–181° C., and is soluble in water and alcohol. See Adam: *Med. Klinik,* 1911, No. 52, 2026.

Eusemin or Eusemine.—A sterile solution in hermetically sealed vials of: Cocain hydrochlorid, 0.0075 gm. (0.116 grain); and adrenalin hydrochlorid, 0.00005 gm. (8/1,000 grain), dissolved in physiologic salt solution, 1 c. c. Littaur (*Deut. med. Woch., 35,* 1277) states that eusemin is a mixture of cocain with adrenalin in physiological salt solution. He considered it of value as a local anesthetic. *Gehe's Codex* (Nov., 1910, 119) states that eusemin is a solution of 0.75 per cent cocain hydrochlorid and 5 per cent of a 1:1,000 adrenalin solution in physiological salt solution. Riedel's "Mentor" (1911, 153) states that each c. c. contains 0.0075 gm. cocain hydrochlorid and 0.00005 gm. adrenalin hydrochlorid in physiological salt solution.

Neuhann (*Med. Klinik, 8,* 780) stated that the toxicity of eusemin was reduced to a minimum on account of its small content of cocain and adrenalin. He reported that it is sterilized in an autoclave.

Falkenstein's Zahnpasta.—A paste said to contain an "antiseptic anesthetic."

Filodentol Bertagnolli.—A red-colored alcoholic solution of oils of cinnamon and peppermint, intended for the treatment of odontalgia.

Formal.—See *Methylal.*

Formaldehyd-kelene.—*Kelene* (*q. v.*) containing formaldehyd for use in treating hay fever, catarrh, etc.

Formanilid.—This compound, phenyl foramid (C_6H_5.NH.CHO), is a reaction product of anilin and formic acid. It occurs in colorless to yellowish crystals, which are soluble in water and alcohol, and which melt at + 46° C. In a paper by Kossa, Tauszk, Preisach, and Meisels (*Magyar Orvosi Arch.,* through *Therap. Blätter,* 1893, 143), formanilid is described as a very powerful antipyretic, also acting as an analgesic, producing local anesthesia, even when employed in smaller quantity than cocain. It is said to be used externally in 20 per cent solution to produce local anesthesia in one hour. Formanilid is also said to be hemostatic.

Formyl Tribromid.—See *Bromoform.*

Fresenius Anæsthesin-bormelin.—See *Anæsthesin-bormelin.*

Frohmann's Solution.—A dental local anesthetic composed of cocain hydrochlorid, 0.2 part; morphin hydrochlorid, 0.25 part; sodium chlorid (sterilized), 0.2 part; antipyrin, ½ guaiacol, 2 drops; and distilled water, 100 parts.

Gajacyl.—See *Guaiacyl.*

Gasoline.—Used as a local anesthetic in 1879. See *Pentane.*

Gasu-basu.—See *Nervocidin.*

Glacial.—A mixture of methyl and ethyl chlorids, intended for use as an anesthetic.

Gleditschin.—See *Stenocarpin.*

Goldschmidt's Anæsthetics.—According to Goldschmidt (*Chem.-Ztg., 26,* 743), p-phenetidin and its homologues give with o-formic acid ester, according to the reaction of Claisen, anesthetic compounds of the type of methenyldi-p-phenetidin. Goldschmidt (see *Pharm. Ztg., 46,* 323) stated that o-anisidin-ethyl-formate and o-phenetidinethylformate are anesthetics.

Gray's Anæstheticum.—Cocain hydrochlorid, 1; anilin, 5; diluted alcohol, 5. For use in ear affections.

Grehant's Anesthetic.—A 4 per cent solution of morphin is given, ¼ c. c. per kilogram of animal, followed in half hour by 10 c. c. per kilogram of a mixture of chloroform 50 c. c. and alcohol and water each 500 c. c. See McNider: *Proc. Soc. Exper. Biol. and Med.,* 1913, *10,* 95.

Guaiacol.—This compound has been used as a local anesthetic; it is said to be innocuous, but irritating. On the production of complete anesthesia by the cataphoresis of a mixture of guaiacol and cocain, see Morton: *Dental Cosmos,* Jan., 1896; Berten: *Berl. klin. Woch.,* 1896, No. 35, 769; Marcus: *Deut. med. Woch.,* 1897, No. 10. On the anesthetic action of Guaiacol, see Cohn: *Pharm. Centralh., 40,* 33.

Holland (*Dental Brief,* 1901, 8; *Odontolog. Blätter,* 1902, No. 13, 254) found guaiacol to be a valuable means for the removal of pains in pulpitis, and also a useful addition to arsenic and cocain caustic paste. Hecht (*Therap. der Gegenwart,* 1909, 354) published a report on the use of guaiacol as an anesthetic and antiphlogistic; this is worthy of careful perusal by every physician, for, although the external use of guaiacol has not met with great favor, this may be largely attributed to a certain prejudice founded on the bad effects displayed by excessive amounts.

Guaiacol dissolved in olive oil has been employed as a local anesthetic, although this solution has not met with general favor. It was introduced by Lucas-Championnière. According to Heineck ("General and Local Anæsthesia," 1909, 79), it does not produce anesthesia as rapidly as cocain; it can cause sphacelus; it does not always produce anesthesia; and there is considerable irritation at the periphery of the area of injection.

On the employment of guaiacol as a local anesthetic, see the following contributions:

Benoit: "Du gaïacol et de la cocaïne considérés comme anesthésiques locaux," *Thèse de Paris,* 1896.

Championnière: "Le gaïacol comme anesthésique local et discussion," *Bull. de l'Acad. de Méd.,* July 23, 1895; *La France méd.,* 1895, No. 31; "Emploi du gaïacol pour l'anesthésie locale en remplacement de la cocaïne," *Bull. de l'Acad. Méd.,* 1895, No. 30; "Emploi du gaïacol pour l'anesthésie locale en remplacement de la cocaïne," *Lyon méd.,* 1895, No. 33; "Anesthésie locale par le gaïacol," *J. de Méd. et de Chir. Pratiques,* 1895, No. 17.

Coutant: "Contribution à l'étude des anesthésiques locaux et en particulier du gaïacol en injections intracutanées," *Thèse de Bordeaux,* 1896.

Malot: "Des injections sous-cutanées de gaïacol chloroforme comme analgesique local," *Thèse de Paris,* 1897.

O'Followell: "L'Anesthésie locale par le gaïacol, le carbonate de gaïacol et le gaiacyl," *Thèse de Paris,* 1897.

Reclus: "Sur la valeur comparée du gaïacol et de la cocaïne dans l'anesthésie locale," *Bull. de l'Acad. de Méd.,* 1896, No. 20.

Guaiacol Benzyl Ester.—See *Benzcain.*

Guajacid, or Guaiacyl.—Calcium guaiacol monosulphonate,

$$[(C_7H_7O_2SO_3)_2Ca]$$

is a grayish-white powder, freely soluble in water and alcohol, but insoluble in fatty oils. It acts like guaiacol, as an innocuous local anesthetic [André: *J. Pharm. Chim.,* 1898, (6), 7, i, 324; and Followell: *Presse médicale,* 1898, No. 25]. Capitain (*Belge medicale,* 1898, 691) praised guaiacyl on account of its antiseptic and anesthetic properties, as well as on account of its harmlessness. It is said to have been used in minor surgery, dentistry, etc.

Guaiasanol (Gujasanol).—Diethylglycocoll-guaiacol hydrochlorid, $C_6H_4(OCH_3).[CH_2N(C_2H_5)_2.COO].HCl = C_{13}H_{19}NO_3HCl$, is the hydrochlorid of diethylglycocoll-guaiacol. It is prepared by the action of chloracetylchlorid on guaiacol and decomposition of the product with diethylamin. It forms small, colorless, prismatic crystals, melting at $+183°$ to $184°$ C. ($361.4°$ to $363.2°$ F.), having a slight odor of guaiacol and a bitter saline taste. It is soluble in its own weight of water and in 25 parts of alcohol, but is insoluble in ether. The solution in water should be clear, colorless, and give a white precipitate with silver nitrate. The oily base separates on the addition of an alkaline hydroxid. When incinerated on platinum it leaves no residue. It is incompatible with alkalies and their carbonates.

Actions and Uses.—It is antiseptic and anesthetic. It is readily absorbed and splits off guaiacol in the organism with facility. Its antiseptic power is said to be about equivalent to that of boric acid. Guaiasanol has been recommended for the treatment of tuberculosis, both internally and subcutaneously. It is also said to be useful as a deodorant and to have given good results in putrid cystitis.

Guaiasanol has been tested pharmacologically by Heinz, bacteriologically by Büchner, and clinically by Einhorn (*Münch. med. Woch.*, 1900, No. 1, 11). Schäfer (*ibid.*, 1903, No. 31, 1363) employed it in the treatment of tuberculosis of the larynx as well as of the bones; and Rahn (*ibid.*, 1905, 783 and 1806) used the preparation successfully in the treatment of oxyuris vermicularis and for a mouth deodorant. It is said that, when a 1 per cent solution is used for superficial wounds of the eye, there is quite a perceptible anesthetic effect.

Dosage.—One to three gm. (15 to 45 grains) in wafers; subcutaneously, 3 to 4 gm. (45 to 60 grains) in 20 per cent aqueous solution; locally it may be used in from 0.1 to 2 per cent solutions.

Gujasanol.—See *Guaiasanol.*

Gummitropakokain.—Sterile ampules containing 1.2 c. c. gum solution and 0.05 gm. *Tropacocain Hydrochlorid* (*q. v.*). On the employment of this combination in lumbar anesthesia, see Hertel: *Münch. med. Woch.*, 1910, No. 16, 844.

Hedonal (Methylpropylcarbinol urethane; pentan-2-ol-urethrane).—Hedonal is pentan-2-ol-urethane, $CH_3.CH_2.CH_2.CH(CH_3)O.CO.NH_2 = C_6H_{13}O_2N$. It is a derivative of urethane, differing from ethyl carbamate, U. S. P., in that the ethyl radicle has been replaced by the radicle of methyl-propylcarbinol (pentan-2-ol),

$$CH_3.CH_2.CH_2.CHOH.CH_3.$$

It is prepared by heating the secondary methylpropylcarbinol or pentan-2-ol. $CH_3.CH_2.CH_2.CHOH.CH_3$ with urea nitrate under pressure (U. S. Patent No. 659,202), also by other methods (German Patents Nos. 120,863, 120,864, 120,865. It is a white, crystalline powder, having a faint aromatic odor and taste, melting at + 74° C. (165.2° F.), and boiling at + 215° C. (419° F.). It dissolves in 120 parts of water at 37° C. (98.6° F.), but is more soluble at higher temperatures, and is readily soluble in alcohol, ether, chloroform, and other organic solvents. It is readily volatilized with the vapors of water or alcohol, and when boiled with alkalies it is split up into its constituents, methyl-propylcarbinol, ammonia, and carbon dioxid.

On boiling with dilute sodium hydroxid, ammonia is evolved, and may be recognized by the odor and the usual reagents; if then an aqueous solution of iodin in potassium iodid is added, and the mixture is allowed to cool, the odor of iodoform, derived from the alcohol, is distinctly manifested. It is incompatible with alkalies, their carbonates, and bicarbonates.

Actions and Uses.—Hedonal appears to have a greater hypnotic effect than ethyl carbamate. It is said to be followed by no bad after-effects, and to be oxidized in the body to urea and carbon dioxid. It is employed in insomnia due to mental overwork, or nervous excitement occurring in the course of neurasthenia or hysteria. It is claimed to be a particularly useful preliminary to anesthesia, a hypnotic dose being given, and anesthesia is effected with chloroform after the patient has been asleep for an hour; and recently it has been found to be applicable by itself as an anesthetic for operations, especially if it is applied intravenously. See *Z. für Chir., 108,* 5-6.

When hedonal is employed as a preliminary to general anesthesia with chloroform, it must be given at least one hour before the anesthetic, for its absorption is slow. There are said to be objections other than this to its use in this manner. On hedonal as an anesthetic when applied intravenously, see Sichkovski: *Russkiy Vrach, 9,* 1447; Fedoroff: *Zentralbl. f. Chir.,* 1910, No. 9; Russisches: *J. f. Geburtshilfe u. Gynäkol.,* 1910, Nos. 5 and 6; Sidorenko: *Zentralbl. f. Chir.,* 1910, No. 37. On chloroform-hedonal anesthesia, see especially Krawkoff: *Russkiy Wratsch,* 1910; *Therap. Monatsh.,* 1910, 444. On intravenous hedonal anesthesia, see Sidorenko: *Zentr. Chirurg.,* 1910, No. 37, 1219; Jeremitsch: *Deut. Z. Chir.,* 1911, *108,* Nos. 5-6; Krzizewsky: *Russkiy Wratsch,* 1911, No. 13; Albinsky: *Ibid.;* Fedoroff: *Therap. Gegenwart,* 1911, 268; *Allg. med. Zentralztg.,* 1911, 305; *Zentr. Chir.,* 1910, No. 19, 675; Lytschkowski: *Petersburger med. Woch.,* 1911, 209. The last five authors confirm the advantages of this method of anesthesia on the whole. For a late report, see Page: *Lancet, 182,* 1258.

Dosage.—One to two gm. (15 to 30 grains), administered dry, followed by a swallow of water, or in wafers or capsules.

Hedonal tablets, 8 grains. Each tablet contains hedonal 0.52 gm. (8 grains).

Helleboreïn.—A glucose from *Helleborus niger* (Winter Rose; Black Bear's Foot), used as a local anesthetic in ophthalmic surgery; on the cornea 3 to 4 drops of a solution containing in 1 drop 0.0005 gm. is said to give complete anesthesia, without irritation, lasting 30 minutes. It is a yellowish powder, possessing the composition $C_{37}H_{56}O_{18}$, and is soluble in water and alcohol.

Heufibrol-crème Stauffer.—This contains *Anesthesin* (*q. v.*) and homorenon (ethylamino-acetobrenzcatechin hydrochlorid).

Heufieber-renitol.—Extract of suprarenal gland with a local anesthetic.

Hewitt's C. E. Mixture.—Chloroform, 2 parts by volume; and ether, 3 parts by volume. Mix. See Hewitt: "Anæsthetics and Their Administration," 3rd ed., 462.

Hexahydrophenanthrene.—According to Brissemoret (*Compt. rend. Soc. Biol., 69,* 497), this compound has a narcotizing power on such warm-blooded animals as the rabbit.

Hexamekol.—This compound of guaiacol with hexamethylene-tetramin is said by Rabow (*Chem.-Ztg.*, 1912, No. 21, 190) to be an anesthetic. On its employment in practice, see Lüdin: *Münch. med. Woch.*, 1911, 48; *Chem.-Ztg.*, Repert., 1911, 554.

Hexane.—This hydrocarbon is said to be actively intoxicant, producing a long stage of excitement, followed by deep anesthesia (Francis and Fortescue-Brickdale's "The Chemical Basis of Pharmacology," 1908, 45). It has never been employed as an anesthetic, however. See *Octane.*

Holocain and Adrenalin Ointment.—An ointment said to consist of holocain, 1 per cent; adrenalin chlorid, 4 per cent; hydrous wool fat, 10 per cent; and white petrolatum, 85 per cent. It is put up in collapsible tubes for application to the eye.

Holocain Hydrochlorid (Holocainæ Hydrochloridum; Ethenyl-para-diethoxy-diphenyl-amidin Hydrochlorid).—Holocain hydrochlorid is phenetidy-acetphenetidin hydrochlorid, $CH_3C(:N.C_6H_4.OC_2H_5)(.NH.C_6H_4.OC_2H_5).HCl = C_{18}H_{22}N_2O_2HCl$. Phenetidyl-acetphenetidin hydrochlorid is the hydrochlorid of a basic condensation product of para-phenetidin (para-ethoxy-amino-benzene) and acetparaphenetidin (phenacetin). It is prepared by the interaction of molecular proportions of para-phenetidin sulphate and acetphenetidin (phenacetin) in the presence of phosphorous oxychlorid, decomposing the resulting holocain sulphate with sodium hydroxid, crystallizing the base from alcohol, neutralizing it with hydrochloric acid, and crystallizing. It was first prepared by Täuber (see *Centr. f. prakt. Augenheilkunde,* 1897, 30).

It forms small, colorless crystals, neutral or faintly alkaline, melting at + 189° C. (372.2° F.), odorless, faintly bitter, and producing transient numbness on the tongue. It is soluble in 50 parts of water and freely soluble in alcohol. On boiling in ordinary glass vessels, the water solution becomes turbid, owing to a separation of a small quantity of the free base by the alkali derived from the glass. It should form a clear, colorless solution in water, neutral or faintly alkaline, yielding a white precipitate on addition of silver nitrate or of ammonia. The base obtained by precipitation with ammonia and crystallized from alcohol forms colorless needles, which melt at + 121° C. (249.8° F.). Incinerated on platinum, it leaves no weighable residue. It is incompatible with alkalies and their carbonates and the usual alkaloidal reagents. Glass vessels should be avoided in preparing the solution, porcelain being used instead. Only distilled water should be employed.

Actions and Uses.—It is a local anesthetic like cocain, but having the advantage of a quicker effect and an antiseptic action. Five minims of a 1 per cent solution, when instilled into the eye, are usually sufficient to cause anesthesia in from 1 to 10 minutes. It is said not to cause the scaliness of the cornea which sometimes results after the use of cocain. It should never be given internally or be employed hypodermically, for it is said to be toxic when so used. In toxic doses it produces general convulsions.

Dosage.—It is applied in a 1 per cent water solution prepared in porcelain vessels. The action and mode of application of holocain hydrochlorid have been discussed in an extensive series of papers; these follow in part.

Kuthe: *Centr. f. prakt. Augenheilk.*, Jan., 1897, 55.

Jaeuber: *Centr. f. prakt. Augenheilk.*, Jan., 1897, 53.

Gutmann: *Deut. med. Woch.*, 1897, No. 11, 165.

Deneffe: *Sem. méd.*, 1897, No. 15, 114.

Berger: *Ibid.*, 1897, No. 31, 25.

Löwenstamm: *Therap. Monat.*, 1897, No. 5, 268.

Winselmann: *Klin. Monat. f. Augenheilk.*, May, 1897, 150.

Hirschfeld: *Monat. f. Augenheilk.*, May, 1897, 157.

Natanson: *St. Petersburg. med. Woch.*, 1897, No. 32, 304.

Coosemanns: *Presse méd.*, 1897, No. 74, 83.

Coosemanns: *Rev. hebd. de Laryng., d'Otol., et de Rhin.*, Dec. 11, 1897.

Chevalier: *Bull. de thérap.*, Oct. 23, 1897; *Nouveau remédes*, 1897, No. 20, 609.

Lagrange and Crosse: *Bull. méd.*, 1897, No. 104, 1209.

Lagrange and Crosse: *Bull. méd.*, Feb. 8, 1898.

Gires: *Thèse de Paris*, 1897.

Heinz: *Centr. f. prakt. Augenheilk.*, March, 1897.

Heinz and Schlosser: *Klin. Monats. f. Augenheilk.*, April, 1897, 114.

Carter: *Lancet*, May, 1897, 1466.

Derby: *Boston Med. and Surg. J.*, June 3, 1897; and *Boston Med. and Surg. J.*, Jan., 1890.

Wood: *Ann. of Ophthalmology*, Oct., 1897.

Holtz: *J. Am. Med. Assn.*, Nov. 13, 1897.

Masselon: *Arch. d'Ophthalm.*, Oct., 1897.

Wurdemann: *Clinique ophthalm.*, 1898, No. 5.

Randolphe-Westcott-Hotz: *Woch. f. Therap. u. Hygiene des Auges*, 1898, No. 47.

De Landsheere: *Clinique ophthalm.*, 1898, No. 16, 191.

Snegirew: *Med. Oboshrenie, 50*, No. 4.

Frassi: *Clinica Moderna*, 1898, 29.

Wurdemann and Black: *Ophthal. Rec.*, Oct., 1897, and Jan., 1898.

Hinshelwood: *Brit. Med. J.*, Sept. 3, 1898; *Glasgow Med. J.*, June, 1904.

Cheatham: *Am. Pract. and News*, Aug. 15, 1898.

Ellett: *Phil. Med. J.*, Nov. 26, 1898.

Randolph: *J. Am. Med. Assn.*, Sept., 1898.

Trousseau: *La Presse méd.*, Apr., 1898, No. 37.
Hinshelwood: *Klin.-therap. Woch.*, Sept., 1898, No. 39.
Scrini: *Archives d'Ophthal.*, Jan., 1899.
Knapp: *Archives of Ophthal.*, May, 1899.
Guttmann: *N. Y. med. Monats.*, Nov. 3, 1899.
Norris: *Ophthal. Rec.*, June, 1899.
Schultz: *Archiv f. Augenheilk.*, 1899, *40*, No. 2, 125.
Jackson: *Col. Med. J.*, Dec., 1899.
Pyle: *West. Med. Rev.*, Jan. 15, 1900.
Hale: *Chicago Med. Rec.*, Feb., 1900.
Deane: *Pac. Med. J.*, June, 1900.
Ellenbogen: *Rev. thérap. méd.-chir.*, Dec. 1, 1900.
Holber Mygind: "Krankheiten der oberen Luftwege" (Verlag Oscar Coblentz, Berlin), 1901.
Brandt: *Zahnärztlich Rundschau,* 1901, Nos. 468 and 469.
Heineck: *The Bacillus,* Jan., 1901.
Zirn: *Zentralb. f. prakt. Augenheilk.*, May, 1901.
Coulter: *Ann. of Otol., Rhinol. and Laryng.*, Feb., 1901.
De Schweinitz: *Therap. Gaz.*, June 15, 1901.
Calhoun: *Ophthal. Rec.*, Jan., 1902.
Knipp: *J. Am. Med. Assn.*, Aug. 9, 1902.
Briggs: *Occidental Med. Times,* Aug., 1902.
Oliver: *Ann. of Ophthal.*, Oct., 1903.
Bock: "Das erste Jahrzehnt der Abteilung für Augenkranke in Laibach," Wien, 1902; *Allgemeine Wiener medicinische Zeitung,* 1908, No. 36.
Wainwright: *The Am. Therap.*, 1904, No. 1.
Church: *Ophthalmology,* July, 1905.

Hydramyl (Amyl Hydrid; Pentylene).—Obtained as a fraction in the distillation of petroleum and proposed as an anesthetic. See *Amyl Hydrid.*

Hydramyl Ether.—A local anesthetic containing equal parts of hydramyl and ether.

Hydramyle.—To quote Richardson (*Sci. Am. Suppl.*, No. 516, 8240): "A mixture made by adding amyl hydrid to zinc in making methylene bichlorid from chloroform. A colorless ethereal fluid. Sp. gr., 0.720. Vapor ethereal, sweet, and very pleasant to breathe; quantity required to produce anesthesia, 2 to 4 fluid drachms. Action extremely rapid, complete insensibility sometimes occurring within the minute. Peculiar in its effect in that insensibility from it intensifies for a few seconds after it is withdrawn. Recovery, when it commences, almost immediate. An excellent anesthetic for short operations like extraction of a tooth. Was administered by author forty-six times to the human subject, with production of insensibility within an average of fifty seconds, and without vomiting or any other untoward symptom." Richardson introduced hydramyle in 1871.

Hydriodic Ether.—See *Ethyl Iodid.*

Hydrobromic Ether.—See *Ethyl Bromid.*

Hydrochloric Ether.—See *Ethyl Chlorid.*

Hyoscin (or Hyoscine) Hydrobromid.—See *Scopolamin Hydrobromid.*

Hyoscin, Morphin, and Cactin.—On the use of this combination as an anesthetic, see Lee: *J. Minn. Med. Assn., 28,* 98.

Hyoscin-morphin Mixture.—This anesthetic has been used in obstetrical medicine in a dose of 1/100 gr. of hyoscin hydrobromid and ¼ gr. of morphin sulphate. See *Practitioner,* July, 1911.

Ice and Salt.—Lemke used ice and salt to anesthetize the site of the insertion of the cannula, previous to injecting nitrogen in tubercular pulmonary cavities (Heineck, "General and Local Anæsthesia," 1900, 87). A mixture of salt and snow was highly recommended by Arnott as a local anesthetic, but such a method is troublesome.

Ichnol.—An alcoholic solution of ethereal oils (eugenol, etc.) colored green by means of chlorophyll. Used in odontolgia. See *Jehnol.*

Idin.—Apparently spirits of camphor. Used in odontalgia. According to Riedel's "Mentor" (1912, 173), a solution of camphor and menthol, or oil of peppermint, in alcohol.

Injection Hirsch.—This is said to be a stable solution containing one per cent of mercury oxycyanid and one half of one per cent of *Acoin* (*q. v.*), used as a local anesthetic.

Iodoform.—Iodoform is said to resemble the other kindred anesthetics in its physiological action; in the lower animals it produces muscular rigidity, anesthesia, sleep, muscular relaxation, and, in sufficient doses, death. It has not received any real consideration as an anesthetic for operations.

Iso-amylene-beta-pental.—This compound has been used for effecting total anesthesia.

Isobutyl Ester of Para-amidobenzoic Acid.—See *Cycloform.*

Isopon.—This preparation contains the alkaloids of opium. See *Pantopon.*

Isopral.—Isopral (trichlorisopropylalcohol), $CCl_3.CHOH.CH_3$, is obtained in prismatic crystals, possessing a camphoraceous odor and pungent taste. It has a melting point of + 49° C. It is soluble in about 30 parts of cold water, more readily in alcohol and ether. Isopral is a hypnotic, the uses of which are, in general, those of chloral hydrate. The dose is 0.3 to 1.3 gm. (5 to 20 grains). Mertens (*Arch. klin. Chir., 95,* No. 3) found isopral to be useful as a preliminary to chloroform anesthesia when given in the form of rectal injections. Burkhardt (*Münch. med. Woch.,* 1911, No. 15) employed isopral intravenously as an anesthetic, finding it to possess several advantages over *Hedonal* (*q. v.*). Intravenous ether anesthesia seems to have special advantages when combined with isopral (Burkhardt: *Münch. med. Woch.*, 1911, 778).

Jehnol.—A solution containing ethereal oils and camphor, colored green with chlorophyll. Used in odontalgia.

Johimbin.—See *Yohimbin.*

Kandol.—See *Canadol.*

Katharin.—See *Carbon Tetrachlorid.*

Kelen or Kelene.—A purified ethyl chlorid, supplied in a special form of container. There are also preparations of cocain and kelene, formaldehyd and kelene, and of the latter with menthol.

Kelene-methyl.—A mixture of ethyl chlorid with methyl chlorid for use as an anesthetic. See *Z. angew. Chem.*, 1901, 261.

Keroselene.—A mixture of hydrocarbons from coal oil, possessing a boiling point of + 90° F.; it was proposed as an agent for producing anesthesia by inhalation (see Bigelow: *Boston Med. and Surg. J.*, July 11, 1861), but it produced in every case disagreeable and alarming symptoms, as irritation of the air passages, lividity of the surface, muscular disturbance, and intermission of the pulse.

Koenig's Æther Anæstheticus.—See *Æther Anæstheticus* (Koenig).

Lamellæ Cocainæ.—Each lamella contains 1/50 gr. cocain hydrochlorid.

Laudanon.—This is an opium preparation containing a combination of different opium alkaloids. See *Pantopon.*

On laudanon, see Faust: *Münch. med. Woch.*, 1912, 2189.

Letargin.—In each c. c. are 0.5 gm. extract hamamelis, 0.015 gm. novocain, 0.0092 gm. sodium chlorid, 0.0002 gm. thymol, 0.5 gm. distilled water, and 1 drop of a 1:1000 suprarenin hydrochlorid solution; it is used as a local anesthetic in the extraction of teeth and in other minor operations.

Letheon.—Morton and Jackson sought to patent their anesthetic under this name. It was soon recognized as ethyl ether (see Chapter I, p. 16). It has been stated that ethyl ether mixed with aromatic oils was termed "Letheon" in 1846.

Linhart's A. C. Mixture.—According to Buxton ("Anæsthetics," 4th ed., 288), "Linhart's Mixture" is composed of alcohol, 1 part, and chloroform, 4 parts. Buxton further states (*ibid.*, 294) that it contains 20 per cent alcohol—more than is necessary—and gives less good results than the 10 per cent mixture. See also Dumont's "Allgemeine u. lokale Anaesthesie," 117.

Linhart's C. E. Mixture.—A mixture of chloroform, 1 part, and ethyl ether, 4 parts. "This mixture is devoid of any danger" (Müller: "Narkologie," 1908, 492).

Liquor Anæstheticus.—A very variable mixture obtained by chlorinating ethyl chlorid.

Liquor Hollandicus.—See *Ethylene Chlorid.*

Locasemin.—A local anesthetic, similar to *Eusemin* (*q. v.*).

Loco-dolor.—A purified ethyl chlorid.

London Medical and Chirurgical Society Mixtures.—A—Alcohol, 1 part; chloroform, 2 parts; ether, 3 parts. B—Chloroform, 1 part; ether, 4 parts. C—Chloroform, 1 part; ether, 2 parts. It was found that mixture B was very similar in physiological action to ethyl ether (see *Med. Chir. Trans., 47,* 1864); that the mixtures A and C were very similar to each other in their action; that A and C exercised a much less depressing effect upon the action of the heart than chloroform alone; that a mixture of ether and chloroform (such as A and C) was as effective as pure chloroform, and a safer agent where deep and prolonged anesthesia was to be induced. In the opinion of the committee, preference was to be given to mixture A. Ellis ("Anæsthesia with Mixed Vapor," London, 1866) found that, when the mixture A was evaporated, during the six or seven minutes required for the evaporation of half a drachm (two grams) of the liquid, the vapor of ether, almost exclusively, was given off during the first minute, the vapor of chloroform predominated during the next three minutes, and the evaporation of alcohol occupied the last three minutes.

On death from the inhalation of a mixture of chloroform and alcohol, see Hammond: *Am. J. Med. Sci.,* July, 1858, 41; and on death from inhaling a mixture of chloroform, ether, and alcohol, see Morton and Hewson: *Ibid.,* Oct., 1876, 415. See *A. C. E. Mixture; Anæsthol* (W. Meyer); and *"M. S."*

Lycoperdon Proteus.—See *Puff-ball.*

Magnesium Salts.—In 1906 S. J. Meltzer (*Berl. klin. Woch.,* 1906, No. 3, 73) conducted experiments with the subcutaneous, intravenous, and intraspinal injection of magnesium sulphate. Meltzer reasoned from the fact that intracerebral injections of magnesium salts produced, not convulsions, but evidences of paralysis. The results of his experiments, which proved that magnesium sulphate has not an inconsiderable anesthetic action, decided Meltzer to employ lumbar anesthesia by means of magnesium sulphate in a number of operations on patients, partly by itself and in part in combination with the inhalation of chloroform. He injected 1 c. c. of a 25 per cent sterile solution of magnesium sulphate for each 12 kg. of body weight, and found that after 3 or 4 hours there appeared paralysis of the legs and the region of the pelvis, thus permitting of the painless performance of an operation in these regions. Meltzer observed, as secondary actions, undue prolongation of the paralysis and retention of the urine, but reported that these could be avoided by washing out the spinal canal with normal saline solution. The heart and blood pressure were said to be unaffected, but the influence on the respiration required careful notice.

Desguin (*Deut. Med.-Ztg.*, 1907, No. 99, 1102) reported on the innocuous nature of magnesium sulphate as leading to its adoption in the place of the customary anesthetics in certain cases; and Tucker (*Therap. Gaz.*, 1907, No. 5; *Revista espec. medicas*, 1907, No. 199, 475; *Merck's Archives*, 1907, No. 6, 178) applied solutions of magnesium sulphate as local anesthetics.

Delhaye (*Presse méd.*, 1908, 397) studied the anesthetic action of magnesium salts from a pharmacological standpoint. He regarded these salts as strong nerve sedatives, able to produce complete anesthesia and even paralysis. They have, according to Delhaye, no toxic action on the heart, although he considered them dangerous to respiration and to the kidneys, and that they should not be employed for producing anesthesia for these reasons. Netter (*J. de Méd. inter.*, 1909, 38) and Griffon and Lian (*Thèse de Paris*, 1908) noted the anesthetic power of solutions of magnesium sulphate, particularly on subcutaneous or intravenous application. Henderson (*J. Pharmacol. and Exper. Therap.*, 1909, *1*, 199) investigated the production of anesthesia by intracerebral injection of magnesium chlorid. More recently the use of magnesium sulphate as an anesthetic has been described by Corrado: *Il Policlinico*, 1910, 124; but especially *Rev. de Thérap.*, 1910, No. 16, 556; Phillips: *Klin.-therap Woch.*, 1910, No. 10, 263; Johnson: *Brit. Med. J.*, 1910, No. 2590, 457; Paterson: *Lancet*, 1910, No. 4518, 922; and Canestro: *Klin.-therap. Woch.*, 1910, No. 19, 455. Canestro found that the spinal anesthesia produced by magnesium sulphate caused no changes in the central nervous system such as had been observed to follow the use of other anesthetics. Hyndham and Mitchener (*J. Am. Med. Assn.*, July 23, 1910) proved that magnesium sulphate injections paralyzed only the sensory cells and not the motor cells of the cerebral centers. The value of magnesium sulphate in the treatment of tetanus is apparently well established; it depends upon the sedative action of the salt, which persists long enough to enable the brain to render the tetanus poison harmless.

Guthrie and Ryan, in a paper on the reported specific anesthetic property of magnesium salts (*Am. J. Physiol.*, *26*, 329), claim that the specific anesthetic properties cannot be ascribed to magnesium salts, despite the assertions of Meltzer and others to the contrary.

Wiki (*Arch. intern. Pharmacodyn.*, *21*, 415) studied the local anesthetizing action of magnesium sulphate. He was able to confirm the local anesthetizing effect and to show that the action is augmented with the concentration of the solution.

Meltzer has more recently injected magnesium sulphate (1 c. c. of a 25 per cent solution in sterile water per kg. of animal) into the femoral muscle, and thereby obtained great relaxation with much smaller amounts of ether. The animal is first anesthetized with ether by the cone method, and the solution injected, the infiltrated muscle being immediately massaged thoroughly. By giving calcium salts just before the ether is discontinued, the subject is brought quickly from under the influence of the magnesium.

Maier's Radikal-anästhetikum.—See *Radikal-anästhetikum Maier.*

Mannin.—Amido-oxybenzoic acid methyl ester, a local anesthetic.

Martindale's Mixture.—A volumetric mixture, the ingredients of which are said to evaporate almost uniformly. It is composed of absolute alcohol (0.795), 1 volume; chloroform (1.497), 2 volumes; and ethyl ether (0.720), 3 volumes. See *A. C. E. Mixture,* from which Martindale's mixture differs only in the specific gravity of the ingredients and from the fact that "the three ingredients are intended to evaporate uniformly." There is said to be no advantage in this mixture over the A. C. E. mixture, and, since the specific gravities mentioned in either differ from those for the corresponding anesthetics used in the United States, the A. C. E. mixture may be defined as alcohol, 1 part; chloroform, 2 parts; and ether, 3 parts; the best quality of ingredients to be employed and the mixture freshly prepared.

On Martindale's mixture, see "The Extra Pharmacopœia," by Martindale and Westcott, 12th ed., 235; and Hewitt's "Anæsthetics and Their Administration," 3rd ed., 467.

Med. Chir. Soc. of London's Mixture. See *A. C. E. Mixture,* and *London Medical and Chirurgical Society Mixtures.*

Menthol Thymate.—Used in odontalgia.

Menthophenol.—An aromatic liquid, soluble in alcohol, ether, and chloroform, but not in water or glycerin, obtained by fusing 3 parts of menthol with 1 part of phenol; it possesses antiseptic and analgesic properties.

Menthophenol Cocain.—A local anesthetic, obtained by fusing equal parts of menthol, crystalline phenol, and cocain hydrochlorid, also known as *Bonaine* (*q. v.*).

Von Mering's Mixture.—A mixture of chloroform, 1 part, and dimethylacetal, 2 parts (Dumont: "Allgemeine u. lokale Anæsthesie," 117). See *Dimethylacetal.*

Metæthyl.—This mixture of ethyl and methyl chlorids is mentioned in *Z. angew. Chem.*, 1901, 261. See *Methethyl.*

Methaform.—Methaform, known also as acetone-chloroform, chlorbutanol, and dimethylcarbinol chloroform, is a white, crystalline compound possessing a camphor-like taste and odor. It occurs in delicate needle-like crystals, sparingly soluble in water, but quite soluble in chloroform, alcohol, ethyl ether, and glacial acetic acid. Water, at the ordinary room temperature, dissolves about 1 part in 100. Methaform is not decomposed by acids or alkalies. It melts at + 96° to 97° C., boils at + 167° C., and sublimes at body temperature in characteristic crystals.

Methaform is hypnotic, analgesic, anesthetic, and antiseptic. In physiological action it closely resembles chloral hydrate, but is said to be less likely to irritate the stomach and to exert a less depressant action on the circulation. In addition, it is said to paralyze the sensory nerve terminals when applied locally, and hence, like cocain, to be applicable for local anesthesia, especially in infiltration anesthesia. In experimental work upon the lower animals, where anesthesia is desired, it is said that methaform is almost an ideal anesthetic when administered in doses of 2 to 5 grains per pound weight of the animal.

Cocain hydrochlorid solution with methaform (2 per cent and 4 per cent cocain) is offered in 1 ounce vials. It is said that methaform, being strongly antiseptic as well as a local anesthetic, is perhaps the best preservative for cocain solutions. It is reported to not only prevent decomposition of the cocain, thus rendering the solution stable, but to be a material aid in the production of anesthesia. It is furthermore said to be of value in preventing infection of the tissues by the hypodermic needle employed to introduce the cocain solution. Cocain solutions with methaform are said to be of value in dental and other minor surgical operations. See *Chloretone*.

Methane.—T. Nunneley, in 1849, and Richardson, in 1867, introduced methane as an anesthetic. Richardson found it to be "a very good anesthetic, but not practical, owing to its being a gas" (*Sci. Am. Suppl.*, No. 516, 8240). He found that it could be breathed without irritation; that the quantity required in air for anesthesia was 35 per cent; and that the anesthesia was slowly induced without any active spasmodic stage.

Methenyl-o-Anisidin.—According to Goldschmidt (*Chem. Ztg.*, *25*, 329), this compound possesses anesthetic properties; its guaiacol sulphonic acid salt also has an anesthetic action.

Methenyl-p-Phenetidin.—A local anesthetic.

Methethyl.—A mixture of ethyl and methyl chlorids, used as a spray for producing local anesthesia.

Methoxycaffein.—This compound [$C_8H_9(OCH_3)N_4O_2$] is a white bulky powder, melting at + 177° C., and slightly soluble in water, more readily soluble in dilute alcohol. It is used subcutaneously as a local anesthetic (1 c. c. of a 2 per cent solution).

Methyl Acetylsalicylate.—Pototzky (*Arch. de Pharmacodyn.*, *12*, 132) found this ester to possess local anesthetic properties.

Methyl Alcohol.—B. W. Richardson introduced methyl alcohol as an anesthetic in 1867. He found that the vapor was pungent to breathe and slightly provocative of coughing. The quantity of liquid required for complete anesthesia was from 1½ to 2 ounces by volume, and the required charge of air was to saturation. The action was very slow, and with distinct symptoms of alcoholic intoxication; a full hour was required to produce insensibility, which at the deepest was insufficient to destroy reflex irritability. The breathing was stertorous, often with bronchial râles; the recovery was very slow, being four to six hours in deep anesthesia; and the temperature was reduced 3° F. Richardson regarded methyl alcohol as an indifferent anesthetic, owing to the length of administration and slow recovery, but considered the danger practically *nil.* He learned that when the inhalation was enforced to the production of death, the circulation and respiration ceased simultaneously (*Sci. Am. Suppl.,* No. 516, 8240).

The use of methyl alcohol as an anesthetic is highly objectionable. Methyl alcohol is less poisonous to lower plants and infusoria than ethyl alcohol, but for higher animals, and especially for man, it is a severe toxic agent. It occasions toxic effects whether it is taken internally or *inhaled through the lungs.* Methyl alcohol is treated fully by Baskerville in his report to the State Factory Investigating Commission of New York, 1913, which should be consulted.

Methyl Bromid.—B. W. Richardson introduced this compound as an anesthetic in 1867. He found the physiological properties to be analogous to those of *Ethyl Bromid* (*q. v.*), but causing more irritation, with salivation. The anesthetic value was stated by Richardson (*Sci. Am. Suppl.,* No. 516, 8240) to be analogous to that of ethyl bromid, but less practical, owing to the extreme volatility and lesser steadiness of action. Methyl bromid is only slightly toxic.

Methyl Chlorid (Methyl Chloridum).—Methyl chlorid (CH_3Cl) is the hydrochloric acid ester of methyl alcohol. It occurs, in the compressed state, as a colorless liquid, having an ethereal odor and a sweet taste.

Methyl chlorid is insoluble in water, more readily in alcohol, freely in ether and chloroform, and also in acetic acid. It should be neutral to litmus paper. At about —25° C. (—13° F.), it has a specific gravity of 0.991, and boils at about —21° C. (—5.8° F.). It burns in the air with a greenish flame, though it is not highly inflammable. The neutral solution is not precipitated by a solution of silver nitrate, nor is there any reaction with potassium iodid and starch paste. If the liquid is allowed to evaporate it is a powerful refrigerating agent. At very low temperatures it forms with water a hydrate, $CH_3Cl.9H_2O$. It should not react alkaline to litmus (absence of ammonia and methylated ammonia —methylamin). It should not immediately form a precipitate with silver nitrate. On evaporating it should leave no residue and emit no odor of methylamin.

Action and Uses.—By its evaporation a temperature of —23° C.

(— 9.4° F.) is produced, while if the evaporation is accelerated by means of a current of air a temperature of — 55° C. (— 67° F.) may easily be reached. On account of this property, it is used as a local anesthetic in the form of a spray, but its use requires caution, since it is apt to produce blisters. The diluted vapor is said to be non-poisonous. Methyl chlorid is said to be an efficient general anesthetic, which has practically no influence on the circulation, but fails to produce complete muscular relaxation. It is used as a general anesthetic, mixed with ethyl chlorid and ethyl bromid. Richardson introduced it as a general anesthetic in 1867. He found the gas very pleasant to breathe, and determined the required charge of air to be 15 per cent. The anesthetic action was found to be rapid and most effective, with the briefest spasmodic stage or with no such stage at all; insensibility was deep, and recovery was rapid, not being longer than five minutes from the deepest narcotism, and with no bad after-effects. Vomiting was rare. Richardson (*Sci. Am. Suppl.*, No. 516, 8240) considered it one of the best and safest of anesthetics—the safest of all anesthetics containing chlorin, but difficult of management, owing to it being a gas. When carried to the point of death, the heart was found to outlive the respiration, and the muscles to retain their irritability after death for periods of three to four hours. The heart pulsated spontaneously, in the case of a rabbit killed by the vapor, for forty minutes.

Methyl Chlorid is less toxic than *Methylene Chlorid* (*q. v.*).

Richet and Marcille (*Sem. méd.*, 1902) reported that methyl chlorid acted on the animal as an efficient anesthetic and that it had practically no influence on the circulation.

Dosage.—When sprayed on the skin, the part should be partly protected by a thin layer of cotton wool. When used locally, cotton wool soaked in liquid methyl chlorid may be applied to the skin over the painful area, but care should be taken that blisters are not formed. In order to avoid this, a mixture with ethyl chlorid has been recommended.

Methyl Chlorid-Alcohol.—The Committee of the British Medical Association (*Brit. Med. J.*, Jan. 4, 1879) reported that methyl chlorid, liberated from its alcoholic solution, was not very potent. A rabbit was subjected to its inhalation, but "after somewhat prolonged use there was not any abolition of reflex action, and the animal almost immediately recovered. The only effect was slight drowsiness."

Methyl Chlorid-Ether.—Hermann and Richardson found the solution of methyl chlorid in ether to be a very efficient and agreeable anesthetic.

Methyl Chloroform.—See *Trichlorethane.*

Methyl Cinnamenylacrylate.—Pototzky (*Arch. de Pharmacodyn.*, *12*, 132) found that this ester had local anesthetic properties.

Methyl Dichlorid (Methyl Bichlorid, Richardson-Merck).—A mixture of 1 volume of methyl alcohol and 4 volumes of chloroform for anesthesia by inhalation. Not to be confounded with *Methylene Bichlorid.*

Methyl Ether (Dimethyl Ether; Methyl Oxid).—This anesthetic gas has been sold in ethereal solution, but is not used in the United States. It was introduced by Richardson as an anesthetic in 1867. He found the gas pleasant to breathe, causing no irritability. The required charge of air was 25 per cent. The anesthetic action was rapid up to complete insensibility, without any manifestation of a spasmodic stage; in fact, Richardson found that methyl ether possessed the remarkable property of destroying sensibility before destroying consciousness. The recovery from deep anesthesia was rapid, and was unattended by any bad symptom or vomiting. The temperature was reduced 1° to 2° F. in deep anesthesia. To quote Richardson (*Sci. Am. Suppl.,* No. 516, 8240): "I consider methylic ether to be the safest of all anesthetics hitherto discovered. Pigeons and rabbits will remain anesthetized in a full anesthetic atmosphere for twelve minutes without dying, and after being allowed to die are recoverable by artificial respiration seven minutes after cessation of all signs of life. The one practical objection to methylic ether as an anesthetic consists in it being a permanent gas at ordinary temperatures. I have administered it successfully twenty-seven times to the human subject."

According to Francis and Fortescue-Brickdale ("The Chemical Basis of Pharmacology," 1908, 104), methyl ether acts very like nitrous oxid, producing a rapid and transient anesthesia. The same authors call attention to the fact that it would be interesting to ascertain whether methyl-ethyl ether ($CH_3.O.O_2H_5$) has any advantages over ordinary ethyl ether.

On the properties of methyl ether, see *J. Pharm. Chim.* (4), *19,* 438.

Methyl Fluorid.—Moissan stated that methyl fluorid possessed anesthetic properties (*Bull. de l'Acad. de Méd. de Paris,* 1890).

Methyl Hydrate or Hydroxid.—See *Methyl Alcohol.*

Methyl Iodid.—This compound was experimented with by Richardson and Simpson, who found that its vapor could be respired, even to the induction of anesthesia. Simpson regarded it as powerful but dangerous. It has also been employed as a local anesthetic.

Methylal (Methylene-dimethyl Ester; Formal; Methylene Dimethylate).—This compound [$CH_2(OCH_3)_2$], prepared by distilling together methyl alcohol, water, sulphuric acid, and manganese dioxid, is a colorless volatile liquid with a chloroform-like odor and a pungent taste; it possesses a density of 0.855 at + 15° C., and boils at + 42° C.; it is easily soluble in water, alcohol, and oils. At the present time it is said to be used as a 10 per cent liniment or ointment as a local anesthetic. Richardson introduced methylal as an anesthetic in 1868. He found that its anesthetic value was the same as that of *Methyl Alcohol (q. v.)*; that its vapor was agreeable to breathe, and that the quantity required to produce anesthesia was from 1 to 3 fluid ounces, the required charge of vapor in air being 35 per cent. "Recovery very prolonged, but without painful symptoms or vomiting" (*Sci. Am. Suppl.,* No. 516, 8240). According to Francis and Fortescue-Brickdale ("The Chemical Basis of Pharmacology," 1908, 104), methylal produces anesthesia slowly; the action is prolonged and deep, but somewhat uncertain; and patients quickly become accustomed to it.

"Methylene."—A mixture of methyl alcohol, 30 per cent (1 volume); and chloroform, 70 per cent (4 volumes), proposed by Regnault and Villejean. It is said to be inferior to and less safe than alcohol-chloroform mixture, 1:10, and is seldom used at the present time.

"Methylene Bichlorid."—See *Narcotil.*

Methylene Chlorid (Methylene Bichlorid; Dichloromethane; Methene Chlorid).—This compound (CH_2Cl_2) is prepared by the action of zinc and hydrochloric acid on a mixture of alcohol and chloroform; it is a colorless liquid which possesses a density of 1.377 at + 15° C., and a boiling point of + 40° C. It is soluble in alcohol and ethyl ether. It is used in the form of a spray to produce local anesthesia, particularly in dental surgery.

Richardson introduced methylene chlorid as a general anesthetic in 1867. He reported that the vapor was pleasant to inhale and was not irritating; that the quantity of liquid required to produce anesthesia was 1 to 6 fluid drachms; that the required charge of air was 5 to 10 per cent; that the action was rapid, with short but rather acute spasmodic stage; and that insensibility was perfect. He found recovery to be rapid, and usually without bad symptoms; that vomiting occurred about once in six administrations; and that the animal temperature was reduced from 2° to 3° F. under deep anesthesia. To quote the conclusions of Richardson (*Sci. Am. Suppl.,* No. 516, 8240): "Pure methene chlorid is one of the best anesthetics, but not free from danger. The deaths from it have been estimated at 1 in 7,000 administrations." Regnault and Villejean (*Compt. rend., 100,* 1146) reported that methylene chlorid, like carbon tetrachlorid, but unlike chloroform and methyl chlorid, exerted a poisonous action when inhaled. See, however, *Carbon Tetrachlorid.* Methylene chlorid is said to be less toxic than chloroform (Francis and Fortescue-Brickdale's "The Chemical Basis of Pharmacology," 1908, 95). It cannot yet be regarded as a safe anesthetic.

For cases of death from the inhalation of methylene dichlorid, see *Brit. Med. J.,* Oct. 23, 1869; *ibid.,* May 7, 1870; *ibid.,* April 29, 1871; *ibid.,* Sept. 16, 1871; *ibid.,* Aug. 31, 1872; *ibid.,* Oct. 12, 1872; *ibid.,* Oct. 19, 1873; *Lancet,* Dec., 1874; *Brit. Med. J.,* July 24, 1875; *Med. Times and Gaz.,* Sept. 22, 1877; *ibid.,* June 23, 1877; and *Brit. Med.*

J., March 2, 1878. While Morgan used this agent 1,800 times without a single accident (*Brit. Med. J.*, Jan. 4, 1879), it will thus be seen that others have been less fortunate.

Methylene Ether.—A mixture of equal parts of absolute ether and methylene bichlorid (Richardson, 1870). Richardson (*Sci. Am. Suppl.*, No. 516, 8240) described methylene ether as a colorless fluid, "more stable than the other anesthetic mixtures," the vapor of which was pleasant to inhale. He found that the quantity required for complete anesthesia was 2 to 8 fluid drachms; that the action was steady and rapid, with a very slight spasmodic stage; and that recovery was quick, with few bad after-effects, and vomiting infrequent. To quote his conclusions: "An exceedingly good combination and deserving a further trial than it has received. Author administered it thirty times with most satisfactory results. One death occurred in the practice of Mr. Lawson Tait, from administration of a fluid supposed to be this mixture, but which contained choloroform in large proportion. In death of lower animals in this vapor, circulation survives respiration." On methylene ether, see also Richardson: *Med. Times and Gaz.*, 1872, 2; and 1873, 1. For cases in which death occurred during its administration, see *Phila. Med. Times, 3,* 718; *Med. Times and Gaz.*, July 5, 1873; and *Brit. Med. J.*, March 2, 1878, 290.

Methylethyl.—A mixture of methyl and ethyl chlorids. See *Methethyl.*

Methylic-Ethylic Ether.—A mixture, proposed by Richardson in 1867, made by saturating ethyl ether with methyl ether gas. It was described by Richardson (*Sci. Am. Suppl.*, No. 516, 8240) as a colorless fluid, very unstable and inflammable, possessing a density of 0.720. He reported that it was found to be extremely pleasant to inhale and that it showed all the effects of methyl ether, except that anesthesia was slower and more prolonged. "Would be among the most valuable of anesthetics if it were more stable and practical in application."

Methylium Bichloratum Richardson.—See *Methylene Ether.*

Methylium Oxyamidobenzoicum.—Para-Amido-m-oxybenzoic acid methyl ester, a local anesthetic.

Methylpropylcarbinolurethane.—See *Hedonal.*

Midy's Mixture.—This is described as a solution of 5/100 gram of subcutin, 1/10 gram of mercuric iodid, 1/10 gram of sodium iodid, 2/100 gram of sodium chlorid, and distilled water to make 1/100 c. c.

Molecular Solution or Molecular Solution Mixture.—See *"M. S."*

Monobromethane.—See *Ethyl Bromid.*

Monochlorethane.—See *Ethyl Chlorid.*

Monochloro-Ethylene Chlorid.—See *Ethylene (Monochloro-) Chlorid.*

Morphin Hydrochlorid.—This compound has been employed as a local anesthetic with ether spray and for general anesthesia with chloroform vapor. Pitha stated (*Wiener med. Woch.*, 1861, 25, 36) that, having unsuccessfully attempted for two hours to anesthetize a patient, first with a mixture of ether and chloroform, and then with chloroform alone, he finally inserted into the rectum a solution of the extract of belladonna; the patient passed into a condition of anesthesia which persisted for twelve hours. In 1863 Nussbaum found that, by the hypodermatic injection of morphin at the commencement of inhalation, the anesthesia produced by chloroform could be prolonged for several hours. In this connection, see also Uterhart: *Berl. klin. Woch.*, 1868, No. 32. Bernard ("Leçons sur les Anaesthesiques," Paris, 1875) collected a large number of cases, illustrating the advantages connected with the combined administration of opiates and chloroform. As a result of his experiments in treating the same patients, sometimes with chloroform alone, and sometimes with chloroform and morphin, making an injection about twenty minutes or half an hour before the operation, Kappeler ("Anæsthetica," 209) concluded that the course of the resulting anesthesia did not materially vary under either set of conditions; he believed, however, that the character of the anesthesia was more tranquil, and that the patient passed more rapidly, and with less excitement, into the stage of insensibility. See *Scopolamin Hydrobromid* and *Pantopon.*

"M. S." (Molecular Solution).—Weidig found that 119.5 gm. of "chemically pure" chloroform and 74 gm. of absolute ether, or, expressed in volume, 43.25 parts of chloroform and 56.75 parts of ether, mixed together, entered into "chemical combination," representing a new anesthetic. To quote Meyer (*J. Am. Med. Assn.*, Feb. 29, 1903): "It contains neither free ether nor free chloroform and has a boiling point of its own at + 125.6° F. (+ 52° C.). We called this product molecular solution (of chloroform and ether) or, abbreviated, 'M. S.'" In the first part of 1898 Meyer administered "M. S." for general anesthesia and found it to be an excellent narcotic. It was used by a number of surgeons at the German Hospital in New York City in 1903. For a discussion of the chemistry of "M. S.," see *Anesthol* (*Meyer*).

Mylocal.—A solution containing cocain and antiseptics, for use as a dental local anesthetic.

Nalicin.—A local anesthetic for dental purposes; it consists of 1 gm. trinitrin and 1 gm. of cocain hydrochlorid in 100 gm. of a mixture of spiritus thymolic comp., alcohol, sodium chlorid, phenol, formaldehyd, and water.

Narcoform.—Said to be a mixture of ethyl chlorid, 60 parts; methyl chlorid, 35 parts; and ethyl bromid, 5 parts, which is the original *sœmnoform* formula of Rolland (see *Somnoform*) but this cannot be definitely asserted.

Narcophin.—Narcophin, described as narcotin-morphin meconate, has been considered in the following contributions:

Straub: *Biochem. Z., 41,* 419; *Münch. med. Woch.,* 1912, 1542.
Schlimpert: *Münch. med. Woch.,* 1912, 1544.
Zehbe: *Ibid.,* 1912, 1543.
Hermann: *Biochem. J., 39,* 216.
v. Issekutz: *Pflügers Arch., 145,* 415.
Caesar: *Biochem. Z., 42,* No. 4.
Zweifel: *Monats. Geburtsh. u. Gynäk., 36; Ergänzungsh.,* 1912.
von Stalewski: *Therap. d. Gegenw.,* 1912.

Narcosin.—A dental local anesthetic which contains extract of hamamelis bark of high tannin content, "obtained by a peculiar process in an autoclave" (Riedel's "Mentor," 1912, 186).

Flury (*Z. angew. Chem., 26,* 242) states that "Narkosin" is extract of hamamelis containing narcotics.

Narcotil (Narkotil) or Narcotile.—This inhalation anesthetic, also known as "Methylene Bichlorid," consisted of a mixture of methyl and ethyl chlorids. It was described as a colorless, very volatile and inflammable fluid, emitting a pleasant odor; and was said to be obtained by the action of hydrochloric acid upon a mixture of ethyl and methyl alcohol. It was recommended by Eastham (*Lancet,* 1903, No. 4155, 1091) for general anesthesia, and was administered with the aid of Junker's inhaler, narcosis being effected within one minute. It was said that return to consciousness was not, as a rule, attended by headache, giddiness, or other unpleasant concomitants; but nevertheless the sale of the preparation was discontinued several years ago, as there were certain objections to its employment. According to *Chem. Centr.,* 1903, *2,* 307, "Narcotil" was a name used in England for "Methylene Chlorid" (*q. v.*).

Narkose-Gemisch "Dr. Hirschlaff."—Each c. c. contains 0.05 gm. morphosan (morphin brommethylate) and 0.00015 gm. euscopol, dissolved in distilled water. It is offered to the trade in sterilized ampoules.

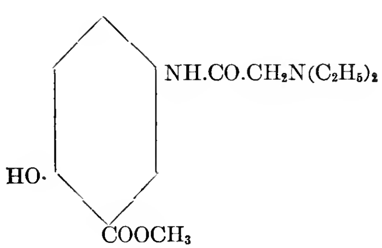
Nealpon.—Flury (*Z. angew. Chem., 26,* 242) states that this preparation contains the alkaloids of opium. See *Pantopon.*

Nerrocidin.—The same as *Nervocidin* (*q. v.*). Dumont ("Allgemeine u. lok. Anesthesie," 1903, 234) and others use this name instead of "Nervocidin," etymologically the correct term.

Nervocidin.—The hydrochlorid of alkaloids contained in the Indian plant "Gasu-Basu" (*Pharm. Ztg., 47,* 317). Nervocidin was isolated by Dalma, its anesthetic properties were discovered by a Hungarian dentist of Fiume, and it was studied by Fenyvessy in the Institute of Bokay, Budapest, pharmacologically. Nervocidin is described as a hygroscopic, yellow amorphous powder, easily soluble in alcohol and ether. Applications of a 0.1 per cent solution are said to produce complete anesthesia on mucous surfaces. It has been used in the eye in doses of 2 minims of a 0.2 per cent solution; stronger solutions are said to cause difficulties. For the cornea a 0.01 per cent solution is used. Nervocidin is used chiefly in dentistry to anesthetize painful pulpa, in the form of the hydrochlorid, which is very soluble in water. Hypodermic injections in animals produce paralysis of the motor centers and peripheral nerves, ending in death. (See *J. de l'Anesthésie,* 1902; Dumont's "Allgemeine u. lok. Anaesthesie," 1903, 234 and 235.)

Neurocain.—Billets containing 1/12 grain (0.005 gm.) of cocain hydrochlorid for use as a local anesthetic in dental practice and in pressure anesthesia. Neurocain is said to be composed entirely of cocain hydrochlorid, without excipient, and to have the advantage over cocain crystals that it dissolves "almost instantly" on contact with water; the shape of neurocain is also said to render it peculiarly suitable for marginal and all other classes of cavities, but particularly for direct introduction into the pulp chamber. The billets are about 1/20th of an inch in thickness and ⅛th of an inch long, and weigh 1/12 grain; they are formed from "absolutely pure" cocain hydrochlorid by special machinery. "No foreign matter of any nature is incorporated with the cocain, either to make the particles adhere or to regulate the weight."

Nirvanin or Nirvanine.—This name was given by a German color works to a new product of theirs, the hydrochlorid of di-ethyl-glycocoll-meta-amido-ortho-oxy-benzoic-methyl-ester,



The preparation was stated to consist of colorless prisms, fusing at + 185° C. and freely soluble in water. The anesthetic properties of *Orthoform* (*q. v.*) suggested the desirability of transforming these sparingly soluble or sensibly acid bodies into freely soluble and non-irritant compounds which should be adapted for subcutaneous injection as well. Nirvanin was said to obviate these objections, and it was stated by Einhorn and Heinz (*Münch. med. Woch.,* 1898, No. 49, 1553) that its principal utility consisted in its power of producing local anesthesia for surgical operations by means of subcutaneous injections. It was said to share with Orthoform its enduring action, but to be less poisonous and at the same time to be antiseptic. Jouanin (*Bull. gén. de Thérap.,* June, 1898, 906; *Repert. de Pharm.,* 1899, 329) and Reynier

(*Rev. de Thérap. Méd.-chirurg.,* 1889, 505) studied the physiological action of nirvanin. The former regarded it as the least toxic of all bodies then employed for local anesthesia, since the lethal dose amounted to 0.7 gm. per kg. Reynier confirmed the statements of Jouanin, but indicated, at the same time, that the anesthetizing power was visibly less than that of cocain. On the pharmacology of Nirvanin, see Didrichson: *Wratsch,* 1900, No. 21. In surgical operations good results were witnessed by Boisseau (*Thèse de Bordeaux,* 1899) and by Luxenburger (*Münch. med. Woch.,* 1899, Nos. 1, 2, and 38), the latter even going so far as to give nirvanin the preference over cocain and cocain mixtures in anesthesia by the infiltration and regionary methods. Hölscher (*Münch. med. Woch.,* 1899, No. 8, 247) and Schmidt (*ibid.,* 1899, No. 38, 1255) employed nirvanin in regionary anesthesia and noted that its use gave rise to violent pains. Experiments on the use of nirvanin in dental surgery were made by Dumont and Legrand: *Rev. de Stomatol.,* March 20 and June, 1899; Stubenrauch: *Münch. med. Woch.,* 1899, No. 38, 1255; Wittkowski: *Odontol. Blätter,* 1898, No. 15; Rotenberger: *Deut. zahnärztl. Woch.,* 1898, No. 38; Fricke, Schröder, and Carras: "*Correspondenz f. Zahnärzte,* 1899, No. 3, 264; Bounard: *L'Odontologie,* April 30, 1899, and others. The first three mentioned writers expressed a favorable opinion on the properties of nirvanin, whereas the last three joint authors condemned it, since its injection was found to invariably produce, in a more or less pronounced degree, pains in the puncture canals and their surroundings, and to give rise to edematic swellings liable to persist for days. In 1899 it was directed that regionary anesthesia according to Oberst be effected by means of a 2 per cent solution of nirvanin; that 0.1 to 0.5 per cent solutions be used in Schleich's method of infiltration; and that 2 to 5 per cent solutions be used in dental surgery. Marcus (*Deut. zahnärztl. Woch.,* 1903, No. 39) published some observations respecting the use of nirvanin in dental surgery, as did Guadagnini (*Bollett. delle scienze med.,* 1903, 77); these operators appeared to be favorably impressed with the anesthetic. Ouwarow (*Wratsch,* 1900, No. 23) found that nirvanin exercised an elective action upon the sympathetic nerve, since its use occasionally gave rise to irregular dilatation of the pupil, acceleration of the action of the heart, flow of tears, and ptyalism.

Nirvanin is no longer on the market.

Nitrogen.—While nitrogen cannot be regarded as an anesthetic, producing, as it does, simple, uncomplicated asphyxia, Sanderson, Murray, and Turner (*Brit. Med. J.,* June 13, 1868) experimented with the gas, finding that its primary effect was to accelerate the movements of respiration and circulation; respiration was then retarded and labored, while the pulse became slow and irregular. The pupils, which had been dilated, now became contracted. The countenance was pallid, and there was no appearance of cyanosis. Continued inhalation caused a renewed acceleration of the pulse, accompanied by retardation of respiration, and the production of a degree of insensibility sufficient for the painless extraction of a tooth.

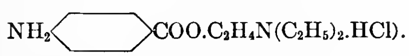
Nitrous Oxid.—See Chapter IV. Hunter (Eng. Pat. 7,343, 1885) proposed mixing nitrous oxid with vapor of alcoholic tinctures of hops, etc.

Nopain.—This dental anesthetic is said to contain 1 part cocain hydrochlorid; ¼ part phenol; 5 parts glycerin; 4 parts adrenalin solution (1 : 1000); and 4 parts absolute alcohol.

Nor-Cocain.—When nor-l-ecgonin has benzoyl and methyl groups introduced, as in ordinary cocain, nor-cocain, a powerful anesthetic, is produced. This is, however, too toxic for practical purposes, owing, probably, to the presence of the imid group (NH).

Novadrin.—A solution containing novocain (0.015 gm.) and adrenalin (0.00005 gm.), for subcutaneous injection.

Novocain or Novocaine (Mon-hydrochlorid of para-amino-benzoyl-diethyl-amino-ethanol,



This compound produces a profound anesthetic action subcutaneously; this passes off quite soon, leaving no symptoms of irritation. Le Brocq (*Pharm. J., 82,* 673) found that novocain is equal in anesthetic power to cocain, and that its toxicity and destructive action are much less. Experiments by Gros (*Arch. exp. Path. Pharm., 67,* 132), with the borate, bicarbonate, secondary phosphate, acetate, and chlorid of novocain, showed their narcotizing power to decrease in the order given.

Novocain crystallizes from alcohol in colorless needles possessing a melting point of + 156° C. It can be heated to + 120° C. without decomposition. It dissolves in equal parts of cold water, and the solution possesses a neutral reaction and may be boiled without decomposition; it dissolves in cold alcohol in the proportion of 1:30. Caustic alkalies and alkaline carbonates precipitate the free base from the aqueous solutions in the form of a colorless oil which soon solidifies to a crystalline mass; on the other hand, sodium bicarbonate mixes with the water solution without producing a turbidity. Alkaloidal reagents, as potassium-mercuric iodid, picric acid, and iodo-potassium iodid solution, produce precipitates even in very dilute water solutions of novocain. Pharmacological investigations show that novocain possesses the same action as cocain upon the peripheral sensory nerves, and that the 0.25 per cent solution suffices completely to anesthetize even the thick nerve trunks, as the sciatic nerve, in about ten minutes. It is said to produce no by-effect when applied locally, and that there are no symptoms of irritation even when strong solutions are used. Experiments on animals showed, it is reported, that novocain is about six times less toxic than cocain, far less toxic than any of the cocain substitutes, and the general effect on the system after its absorption is scarcely perceptible, neither the circulation nor the respiration being affected. Moreover, that the cardiac activity does not suffer, and that no mydriasis is produced. It has been shown that novocain not only does not reduce the action of suprarenalin, but increases it. The indications are the same as for cocain, and it is said to be useful in cases in which cocain is indicated.

Dosage.—For infiltration anesthesia, solutions of 0.25 gm. (4 grains) novocain in 100 or 50 gm. (3.2 or 1.6 ounces) physiologic salt solution, with 5 or 10 drops of epinephrin solution (1:1000); for instillations and injections, solutions of 0.1 gm. (1½ grains) novocain in 10 or 5 gm. (150 or 75 grains) salt solution, with or without 10 drops of epinephrin solution (1:1000). In ophthalmology, 1 to 5 to 10 per cent solution, in rhinolaryngology, 5 to 20 per cent solutions are recommended, with the addition of 6 to 8 drops of epinephrin solution (1:1000) to each 10 c. c. (160 minims). Internally, owing to its feeble toxicity, it may be given in doses up to 0.5 gm. (7½ grains) to adults.

The literature relating to novocain is quite extensive; a number of the references follow in chronological order:

Braun, H.: *Deut. med. Woch.*, 1905, No. 42.
Biberfeld, Joh.: *Med. Klinik*, 1905, No. 48.
Heineke, H., and Läwen, A.: *Deut. Z. f. Chir.*, *80*, 180.
Sachse, B.: *Deut. zahnärztliche Woch.*, 1905, No. 45.
Danielsen, Wilh.: *Münch. med. Woch.*, 1905, No. 46.
Schmidt, Erhardt: *Münch. med. Woch.*, 1905, No. 46.
Duhot: *Ann. de la policlin. centrale de Bruxelles*, 1905, No. 12.
Krecke: *Münch. med. Woch.*, 1906, No. 6, 287.
Liebl, Fritz: *Münch. med. Woch.*, 1906, No. 5.
Cisler, Josef: *Casopis Lekaruv Ceskych* (Prag), 1906, No. 5.
Klein: *Les Nouveaux Remèdes*, 1906, No. 3.
Sonnenburg, Ed.: *Von Leuthold-Gedenkschrift*, 1906, *2*.
Best, F.: *Med. Woch.*, 1906, No. 10.
Lucke, Robert: *Monats. f. Harnkrankh. und Sex. Hygiene*, 1906, *3*.
Mayer, Theodor. *Dermatologische Z.*, 1906, *13*, No. 3.
Hermes, O.: *Med. Klinik*, 1906, No. 13.
Ciezynski, A.: *Deut. Monats. f. Zahnheilk.*, Apr., 1906.
Opitz: *Münch. med. Woch.*, 1906, No. 20.
Willke, O.: *Medico*, 1906, No. 19.
Euler: *Deut. zahnärztl. Woch.*, 1906, No. 20.
Gebb, H.: *Archiv für Augenheilk.*, May, 1905, *55*, Nos. 1 and 2.
Lazarus, Paul: *Z. f. physikal. und diätet. Therap.*, 1906, *10*, No. 2.

Freemann: *Dermatol. Zentralb.*, 1906, No. 8.
Brunner: *Münch. med. Woch.*, 1906, No. 23.
Pinet and Jeay: *L'Odontologie*, May 30, 1906, No. 10.
Fischer, Guido: *Deut. Monats. f. Zahnheilk.*, June, 1906.
Graeser, Carl: *Jahresber.*, 1905 and 1906, *d. Deut. Kranken.* Neapel, 42.
Haug: "Therap. von Ohraffektionen," *Archiv f. Ohrenheilk.*, 1906, 69.
Misch, Julius: *Oesterreichisch-Ungarische Vierteljahres. f. Zahnheilk.*, July, 1906, No. 3.
Freund, Rich.: *Deut. med. Woch.*, 1906, No. 28; and *Münch. med. Woch.*, 1906, No. 30.
Stieda, A.: *Münch. med. Woch.*, 1906, No. 30, 1490.
Katz, Leo: *Deut. med. Woch.*, 1906, No. 36.
Hoppe: *Die ärztliche Praxis*, 1906, No. 16.
Lindenstein: *Deut. med. Woch.*, 1906, No. 45.
Blondel, Paul: *Rev. de Thérap. Méd.-chir.*, 1906, Dec. 23.
Hamecher, Hans: *Odontol. Blätter, 11*, Nos. 7-8.
Hoffmann, C.: *Münch. med. Woch.*, 1906, No. 52.
Remien, Carl: *Allgem. med. Central-Zeitung*, 1906, No. 8.
Regnier: *Bull. de l'Acad. de Méd.*, 1907, 484.
Nast-Kolb: *Münch. med. Woch.*, 1908, No. 13.
Struthers: *Ednb. Med. J.*, Feb., 1908.
Bier, August: *Archiv f. klin. Chir.*, *86*, No. 4; *Surg. Gynec. and Obstet.*, Nov., 1908.
Cramer: *Dissert.*, Freiburg, 1908.
Stoekel, W.: *Central. f. Gynäk.*, 1909, No. 1.
Albright, J. D.: "Albright's Office Pract.," July, 1909.
Hahn: *Deut. zahnärztl. Woch.*, 1909, No. 5.
Nyström: *Zentralb. f. Chir.*, 1909, No. 5.
Blum: *Z. f. Urologie*, 1909, No. 2.
Bolze: *Zahntechn. Rundschau*, 1909, No. 9.
Erhart: *Zahntech. Rundschau*, 1909, No. 1.
Prinz: *Zahnärztl. Rundschau*, 1909, Nos. 4-10; and *Deut. zahnärztl. Zeit.*, 1909, No. 10.
Sieber: *Münch. med. Woch.*, 1909, No. 10.
Bier: *Berl. klin. Woch.*, 1909, No. 11.
Le Brocq: *Brit. Med. J.*, 1909, No. 2517, 783.
Petrow: *Zentralbl. f. Chir.*, 1909, No. 14.
Bäärnhielm: *Allmänna Svenska Läkartidningen*, 1909, No. 11.
v. Lichtenberg: *Deut. med. Woch.*, 1909, No. 16.
Busse: *Therap. der Gegenwart*, 1909, No. 5.
Spisharny: *Russkiy Wratsch*, 1909, No. 9.
Braun: *Deut. med. Woch.*, 1909, No. 16.

Ruprecht: *Monats. f. Ohrenheilk. und Laryngo-Rhinol.*, 1909, Nos. 3 and 4.

Braun: *Beitr. z. klin. Chir.*, 1909, *62*, No. 3.

Düwawis: *Prakt. Wratsch*, 1909, No. 11.

Scheff: *Osterr.-ungar. Vierteljahressch. f. Zahnheilk.*, 1909, No. 1.

Fischer: *Deut. zahnärztliche Woch.*, 1909, No. 22.

Lemire and Ducrotoy: "Récueil de mémoires et observations sur l'hygiène et la médecine veterinaires militaires," 1908, 10.

Canny Ryall: *The Clin. J.*, 1909, No. 871.

Hammer: *Deut. militäräztliche Z.*, 1909, No. 11.

Gros: *Münch. med. Woch.*, 1910, No. 39.

Läwen: *Ibid.*

Krecke: *Münch. med. Woch.*, 1910, No. 26, 2447.

Gross: *Gynäkol. Rundschau*, 1910, No. 17.

Kraatz: *Zentralbl. f. Gynäkol.*, 1910, No. 22.

Kutscher: *Deut. med. Woch.*, 1910, No. 24, 1129.

Bünte-Moral: *Deut. Monats. f. Zahnheilk.*, 1910, No. 2.

Senator: *Münch. med. Woch.*, 1910, No. 10, 524.

Schlüter: *Klin. Monatsbl. Augenheilk.*, *45*; *Biochem. Centr.*, *8*, 900.

Möller: *Deut. zahnärztl. Woch.*, 1910, No. 35; 1911, No. 16.

Gros: *Arch. exp. Path. Pharm.*, 1912, *67*, 132-6.

Prinz: *Dental Summary*, Feb., 1912; *Pharm. J.*, *88*, 779.

Novocain, Adrenalin, and Sodium Bicarbonate.—Novocain, adrenalin, and sodium bicarbonate solutions have been proposed for renal operations. See *Münch. med. Woch.*, 1911, No. 26; *Therap. Gaz.*, Aug. 15, 1911.

Novocain Bicarbonate Solutions.—Gros (*Münch. med. Woch.*, 1910, No. 39) demonstrated that, in animals, solutions of salts of cocain, novocain, alypin and eucain, to which an alkali had been added, showed a considerable increase in their anesthetic properties. In practice, sodium bicarbonate was recommended for this purpose. For local anesthesia Läwen (*ibid.*) tested this method especially with novocain. He found on using a solution of novocain, sodium chlorid, and sodium bicarbonate that the resulting anesthesia occurred earlier than was the case when novocain solution was employed, while it continued for a far longer time. He gave formulas for preparing three different strengths of solutions to be used for sacral, regional, and dental anesthesias. It is said that for pure infiltration anesthesia no special advantages are to be obtained from solutions of novocain bicarbonate.

Novocain Nitrate (Novocainæ Nitras).—Novocain nitrate is 1-para-aminobenzoyl-2-diethylamino-ethane nitrate [$C_6H_4NH_2COO.C_2H_4.N(C_2H_5)_2.HNO_3 = C_{13}H_{21}O_5N_3$], the nitrate of p-aminobenzoyldiethylaminoethanol, the base contained in novocain. Novocain nitrate is obtained in small colorless and odorless crystals, soluble in water and alcohol. The aqueous solution is neutral in reaction. Melting point, + 100°-102° C. (212-215° F.). If 0.1 gm. novocain nitrate is dissolved in 1 c. c. concentrated sulphuric acid and a solution of ferrous sulphate is carefully floated above it, a brown zone is formed at the surface of contact of the two solutions. One part of novocain nitrate dissolved in 10 parts water and acidified with nitric acid should yield no precipitate upon the addition of silver nitrate solution.

Actions and Uses.—As for novocain, it may be prescribed in combination with silver salts, with which it forms no precipitate.

Dosage.—Used in 3 per cent solutions.

Novocain-Suprarenin Solutions.

0.5	per	cent	solution	=	Tablet	A	in	25 c. c.	water.
2.0	"	"	"	=	"	B	"	5 "	"
5.0	"	"	"	=	"	C	"	1 "	"
10.0	"	"	"	=	"	D	"	2 "	"
2.0	"	"	"	=	"	E	"	1 "	"

Novocain-Suprarenin Tablets.—A.—0.125 gm. novocain + 0.00016 gm. suprarenin borate, for infiltration anesthesia; B.—0.1 gm. novocain + 0.00045 gm. suprarenin borate; C.—0.05 gm. novocain + 0.000108 gm. suprarenin borate, for medullary anesthesia; D.—0.2 gm. novocain + 0.00015 gm. suprarenin borate + 0.09 gm. sodium chlorid, for dental operations; E.—0.02 gm. novocain + 0.000015 gm. suprarenin borate + 0.009 gm. sodium chlorid, for dental operations.

Novoconephrin.—Novocain, 0.018 gm.; paranephrin, 0.00007 gm.; with a trace of thymol, in physiological salt solution, 1.25 gm. An injection-anesthetic in dentistry.

Novo-Dentæsthin.—This dental local anesthetic contains in 1 c. c. of a physiological salt solution 0.01 gm. beta-eucain lactate, 0.015 gm. novocain, and 0.05 gm. of synthetic suprarenin.

Novorenal.—The 0.25 per cent solution contains 0.0125 gm. of novocain, 5 gm. of physiological salt solution (NaCl), and 0.00001625 gm. suprarenin hydrochlorid; the 0.5 per cent solution contains double the above quantities of novocain and suprarenin; the 1 per cent solution contains 0.01 gm. novocain, 1 gm. of physiological salt solution, and 0.00009 gm. of adrenalin hydrochlorid; the 2 per cent solution contains 0.02 gm. of novocain, 1 gm. of physiological salt solution, and 0.00009 gm. of suprarenin hydrochlorid. These solutions are employed as local anesthetics; novorenal 2 per cent is most used by dentists, and the experiences are reported to be very good.

Novorobiol.—See *Robiol.*

Nussbaum's Mixture.—Alcohol, 1 part; chloroform, 1 part; and ether, 3 parts. Mixed. See Potter: "Mat. Med. Pharm. Therap.," 10th ed., 88.

Obalgo.—A dental local anesthetic of unknown origin.

Obtundo.—A dental local anesthetic consisting of chloretone, cocain, nitroglycerin, thymol, menthol, and oils of wintergreen, eucalyptus, and cloves.

Octane.—This hydrocarbon, which is contained in commercial ligroine in crude petroleum, produces an anesthesia similar to that caused by *Hexane* (*q. v.*); in addition, according to Versmann, there is a tendency to vomiting. The unsaturated hydrocarbons ethylene, propylene, and butylene are said to have a very similar action.

Odiot.—Tincture of benzoin, with balsam of Peru and oil of cloves. Used in odontalgia.

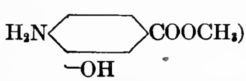
Oil Absinthium, or Oil Wormwood.—This oil possesses anesthetic properties.

Omnopon.—See *Pantopon.*

O-phthaloyl-bis-methylecgonin.—Einhorn and Klein (Ber., 1888, *21*, 3335) have shown that this compound possesses a physiological action similar to that of cocain.

Opiopon.—According to Flury (*Z. angew. Chem.*, *26*, 242), this preparation contains the alkaloids of opium. See *Pantopon.*

Opon.—According to Flury (*Z. angew. Chem.*, *26*, 242), Opon is a morphin-free Pantopon (*q. v.*).

Orthoform (Orthoform-Proper; Para-amido-meta-oxybenzoic acid methyl ester, 

). See *Orthoform-New,* which is a finer, whiter, more homogeneous powder and is less expensive than orthoform-proper. Like orthoform-new, orthoform-proper exercises its full local anesthetic action even in a 10 to 20 per cent mixture with amylum or talcum. It is very slightly soluble and is also but feebly toxic. It is said, however, that it is only active when directly applied to the nerve endings, and that it is useless when applied to the unbroken skin or mucous membranes. The soluble hydrochlorid of orthoform-proper is not used in practice, owing to the fact that its injection produces pain. According to Francis and Fortescue-Brickdale ("The Chemical Basis of Pharmacology," 1908, 310), orthoform has also been observed to produce severe dermatitis of an erythematous, pustular, or even gangrenous type.

Orthoform-New (Meta-amido-para-oxybenzoate of methyl).—Orthoform-New is methyl meta-amino-para-oxybenzoate,

$$C_6H_3.NH_2.OH.COO(CH_3),\ 3:4:1 = C_8H_9O_3N,$$

the meta-amino-para-oxybenzoic acid ester of methyl alcohol. It is prepared by the nitration of para-oxybenzoate of methyl and reduction of the nitro product obtained. A large number of bodies have been prepared which resemble orthoform, but only a few are of any practical use. It is obtained in a fine, white, crystalline powder, neutral in reaction, and melting at + 141° to 143° C. (285.8° to 289.4° F.), odorless and tasteless. It is scarcely soluble in water, but is soluble in 5 or 6 parts of alcohol and 50 parts of ether. It is decomposed by boiling with water, or by warming with alkalies or their carbonates, into methyl alcohol and paroxybenzoic acid. When crystallized from chloroform it sometimes assumes the form of white crystals melting at + 110° to 111° C. (230° to 231.8° F.), returning, on melting, to the ordinary form. The filtrate obtained after shaking a small portion with water produces a fugitive color with ferric chlorid, and should not give a reaction with silver nitrate. A solution of 0.1 gm. in 2 c. c. of water by the aid of hydrochloric acid is colored yellowish red on addition of sodium nitrate, and then deposits a yellow precipitate, deepening to red on exposure to the air.

It is decomposed by heating with water; it is incompatible with alkalies and their carbonates. Orthoform is also incompatible with silver nitrate (see Bock: *Therap. Monatsh.*, 1898, 413), the organic silver albuminoid preparations, formaldehyd, potassium permanganate, ferric chlorid, antipyrin, and bismuth subnitrate. It may, however, be combined with solutions of mercuric chlorid, tincture of iodin, turpentine, solutions of copper sulphate, iodoform, dermatol, zinc oxid, europhen, aristol, calomel, and salicylic acid. It is also applicable in 3 to 5 per cent solutions of phenol, and with lysol and cresol solutions. Its hydrochlorid is soluble, but irritant.

Actions and Uses.—Orthoform-New is a local anesthetic, resembling cocain in its local action, but not penetrating the tissues on account of its insolubility. It has practically no action on the unbroken skin, except for a slight irritation which it produces about the place of application. It is somewhat antiseptic and practically non-toxic in the usual doses. It is used internally to relieve the pain of gastric ulcer. Since it acts only on ulcerated surfaces, the relief of pain has been assumed to be evidence of the existence of an open ulcer. It has been applied locally as an analgesic to wounds of every description. It has been used in dentistry, in nasal catarrh, hay fever, etc.

Orthoform paralyzes, just as cocain, all the peripheral sensory nerve endings and nerve trunks with which it is brought into direct contact. Therefore, because of its insolubility, it can only exercise its properties when applied to wound surfaces where the nerve endings are exposed, and does not penetrate the tissues. Its antiseptic action is weak. Heinz determined experimentally, and this point has been confirmed by clinical work, that the drug exerted practically no toxic action on the economy at large when administered in the doses recommended. Cf. Soulier and Guinard: *Répert. de Pharm.*, 1898, 420. Owing to the slow solubility of orthoform, only small quantities are absorbed at a time, thus prolonging anesthesia for hours or days. It is said to be applicable whenever pain is in evidence, and to be of value as a sprinkling powder, pure or mixed with some bland powder, in solution in alcohol, ethyl ether, or collodion, and in an ointment.

Dosage.—Internally, 0.5 to 1 gm. (8 to 15 grains) in emulsion; locally, in substance as a dusting powder or mixed with milk sugar for insufflation, dissolved in ether and mixed with oil for pencilings, or as a salve with wool fat, etc.

The following are some of the references to the literature of orthoform.

Einhorn and Heinz: "Orthoform; ein Lokalanästhetikum für Wundschmerz, Brandwunden, Geschwüre usw.," *Münch. med. Woch.*, 1897, No. 34; No. 37, 555.

Neumayer: Über Orthoform," *Münch. med. Woch.*, 1897, No. 44, 1230.

Klaussner: "Über Orthoform," *Münch. med. Woch.*, 1897, No. 46, 1289.

Boisseau: "De l'orthoforme; son emploi en oculistique," *Gaz. hebd. d. Sciences méd. d. Bordeaux*, 1897, 603-607.

Kallenberger: "Über Orthoform," *Inaug.-Dissert.* München, 1897.

Lichwitz and Sabrazès: "L'Orthoforme comme anesthésique et comme antiseptique," *Bull. méd.*, Nov., 1897, No. 94.

Tschernogoubov: "Orthoforme pour injections souscutanées," *Sem. méd.*, 1897, No. 16.

Hirschbruch: "Orthoform," *Berl. klin. Woch.*, 1897, No. 51.

Boisseu: "L'Orthoforme en laryngologie et en stomatologie," *Gaz. hebd. d. Sciences méd. d. Bordeaux*, Jan., 1898, 39-41; also, *Presse méd.*, 1898, 89.

Yonge: "Treatment of Painful Ulcerations," *Brit. Med. J.*, Feb., 1898; see, also, *Canadian J. Med.*, 1898, No. 3.

Cumston: *Boston Med. and Surg. J.*, Mar. 24, 1898.

Kindler: "Orthoform," *Fortsch. d. Med.*, Apr., 1898, No. 7.

Bernould and Garrel: "L'Orthoforme en laryngologie," *Lyon méd.*, 1898, No. 13.

Kallenberger: "Über Orthoform," *Berl. klin. Woch.*, 1898, No. 12; *Inaug.-Dissert.*, München, 1898.

Dreyfuss: "Kombination von Infiltrationsanästhesie und Orthoform," *Münch. med. Woch.*, 1898, No. 17.

Nogouès: "L'Orthoforme dans les affections douloureuses de la vessie," *Annales des maladies des organes génito-urinaires*, Paris, 1898, 547.

Fromaget: "Orthoform bei Augenaffektionen," *Berl. klin. Woch.*, 1898, No. 9.

Ginestoux: "Acide arsénieux et orthoforme dans le traitement du cancer épithélial," *Sem. méd.*, Apr., 1898, No. 20.

Cerry and Tourecek: "Emploi de l'orthoforme," *Sem. méd.*, Apr. 13, 1898.

Bonnard: "L'Orthoforme et le chlorhydrate d'Orthoforme en art dentaire," *L'Odontologie*, May 30 and June 15, 1898.

Brocq: "Accidents produits par l'orthoforme,' *Sem. méd.*, 1898, No. 17.

Bornstein: "Orthoform," *Zahnärzt. Runds.*, May 15, 1898, No. 306.

Lichtwitz: "Traitement de la rhinite vaso-motrice (hydrorrhée nasale, fièvre des foins) par l'orthoforme," *Le Bull. méd.*, 1898, No. 7; *Arch. internat. Laryngol.*, 1898, No. 1.

Loeb: "Orthoform als Anästhetikum bei intramuskulären Injektionen," *Monats. f. prakt. Dermatol.*, Jan. 27, 1898.

Jessen: "Orthoform," *Deut. zahnärzt. Woch.*, 1898, No. 10.

Blondel: "L'Orthoforme en gynécologie," *Rev. d. Thérap.*, May, 1898, No. 10.

Manquat: "Deux nouveaux anesthésiques locaux, l'orthoforme et la nirvanine," *Bull. méd.*, 1898, 984.

Pozzi: "L'Orthoforme en gynécologie," *Le Scalpel*, May, 1898, No. 46.

Mosse: "Verhalten des Orthoforms im Organismus," *Deut. med. Woch.*, 1898, No. 26; see, also, *Klin.-Therap. Woch.*, 1898, No. 25.

Mosse, Herzfeld, Jastrowitz, v. Leyden, Goldscheider, Fränkel, Ehrlich: Discussion: "Verhalten des Orthoforms in Organismus," *Allge. med. Central-Zeit.*, June, 1898, No. 47; *Deut. med. Woch.*, 1898, No. 17.

Bezold: "Orthoform," *Münch. med. Woch.*, 1898, No. 26.

Gianelli: "L'Orthoformio in ginecologia," *Archiv. Ital. di Ginecol.*, 1898, 508-511.

Schech: "Orthoform," *Münch. med. Woch.*, 1898, No. 26.

Fink: "Orthoform in der Rhino-Laryngologie," *Ärztl. Praxis*, 1898, No. 20.

Jessen: "Orthoform," Jahresbericht der Poliklinik für Zahnkrankheiten, Strassburg, 1898-1899; *Deut. zahnärztl. Woch.*, 1898, No. 10.

Korn: "Orthoform bei Prurigo und bei Herpes Zoster," *Die ärztl. Praxis*, July, 1898, No. 13.

Hecker: "Über Orthoform," *Inaug.-Dissert.*, Berlin, July, 1898.

Bock: "Beiträge zur Kenntnis des Orthoforms," *Therap. Monatsh.*, 1898, 413.

Rotenberger: "Orthoform und 'Orthoform neu' und Nirvain," *Deut. zahnärz. Woch.*, 1898, No. 38.

Klaussner: "Uber Orthoform und 'Orthoform neu,'" *Münch. med. Woch.*, 1898, No. 42, 1338.

Kassel: Über Orthoformemulsion," *Therap. Monatsh.*, Oct., 1898, 556.

Heinzel: "Über Orthoform," *Wiener klin. Woch.*, 1898, No. 48.

Wohlgemuth: "Über Orthoform," *Deut. med. Woch.*, 1898, No. 44.

Hanszel: "Orthoform," *Wiener klin. Woch.*, 1898, No. 49.

North: "Orthoform as a Local Anesthetic, Analgesic, and Antiseptic," *Am. Med. Compend.*, Nov., 1898.

Maygrier and Blondel: "Zur Behandlung der Rhagaden der Brustwarze bei stillenden Frauen," *Revue de Thérap.*, 1898, 797.

Apfelstädt: "Orthoform," *Deut. zahnärzt. Woch.*, 1898, No. 40.

Hildebrandt: "Beitrag zur Orthoformanästhesie," *Deut. med. Woch.*, 1898, No. 48; *Therap. Beil.*, No. 12, 95.

Löbisch: "Orthoform," *Enzyklopädische Jahrb.*, 1898, viii.

Lipowski: "Larynxerkrankungen," *Therap. Monats.*, *18*, No. 12.

Denigès: "Sur les orthoformes, caractères et différences," *Bull. d. la Soc. d. Pharmacol. d. Bordeaux*, Dec., 1898.

Ducray: "L'Orthoforme et ses indications en laryngologie," *Inaug.-Dissert.*, Lyon, 1898.

Herzfeld: "Verhalten des Orthoforms im Organismus," *Allge. med. Centr.-Ztg.*, June, 1898, No. 47.

Teisseire: "Traitement des gerçures et crevasses du sein par d'orthoformè," *Inaugural-Dissertation*, Paris, 1898; also, *Sem. méd.*, 1898, No. 57, 226.

Kionka: "Über neuere Arzneimitte," *Therap. der Gegenwart*, 1899, No. 1.

Holmes: "The Use of Orthoform in Surgery," *Woman's Med. J.*, Jan., 1899, No. 1.

Johnson: "Orthoform," *Woman's Med. J.*, 1899, No. 1.

Maygrier: "Treatment of Fissures of the Nipples," *Med. Press*, Jan. 25, 1899.

Danlos: "Orthoform," *La Presse méd.*, Jan. 14, 1899; "Injections de calomel additionées d'orthoforme à titre d'analgésique," *J. d. Malad. Cutan. et Syphilit.*, 1899, *60*.

Epstein: "Über Orthoform, bezw. 'Orthoform neu' als Zusatz zu Quecksilberparaffin-Emulsionen," *Dermat. Centralblatt*, February, 1899, No. 5.

Göppert: "Orthoform," *Fortsch. der. Med.*, 1899, No. 35; "Orthoform," *Jahrbuch f. Kinderheilk.*, N. F., Feb., 1899, No. 49.

Asam: "Erfahrungen mit Orthoform," *Münch. med. Woch.*, 1899, No. 8, 252.

Cheatham: "A Note on Orthoform," *Amer. Therap.*, Feb., 1899, No. 8.

Mailland: "Accidents provoqués par l'orthoforme employé comme topique des plaies," *Province méd.*, 1899, 135.

Meyer: *Laryngologist,* March, 1899.

Sims: "Experience with Orthoform," *Therap. Prog.*, 1899, No. 3.

Dickenson: "Orthoform in Rectal Affections," *Therap. Prog.*, 1899, No. 3.

Crisand: "Clinical Note on Orthoform," *Therap. Progress,* 1899, No. 3.

v. Zander: "Das Orthoform in der Laryngologie," *Charité-Ann.*, March, 1899, *23.*

Freudenthal: "Behandlung des Hustens und der Tuberkulose," *Monat. f. Ohren-, Kehlkopf-, Nasen- und Rachenkrankheiten,* 1899, No. 3.

Schröppe: "Orthoform-Exanthem," *Petersburger med. Woch.*, Mar., 1899, No. 12; No. 13, 100.

Kindler: "Weitere Mitteilungen über den Gebrauch von Orthoform," *Fortsch. der Med.*, 1899, No. 7.

Miodowski: "Orthoform," *Münch. med. Woch.*, 1899, No. 12, 382.

Boisseau: "Contribution à l'étude de l'orthoforme," *Inaug.-Dissert.*, Bordeaux, Mar. 24, 1899.

Albertin: "Intoxication par l'orthoforme employé comme topique dans le pansement des plaies," *Lyon méd.*, May, 1899.

Darier: "De l'action analgésiante de l'orthoforme dans certaines affections oculaires," *La Cliniq. Ophthal.*, Apr., 1899, No. 8.

Brocq: "De l'orthoforme en dermatologie," *J. d. Pratic.*, 1899; *Presse méd.*, 1899, No. 30; "Intolérance par l'orthoforme," *Soc. franç. d. Dermatol.*, Paris, Apr., 1899.

Dauchez: "*Progrès. méd.*, May 20, 1899.

Brocq and Besnier: "Éruptions orthoformiques," *Soc. franç d. Dermatol.*, Paris, April, 1899.

Brocq and Thibierge: *Gaz. hebd. de Méd. et de Chir.*, 1899, No. 32.

Denigès: "Prüfung des Orthoforms," *Les Nouveaux Remèdes,* 1899, 400.

Wunderlich: "Zur Anwendung von Orthoform," *Münch. med. Woch.*, 1899, No. 40, 1296.

Gomberz: "Über Versuche mit einigen neuren Mitteln," *Monat. f. Ohrenheil.*, 1899, No. 6, 256.

Kassel: 'Orthoform-Neu," *Monat. f. Ohrenheil.*, 1899, No. 6.

Dunogier: "L'Orthoforme," *J. de Méd.*, June, 1899.

Soulier and Guinard: "Contribution à l'étude pharmacodynamique de l'orthoforme," *Archiv. Internat. d. Pharmaco.- et d. Thérap.*, 1899, 6.

Bleuler: "Orthoform," *Neurolog. Central.*, 1899, No. 14.

Wright: "The Prevention of Hayfever," *N. Y. Med. J.*, May 6, 1899.

Ott: "Orthoform," *Med. Arena*, Sept., 1899.

Madden: "Observation on Uterus Cancer Treatment," *Dublin J. Med. Sci.*, 1899, 409.

Maire: "Behandlung der Papilla fissurata," *Zentralb. f. Gynäkol.*, Aug., 1899, No. 32.

Salzer: "Orthoform bei Augenaffektionen," *Die ophthal. Klinik*, Sept., 1899, 257.

Stubenrauch, Klaussner, Gossmann, Krecke, Moritz: "Diskussion über Orthoform"; Auszug: *Münch. med. Woch.*, 1899, Nos. 38, 39, Seite 1254.

Whien: "Des éruptions dues à l'orthoforme," *Bull. d. l'Hôpital franç. d. Tunis*, 1899, 243.

Mirabeau: "Orthoform," *Zentralbl. f. Gynäkol.*, 1899, No. 11; *Monat. f. Geburts.*, 1899, 9.

Decker: "Dermatitis Following the Use of Orthoform," *N. J. Med. J.*, 1899, 780.

Sauer: "Orthoform-Idiosynkrasie?" *N. Y. Med. Monat.*, 1899, No. 12.

Bardet: "Note sur les modes d'administration de l'orthoforme et sur quelques applications," *Bull. gén. d. Thérap.*, Feb., 1900, 262.

Blondel: "Traitement des crevasses du mamelon par l'orthoforme," *Soc. d. Thérap.*, Feb., 1900.

Dejace: "Orthoforme," *Le Scalpel*, July, 1900, No. 5.

Luxenburger: "Experimentelles und Klinisches über Orthoform," *Münch. med. Woch.*, 1900, Nos. 2, 3, 48, and 82.

Sprague: "Orthoform Facts," *Am. Therap.*, Sept., 1900, No. 3.

Thelberg: "Treatment of Anal Chancroids," *N. Y. Med. J.*, May 26, 1900.

Norbury: "Orthoform in the Treatment of Epithelioma," *Med. Fortnightly*, March 26, 1900.

Hélouin: "L'Orthoforme," *Bull. des Sci. pharmacol.*, Nov., 1900, No. 11.

Gleason: *Internat. Med. Mag.*, Oct., 1900.

Friedländer: "Orthoformvergiftung," *Therap. Monat.*, Dec., 1900, No. 12, 676.

Ruhemann: "Ein Fall von Orthoformvergiftung," *Therap. Monat.*, Dec., 1900-1901, No. 12.

Lang: "Erfahrungen mit Orthoform und Nirvanin," *Zahnärzt. Rundschau*, 1900, 6359-6360.

Plique: "L'Orthoforme," *La Presse méd.*, 1900, 204-205.

Vacek: "Sur l'orthoforme," *Casopis Lakaruv. Ceskych*, Prag, 1900, 154.

Villa: "Contribution à l'étude expérimentale et clinique de l'orthoforme," *Inaugural-Dissertation*, Lyon, 1900.

Villa: "À propos des accidents produits par l'orthoforme," *Echo méd. de Lyon*, 1900, 161-171.

Vogt: "Traitement de la période éruptive du zona par les applications d'orthoforme," *Bull. gén. d. thérap.*, 1900, 576.

Garnault: "Traitement de la tuberculose par la viande crue et par les injections intratrachéales d'orthoforme," *Bull. d. la Soc. d. Thérap.*, Jan., 1901.

Heineck: "Newer Local Anesthetics. Holocain, Nirvanin, Orthoform," *The Bacillus*, Jan., 1901.

Brewster: "A Review of Some of the Modern Medicinal Preparations Used in Dentistry," *Items of Interest*, Jan., 1901, No. 1.

Spiess: "Ein neuer Gesichtspunkt in der Behandlung des Keuchhustens," *Münch. med. Woch.*, Apr., 1901, No. 15, 596.

Spiess: "Ein neuer Gesichtspunkt in der Behandlung des frischen Schnupfens," *Archiv f. Laryngol.*, 1901, *12*, No. 1.

Colleville: "Sur un cas de névralgie sacro-lombaire traité par des injections épidurales de guaïacol orthoforme," *Union méd. du Nord-est*, May 30, 1901.

Graul: "Über Nebenwirkungen des Orthoforms," *Deut. med. Woch.*, 1901, No. 24, 390.

Friedrich: "Sammelreferat über neuere Arbeiten aus dem Gebiete der Nasen und Kehlkopfkrankheiten," *Fortsch. der Med.*, Sept., 1901, No. 25.

Siebourg: "Beitrag zur Behandlung des Pruritus vulvæ," *Zentralbl. f. Gynäkol.*, 1901, No. 26.

Hornberger: "Über Orthoform," *Therap. Monats.*, October, 1901, 519.

Boennecken: *Prager med. Woch.*, 1901, No. 37.

Memmi: "L'Orthoformio per la diagnosi dell'ulcera gastrica," *Riforma méd.*, *17*, Nos. 112-116.

Dubreuilh: "Des Éruptions orthoformiques," *La Presse méd.*, May 18, 1901, No. 40.

Holger-Mygind: "Lehrbuch der Krankheiten der oberen Luftwege," 1901.

Bouveyron-Siraud: "Orthoform innerlich." *Sem. méd.*, 1901, No. 50, 400.

Horn: "Ein Fall von mit Menthol-Orthoform-Emulsion behandeltem Pharynx," *N. Y. Med. Monat.*, 1901, 134.

Solis-Cohen: "Orthoform Lozenges to Mitigate Odynophagia," *Am. Med.*, Nov. 9, 1901.

Odenthal: "Schädliche Wirkung des Orthoforms," *Deut. zahnärzt. Woch.*, 1901, 1623.

Heryng: "Zur Anwedung des Orthoforms," *Gazeta Lekarska,* 1901, No. 39.

v. Tovölgyi: "Über di Behandlung der Kehlkopftuberkulose, mit Rücksicht auf die neuren Heilmittel," *Therap. der Gegenwart,* Mar., 1902.

Melenowski: "Ein Fall von Orthoformvergiftung," *Gazeta Lekarska,* 1901, No. 48.

Friedländer: "Entgegnung auf den Artikel von Homberger," *Therap. Monat.,* Nov., 1901.

Haug: "Orthoform gegen die Schmerzen bei Furunkeln des Meatus auditorius," *Monats. f. Ohrenheilk.,* 1901, No. 12.

Homberger: "Schlussbemerkung über Orthoform," *Therap. Monats.,* Feb., 1902.

Wright: *Med. News,* Jan. 19, 1902.

Bowen: "Orthoform Eruptions," *Boston Med. and Surg. J.,* Mar. 20, 1902.

Spiess: "Die Heilwirkung der Anästhetika," *Zentralbl. f. innere Med.,* Mar., 1902, No. 9.

Veis: "Ein Beitrag zum Verlaufe von Larynxtuberkulose in der Gravidität," *Monat. f. Ohrenheilk.,* 1902, No. 4.

Freytag: "Über Kehlkopftuberkulose," *Münch. med. Woch.,* 1902, No. 19.

Wassermann: "Über Nebenwirkungen des Orthoforms und ihre bisher ungelklärte Ätiologie," *Von Leyden-Festschrift,* 1902, *2,* 317.

Dalche: "Les leucorrhées virginales et leur traitement," *Gaz. méd. Belge,* 1902, No. 41.

Czaplicki: "Orthoform," *Przeglad Lekarski,* Kraku, 1902, 305-306.

Gardner and Wilson: "Clinical Report of Some Genito-Urinary Cases," *Buffalo Med. J.,* July, 1902.

Schalenkamp: "Zur Frage der schädlichen Nebenwirkungen des Orthoforms," *Reichs-Med.-Anzeiger,* 1902, No. 16.

Murdoch: "Orthoform in the Diagnosis of Gastric Ulcer," *N. Y. Med. J.,* Nov. 29, 1902, No. 22.

Plesch: "A Tüdövész és Tüneti Kezelése," Budapest, 1902, 41.

Aveline: "Contribution à l'étude de l'orthoforme," *Monograph,* Paris, 1902; also, *Gaz. des Hôp.,* 1903, 20.

Robertson: *J. Am. Med. Assn.,* Jan. 17, 1903.

Luntz: "Zur Behandlung der Fissuren des Anus," *St. Petersburger med. Gesells.* (*Arztl. Runds.,* 1903, No. 25).

Dumont: "Handbuch der allgemeinen und lokalen Anästhesie," Berlin and Wien, 1903, 230.

Dickinson: *Detroit Med. J.,* Aug., 1903.

Cohn: "Tuberculosis of the Larynx," *Occidental Med. Times,* Sept., 1903.

Mayer und Thiesen: "Discussion of a paper, "The Early Appearances, Diagnosis, and Treatment of Tuberculosis of the Upper Air Passages," by Chappell. *J. Am. Med. Assn.,* Feb. 21, 1903.

Allen: "The Treatment of Cancer by Caustic Paste," *N. Y. Med. Record,* Dec. 12, 1903.

Teissier: "Action anesthésique de l'orthoforme dans le traitement par l'injestion iodée de l'hydrocèle," Ref.: *Le Scalpel,* 1903, No. 21.

Bardet: "Les Intoxications par l'orthoforme, le meilleur mode de prescription de l'orthoforme," *Bull. d. la Soc. d. Thérap.,* 1904, No. 9; also, *Nouveaux Remèdes,* 1904, No. 11, 21.

Murdoch: "Further Remarks on Orthoform in the Diagnosis of Gastric Ulcer," *Med. News,* 1904, No. 15.

Audebert: *Tribune méd.,* 1904, No. 40.

Tolnai: "Einige pulverförmige Antiseptika," *Budapesti Orvosi Ujság,* 1905, No. 11.

Baumgarten: "Therapeutische Erfahrungen auf dem Gebiete der Rhinolaryngologie; Orthoform und Anaesthesin," *Budapesti Orvosi Ujság,* 1905, No. 13.

Saxtorph-Stein: "Behandlung der Larynxtuberkulose," *Deut. Med.-Ztg.,* 1906, No. 24.

Schröder: "Diagnose und Behandlung des chronischen Magengeschwürs," *Lancet Clinic,* Dec. 15, 1906.

Hoffman: "Daueranästhesie im tuberkulösen Kehlkopf," *Münch. med. Woch.,* 1908, No. 14.

Limburger: "Über Lokalanästhesie," *Zahnärztliches Centralbl.,* 1908, No. 4.

Orthoform-New Hydrochlorid.—Orthoform-new hydrochlorid

$$(C_8H_9O_3N.HCl)$$

is the hydrochlorid of methyl meta-amino-para-oxybenzoate. It is a white, crystalline powder, having an indefinite melting point and an acid reaction. It is soluble in 10 parts of water. Its reactions are the same as those of Orthoform-New, except that it gives a reaction for chlorids with silver nitrate and has an acid reaction; 3.65 gm. dissolved in 50 c. c. of alcohol require not less than 17.8 c. c. nor more than 18 c. c. of normal solution of sodium hydroxid to produce a neutral liquid. Its incompatibilities are the same as those of *Orthoform-New* (*q. v.*).

Actions and Uses.—The actions, uses, and dosage of this compound are similar to those of *Orthoform-New* (*q. v.*); but it is freely soluble in water. It has been employed hypodermically, but this method of application is not always satisfactory, for the reason that solutions are inclined to be somewhat acid and have been known to produce irritation at the site of injection.

Orthonal.—The name is given to a local anesthetic intended for dental use. It consists of cocain hydrochlorid, 0.5 gm.; alypin, 0.75 gm.;

adrenalin solution (1 to 1,000), 6 gm.; physiological salt solution, enough to make 100 gm. It is put up in ampules holding 1 to 2 c. c.; 1 to 3 c. c. are used subcutaneously for anesthesia, according to Schleich's infiltration or Oberst's method.

On Orthonal, see:

Barry: *Zahnärztl. Rundschau, 19,* No. 10; Friedrich: *Berlin zahnärztl. Halbmonatsschr.,* 1911; Sander-Calbe: *Zentr. Zahnheilk., 4,* No. 8; Brandes: *Deut. Monat. Zahnheilk.,* 1910, No. 3; Schulze: *Zahnärztl. Rundschau, 19,* No. 27; Seefeld: *Ibid., 19,* No. 50; Moses: *Deut. med. Woch., 37,* No. 46, 2138; Rabow: *Chem.-Ztg.,* 1912, No. 29, 258; Flury: *Z. angew. Chem., 26,* No. 35, 242.

Otis Mixture.—Chloroform, 3 parts; alcohol, 4 parts; and ethyl bromid, 1 part (Müller: "Narkologie," *1,* 492). Otis employed this mixture extensively in general and obstetric surgery.

Ouabain.—Ouabain ($C_{30}H_{46}O_{12}$) is a glucosid from the ouabai root, an acocanthaceæ, and is also found in one of the strophanthus species (*Strophanthus gratus*). In 1882 Arnaud obtained from an unidentified species of the genus Acocanthera a crystalline glucosid, and, in 1893, Lewin separated from the cocanthera deflersii an amorphous glucosid. Arnaud assigned to ouabain the formula $C_{30}H_{46}O_{12}$. Gley (*Compt. rend. Soc. biol.,* 1895, ii), whose statements have been largely corroborated by Sailer, Lewin, and others, reported that ouabain was a local anesthetic, having ten times the power of cocain.

On ouabain as a local anesthetic, see Panas, "Sur l'action anesthésique locale da la strophantine et de l'ouabaine," *Bull. de l'Acad. de Méd. de Paris,* 1890, No. 7.

Strophanthus glaber contains ouabain, which, according to Karsten (*Compt. rend., 126,* 346), is identical with *Strophanthin* (*q. v.*).

Oxygen.—Gray (1874) found oxygen to serve as an anesthetic for short operations (see *Richmond Med. Mon.,* June, 1879); it is not a true anesthetic, however.

Oxysparteinum Hydrochlorid.—The hydrochlorid of oxyspartein, an oxidation product of the alkaloid spartein from Spartium scoparium. It forms white crystals, melting at + 48–50° C., and is soluble in water and alcohol. It is used to prevent cardiac disturbances during chloroform narcosis.

Pantopon (Omnopon).—The preparation introduced by Sahli (*Therap. Monatsh.,* 1909, No. 1; see, also, *Pharm. Centrh., 50,* 49), under the name "Pantopon," is said to contain the alkaloids of opium in the same proportion in which they occur in nature in opium itself (89.77 per cent alkaloids as hydrochlorids, 50 per cent of which is morphin). It is a brownish powder, soluble in water, forming with the latter a brown solution. The alkaloids are combined with hydrochloric acid. The variable composition of opium would seem to render it almost impossible to obtain a preparation of uniform composition and of uniform therapeutic action in every case, and further experience is required to enable us to decide on the special indications of pantopon. Sahli stated that it could not be regarded as an exact substitute for morphin; but Rodari (*Therap. Monatsh.*, 1909, 540) came to the conclusion that the narcotic and hypnotic action observed clinically by Sahli could also be obtained on animals, and that this action determined its chief advantage. The pharmacological studies of Wertheimer-Raffalovich (*Deut. med. Woch.*, 1910, No. 37) demonstrate that pantopon has a decided hypnotic action on animals and affects the respiratory center less than morphin. Similar results were obtained by Loewy and Bergien (*Münch. med. Woch.*, 1910, No. 46), the latter also showing that pantopon had no effect upon the circulation. These characteristics indicated that pantopon would be a suitable substitute for morphin in scopolamin-morphin anesthesia, and Brüstlein (*Correspondenz. f. schweizer Aerzte*, 1910, No. 26) proposed its use for this purpose. Gräfenberg (*Deut. med. Woch.*, 1910, Nos. 34 and 39) considered that the scopolamin might be omitted. He also tried general anesthesia by means of ethyl ether with pantopon injections alone, and procured very satisfactory results.

On the action of pantopon on the digestive canal, see Cohnheim and Modrakowski: *Z. physiol. Chem.*, *71*, 273. Brüstlein (*Corr.-Blatt. f. schweiz. Aerzte*, *40*, 826) reported that scopolamin hydrobromid in 75 parts of water and 25 parts of glycerol containing 2 per cent of pantopon made a clear solution which was narcotic. He considered that pantopon was entirely devoid of disturbing substances and side actions. German Patent 229,905, of October 10, 1909, of F. Hoffman-La Roche & Co., claims a process for the manufacture of preparations containing all the alkaloids of opium in a readily soluble form suitable for subcutaneous injection. An aqueous acid extract of opium is precipitated with alkalies, the alkaline precipitant, separated from the precipitate, is shaken with organic solvents, the alkaloids are removed by shaking out with acids yielding water-soluble salts, the alkaloids precipitated with alkalies and purified are dissolved in the acid alkaloid solution, and the solution is dried. The products are stated to give the reactions for morphin, narcotin, papaverin, and thebain.

On morphin-free pantopon, see Winternitz, *Münch. med. Woch.*, *59*, 853.

On pantopon anesthesia, see the following:

Sahli: *Münch. med. Woch.*, 1909, No. 26; *Therap. Monatsh.*, 1909, No. 1.

Hallervorden: *Therap. der Gegenwart*, 1910, No. 5, 206.

Heimann: *Münch. med. Woch.*, 1910, No. 7, 357.

Rodari: *Therap. Monatsh.*, Oct., 1909.

Gottlieb and v. d. Eeckhart: *"Festschr. f. Schmiedeberg,"* 1910, 235.
Becker: *Reichs-Med.-Anz.,* 1910, No. 18, 273.
Witowski: *Arch. f. exper. Path. u. Pharmakol., 17.*
Jäger: *Münch. med. Woch.,* 1910, 2238.
Raffalovitch: *Deut. med. Woch.,* 1910.
Brüstlein: *Correspondenz. f. schweiz. Aerzte,* 1910; *Zentr. Chirurg.,* 1911, No. 10, 345.
Ewald: *Berl. klin. Woch.,* 1910, No. 35; *Münch. med. Woch.,* 1910, No. 25, 1326.
Burgi: *Deut. med. Woch.,* 1910.
Sahli: *Zentralbl. f. d. gesammte Therapie,* 1909; *Berl. klin. Woch.,* 1910, No. 35, 1609.
Gräfenberg: *Deut. med. Woch.,* 1910, No. 34, 1569.
Döblin: *Therap. Monatsh.,* 1911, No. 4, 216.
Leipoldt: *Lancet,* Feb. 11, 1911, 368.
Zollinger: *Correspondenz. f. schweiz. Aerzte,* 1911, No. 10.
Robertson: *Lancet,* Oct. 7, 1911.
Fowelin: *Zentr. Chirurg.,* 1911, No. 27, 921.
Hellman: *Am. Med.,* n. s., 7, No. 1, 39.
Voigt: *Therap. Monatsh.,* 1911, 601.
Haymann: *Münch. med. Woch.,* 1911, No. 2, 82.

In employing omnopon in the induction of anesthesia before operations, Leipoldt found that omnopon injections are more effectual than a combination of *Omnopon* and *Scopolamin* (*q. v.*), since it occasions neither nausea nor vomiting.

Krauss: *Zentr. Chirurg.,* 1911, No. 20.
Zahradnicky: *Ibid.,* 1911, No. 30, 1017.
Aulhorn: *Münch. med. Woch.,* 1911, No. 12, 618.
Johannsen: *Zentr. Gynäk.,* 1911, No. 19, 702.
Zeller: *Münch. med. Woch.,* 1911, No. 25, 1355.
Kolde: *Ibid.,* 1911, No. 28, 1499.
Simon: *Ibid.,* 1911, No. 32, 1725.
Dornblüth: *Deut. med. Woch.,* 1911, No. 15, 697.
Kafemann: *Med. Klin.,* 1911, No. 26, 1002.
Heinsius: *Berl. klin. Woch.,* 1911, No. 41, 1837.
Anneler: *Arch. Pharm., 250,* 186.
Mannich and Schwedes: *Apoth.-Ztg., 28,* 82.

For other preparations containing the alkaloids of opium, see *Isopon, Nealpon, Opiopon, Opon,* and *Summopon.*

Paraldehyd.—This compound was found to act similarly to chloral, but caused deep sleep and no convulsive movements. (See *Archiv f. exper. Pathol. u. Pharmakol.,* 1882.) Noto (*New Orleans Med. and Chir. J.,* 1900, No. 9) believed that paraldehyd was a remedy which, when administered internally in hypnotic doses of 2 to 3 gm., 30 minutes to one hour previous to narcotization by chloroform, completely divested the latter of its attending dangers. The anesthetic properties of paraldehyd are more marked than those of acetaldehyd; it is less toxic than metaldehyd. It acts first on the higher cerebral centers and then on the other parts of the central nervous system, finally causing spinal anesthesia and death. It is said to have no depressant action on the heart. However, it possesses a very unpleasant odor and taste, and has an irritant action on the gastric mucosa (Francis and Fortescue-Brickdale: "The Chemical Basis of Pharmacology," 1908, 107-8).

On employment of paraldehyd in intravenous anesthesia, see, also: *Lancet,* Sept. 21, 1912, 818; Nov. 2, 1912, 1220.

Para-amidobenzoic Acid Ethyl Ester.—A white powder, melting at + 90–91° C., and possessing the following composition:

$$NH_2.C_6H_4.COOC_2H_5.$$

It is used as a local anesthetic.

Para-amidobenzoic Acid Isobutyl Ester.—Soft, colorless needles, melting at + 65° C., possessing anesthetic properties.

Paranephrin.—An extract from the suprarenal glands which is free from albumoses and peptones. In dental practice it is employed in combination with tropacocain; see, also, combinations which follow (*infra*).

Paranephrin-cocain Mixture.—A dental anesthetic consisting of paranephrin 1:1,000 and 1 per cent of cocain.

Paranephrin-cocain-subcutin.—A hemostatic local anesthetic for surgical and dental practice.

Paranephrin-novo-subcutin.—This preparation contains novocain, and is employed as a general as well as a local anesthetic, especially in dental surgery.

Pâte de Vido.—Bonbons containing aconitin, heroin, and stovain.

Pental (Trimethylethylene; beta-isoamylene).—Pental $[(CH_3)_2C = CH.CH_3]$ is an anesthetic which has been used in minor surgical cases, as tooth extraction; but it possesses toxic properties, and hence is not favored. Pental was highly recommended by W. Lombardino as an anesthetic of great practical value. Wood and Cerna have shown, however, that it acts on lower animals as a powerful cardiac depressant, and is probably a dangerous anesthetic. That it possesses real danger is shown in the statistics gathered by Gurlt, who recorded that there were 6 deaths in 600 pental narcoses; and, moreover, Kleindienst found that very frequently in man severe albuminuria results and that not infrequently hematuria and hemoglobinuria occur three or four days after pental narcoses.

On the employment of pental, see the following:

Breuer and Lindner: "Ueber Pentalnarkosen"; v. Hacker's "Chir. Beitr. a. d. Erzherzogin-Sophien-Spital," Vienna, 1892; *Zentr. Chir.,* 1893, 91.

Gurlt: "Zur Narkotisierungsstatistik," *Verh. d. XXVI. Deut. Chirurgenkongr.*, 1897, Teil ii, 202.

Holländer: *Therap. Monatsh.*, 1891 and 1892; *Deut. med. Woch.*, 1892, 757; *J. f. Zahnheilk.*, 1893; *Zentr. Chir.*, 1893, 517.

Kleinschmidt: "Ueber Pental als Anästhetikum," *Deut. Z. f. Chir.*, *35*, 333.

Philipp: "Ueber Pentalnarkose in der Chirurgie," *Verh. d. XXI. Deut. Chirurgenkongr.*, 1892, Teil ii, 367.

Van Reysschoot: "Contribution à l'étude expérimentale du pental," Gand, 1892.

Rieth: "Ueber die Pentalnarkose," v. Bruns' *Beitr.*, 1893, *10*, 189.

Von Rogner: "Das Pental in der chirurgischen Praxis," *Wiener med. Presse*, 1891, No. 51; *Zentr. Chir.*, 1892, 93.

Weber: "Pental, ein neues Anästhetikum," *Dissertation*, Halle, 1891; *Münch. med. Woch.*, 1892, No. 7.

Pentane (Amyl Hydrid).—A liquid hydrocarbon from naphtha, proposed as an anesthetic. See *Hydramyl.*

Pentylene.—See *Hydramyl.*

Peronin.—This morphin derivative, benzyl-morphin hydrochlorid [$C_{17}H_{18}NO_2.O.C_6H_5.CH_2.HCl$] has been shown to act as a local anesthetic for the eye. Buffalini (*Settimana med.*, 1899, No. 27) found that the instillation of a few drops of a luke-warm 1 to 2 per cent solution of peronin into the conjunctival sac induced complete and deep anesthesia of the cornea enduring for many hours. Guaita (*ibid.*, 1899, No. 40) confirmed the statements of Buffalini.

On Peronin as a local anesthetic, see the following literature:

Buffalini: "La Peronina, nuovo anestesico locale," *Settimana med.*, 1899, No. 27; Virchow-Hirsch's *Jahresber.*, 1899, *1*, 393.

Guaita: "Sopra l'azione anestetica locale della peronina," *Ann. di Farmacoterap.*, 1899, No. 9, 10.

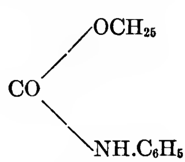
Pierard: "Quelques experiences sur l'action physiologique de la Peronine," *Ann. de la Soc. des Sci. méd. de Bruxelles*, 1899, No. 8.

Phenol.—See *Carbolic Acid.*

Phenol Camphor.—See *Camphor, Phenylated.*

Phenolcocain.—See *Cocainum Phenylicum.*

Phenyl-urethane.—This compound, also known as *euphorin*, has the following formula:



It forms colorless, crystalline needles, melting at + 49°–50° C., and dissolving in alcohol and ethyl ether. Ströll (*Münch. med. Woch.*, 1907, No. 45, 2262) drew attention to the use of phenyl-urethane in the treatment of painful ulcers of the foot; in his experience the preparation was superior in anesthetic power even to anesthesin and orthoform.

Phenyphrin.—A dental local anesthetic containing, per c. c. of physiological salt solution, 0.02 gm. alypin and 0.1 gm. "Nebennierenextraklösung" (1:1,000).

Phœnixin.—*Carbon Tetrachlorid* (*q. v.*).

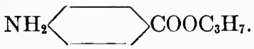
Plecavol.—A tooth cement. A flask with plevacol powder: Paraamidobenzoyleugenol, eugenol, zinc oxid, zinc sulphate, and gum arabic. A flask containing a solution of tricresol-formalin is also required. Anesthetic and antiseptic acting pulpa-capping material and filling material for roots, used in dentistry. It is said to act without irritation, conserving the pulpa, and hardening in a short time.

Pleistopon.—Narcotin-free *Pantopon* (*q. v.*).

Polychloral.—This is obtained by adding pyridin, drop by drop, to chloral, washing out the resulting solid with dilute hydrochloric acid and then drying. It dissolves slowly in water, more quickly in alcohol, forming chloral hydrate and chloral alcoholate respectively. An anesthetic and hypnotic.

Polychlorated Hydrochloric Ether.—See *Ethyl Chlorid Polychlorated.*

Potassocain or Pottasocain.—This contains cocain dissolved in alcohol and ether.

Propesin (Propäsin).—A German local anesthetic; it is the propyl ester of paramido-benzoic acid, 

It is a white crystalline powder which melts at + 73-74° C. It is readily soluble in alcohol, ether, and chloroform, but dissolves with difficulty in water. Said to be practically nontoxic, and to act very promptly and effectively on mucous membranes.

On propesin, see the following:

Kluge: *Therap. Monatsh.*, Feb., 1909, 77.

Stürmer and Lüders: *Deut. med. Woch.*, 1908, No. 53, 2310.

Dietrich: *Deut. zahnärztlichen Ztg.*, 1910, No. 16.

Perl: *Med. Klinik,* 1909, No. 50, 1892.

On the use of propesin in urology and gynecology, see *Medizin. Klinik,* 1908, 1769. Kluge states that the only disadvantage of propesin is that its slight solubility in water renders it unsuitable for subcutaneous injection.

Propesin-colloid contains, according to *Pharm. Ztg., 55,* 858, 20 per cent propesin, 72.5 per cent glycerin, 2.5 per cent starch, and 5 per cent ethyl alcohol. On propesinöl, see Unger: *Apoth.-Ztg., 27,* 1023.

See *Dipropesin.*

Propion.—Diethyl ketone ($C_2H_5.CO.C_2H_5$), also known as metacetone, propione, and ethylpropionyl, is a colorless, mobile liquid, possessing an acetone odor; it boils at + 101° C. Propion was recommended as a hypnotizing agent by Albanese and Barabini (*Ann. di chem. e farmacol.*, Feb., 1892, 124; April, 1892, 225), who observed that it caused, when administered to dogs and rabbits in doses of 1.0 to 1.5 gm., deep, tranquil, and enduring sleep, the compound being readily absorbed when introduced into the stomach or rectum, or when injected in subcutaneous tissue. The inhalation of diethyl ketone also induced sleep, but this property did not seem to be of any practical value, since, in this method of application, the narcosis was effected too slowly. See, also, Noera: *Arch. di farmacol. e terap.*, 1896, *4*, f. ii, 12. The solubility of propion in water is not great and, in addition, its taste is unpleasant.

Puff-Ball.—In 1853, Richardson, having learned that the "smoke" (cloud of brown dust-like spores) of that curious fungus, the common puff-ball, had been used by country folk for the stupefaction of bees, conceived the idea that it might be used as a general anesthetic. He conducted experiments upon dogs, cats, and rabbits, and in one case removed a tumor from a dog without observing any indications of pain during the operation (*Med. Times and Gaz.*, 1853, 610). To quote Lyman ("Artificial Anesthesia and Anesthetics," 1881, 328), when a moderate quantity of the smoke was gradually inhaled, anesthesia appeared and disappeared slowly. The animal exhibited all of the symptoms of intoxication, accompanied by convulsions and sometimes by vomiting. Life ceased by degrees; after the induction of complete insensibility, a dog might inhale the smoke for twenty minutes or even half an hour before death resulted. Respiration always ceased before the action of the heart. Herapath made experiments which proved that the active agent in producing the preceding phenomena was carbon dioxid, generated during combustion; his conclusion, confirmed by Snow, was accepted by Richardson. It would seem from these experiments (*Phil. Mag.*, July, 1855) that the anesthetic effects are not owing to a narcotic. See *Carbon Dioxid.*

Pyridin.—This is a liquid of a powerful odor, the vapor of which, if inhaled, stimulates the fifth nerve and produces dyspnea, then slow, shallow breathing, and finally sleep. In very large doses it paralyzes the sensorium, producing complete anesthesia and abolition of reflexes; smaller doses may inhibit respiration. Piperidin and pyrollidin have much the same action (Francis and Fortescue-Brickdale's "The Chemical Basis of Pharmacology," 1908, 250).

Pyrocain.—A guaiacol-benzyl ester, said to be a nontoxic local anesthetic.

Pyrrol (Pyrrhol).—Pyrrol was experimented with by the Committee of the British Medical Association. In the frog it produced anesthesia with considerably less rapidity than chloroform, and great excitement and muscular spasms preceded complete anesthesia. Its hypodermatic administration to three young rabbits produced spasmodic movements, principally involving the jaws and fore-paws; these rabbits were not decidedly anesthetized.

Quinin Alkaloids.—Morgenroth and Ginsberg (*Berl. klin. Woch., 50,* No. 8) investigated the effect of the quinin alkaloids upon the cornea. The compounds studied combine with ethylhydrocuprein to form isopropyl, isobutyl, and isoamyl hydrocuprein. A 3 per cent solution of quinin hydrochlorid and 1.0 to 1.25 per cent solutions of hydroquinin and ethylhydrocuprein hydrochlorid produced complete anesthesia of the cornea; with the transformation of the ethyl to the propyl compound, a marked increase in anesthetic action resulted, for with isoamylhydrocuprein a 0.1 to 0.125 per cent solution was sufficient. Isoamylhydrocuprein proved to be at least 20 to 25 times more active than cocain.

Quinin and Urea Hydrochlorid (Quininæ et Ureæ Hydrochloridum; Chininum bihydrochloricum Carbamidum).—Quinin and urea hydrochlorid ($C_{20}H_{24}N_2O_2.HCl + CH_4N_2O.HCl + 5H_2O$) is a compound of quinin hydrochlorid and urea hydrochlorid containing approximately 60 per cent of anhydrous quinin. The preparation is made by dissolving 400 parts quinin hydrochlorid in 300 parts of dilute hydrochloric acid, sp. gr. 1.061, mixing the solution with 60 to 61 parts of pure urea [$CO(NH_2)_2$], warming the mixture until dissolved, filtering it through glass wool and setting the filtrate aside for crystallization. After twenty-four hours the crystals are brought on a filter, drained, washed with very cold distilled water, spread on flat plates and dried at room temperature. The mother-liquor is evaporated and again set aside for crystallization. The second mother-liquid, which is colored brown, is exposed in a dish to spontaneous evaporation, during which all of the double salt of quinin slowly crystallizes out and may be separated.

The hydrochlorid of quinin and urea crystallizes from hot solutions in hard, white, interlaced four-sided prisms. On spontaneous evaporation of a concentrated solution, very large transparent prisms are found. The salt dissolves at ordinary temperature in its own weight of water, forming a somewhat viscid straw-colored liquid, not altered by exposure to light. During its solution a marked lowering of temperature occurs. It is not hygroscopic and is unalterable in the air, excepting that when warmed the crystals lose their transparency and become yellowish. They fuse at from 70° to 75° C. (158° to 167° F.) with the loss of 10 per cent of water, forming a yellowish liquid which congeals, on cooling, to a yellow mass. If this mass is allowed to stand in the air, it takes up water, after a few days, equal in amount to that expelled, and again becomes white. If the melted salt is dissolved in water, it may be completely recovered in a crystalline form. It is also soluble in alcohol, and from this solution a salt of somewhat variable composition is precipitated by ether. It is soluble in about 800 parts of chloroform. Its water solutions are of a strong acid reaction. A solution of the salt in water (1 to 20) shows no fluorescence; but if one drop of this solution is added to 10 c. c. of distilled water in a test tube, a vivid blue fluorescence is developed. On drying the salt at + 125° C. to constant weight and cooling in a desiccator, it should not lose more than 16.5 per cent of its weight (corresponding to five molecules of water of crystallization). On ignition, the pure salt is slowly consumed, leaving no residue. Ammonia water, alkaline hydroxids or alkali carbonates throw down from the water solution of quinin and urea hydrochlorid a white precipitate of alkaloidal quinin, which, when carefully washed with cold distilled water until free from chlorids, and dried at a low temperature, should conform to the reactions and tests given in the *United States Pharmacopœia* under *quinin.* One gram dissolved in 2 c. c. of distilled water, and well shaken in a stoppered test-tube with 6 c. c. of ether and 2 c. c. of 10 per cent ammonia water, should be dissolved completely, and no crystals should separate out from the ethereal solution on standing for six hours. If the ethereal stratum is removed to a tared beaker, and the contents of the test-tube are washed successively with three portions of 5 c. c. each of ether and these ether washings be also added to the tared beaker, the alkaloidal quinin remaining after evaporating off the ether, dried at + 125° C. to constant weight, should weigh not less than 0.592 gm. On the chemical and physical properties of Quinin and Urea Hydrochlorid, see Schaefer: *The Drug. Cir.,* Feb., 1910.

Actions and Uses.—Quinin and urea hydrochlorid has the actions of quinin. It is non-irritating when injected hypodermically. Recent investigations have shown that, when injected hypodermically or when applied locally to mucous membranes, it exerts an anesthetic action similar to that of cocain. It is reported that the anesthesia is in some cases prolonged for several days. Sylvester, of Wellston, Ohio, is reported as having employed quinin for more than twenty years as an anesthetic to denuded and mucous surfaces, but not hypodermically. In July, 1896, before the Chautauqua County, N. Y., Medical Society, Griswold reported on its hypodermic use as an efficient local anesthetic. It was Henry Thibault who found that quinin and urea hydrochlorid, employed extensively in the South for the hypodermic treatment of malaria, rendered the site of the injection anesthetic for a considerable period. He experimented further and learned that 1 to 2 per cent solutions produced local anesthesia which lasted from 1 to 6 hours and proved to be safer than cocain.

On the use of the preparation in various operations, consult the following:

Hertzler, Brewster, and Rogers: *J. Am. Med. Assn.,* Oct. 23, 1909, 1393; *The Prescriber,* 1910, 19; *Klin.-therap. Wochenschrift,* 1910, 96.

MacCampbell: *J. Am. Med. Assn.,* May 14, 1910.

Hertzler: *Ibid.,* April 23, 1910, 1375; and June 11, 1910, 1940.

Hirschman: *Lancet-Clinic,* July 9, 1910.

Med. Council, April, 1910, 116; May, 1910.

Green: *J. Am. Med. Assn.,* June 11, 1910.

Merck's "Report," Nov., 1911, 356.

Ellis: *Therap. Notes,* January, 1912, 7.

These contributions show that subcutaneous injections of a 1 to 2 per cent solution of quinin hydrochloro-carbamid and the local application of a 10 to 20 per cent solution occasionally have a better anesthetic action than cocain. See *Chevanne's Local Anesthetic.*

Dosage.—The same as quinin. For the production of local anesthesia, injections of a solution of from ¼ to 1 per cent strength are used. The ¼ per cent solution is said to be free from the risk of producing fibrous indurations, which sometimes occur with the stronger solution. For application to mucous membranes solutions varying in strength from 10 to 20 per cent should be used.

Radestock's Mixture.—An anesthetic mixture of chloroform, 2 parts, and ethyl ether, 3 parts (Müller, "Narkologie," *1,* 493).

Radikal-Anästhetikum Apotheker Maier.—A solution containing cocain, phenol, iodin, and pyrazolin.

Radinin.—A preparation insensitive to light and air; it will keep in a 1 per cent cocain solution without adrenalin.

Rapid Respiration, Anesthesia by.—Bonwill and Hewson called attention to a form of insensibility to pain induced by rapid respiration, and the matter was discussed by the Philadelphia County Medical Society (*Med. Rec.,* Aug. 21, 1880). Bonwill and Lee reported that the best method of producing this kind of analgesia was by causing the patient to lie upon the side, with a handkerchief over the eyes in order to avoid distraction of the attention. He was then directed to breathe about one hundred times per minute, expelling the air by a succession of puffing expirations. After from two to five minutes of this exercise, there was developed a degree of insensibility to pain which persisted for as long as thirty seconds. The movements of the heart were accelerated and the force of the pulse was diminished. Consciousness and the sense of touch were not abolished. After the production of this condition, a smaller quantity than usual of the ordinary anesthetics were required to produce complete insensibility. For a discussion of this method, see Lyman: *Loc. cit.*

For a consideration of superventilation by means of oxygen, see Chapter II.

Reichel's Zahnschmerzstillende Tropfen.—A Japanese peppermint oil free from menthol, also known as "Poho Oil."

Renocain.—An adrenalin solution containing cocain, intended for use as a local anesthetic.

Renoform.—The active principle of the suprarenal gland. It is a white, crystalline powder, difficultly soluble in cold water, easily soluble in acidified water; used in operations for localizing anesthetics, in combination therewith.

Rhigolene.—A petroleum ether of low boiling point. Rhigolene was introduced by Bigelow in 1866. See *Æther Anæstheticus* (*Koenig*).

Rhinosol.—A hay-fever remedy containing *Anesthesin* (*q. v.*) and paranephrin.

Richardson's Methylen Chlorid.—A mixture of chloroform and methyl alcohol.

Richardson's Mixture.—Chloroform, 2 parts; alcohol, 2 parts; and ethyl ether, 3 parts (Müller, "Narkologie," *1*, 492). Richardson (*Sci. Am. Suppl.,* No. 516, 8240) said, in reference to the varying proportions of alcohol, chloroform, and ether used by different administrators in compounding A. C. E. Mixture, that he thought that 4 parts ether, 2 parts chloroform, and 2 parts alcohol, by fluid measure, were the best proportions, and that it was "altogether a very good mixture."

Robiol.—Robiol and Novorobiol are combinations of suprarenin with local anesthetics (Flury: *Z. angew. Chem., 26*, 242).

Royal Medical and Chirurgical Society Committee Mixture.—Alcohol (sp. gr., 0.838), 1 part; chloroform (sp. gr., 1.497), 2 parts; ether (sp. gr., 0.735), 3 parts (Hewitt: "Anesthetics and Their Administration," 3rd ed., 466).

Sal Anæstheticum Schleichii.—A varying mixture of cocain hydrochlorid, morphin hydrochlorid, and sodium chlorid, to induce anesthesia by infiltration according to the method of Schleich. In 1894 Schleich ("Schmerzlose Operationen," Berlin, 1894) first propounded the doctrine of anesthesia by artificial edematization of the tissues by means of morphin-cocain injection. A number of papers were subsequently published on the practical aspects of the subject: Krecke: *Münch. med. Woch.,* 1897, No. 42; Reichold: *Ibid.,* 1167; Briegleb: *Therap. Monatsh.,* 1897, No. 12, 651; Haberern: *Ungar. med. Presse,* 1897, No. 46, 1094; Simon-Cohn: *Berl. klin. Woch.,* 1897, No. 30.

The anesthetizing mixture originally proposed by Schleich was of three different degrees of strength, namely:

1. Sal anæstheticum Schleichii I (strong):

Cocain Hydrochlorid	0.2	(gr. 3);
Morphin Hydrochlorid	0.025	(gr. 1/3);
Sodium Chlorid	0.2	(gr. 3).

2. Sal anæstheticum Schleichii II (normal):

Cocain Hydrochlorid	0.1	(gr. 1 2/3);
Morphin Hydrochlorid	0.025	(gr. 1/3);
Sodium Chlorid	0.2	(gr. 3).

3. Sal anæstheticum Schleichii III (weak):

Cocain Hydrochlorid	0.01	(gr. 1/6);
Morphin Hydrochlorid	0.005	(gr. 1/12);
Sodium Chlorid	0.2	(gr. 3).

Each of the three mixed powders was dissolved shortly before use in 100 c. c. of boiled distilled water, and these solutions were directed to be used only when cold, since otherwise their anesthetic properties were lost. It was known in 1897 that cocain could be suitably replaced by *Tropacocain* (*q. v.*). Ethyl chlorid was usually employed as a precursor of infiltration anesthesia. In 1898 Custer (*Münch. med. Woch.,* 1898, No. 22) showed that tropacocain was decidedly preferable to cocain, especially when required for Schleich's infiltration method. The solutions required for infiltration were stated to be of the same degree of concentration as cocain hydrochlorid, *i. e.,* 0.2 per cent in the case of solution I; 0.1 per cent in that of solution II; and 0.01 per cent in the case of solution III, which was found to act as an *"anæstheticum dolorosum."* For further details, Custer's paper should be consulted. In 1901 Schleich (*Deut. Klinik,* 1901, parts 22 and 23) recommended exclusively one of the three infiltration fluids originally formulated by him, namely, the normal solution II, which might, according to the requirements of the case, be intensified by the addition of tropacocain or weakened by that of a sterilized 0.2 per cent solution of sodium chlorid. In 1906 Schleich ("Schmerzlose Operationen," 5th ed.; *Allg. med. Zentral-Ztg.,* 1906, No. 48, 872) reported that he had found it of advantage, in his method of producing anesthesia, to use a combination of cocain with *Alypin* (*q. v.*), since a greater effect was obtained in this manner. He consequently advised the substitution for the older solutions of the following:

	I	II	III
Cocain Hydrochloride	0.1	0.05	0.01
Alypin	0.1	0.05	0.01
Sodium Chlorid	0.2	0.2	0.2
Distilled Water	100.0	100.0	100.0

He avoided the addition of adrenalin for fear of unpleasant secondary effects.

Salolcamphor (Salolum Camphoratum).—A mixture of 3 parts of salol and 2 parts of camphor. A local antiseptic and anesthetic.

Sanoform-Preparations.—Sanoform-cocainol-streupulver contains 10 per cent of sanoform (diiodosalicylic acid methyl ester) and 10 per cent of *Anæsthesin* (*q. v.*).

Sanovagin.—See *Cocainol-Crême.*

Sansom's A. C. Mixture.—Alcohol, 1 part by volume; and chloroform, 1 part by volume. See *Med. Times and Gaz.,* 1870, *2,* 107. Sansom found that alcohol "had the greatest effect in sustaining the heart's action during the influence of chloroform." He found it impossible to kill with chloroform a frog which had previously inhaled the vapor of alcohol. In the opinion of Sansom, if chloroform is to be used without an inhaling apparatus, in order to insure a supposed uniformity of strength of vapor, it should be mixed with alcohol, or with alcohol and ethyl ether.

Schäfer and Scharlieb's A. C. Mixture.—A mixture of absolute alcohol, 1 part by volume, and chloroform, 9 parts by volume. See *Trans. Roy. Soc. Ednb., 41,* part ii, No. 12.

Schleich's Anesthetics.—Owing to their low boiling points, these mixtures are said to be rapidly eliminated from the system.

(1) Chloroform, 45 parts; petroleum ether (+ 60° C.), 15 parts; ether, 180 parts; boils at + 38° C. (2) Chloroform, 4 parts; petroleum ether, 15 parts; ether, 150 parts; boils at + 40° C. (3) Chloroform, 30 parts; petroleum ether, 15 parts; ether, 80 parts; boils at + 42° C.

Mixture 1 is used in short operations, while 2 and 3 are for major periods.

For a full discussion of Schleich's Anesthetic Mixtures, see Meyer: *J. Am. Med. Assn.,* Feb. 28, 1903; and *Med. Rec.,* Aug. 15, 1908. See *Anesthol.* Schleich's narcotic mixture contains 2 parts of ethyl chlorid, 4 parts of chloroform, and 12 parts of ethyl ether. It is said to suppress local pains with rapidity and certainty. See Schleich: *Therap. der Gegenwart,* March, 1902. Cf. *Sal Anæstheticum Schleichii.*

Scopolamin Hydrobromid.—Scopolamin hydrobromid (Scopolaminæ hydrobromidum) is the hydrobromid ($C_{17}H_{21}NO_4HBr.3H_2O$) of an alkaloid obtained from plants of the *Solanaceæ;* it is chemically identical with hyoscin hydrobromid U. S. P. According to the *British Pharmacopœia,* it is "the hydrobromid ($C_{17}H_{21}NO_4.HBr.3H_2O$) of an alkaloid contained in hyoscyamus leaves, different species of scopola, and possibly other solanaceous plants."

Hyoscin hydrobromid was introduced in the *United States Pharmacopœia* in 1890. Hyoscin ($C_{17}H_{21}NO_4$) is found in the leaves and seeds of Hyoscyamus niger, Duboisia myropoides, Scopola japonica, Atropa belladonna, and other solanaceous plants; it forms, when pure, a sirupy liquid. The hydrobromid forms colorless, transparent, rhombic crystals, odorless, possessing an acrid, slightly bitter taste, and slightly efflorescent. It is soluble in 1.5 parts of water, 16 parts of alcohol, and in 750 parts of chloroform at + 25° C.; it is insoluble in ethyl ether. The water solution shows a slightly acid reaction to blue litmus paper. When hyoscin hydrobromid is heated, it softens at about + 100° C.; it first fuses and then loses its water of crystallization at + 110° C. When dried over sulphuric acid until it is completely deprived of its water of crystallization, it melts at from + 191°-192° C. When ignited, it leaves no residue. Schmidt (*Pharm. Ztg.,* 1891, 522) considered that the hyoscin hydrobromid of commerce was essentially scopolamin hydrobromid, and Hesse (*Ann.*, 1893, 304) confirmed this view. The *United States Pharmacopœia* introduced, in the Eighth Revision, Scopolaminæ hydrobromidum production as a separate title, but referred to Hyoscinæ hydrobromidum for the description and tests; it considered them to be identical compounds.

Schneiderlin (*Aerztl. Mittheilg. aus und f. Baden,* 1900, No. 10) recommended operations under anesthesia by morphia-scopolamin, which method consisted essentially in administering to the patients subcutaneously, 1½ to 2 hours previous to the operation, scopolamin and morphia separately, which induce deep anesthesia. Korff (*Münch. med. Woch.*, 1901, No. 29; 1902, No. 27); Blos (*Burns' Beit. z. klin. Chir., 35,* No. 3, 565); and von Steinbüchel (*Centralb. f. Gynäkol.*, 1902, No. 48) supplied most favorable reports on the anesthesia obtained in this manner; but Shicklberger (*Wien. klin. Woch.*, 1902, No. 51) maintained that the morphia-scopolamin method was adapted only for those cases which rendered a general anesthesia absolutely requisite and where at the same time chloroform or ether were contraindicated. The Schneiderlin-Korff method of anesthesia by morphia and scopolamin is based upon the fact that the hypnotic and anesthetic properties of morphia and scopolamin associate themselves, while their toxic effects on the respiration and circulation, being antagonistic, counterbalance each other.

On this method of anesthesia, see the following additional contributions:

Grevsen: *Münch. med. Woch.*, 1903, No. 32, 1383.

Bloch: *Ibid.*, 1903, No. 26, 1135.

Volkmann: *Deut. med. Woch.*, 1903, No. 51, 967.

Heinatz: *Russkiy chir. Archiv,* 1902, No. 6.

These authors appeared to be satisfied with the method; in fact, the first three regarded it with favor.

Korff: *Münch. med. Woch.*, 1903, No. 46, 2005.

Stolz: *Wiener klin. Woch.*, 1903, No. 41.

Stolz ascribed the tranquil nature of the anesthesia to morphia rather than to scopolamin, and considered that it was procurable more perfectly and with less danger by an injection of morphia or of morphia-atropin before the administration of the ordinary anesthetic.

Wild: *Berl. klin. Woch.*, 1903, No. 9, 188.

Flatau: *Münch. med. Woch.*, 1903, No. 28, 1198.

These two authors regarded the morphia-scopolamin method of anesthesia as risky and cautioned against its application.

Hartog: *Ibid.*, 1903, No. 46, 2003.

Hartog found that the combination of the morphia-scopolamin and ethyl-ether methods of anesthesia was free from danger and thoroughly reliable. See, also, Robertson: *Sem. méd.*, 1903, No. 26, 220.

Schneiderlin: *Münch. med. Woch.*, 1903, No. 9, 371.

Bumke: *Monats. f. Psych. u. Neurol.*, 1903, 62.

Kochmann: *Archives internationales de pharmacod. et de thérap.*, 1903, 99.

Liepelt: *Berl. klin. Woch.*, 1904, No. 15, 387.

Rose: *Brit. Med. J.*, 1903, No. 2242, 1589.

Korff: *Berl. klin. Woch.*, 1904, No. 33, 882.

Wiesinger: *Deut. med. Woch.*, 1904, No. 36, 1335.

Wiesinger considered that the method possessed important advantages and certainly appreciated it.

Bonheim: *Wiener klin.-therap. Woch.*, 1904, No. 11, 329. Bonheim recommended the combination of the anesthesia by scopolamin and morphin with the administration of chloroform. Cf. Korff: *loc. cit.*

Landau: *Deut. med. Woch.*, 1905, No. 28, 1108.

Rys: *Csasopis lekaruv cesky,* 1905, No. 18.

Lasek: *Ibid.*, No. 2.

Menod: *Presse méd.*, 1905, No. 60.

The last four authors recorded failures with the method.

Kochmann: *Münch. med. Woch.*, 1905, No. 17.

Wartapetian: *Aerztl. Rundschau,* 1905, No. 17, 202.

According to these two authors, the method unquestionably possessed advantages, yet its improvement was necessary.

Zahradnicky: *Wiener med. Ztg.*, 1905, No. 5, 55.

Stein: *Deut. med. Ztg.*, 1905, No. 29, 313.

Roith: *Münch. med. Woch.*, 1905, No. 46, 2213.

Rotter: *Deut. med. Ztg.*, 1905, No. 2, 21.

Wiesinger: *Deut. med. Woch.*, 1905, No. 38, 1525.

Defontaine: *Sem. méd.*, 1905, No. 29, 345.

Puschnig: *Wiener klin. Woch.*, 1905, No. 16.

Ries: *Ann. of Surg.*, *42*, 193.

Stien: *Hospitalstidende*, 1904, No. 43.

Terrier and Desjardin: *Presse méd.*, 1905, No. 18.

Ziffer: *Monats. f. Geburtshilfe u. Gynäk.*, 1905, No. 1.

Seelig: *St. Louis Med. Rev.*, Aug. 12, 1905.

Rochard: *Merck's Arch.*, 1905, No. 6, 187.

Dirk: *Deut. med. Ztg.*, 1905, No. 2, 21.

Weingarten: *Dissertation,* Giessen, 1904.

The last twelve mentioned authors recognized the value of the method.

Gauss: *Münch. med. Woch.*, 1905, No. 41, 1998.

Krönig: *Ibid.*, 1905, No. 52, 2536.

Korff: *Ibid.*, 1905, No. 52, 2539.

Roussy: *Revue neurol.*, 1905, 644.

Laurendeau: *Presse méd.*, 1905, No. 93. 749.

Cremer: Textbook on "Painless Confinements"; also Welmans: *Pharm.-Ztg.*, 1906, No. 2, 17.

Roith (*loc. cit.*), to simplify the application of scopolamin, recommended the introduction of scopolamin tablets; but Laurendeau and Cremer stated their emphatic opposition to the use of tablets in connection with subcutaneous injections.

Kionka: *Therap. der Gegenwart*, 1908, No. 8.

Kreuter: *Münch. med. Woch.*, 1907, No. 9.

Bass: *Ibid.*, 1907, No. 11.

Hocheisen: *Ibid.*, 1907, No. 11.

Holzbach: *Ibid.*, 1907, No. 25.

Korff: *Berl. klin. Woch.*, 1906, No. 51.

Janson: *Psych.-neurolog. Woch.*, 1907, No. 25.

Klein: *Zentr. f. Gynäkol.*, 1907, No. 27.

Hirsch: *Wiener klin. Rundschau*, 1907, No. 52.

Mansfeld: *Wiener klin. Woch.*, 1908, No. 1.

Doucet: *Gaz. méd. de Nantes*, 1907, No. 2.

Ebert: *The Military Surgeon*, May, 1907.

Steffen: *Archiv f. Gynäkol.*, 1907, No. 2.

Cazin: *Sem. méd.*, 1907, No. 42.

Segelken: *Klin. Monats. f. Augenheilk.*, 1907, 75.

Rochard: *Bull. Gén. de Thérap.*, 1907, No. 15.

With the exception of Steffen and Rochard, all the last mentioned sixteen authors give, as a result of their experience, a favorable opinion of the value of scopolamin anesthesia. It may therefore be assumed with Kionka that failures are attributable to the use of impure preparations, of faulty method, or of applying the method to patients who are too feeble. Klein, who studied scopolamin sleep and spinal anesthesia, by themselves and in combination, in gynecological operations, held this view; he reported that scopolamin anesthesia in combination with spinal anesthesia was especially indicated when anesthesia by inhalation was contraindicated.

Bass stated that "The pain of delivery was considerably reduced in a large majority of the cases (he made observations on more than 100 confinements) by the scopolamin-morphin injections." Kreuter described the value of scopolamin-morphin-chloroform anesthesia as used in more than 100 operations.

Baisch: *Berl. klin. Woch.*, 1907, No. 11.

Moore: *Lancet*, 1907, No. 4364, 1084.

Lindenstein: *Münch. med. Woch.*, 1908, 2064.

The experience of Lindenstein extended to some 150 surgical cases. He recommended the use of solutions which were as fresh as possible, and he ascribed the want of uniformity of action to individual differences.

Caro: *Berl. klin. Woch.*, 1908, 246.

Caro advised that scopolamin-morphin anesthesia be used only in persons whose heart is found to be sound.

Martin: *Württemberg. med. Korrespond.*, 1908, No. 50.

Boesch: *Zentralbl. f. Gynäkol.*, 1908, No. 49.

Hotz: *Deut. med. Woch.*, 1908, 534.

Gminder: *Beitr. z. Geburts. und Gynäkol.*, 1908, No. 2.

Krönig: *Deut. med. Woch.*, 1908, No. 23.

Mayer: *Zentr. f. Gynäkol.*, 1908, No. 21.

Keyserlingk: *Petersburger med. Woch.*, 1908, No. 21.

Bruck: *Allg. med. Zentral-Ztg.*, 1908, No. 44.

Kleinertz: *Zentralbl. f. Gynäkol.*, 1908, No. 42.

Veit: *Therap. Monatsh.*, 1908, No. 12.

Zuntz: *Deut. Aerzte-Ztg.*, 1908, No. 4.

The last eight mentioned authors published communications on the production of scopolamin-morphin partial anesthesia ("Dämmerschlaf") in gynecological practice; they were almost all in favor of the method. Some of them thought that its use should be limited to clinical cases, while Veit thought that it should be limited to urgent cases and only used in neurasthenic women. Compare, however, the extensive experience of Krönig.

Nicholson: *J. Am. Med. Assn.*, 1909, No. 14.

Nicholson studied the harmful effects from the use of scopolamin. In his opinion, no fatal case had been described in the literature which could be definitely proved to be due to the use of scopolamin. Nicholson employed scopolamin injections in 650 cases, and found their excellent effect and their well known advantages fully manifested in 94 per cent of the cases.

Blisnianski: *Zentr. f. Gynäkol.*, 1909, No. 9.

Schoemaker: *Deut. med. Woch.*, 1909, No. 7.

This author used scopolamin-morphin-ether-chloroform anesthesia in 3,000 cases, being well satisfied with the results; no by-effects were produced on the patient.

Trancu-Rainer: *Revista sciintelor medicale*, 1909, Nos. 5 and 6.

Zadro: *Wiener klin. Woch.*, 1909, No. 13.

Berutti: *Med. Klinik*, 1909, No. 14.

Avarffi: *Gynäkol. Rundschau*, 1909, No. 9.

Kroenig, Gauss, van Hoosen, Frogyesi, and Zweifel: *Münch. med. Woch.*, 1909, No. 41.

Stuelp: *Klin. Monatsbl. f. Augenheilk.*, 1909, No. 6.

Beer: *Dissertation*, Freiburg i. Br., 1910.

Beer enumerates the advantages and disadvantages of scopolamin-morphin anesthesia. This dissertation should be consulted by all interested in scopolamin anesthesia.

Rinne: *Deut. med. Woch.*, 1910, No. 3, 110.

Sick: *Ibid.*, 1910, No. 9, 406.

Hatcher's report to the Council of Pharmacy and Chemistry of the American Medical Association (*J. Am. Med. Assn.*, Feb. 5-12, 1910) is probably one of the most conservative papers written on this subject. We quote from this paper:

"Scopolamin and hyoscin are now considered interchangeable words. Scopolamin acts similarly to atropin in large doses, but in small doses has a different action. After small doses there is a rise of blood-pressure but little change in the pulse rate. Clinically, it produces sleep without analgesia, if used alone. It is excreted by the kidneys. When used in combination with morphin, there is no antagonism in regard to its action on the respiration.

"Statistics give us over thirty lives lost in an unknown number of administrations. These deaths have not occurred so frequently of late because very few attempt to use this combination without any other anesthetic. All insist that exceptional cases only can be narcotized without any chloroform or ether. When this occurs we are on dangerous ground. Schneiderlin, one of the earliest advocates of scopolamin and morphin in narcosis, recommends as high as 1/25 grain of scopolamin and 1⅙ grains of morphin in a space of 1¼ hours.

"Scopolamin and morphin may cause death from paralysis of respiration. When this occurs, artificial respiration is usually ineffective and sometimes useless." Hatcher states that no deaths had been recorded up to 1910 in which the dose did not exceed 1/130 grain of scopolamin and 1/6 grain of morphin. Ely (*N. Y. Med. J.*, 1906, 799) reports the death of a patient from 1/100 grain of scopolamin and ⅛ grain of morphin.

Contraindications to this form of medication are when from disease or accident the respiratory function is decreased, also in all cardiac diseases and other conditions which interfere with the circulation. Graves' disease also contraindicates its use. In acute or subacute nephritis a very rapid heart also indicates a smaller dose of hyoscin. Grave symptoms sometimes arising after the operation is completed are probably some of the causes that led to the discontinuance of this form of anesthesia. H. C. Wood, Jr., places the death rate at one in two hundred and fifty; Roth places it at one in two hundred and twenty-two; another writer, at one in eighty.

"Some of the minor after-effects, when used in large doses, are intense thirst, dryness of the mouth and throat, and difficulty in swallowing. In obstetrical cases 1/200 grain of scopolamin and 1/6 grain of morphin is the proper medication for the average case. The principal advantage in obstetrical cases is that the memory is abolished, the patient being often surprised when told that it is all over. There is often entire absence of pain, or this factor is greatly lessened. The principal objection to its use is on account of the danger to the child. Some are born asphyxiated, or die asphyxiated a short while afterwards."

The conclusions of Hatcher are as follows:

(1) An attempt to use scopolamin and morphin alone without the addition of some other drug is most dangerous.

(2) There is no possible excuse for the employment of ready-made mixtures of scopolamin and morphin. They should be prescribed separately as indicated by the patient's condition.

Otto: *Med. Klinik,* 1910, No. 10, 380.

Thomson: *Ednb. Med. J.,* Dec., 1909; *Deut. Med.-Ztg.,* 1910, No. 16, 276.

Kümmel: *Klin. Monatsh. f. Augenheilk.,* 1910, No. 4; *Fortschr. d. Med.,* 1910, No. 9.

Collins: *J. Obstet. and Gynæcol.,* 1910, No. 6, 549; *J. Am. Med. Assn.,* 1910, 1051.

Ruckert: *Z. f. Geburtshilfe u. Gynäkol.,* 1910, *66,* No. 2.

Faust: *Deut. med. Woch.,* 1910, No. 11, 508.

See the papers by Sick, Otto, Ruckert, Collins, Thomson, and Kümmel for the value of scopolamin-morphin in inhalation anesthesia.

Kretz: *Med. Klinik,* 1910, No. 40, 1568.

Bosse and Eliasberg: *Sammlung klin. Vorträge,* 1910, Nos. 599 to 601; *Gynäkologie,* Nos. 215 to 217.

Cremer: *Med. Klinik,* 1910, No. 28, 1092.

Salzberger: *Dissertation,* Freiburg i. Br., 1910.

Bürgi: *Korrespond. f. Schweizer Aerzte,* 1909.

Hauckold: *Z. f. exper. Path. u. Therapie,* 1910, No. 7, 743.

Brüstlein: *Schweiz. Korresp.-Bl.,* 1910, No. 26.

Ewald: *Wiener med. Woch.,* 1910, 1214.

Luxardo: *Gazzetta degli ospedali e della cliniche,* June 9, 1910.

Neu: *Münch. med. Woch.,* 1910, No. 36, 1873.

Neu made experiments to learn whether nitrous oxid anesthesia might not be improved by the previous use of scopolamin-morphin; the results obtained by experiments on animals showed that this was in fact the case.

Korff: *Med. Klinik,* 1911, No. 2.

Hastrup: *Ugeskrift for Læger,* 1911, Nos. 1 and 2.

Rood: *Brit. Med. J.,* 1911, *2,* 652.

Grigorjan: *Wratschebuaja Gaceta,* 1911, No. 31.

Brüstlein: *Zentr. Chir.,* 1911, 345.

Eckert: *Ibid.,* 1911, 857.

Brant: *Russkiy Wratsch,* 1911, No. 13.

Neuber: *Z. f. ärztl. Fortbildung,* 1911, No. 12.

Hippel: *Fortschritte der Med.,* 1911, 229.

Bosse: *Berl. Klinik,* 1911, No. 272; *Monats. f. Geburtsh. u. Gynäk.,* 1911, No. 3.

Dietschky. *Korrespond. f. Schw. Aerzte,* 1908, No. 15.

Klauber: *Münch. med. Woch.,* 1911, No. 41, 2160.

Gauss: *Ibid.,* 1911, 2355.

Burkhardt: *Münch. med. Woch.,* 1911, No. 15, 778.

Hagemann: *Ibid.,* 1911, No. 28, 1427.

Björkenheim: *Zentr. Gynäk.,* 1911, No. 20, 759.

On the value of scopolamin-morphin in midwifery, see:

Freeland-Solomons: *Brit. Med. J.,* 1911, i, 187.

Strassmann: *Berl. klin. Woch.,* 1911, No. 23.

Iljin: *Russkiy Wratsch,* 1911, No. 12.

Tichauer: *Dissertation,* Freiburg i. Br., 1911.

Corbett: *Brit. Med. J.,* 1911, *1,* 868.

On pantopon-scopolamin anesthesia, see:

Häni: *Therap. der Gegenwart,* 1911, No. 2.

Deschwanden: *Korrespond. f. Schw. Aerzte,* 1911, No. 4.

Brunn: *Zentr. Chir.,* 1911, No. 3.

Brüstlein: *Ibid.,* 1911, No. 10.

Johannsen: *Zentr. Gynäk.,* 1911, No. 19.

Zeller: *Münch. med. Woch.,* 1911, No. 25.

Eckert: *Zentr. Chir.,* 1911, No. 25.

Fowelin: *Ibid.,* 1911, No. 27.

Simon: *Münch. med. Woch.,* 1911, No. 32.

Kolde: *Ibid.,* 1911, No. 28.

Aulhorn: *Ibid.,* 1911, No. 12.

Haeberlin: *Ibid.,* 1911, No. 33.

Heinsius: *Berl. klin. Woch.,* 1911, No. 41.

Gray: *Lancet,* Sept. 2, 1911.

Scopomorphin.—Sterilized *euscopol-* (*q. v.*) morphin solutions are marketed in glass tubes of 1 and 2 c. c. capacity. Each c. c. contains 0.0006 gm. euscopol and 0.015 gm. morphin hydrochlorid. The combination is used for the production of total and semi-narcosis, and as an analgesic and sedative. See Neuber: *Z. f. ärztl. Fortb.,* 1911, No. 12, 340; Fonyo: *Obste. Aerzte.-Ztg.,* 1910, No. 2; Korff: *Med. Klinik,* 1911, No. 2; Salzberger: *Zentr. f. ges. Therap.,* 1910, No. 10, 558; and Meyer: *Münch. med. Woch.,* 1910, No. 45, 2370.

Septicylat.—This contains eugenol, methyl salicylate, geranoil, formaldehyd, and alcohol; it is used in dentistry.

Sicherheitsbenzin.—A mixture of 1 volume of benzin and 2 volumes of *Carbon Tetrachlorid* (*q. v.*).

Sinecain.—Sinecain is a 3 per cent water solution of quinin hydrochlorid, containing, in addition, 3 per cent of antipyrin and 0.05 mg. of adrenalin, intended for employment as a local anesthetic.

See E. Schepelmann: *Med. Klinik,* 1912, No. 43.

Skopomorphin.—See *Scopomorphin.*

Sœmnoforme.—See *Somnoform.*

Soloid "Hemisine" Comp. c. Eucaino.—0.001 gm. hemisin, 0.8 gm. sodium chlorid, and 0.2 gm. *Eucain Hydrochlorid* (*q. v.*).

Soluble Hypodermic Tablets Novocain, 1/3 grain.—Each tablet contains *Novocain* (*q. v.*), 0.02 gm. (1/3 grain).

Soluble Tablets Novocain, 1 1/7 grains.—Each tablet contains novocain, 0.074 gm. (1 1/7 grains).

Solution Atoxyl, 10 per cent, with Novocain, 1 per cent (sterilized). —Each 100 c. c. contain: atoxyl, 10 gm.; and novocain, 1 gm. (each fluid ounce contains atoxyl, 48 grains; and novocain, $4\frac{8}{10}$ grains), dissolved in distilled water.

Somnoform.—This anesthetic, a mixture of ethyl chlorid, 83 parts; methyl chlorid, 16 parts; and ethyl bromid, 1 part (60 of ethyl chlorid and 5 of ethyl bromid, according to *Géhé's Codex,* 1911, 328), is made in Bordeaux, France. In 1901 Rolland, of Bordeaux, read a paper on a new anesthetic he had discovered and named by him sœmnoforme; this was a mixture of ethyl chlorid, 60 parts; methyl chlorid, 35 parts; and ethyl bromid, 5 parts (see *Chem. Centr.,* 1903, i, 188). It was marketed by a London and by a Philadelphia firm. The latter firm later came under the control of a New York company, but retained, as far as somnoform was concerned, the old name. Still later, after the decomposition of somnoform had been shown to be due largely to the ethyl bromid contained therein, this compound was omitted by the London firm from the mixture without notification being given to the American company, and without change of label. The United States Government detected the inconsistency between the label and the product. Then the American firm asserted it knew nothing of it. When summoned by the Government, the firm had the product analyzed, found no ethyl bromid, pleaded guilty, and had a fine of $25.00 imposed (see *Judgment No. 571, Food and Drugs Act*). Then the present formula for somnoform was determined upon. It may be said, therefore, that somnoform, or sœmnoforme, was formerly the same as the present *Narcoform* (*q. v.*), but at present is a mixture of ethyl chlorid, 83 parts; methyl chlorid, 16 parts; and ethyl bromid, 1 part.

Somnoform was recommended by Rolland and Robinson (*Brit. Med. J.,* 1903, No. 2215, 1408) as an excellent and harmless anesthetic and narcotic, since it acted promptly, and, if allowed to act for 50 seconds to 2 minutes, did not give rise to undesirable sequelæ, such as nausea and vomiting. Somnoform has been employed in a very large number of cases, especially in dentistry, as a substitute for nitrous oxid, as recorded by Gross: *Lancet,* 1903, No. 4156, 1169; Secretan: *Ibid.,* 1903, No. 4172, 1169; Cole: *Presse méd.,* 1903, No. 63, 572; Maguire: *Lancet,* 1903, No. 4174, 632; Lankester: *Revue de Thérap.*, 1903, No. 8, 272; Kirkpatrick: *Med. Press and Circular*, April 22, 1903; Gilmour: *The Dental Rec.*, 1903, 496; Ronnet: *Brit. Dental J.*, 1903, 215; Callum: *Ibid.*, 1903, 267; and Vierthaler: *Z. f. Stomatologie*, 1903, No. 11, 349. All these writers concur in formulating the opinion that it induces complete relaxation of the muscles without cyanosis, and they state that the patients nearly always return to consciousness with a smiling countenance; but, to quote Merck: *Ann. Rep.*, *17*, 168): "It is, however, in its application in small operations that its utility will probably be greatest." Rolland devised a special mask for the administration of somnoform.

On the physiological action of somnoform, see Cole: *Brit. Med. J.*, June 20, 1903, 1421; and Webster: *Bio-Chemical J.*, 1906, *1*, 328.

Stenocarpin.—An alkaloid from the leaves of the "tear blanket" tree of Louisiana; said by Claiborne (*Sci. Am. Suppl.*, No. 608) to possess local anesthetic properties.

On the application of stenocarpin as a local anesthetic, consult the following literature:

Claiborne: "A New Local Anesthetic," *N. Y. Med. Rec.*, July 30 and Oct. 1, 1887.

Goodmann: "Stenocarpin," *Med. Rec.*, July 30, 1887.

Jackson: "Observations on the Action of Stenocarpin, the New Local Anesthetic and Mydriatic," *Am. Med. News*, 1887, 255.

Knapp: "Experiments with Stenocarpin," *Med. Rec.*, 1887, 180.

Morse: "Gleditschine (Stenocarpin)," *Phila. Med. Surg. Rept.*, 1887, 701.

Novy: "What Is Stenocarpin?" *Am. pharm. Rund.*, 1887, 248.

Stephen's Mixture.—An anesthetic mixture containing chloroform and alcohol, *āā;* and *Cologne Water, q. s.* (Müller: "Narkologie," *1*, 493).

Stovain or Stovaine (Benzoyl-Ethyl-Dimethylaminopropanol Hydrochlorid.—Stovain is 2-benzoxy-2-methyl-1-dimethyl-amino butane hydrochlorid, $CH_3.CH_2C(C_6H_5COO)(CH_3)CH_2N(CH_3)_2.HCl = C_{14}H_{22}O_2NCl$. It is closely related to *Alypin* (which see); it was produced synthetically by Fourneau (hence its name) in 1904, and was first used in subarachnoid analgesia by Chaput.

Stovain is prepared by causing a reaction of benzoyl chlorid on the α-dimethyl-amino-pentonal-β, which is itself the product of reaction of ethylmagnesium chlorid on methylaminoacetone. It crystallizes in small, brilliant scales, which melt at + 175° C. (347° F.). It is extremely soluble in water and easily in methyl alcohol and acetic ether, but requires 5 parts of absolute ethyl alcohol for solution and is only slightly soluble in acetone. It is quite stable and its solutions may be sterilized at + 115° C. (239° F.) without suffering decomposition. The water solution is slightly acid to litmus, but is neutral to methyl orange. It is precipitated by all the alkaloidal reagents and is decomposed by even very dilute alkalies. It is incompatible with alkalies and all alkaloidal reagents.

Actions and Uses.—Stovain acts as a local anesthetic. It has about the same power as cocain, but dilates the blood vessels, whereas cocain contracts them. It is only one-third to one-half as toxic as cocain. Stovain is also said to exert a tonic action on the heart.

It is used as a local anesthetic; while most reports are favorable, one case of gangrene has been reported following the use of a 10 per cent solution. On the physiological properties of the methyl-, amyl-, phenyl-, and benzyl-homologues of stovain, see Veley and Symes: *Chem. News, 103,* 92. Fourneau has more recently prepared a new compound, the propyl ester of dimethyl-amino-oxy-benzoyl-isobutyric acid, which possesses pronounced local anesthetic properties; it abolishes the contractility of muscle less rapidly than does stovain or methyl-stovain, and has also less effect on blood pressure and on respiration.

Dosage.—Internally, 0.002 gm. (1/30 grain), pill form. Locally it may be used in the eye in 4 per cent solution and applied to other mucous membranes, as in laryngology, in from 5 to 10 per cent solution. For hypodermic injections for local anesthesia, it can be used in 0.75 to 1 per cent solution.

For further information on stovain, consult the following contributions:

Adam, C.: *Münch. med. Woch.,* 1906, No. 8.

Alessandri: "Rachistovainisation," *Congrès de Chir. de Paris,* Oct., 1906.

D'Almeida: "La Stovaïne comme anesthésique," *Acad. Nacional de Med.,* Rio de Janeiro, May 11, 1905.

Andhelovici-Joanitescu: "Das Stovaine als intrarachidianes Analgesikum in der Venerologie," *Romania med.,* No. 22, 1905; abstracted in *Münch. med. Woch.,* 1906, No. 13.

Arnezzi: *Brit. Med. J.,* 1905, No. 2320, 92.

Audbert, A.: "La rachistovainisation en obstétrique," *Thèse de Paris,* Apr. 4, 1906.

Babcock, W. W.: "Spinal Anesthesia with Special Reference to the Use of Stovaine," *Therap. Gaz., 30,* 239, Apr. 15, 1906. "Spinal Anesthesia; a Clinical Study of 658 Administrations," paper read before the Section on Surgery—Medical Society of the State of Penn., Cambridge Springs, Sept. 14-17, 1908. (Printed in *Penn. Med. J.,* Aug., 1909.) The Obstetrical Society of Philadelphia—Meeting Thursday, March 4, 1909. Barton Cooke Hirst: "A Note on Sacral Anesthesia"; "A Study of a Case of Spondylolisthesis." W. Wayne Babcock: Discussion.

Badini: *L'Ospedale maggiore,* 1907, 261.

Bardescu: "La stovaïne en chirurgie," *Spitalul,* 1904, No. 23.

Barker, A. E.: "A Case of Embolus Blocking the Bifurcation of the Aorta. Gangrene of One Leg. Amputation under Lumbar Analgesia," *London Clin. J., 28,* No. 4 (May 9, 1906).

Barker, A. E.: "A Report on Clinical Experiences with Spinal Analgesia in 100 Cases," *Brit. Med. J.,* March 23, 1907.

Baylac, M. J.: "Note sur la toxicité comparée de la stovaïne et de la cocaïne," *Soc. de Biol.,* Paris, Feb. 3, 1906 (*Revue Internat. de Méd.,* 1906, No. 4).

Becker: "Operationen mit Rückenmarksanästhesie," *Münch. med. Woch.,* 1906, No. 28, 1344.

Bell, R. R.: "Stovaine, a New Local Anesthetic," *N. Y. Amer. Vet. Rev.,* Jan., 1905, 28, No. 10.

Benitez Fco, Cabrera: "La Stovaina," *Rev. de la Escuela de Méd. de la Habana,* 1906, *5,* No. 3.

Beurmann (de) and Tanon: "Emploi de la stovaïne en dermatologie," *Bull. Soc. Franç. de Dermatol.,* 1904, No. 9.

Bier: "Ueber den jetzigen Stand der Rückenmarksanaesthesie, ihre Berechtigung, ihre Vorteile und Nachteile gegenüber anderer Anaesthesierungs Methoden," 34 Kongress der deutschen Gesellsch. für Chirurgie, Apr., 1905. (Ref. *München. med. Wchnschr.,* 1905, No. 23, 1117.)

Billon, F.: "Sur un médicament nouveau, le chlorhydrate d'amyléine," *Acad. de Méd. de Paris,* March 29, 1904.

Blondeau: "Sur l'emploi de la stovaïne adrénalisée," *J. de Méd. d. Chir. pract., 76,* No. 16, Aug. 25, 1905; *Therap. Neuheiten,* 1906, No. 1.

Boeckel: *Deut. med. Woch.,* 1906, 1724.

Bonachi: "Vingt.-trois cas de rachistovainisation," *Bull. et Mém. d. la Soc. de' Chirurg. d. Bucharest, 8,* 68.

Bradburne: "Affections of the Eye (Stovaine)," London, *Treatment,* March, 1906.

Braun: "Ueber Medullaranaesthesie," *Münch. med. Woch.,* 1905, 1335; "Ueber einige neue örtliche Anästhetica," *ibid.,* 1667; "Die Leistungen und Grenzen der lokal Anästhesie," *Deut. med. Woch.,* 1906, *42,* 1668.

Bruni, C.: "Il metodo Cathelin nella cura dell incontinenza essenziale dorina," *Ac. d. méd. chir.,* Naples, 1905.

Bruno, D.: "La Stovaina in Terapia oculare," *Rev. internaz. de Clinica e Terapia,* Naples, *1,* No. 4.

Busse: "Ueber die Verbindung von Morphium-Skopolamin Injektionen mit Rückenmarksanästhesie bei gynäkologischen Operationen," *Münch. med. Woch.,* 1906, 1858.

Cavazzani and Balao Venturo: "Su alcune nueve maniere di anestesia generale e locale," *Rev. veneta di sc. med.,* 1905, *25,* No. 1. "Contributo alla anestesia lombare e generale con la Stovaina e la Scopolamina," *ibid.*, 1906, *23*, No. 7.

Cernezzi: "L'Anestesia locale con la stovaina e con la miscela stovaino-adrenalinica nella chirurgia generale," *Riforma medica*, Mar. 11, 1905.

Chaput: "La stovaïne, anesthésique local. Valeur de la stovaïne comparée à la cocaïne," *Bull. Soc. biol.*, May 12, 1904. "L'Anesthésie rachidienne à la stovaïne," *Archives de Thérap.*, Nov. 15, 1904. "Anesthésie lombaire à la stovaïne," *ibid.*, April 1, 1905. "D'anesthésie totale au moyen de la rachi-stovainisation," *Bull. Soc. biol.*, July 6, 1907; *Presse méd.*, 1907, 121. "De la rachistovainisation," Soc. de chir., séance du 4 mars 1908; cf. *Bull. Soc. chir.*, 1904, No. 30.

Chartier: "La rachistovainisation en obstétrique," *La Gynécol.*, Oct. 3, 1904.

Chevalier and Scrini: "Sur l'action pharmacodynamique et clinique de la novocaine," Paris, *Soc. d. Thérap.*, July 27, 1906.

Chiene, George: "The Use of Stovaine as a Spinal and Local Anesthetic," *Scot. Med. Surg. J.*, 1906, No. 3.

Christie, W. W.: "The Use of Stovaine as a Local Anesthetic in Throat and Nose Operations," *Glasgow Med. J.*, Feb., 1906.

Cisler, Jos.: "Nová anaesthetika vrhino laryngologie," *Csasopsis lekaruv cesky*, Prague, Jan. 3, 1906.

Coakley, C. G.: "Report on the Use of Stovaine," *N. Y. Acad. Med.*, Feb. 22, 1905; *Zahntechn. Reform.*, 1906, No. 3.

Coderque: *Rev. de med. y cir.*, Sept. 7, 1907.

Cohn: "Medullaranästhesie in der Geburtshilfe," *Mediz. Gesell. in Giessen*, Jan. 30, 1906; *Deut. med. Woch.*, 1906, 22.

Couteaud: *Bull. d. l'Acad. d. Méd.*, 1908, No. 26.

Czermak: "Nouvelles observations démontrant l'inocuité de la rachistovainisation pour les reins," *Zentralbl. f. Chir.*, Feb. 15, 1908.

Czerny: *34 Kongress der Deut. Gesellsch. f. Chir.*, Apr., 1905.

Dean, H. P.: "The Importance of Anesthesia by Lumbar Injections in Operations for Acute Abdominal Disease," *Brit. Med. J.*, 1906, No. 2367.

Demaillasson: "Les injections analgésiantes 'loco dolenti' dans les névralgies périphériques," *Thèse de Paris*, 1905.

Deetz: "Erfahrungen ueber 360 Rückenmarksanästhesien mit Demonstrationen," *Münch. med. Woch.*, 1906, No. 28; *Z. f. Krankenpf.*, 1906, No. 3.

Delattre, G.: "Accidents consecutifs à l'introduction des substances médicamenteuses dans le liquide céphalorachidien," *Thèse de Paris*, 1905.

Deupès, E.: "La stovaïne: étude expérimentale et clinique," *Thèse de Toulouse*, 1906.

Dion, G.: "Stovaïne; son emploi en chirurgie oculaire," *Thèse de Bordeaux,* 1905.

Dolèris: "La stovaïne," *Soc. d'Obstétriq., de Gynéc. et de Pédiatr.,* Paris, July 11, 1904.

Dolèris and Chartier: "La rachistovainisation en gynécologie," *La Gynécol.,* Feb., 1905.

Dönitz: "Technik, Wirkung u. specielle Indication der Rückenmarksanästhesie," *Arch. f. klinisch. Chir.,* 1906, 77, No. 4.

Dönitz: "Wie vermeidet man Misserfolge bie der Lumbalanästhesie," *Münch. med. Woch.,* 1906, 1339.

Dubar: "La stovaïne en oto-rhino-laryngologiè," *Progrès méd.,* Nov. 26, 1904; *Rev. de Thérap.,* 1905, 57, No. 2.

Duffour: "Etude sur la stérilisation et l'emploi des solutions hypodermiques," Toulouse, July, 1905, *Thèse.*

Elting, A. W.: "The Method and Indications for the Use of Spinal Anæsthesia," *Albany Med. Ann.,* May, 1906.

Feliziani: "Sull'anestesia rachistovainica," *Policlinico,* 1908, sez. prat., fasc. 7.

Fernandez, J. S.: "Le estovaina en nuestra oftamológica," *Crónica med.-quir. de la Habana,* May, 1905.

Finckelnburg: "Neurologische Beobachtungen und Untersuchungen bei der Rückenmarksanästhesie mittelst Kokain und Stovain," *Münch. med. Woch.,* 1906, No. 9, 397.

Fischer, R.: "Ueber Stovaine in der oto-rhino-laryngologischen Praxis," *Deut. med. Ztg.,* 1906, No. 38.

Foisy: "La stovaïne, ses advantages, ses inconvénients, son incompatibilité avec l'adrénaline," *Tribune méd.,* 1904, No. 37.

Forns: "La estovaina in obstetrica," *Rev. d. l. especialidades med.,* Madrid, Sept. 20, 1904.

Fourneau, E.: "Sur les amino-alcools tertiares," *Acad. d. Sci.,* Paris, Feb., 1904; "Anesthésiques locaux," *Rev. gén. d. Sci.,* Sept. 30, 1904; *Bull. Sci. pharmacol.,* 1904, No. 9.

Fourneau, C.: "Un nouvel anesthésique local. La stovaïne," *J. Pharm. Chim.,* Aug. 1, 1904.

Freund: "Weitere Erfahrungen mit der Rückenmarksnarkose," *Münch. med. Woch.,* 1906, 1109.

Fromaget and Dion: "Action mydriatique de la stovaïne," *Presse méd.,* Oct. 1, 1904.

Galceran, A. B.: "La estovaina como anestésico y analgesico," Barcelona, *Archives d. Thérap.,* 1905, No. 11.

Galletta: "Contribuzione clinica alla rachistovainizzazione," *Policlinico,* 1908, sez chir., fasc. 1 and 2.

Garcia Tapia: "La stovaïne; Sus applicaciones in oto-rinilaringologia," *Bolet. di laringol.,* Madrid, Nov. 3, 1904.

Gaudier: "De la rachi-stovainisation chez les enfants," Soc. de Chir., séance du 16 janvier, 1907.

Gauss: "Die Narkose in der operativen Geburtshülfe," *Therap. der Gegenwart,* 1906, 453.

Gemuseus: "Das Stovain," *Dissert.,* Bern, 1905.

Gironi: "Contribution clinique à la rachistovainisation," *Gaz. degli ospedali,* July 7, 1907.

Goldscheider: *Therap. der Gegenwart,* 1905, No. 12.

Greiffenhagen: *Zentralbl. f. Chir.,* 1906, No. 19.

Hackenbruch: "Lumbalanästhesie," *Wiesbaden Centralbl. f. Chir.,* 1906, No. 14.

Halbron and Chartier: "Note sur la réaction méningée après la rachistovainisation," Paris, Feb., 1905.

Heinecke and Löwen: "Lumbalanästhesie mit Stovaine und Novocain," *Brunssche Beit. z. kl. Chir.,* Leipzig, 1906, *50,* Part 2.

Hermes: "Rükenmarksanästhesie," 34th *Deut. Chir. Kongress in Berl.,* Apr., 1905; "Weitere Erfahrungen über Rückenmarks-anästhesie mit Stovaine und Novocaïn," *Med. Klinik,* 1906, No. 13.

Hildebrandt: "Die Lumbalanästhesie," *Berl. klin. Woch.,* Aug. 21, 1905.

Holzbach: "80 Lumbalranästhesien ohne Versager," *Münch. med. Woch.,* Jan. 22, 1908.

Hosemann: "L'Inocuité pour le rein de la rachi-stovainisation," *Zentralbl. f. Chirurg.,* Jan. 10, 1908.

Huchard: "Quelques Faits thérapeutiques sur la stovaïne," *Acad. de Méd.,* Paris, July 12, 1904; *J. des Practiciens,* 1904, 33.

Impallomeni, G.: "Le iniezoni intramuscolare di salicilato sodico e stovaina. Loro applicazioni therapeutiche," *Il Policlinico,* May 6, 1906, *13,* No. 18.

Jonnesco: "Sur la rachistovainisation," *Bull. et Mém. de la Soc. de Chir. de Bucharest, 8,* 60-63; "Remarks on General Spinal Analgesia" (letter to the editor), *N. Y. Med. J.,* Jan. 1, 1910; "Remarks on General Spinal Analgesia," *Brit. Med. J.,* Nov. 13, 1909 (Abstr. *N. Y. Med. J.,* Dec. 4, 1909, 1133); "General Rachianæsthesia," *Med. Times* (N. Y.), Feb., 1910; "Concerning General Rachianæsthesia," *Am. J. Surg.,* Feb., 1910.

Joris, L.: "La stovaïne," *Bollet. dell. Assoc. medica. Tridentina,* Jan. 1, 1906.

Kaménzave, L.: "La Stovaïne, étude expérimentale," *Thèse de Genève,* 1905.

Kendirdjy, L.: "L'Anesthésie chirurgicale par la stovaïne," Paris; Masson et C., edit. 1906. "General Indications for and Technique of Local Anæsthesia," *J. d. Méd. et d. Chir. Pratiques,* Apr. 10, 1909, *80,* No. 7.

Kendirdjy and Bertreaux, R.: "L'Anesthésie chirurgicale par injection sousarachnoïdienne de stovaïne," *Presse méd.*, 1904, 660.

Kendirdjy and Burgaud, V.: "Cent quarante nouveaux cas de rachistovainisation," *ibid.*, May 31, 1905; *Allg. med. Zentral.-Ztg.*, 1905, No. 24.

Koenig, C. J.: "L'Analgésie locale par le stovaïne," *Arch. Intern. de Laryngol.*, 1905, *18*, 5, 9.

Krecke: *Münch. med. Woch.*, 1906, No. 6.

Kroemer: "Beckenerweiternde Operationen," *Mediz. Gesell. in Giessen*, Jan. 30, 1906; *Deut. med. Woch.*, 1906, 900.

Kroner: "Ueber einige neuere Arbeiten zur Lumbalpunktion und Lumbalanästhesie," *Therap. der Gegenwart*, 1906, 361.

Kroenig, M.: "Deux cents cas de narcose mixte par combinaison de la scopalamine-morphine avec la rachistovainisation," *Presse méd.*, Apr. 14, 1906.

Kroenig and Gauss: "Observations anatomiques et physiologiques au cours d'un premier millier de rachi-anasthésies," *Münch. med. Woch.*, Oct. 1 and 7, 1907.

Kugel, L.: "Stovaine ein neues Anästhetikum," *Wien. klin. therap. Woch.*, 1906, No. 7.

Kümmel: "Stovainlumbalanästhezien," *Deut. med. Woch.*, 1906, 126.

Lacceti, C.: "A proposito dell'anestesia locale stovainica in chirurgia," *Gaz. internaz. di medic.*, July, 1906.

Laewen: *Beitr. zur klin. Chir.*, 1906, *2*, 50.

Lang: *Deut. med. Woch.*, 1906, No. 35.

Lasio: "La rachistovainisation en chirurgie urinaire," *Clin. Chir.*, 1907, fasc. 9.

Lapersonne, F. de: "Un nouvel anesthésique local, la stovaïne," *Presse méd.*, 1904, No. 30, 233.

Launoy, L.: "Action du chlorhydrate d'amyléine sur le mouvement ciliare," *Acad. des Sciences*, Paris, July 11, 1904.

Launoy and Billon: "Sur la toxicité du chlorhydrate d'amyléine," *Acad. des Sciences*, Paris, 15 May, 1904; *Compt. rend.*, March 15 and July 11, 1904; *Presse méd.*, 1904, 368.

Lazarus, P.: "Zur Lumbalanästhesie," *Berl. klin. Woch.*, Mar. 19, 1906.

Lennender: "Sur l'anesthésie locale et la sensibilité du corps et des tissus," *Centralb. f. Chir.*, 1906, No. 9.

Loeser: *Deut. med. Woch.*, 1906, 483.

Löffler: "Lumbalanästhesie mit Stovaine," *Frankfort-Münch. med. Woch.*, 1906, 95.

Lohmann, W.: "Das Stovaine in der Infiltration-Anästhesie," *Fortschr. d. Mediz.*, Nov. 20, 1905, No. 33.

Löhrer: "Zur Behandlung hysterischer Kontrakturen der unteren Extremitäten durch Lumbalanästhesie," *Münch. med. Woch.*, 1906, 1568.

Lucangelli, G. L.: "La Stovaine l'Alipina," *Gaz. méd.*, Dec., 1905.

Luke, T. D.: "Stovaine: a Synthetic Analgesic," *Scot. Med. Assn. J.*, Edinburgh, 1905, *17*, 143.

McGavin: "A Report of 250 Cases of Spinal Analgesia by the Use of Stovaine-Glucose Solution," *The Practitioner*, Aug., 1909.

McKenzie, D.: "The Local Anæsthetic Action of Stovaine," *Brit. Med. J.*, 1906, No. 2367.

Marchetti, L.: "La stovaina como anestetico locale nella practica chirurgia," *Gaz. degli osped. e. del. clin.*, Nov. 26, 1905.

Martin, Collier F.: "The Use of Spinal Anesthesia in Rectal Surgery," *The Proctologist*, Sept., 1909.

Mercier, O. F.: "L'Anesthésie chirurgicale par la stovaine," Montreal, *L'Union méd. du Canada*, May 1, 1906, *35*, No. 5.

Meyer, A.: "Zwei neue Lokalanästhetica in der rhinolaryngologischen Praxis," *Therap. Monats.*, 1905, No. 5, 240.

Milko: "Spinalanalgesie mit Stovaine," *Deut. med. Woch.*, 1906, 1400.

Mösetig: "La stovaine," *Deut. Naturforsch. Versammlung*, 1905.

Müller, Benno: "Stovaine als Anästhetikum," *Sammlung klin. Vorträge*, 1906, *15*, No. 428, No. 8, 495.

Narewski: *Zahnärztliche Rundschau*, 1907, No. 19.

Nogué, R.: "La stovaine en stomatologie," *Arch. de Stomatolog.*, 1904, Nos. 4 and 5.

Noland, Lloyd: "Stovaine Spinal Anæsthesia, a Report of Twenty Cases," *Ann. of Surg.*, Apr., 1910.

Nigoul, M.: "Constatations cliniques au sujet de la stovaine," *Concours médicale*, Paris, June 24, 1905.

Ostwald, T.: *Berl. klin. Woch.*, 1906, No. 1.

Pauchet, Amiens: "La chirurgie rurales; rachistovainisation," *La Clinique*, 1906, 633. "Petite chirurgie; traitement du panaris," *La Clinique*, 1906, 681.

Penkert: "Lumbalanästhesie im Morphium-Skopolamin Dämmerschlaf," *Münch. med. Woch.*, 1906, 646; 1907, No. 25.

Perez: *Il Policlinico*, 1907, No. 3.

Piedallu, R.: "La stovaïne," *Thèse de Paris*, July, 1905.

Piga, A.: "Contribución al estudio de los efectos fisiológicos y terapeuticos de la estovaina," Madrid, *Los nuevos remedios*, Apr. 30 and May 30, 1905.

Pochhammer: "Zur Teknik und Indikationstellung der Spinal-analgesie," *Deut. med. Woch.*, 1906, No. 24.

Poenaru Caplescu: "Rachistovaine," *Spitalul*, 1905, 19-20; "La stovaine en chirurgie," *ibid.*, 1904, 21-22.

Poenaru: *Deut. med. Woch.*, 1910, No. 8.

Poinsot, A.: "La cocaïne en art dentaire," *Thèse de Paris*, 1905.

Pont, A.: "À propos d'un nouvel anesthésique local, la stovaïne," *Bull. de Lyon méd.*, May 15, 1904.

Polini, G.: "La stovaina in chirurgia," *Gazz. internaz. di medic.*, Naples, Oct., 1905.

Poth, H.: "Ueber Stovaine als lokales Anaesthetikum in der kleinen Chirurgie," *Med. Klinik*, 1905, No. 15.

Pouchet: "Étude pharmacodynamique de la stovaïne," *Acad. de Méd.*, Paris, July 12, 1904; *Revue de Thérap.*, 1904, 543.

Pouliquen: "La rachistovainisation," *Thèse de Paris*, 1905.

Preindlsberger: *Allg. med. Zentral-Ztg.*, 1905, No. 42, 808.

Preliminary Report of the Anesthesia Commission of the American Medical Association. Transactions of the Section on Surgery and Anatomy of the American Medical Association, 1908, 426-427, *A. M. A. Press.*

Pringle: "Notes of an Experience of Stovaine as a Spinal Analgesic in 100 Cases," *Brit. Med. J.*, 1907, No. 2427, 12.

Pussep: *Arch. f. Psych.*, 1911, No. 48, 2.

Rabourdin, A.: "Topographie des altérations sensitives dans rachistovainisation," *Thèse de Paris*, 1906.

Rahn, A.: "Die Ersatzmittel des Kokains," *Pharm. Cent.*, Sept. 28, 1905; "Ueber Stovaine in der Lumbal-Anæsthesie," *Deut. Aerzte-Ztg.*, Apr. 15, 1906.

Ravant: "Anesthésie chirurgicale limitée à la région génito-périnéoanale par l'injection intra-rachidienne de solution concentrée," *Soc. de Biol., séance du 22 juin*, 1907.

Reclus, P.: "L'Analgesie locale par la Stovaïne," *Académie de Médecine*, Paris, July 5, 1904; *Revue de Thérap.*, 1904, 595. "La Stovaïne," *Presse méd.*, Jan. 3, 1906.

Roith: *Münch. med. Woch.*, 1907, No. 19.

Royet: "Behandlung der Ozæna mit Stovaine," *Wiener klin. therap. Woch.*, 1906, No. 10.

Ruschhaupt: "Lumbalanästhesie mit Stovaine," *Med. Gesell. in Giessen*, Feb. 20, 1906.

Ruthon: "Sur un nouvel anesthésique: la stovaïne," *Thèse de Paris*, 1904.

Sandberg, J.: "Spinalanalgesie," *Med. Rev.*, Dec., 1905.

Saratucci: *Il Policlinico*, 1907, No. 9.

Sauvez, E.: "Un nouvel anesthésique local: la stovaïne," *Soc. d'Odontologie*, Apr. 9, 1904; *Rev. internat. Méd. et Chir.*, 1904, 191. "L'Anesthésie locale pour l'extraction des dents," *Archiv. de Thérap.*, Aug. 1, 1905. "Quelle est la meilleure méthode d'anesthésie locale pour l'extraction des dents?" *La clinique*, Aug. 3, 1906, 505.

Schiff: "Ueber Stovaine als lokales Anæsthetikum," *Deut. med. Woch.*, Aug. 31, 1905.

Schwarz: *Zentr. f. Chir.*, 1907, No. 13.

Scrini: "Précis de thérapeutique oculaire," Paris: G. Steinheil, édit. 1904. "La stovaïne," *Arch. d'Ophthalmol.*, June 15, 1905. "Sur la stovaine," Paris, *Soc. de Thérap.*, Oct. 10, 1906.

Silbermark, M.: "Ueber Spinalanalgesie," *Wiener klin. Woch.*, Nov., 1904, No. 46.

Sinclair, A.: "Gangrene of the Skin Following the Use of Stovaine, a New Local Anesthetic," *Cutan. Dis. incl. Syph.*, 1904, *13*, 307, 310; *Therap. Monats.*, 1905, No. 11, 595.

Sluss, J. W.: "Spinal Analgesia," *Indiana Med. J.*, June 12, 1906.

Sonnenburg: "Rückenmarksanästhesie mittels Stovaine," *Deut. med. Woch.*, 1905, No. 9.

Spiller and Leopold: *Deut. med. Woch.*, 1910, 1292.

Stephenson: "Stovaine: a New Local Anesthetic," *Ophthalmoscope*, Nov., 1904; *Rev. de Thérap.*, 1905, 128.

Tilmann, O.: "Lumbalanästhesie mit Stovaine," *Berl. klin. Woch.*, Aug. 21, 1905.

Tomai, G.: "L'anestesia stovainica," *Giorn. internaz. d. sc. mediche*, Feb. 28, 1906.

Trautenroth: *Deut. med. Woch.*, 1906, No. 7.

Tuffier, Th.: "Die Rückenmarksanästhesie mit Stovaine," *Klin. therap. Woch.*, 1905, 378.

Varvaro, E.: *Il Policlino*, 1906, Nos. 6, 7, 8.

Wainwright, J. M.: "On the Value of Spinal Analgesia in Shock," *Penn. Med. J.*, Nov., 1905.

Wendel: "Die modernen Bestrebungen zur Verminderung der Narkowengefahr," *Münch. med. Woch.*, 1906, 1601.

Wilms: "Heilung hysterischer Kontrakturen durch Lumballähmung," *Deut. med. Woch.*, June 14, 1906.

Wolff, L.: "Ein neues cocainfreies Injections-Anästhetikum," *Allg. mediz. Central.-Ztg.*, 1906, No. 13.

Woskresenski, A. W.: "Ueber lokale Stovaine Anästhesie," *Fortschr. der Med.*, 1905, 506.

Zahradnicky: "The Results of Spinal Anæsthesia, Especially in Laparotomy," *Archiv f. klin. Chir.*, *98*, No. 2; Extract in *Therap. Gaz.*, Sept. 15, 1909.

Zernik (F): "Stovaine," *Apoth.-Ztg.*, 1905, No. 19.

Zwintz (J.): "Ueber Stovaine, ein pharmako-dynamische Studie," *Wien. med. Presse*, Feb. 4, 1906, No. 5.

Stovain Billon.—Contains, in 1 c. c., 0.00013 gm. epirenin borate, 0.04 gm. stovain, and 0.0011 gm. sodium chlorid.

Stovain with Strychnin.—On the use of stovain with strychnin for spinal anesthesia, see *Z. für Chir., 107,* 1-3; *Therap. Gaz.,* June 15, 1911.

Strophanthin.—Strophanthin (strophanthinum, strophantin) is, according to the *United States Pharmacopœia,* a glucosid, or mixture of glucosids, obtained from strophanthus; it was made official in the eighth revision of the *Pharmacopœia.* It is officially described as a white or faintly yellowish crystalline powder, containing varying amounts of water of crystallization, which it does not lose entirely without decomposition. Its taste is intensely bitter, and it is permanent in the air. It is very soluble in water and in dilute alcohol, but is less soluble in absolute alcohol, and is nearly insoluble in ether, chloroform, and benzene. It commences to fuse at + 170° C., and is not completely melted until the temperature of + 190° C. is reached. Its solutions are dextrogyrate, and are neutral to litmus. Fraser (*Am. J. Pharm.,* 1889, 532) found that strophanthin was difficult to separate, but obtained it pure by a process depending upon the formation of a tannate and subsequent decomposition by lead oxid. It yielded, upon analysis, results corresponding to the formula $C_{20}H_{34}O_{10}$. Thoms (Ber., 1898, 534) prepared pure strophanthin. Arnaud gave its formula as $C_{31}H_{48}O_{12}$, and his results were confirmed by Kohn and Kulisch; Feist reported $C_{40}H_{66}O_9$. Thoms found that the strophanthins as obtained from different species differed somewhat in composition; he proposes designating them as follows: *k-strophanthin* when obtained from *S. kombe; g-strophanthin* when prepared from *S. gratus; e-strophanthin* when from *S. emini;* and *h-strophanthin* when from *S. hispidus.*

On the properties of strophanthin, see Hardy and Gallois: *J. Pharm. Chim.* (3), *25,* 176, and Fraser: *Pharm. J.,* July 23, 1886. On the physiological action of strophanthus preparations, see Steinach: *Wiener klin. Woch.,* 1888. The local anesthetic action of strophanthin and *Ouabain* (*q. v.*) has been discussed by Panas: *Bull. de l'Acad. de Méd. de Paris,* 1890, No. 7.

Sturmann's Solution.—A local anesthetic containing: Cocain hydrochlorid, 1.0; tincture iodin (decolorized), phenol, āā., 0.3; glycerin, 10.0; water to 100.0; and 2 drops of a 1:1,000 suprarenin hydrochlorid solution are added per c. c.

Subcain.—A solution containing 1 per cent cocain, 0.0065 suprarenin borate, 0.1 per cent salicylic acid, 0.8 per cent sodium chlorid, and eucalyptol.

Subcutin (Subcutol; *Anæsthesinum solubile;* paraphenol sulphonate of anæsthesin; paraphenol sulphonic acid of para-amidobenzoic acid ethyl ester).—A local anesthetic used like *anæsthesin.*

Subcutin.—$\left(C_6H_4\begin{cases}NH_2.SO_3H.C_6H_4OH\\COOC_2H_5\end{cases}\right)$ is a fine, white, needle-shaped crystalline powder, melting at + 195.6° C., and soluble in cold water, 1:100, and in warm water (body temperature), 2.5:100. On contact with the tongue, it produces a sensation of numbness. It is stable in solution and on boiling—an advantage over cocain, which does not keep so well. On the chemistry of subcutin, see Ritsert: *Pharm.-Ztg.*, *54*, 797. The fact that *Anæsthesin* (*q. v.*) is almost insoluble in water and that it therefore is not well adapted for the preparation of media suitable for injection led Ritsert to study a whole group of anesthesin compounds with a view of determining whether any of them was endowed with greater solubility, and yet mild in its action and free from irritating properties. He ascertained that the phenol sulphonate, or subcutin, answered these requirements.

It has been shown that subcutin exerts an inhibitory action on the propagation of the pathogenic micro-organisms of typhoid and cholera. It is said to be free from all untoward by-effects; and it has been demonstrated experimentally that doses such as are not required in major operations are always well tolerated. It may be said, therefore, that subcutin is nontoxic for all practical purposes, especially since experiments on animals demonstrated that 1.6 gm. per kg. of body weight might be administered without danger. See *Anæsthesin*. On subcutin, see especially Becker: *Münch. med. Woch.*, 1903, *50*, No. 20, 857. "Subcutin-mundwasser" is a 2 per cent subcutin solution.

Sulzberger's Local Anæsthetic.—Nathan Sulzberger, in U. S. Patent 949,134, February 15, 1910, announces a local anesthetic, consisting of a 10 per cent solution of cocain in phenyl acetate with a very small percentage of adrenalin. Ethyl acetate and phenyl stearate are also claimed as solvents of menthol or cocain.

Summopon.—This preparation contains the alkaloids of opium (*Chem.-Zentr.*, 1912, *1*, 1672). See *Pantopon*.

Suppositoires Adreno-styptiques.—Each contains 0.00025 gm. adrenalin and 0.2 gm. anæsthesin-stovain. These are used in the treatment of hemorrhoids.

Suprarenal-tonogen.—A water solution of 0.1 per cent suprarenal extract, 0.5 per cent chloretone, and 0.7 per cent sodium chlorid.

Suprarenin.—*o*-Dioxyphenylethanolmethylamin

$$[(OH)_2C_6H_3.CHOH.CH_2.NHCH_3]$$

is a grayish white powder which has a melting point of + 210–212° C. It is a hemostatic and astringent, and is used in combination with various local anesthetics, as, for example, *Novocain* (*q. v.*). Synthetic suprarenin has the same uses; suprarenin borate and hydrochlorid are also used in combination with cocain and other local anesthetics.

Suprarenin-cocain Tablets.—See *Braun's Suprarenin-tabletten*.

Terpentinchlorhydrate.—See *Terpin Hydrochlorid*.

Terpentinkampfer.—See *Terpin Hydrochlorid*.

Terpin Hydrochlorid (Terpinchlorhydrate).—$C_{10}H_{16}.HCl$ is a camphoraceous mass, melting at + 125° C.; it is said to be used as a local anesthetic in combination with phenol.

Tetrachlorethane (Sym.).—Symmetrical tetrachlorethane (acetylene tetrachlorid; "westron"), $C_2H_2Cl_4$, is slightly anesthetic (Clement and Revière: "Caoutchouc et Gutta-percha," 7, 4021); but under the conditions of its use as an extraction material and solvent in factories, its narcotic effects, as well as those of trichlorethylen, which is less active physiologically, are said to be less than those of some of the other solvents (see, on this point, *Chem.-Ztg., 32,* 529).

Tetrahydronaphthalene.—According to Brissemoret (*Compt. rend. Soc. biol., 69,* 497), this compound has a narcotizing power on such warm-blooded animals as the rabbit.

Tetramethyldiaminodimethylethylcarbinol Cinnamate Hydrochlorid.—This is an alypin, in which cinnamic acid takes the place of benzoic acid; it is said to produce an anesthetic effect lasting twice as long as that effected by the same quantity of cocain (Farbenfabriken vorm. Friedr. Bayer & Co., German Patent 173,631).

Thibault's Local Anæsthetic.—In 1907 Thibault suggested the employment of quinin and urea hydrochlorid as a local anesthetic in operations usually performed with cocain.

See *Quinin and Urea Hydrochlorid.*

Thymocain.—This local anesthetic, said to be without toxic action when used subcutaneously, contains about 1 per cent cocain hydrochlorid and 1 per cent sodium chlorid in water solution, also very small amounts of alcohol, thymol, and a suprarenal gland preparation.

Thymoform.—This preparation, intended for use in the treatment of teeth, contains thymol, alum, formaldehyd, and creosote.

Tonocainum Suprarenale Richter.—A sterilized tonogen-eucain solution.

Tonogen Suprarenale Richter.—A solution (1:1,000) of extract of suprarenal gland with an addition of 0.5 per cent of chloretone and 0.7 per cent sodium chlorid.

Townley's Anodyne Mixture.—James Townley ("Parturition Without Pain or Loss of Consciousness," London, 1863) recommended the employment of an anodyne mixture composed of "alcohol, two ounces; one drachm of aromatic tincture; with sufficient chloroform added short of the production of a turbid state of the fluid." The formula of the aromatic tincture was as follows: "One drachm of nutmegs; two drachms of cloves; pterocarp chips, a drachm and a half; water, four ounces; alcohol, five ounces." This mixture was successfully used by Townley in obstetrical practice for the purpose of blunting the sensibility to pain without the abolition of consciousness.

Trichlorethane.—*a*-trichlorethane (monochlorethylene chlorid),

$CH_2Cl.CHCl_2$, is a colorless liquid, boiling at + 37° C. The readiness with which it is formed by the action of potassium hydroxid upon trichlorethane suggested the hypothesis that the anesthetic effects of this last are really attributable to the liberation of dichlorethylene in the blood. This view was advanced by Tauber, of Jena, who experimented with the isomeric trichlorethanes for the purpose of determining their anesthetic value. His observations were made upon frogs, pigeons, guinea-pigs, rabbits, and dogs; a few drops were sufficient to produce complete anesthesia in the smaller animals.

Methylchloroform (mono-chlorethylidene chlorid), $CH_3.CCl_3$.—This was also studied by Tauber. Administered in the form of vapor to frogs and rabbits it produced a satisfactory anesthesia, without any marked effect upon respiration or circulation. Upon himself Tauber experimented by inhaling the vapor of about 20 gm. under the supervision of von Langenbeck. There was no stage of excitement preceding anesthesia; respiration remained undisturbed; the pulse did not exceed eighty-four beats per minute; it was regular, and exhibited no evidence of diminishing blood pressure. Complete anesthesia was reached in five and a half minutes, and it continued for 10 minutes longer. Vomiting occurred soon after the recovery of consciousness, breakfast having been eaten about two hours before the experiment. A feeling of general discomfort persisted for about an hour, after which it disappeared, leaving no unpleasant effects behind. See *Brit. Med. J.*, Nov. 13, 1880.

Trichlorethylene Dichlorid.—See *Æther anæstheticus aranii.*

Trichlorurum Formili.—See *Chloroform.*

Trimethylbenzoxypiperidinum hydrochloricum.—See *Eucain-B.*

Trimethylethylene.—Prepared, according to von Mering (Eng. Pat. 11,844, 1891), from tertiary amyl alcohol by action of water-abstracting agents; claimed by him to be superior to "amylene" from fusel oil. See *Pental.*

Tropacocain or Tropacocain Hydrochlorid (Tropacocainæ Hydrochloridum).—Benzoylpseudotropein hydrochlorid, tropein, tropacocain hydrochlorid [$C_8H_{14}NO(C_7H_5O)HCl = C_{15}H_{19}NO_2.HCl$] is the hydrochlorid of synthetic tropacocain. It was found in 1891 by Giesel (*Pharm.-Ztg.*, 1891, 419) in the leaves of the Japanese coca plant, and subsequently it was examined by Liebermann very accurately (*Ber.*, 1891, 2336; 1892, 927). Liebermann also succeeded in reproducing it by synthesis from its components, and in this manner he obtained a purer and more active preparation than the natural vegetable base. Willstätter (*Ber.*, *29*, 393, 936, 1575, 2216) indicated a method by which benzoylpseudotropeine might be obtained from tropin, and this method was patented and a cheaper preparation was obtained.

Pseudotropin-Liebermann.—Pseudotropin-Liebermann is obtained from tropinon or from tropin by electrolytic reduction, and from this the benzoyl derivative is obtained, and this is converted into the hydrochlorid. It forms colorless, needle-shaped crystals, melting at + 271° C. (519.8° F.). It is readily soluble in water, and its solution keeps well for several months. Heated in the presence of hydrochloric acid, it is split up into benzoic acid and tropin. Its incompatibilities are the same as those of the alkaloids in general.

Benzoylpseudotropein.—Benzoylpseudotropein was tested physiologically by Chadbourne (*Brit. Med. J.*, 1892, 402) soon after its discovery, and it was he who recommended it under the name of tropacocain as a local anesthetic and cocain substitute. He found it to be less than half as poisonous as cocain, and he regarded it in particular as a much milder poison in its action upon muscles and motor centers. Its solutions may be boiled indefinitely for purposes of sterilization.

Tropacocain Hydrochlorid.—Tropacocain hydrochlorid is now employed as a local anesthetic instead of cocain hydrochlorid; the solution is said to be more stable, easily sterilizable, and to have a less depressing action on the heart. It is used in ophthalmology, dentistry, general surgery by the Schleich infiltration method, in regional anesthesia according to Oberst, and in lumbar anesthesia in accordance with Bier's method.

Dosage.—It is applied in 3 to 10 per cent water solutions containing 0.6 per cent sodium chlorid.

On Tropacocain Hydrochlorid, see the following contributions:

Chadbourne: *Therap. Monatsh.*, 1892, 471; *Brit. Med. J.*, 1892, No. 2.

Schweigger and Silex: *Therap. Monatsh.*, 1892, 473.

Pinet and Viau: *Comm. faites à la Soc. d'Ontolog. de Paris.*, Dec. 6, 1892; Jan. 10, 1893.

Hagenschmidt: *Sem. méd.*, 1893, No. 6.

Ferdinands: *Brit. Med. J.*, 1893, 1318.

Groenouw: *Deut. med. Woch.*, 1893, No. 26, 331.

Bockenham: *Sem méd.*, 1893, 526; *Brit. Med. J.*, Nov. 18, 1893.

Veasey: *N. Y. Med. J.*, Nov. 25, 1893.

Seifert: *Internat. klin. Rundschau*, 1893, No. 8.

In 1893 a 3 per cent solution was generally used to produce local anesthesia, and it was observed that stronger solutions, such as a 5 per cent one, under certain circumstances, caused undesirable results.

Vamossy: *Therap. Woch.*, 1896, No. 9.

Hattyasy: *Oest.-ungar. Vierteljahrs. f. Zahnhlkde*, 1896, 161.

Rogman: *Clin. ophthal.*, 1897, Nos. 17 and 19.

Blaskovics: *Pest. méd. chir. presse*, 1896, No. 50.

Dillenz: *Dissertation*, Zürich, 1897.

Custer: *Münch. med. Woch.*, 1898, No. 32.

Braun: *Centralb. f. Chir.,* 1897, No. 17; Volkmann's: *Sammlung klin. Vorträge,* 1898, No. 228.

Hilbert: *Ophthalmiat. Klinik,* 1899, No. 11.

Schmitt: *Rev. méd. de l'Est,* 1898, No. 20.

Brieglieb: *Z. f. praktische Aerzte,* 1899, No. 6.

Dorn: *Odontol. Blätter,* 1899.

Seifert: *Inter. klin. Rundschau,* 1899, No. 8.

Lang: *Gyógyászat,* Dec. 10, 1899.

Albrecht: *Odontol. Blätter,* Apr., 1899.

Bloch: *Centralb. f. d. gesammte Therap.,* 1900, No. 1.

Bauer: *Oest.-Ungar. Vierteljahrs. f. Zahnheilk.,* Apr., 1900.

Zander: *Deut. zahnärztl. Woch.,* 1900, No. 128.

Vennerholm: *Z. f. Thiermedizin,* 1900, 164.

Schwarz: *Centralb. f. Chir.,* 1901, No. 9, 248.

Meyer: *Med. News,* Apr. 13, 1901.

Neugebauer: *Wien. klin. Woch.,* 1901, Nos. 50 and 52.

The last three authors advocated the preparation for medullary anesthesia by Bier's method.

Kopfstein: *Wien. klin. Rundschau,* 1901, No. 49.

Saum: *Deut. zahnärztl. Woch.,* 1901, 156.

Reissenbach: *Deut. zahnärztl. Ztg.,* 1901, No. 5.

Bloch: *Wien. zahnärztl. Woch.,* 1901, Nos. 2 and 3.

Deak: *Magyar Fogaszati Szemle,* 1901, No. 2.

The last four authors unanimously praised the prompt anesthetic properties of the preparation in extractions of teeth.

Annin: *Wratsch,* 1901, No. 11, 346.

Annin used the preparation successfully in ophthalmic surgery.

Schwarz: *Münch. med. Woch.,* 1902, No. 4.

This author reported on over 100 cases of medullary analgesia by Tropacocain.

Illing: *J. Am. Med. Assn.,* 1901, No. 12.

Neugebauer: *Münch. med. Woch.,* 1902, No. 44, 1862.

Kozlowsky: *Przeglad lekarski,* 1902, No. 4.

Kamann: *Münch. med. Woch.,* May 20, 1902.

Schleich: *Deut. Klinik,* 1902, 22.

Mobilio: *Archivio d'oftalmologia,* Sept. and Oct., 1902.

Fuchs-Gölding: *Zahnärztl. Rundschau,* 1902, No. 499.

Vogt: *Oest.-Ungar. Vierteljahrs. f. Zahnheil.,* 1902, No. 1.

Loves: *Die Zahnkunst,* 1902, No. 26.

The last three authors used the preparation with advantage in dentistry, for the production of local anesthesia during extractions.

Preindlsberger: *Wiener med. Woch.,* 1903, No. 34.

This author confirmed the observations recorded by Neugebauer and others on the application of the preparation in the method of anesthesia of the spine.

Bloch: *Deut. med. Woch.*, 1903, No. 24; *Ver. Beil.*, 188.

Triesch: *Bericht über die 31. Hauptversammlung hessicher Zahnärzte*, 1902; *Odontol. Blätter, 7,* Nos. 15-17.

Triesch used 5 per cent injections of tropacocain in dentistry, being thus able to induce a satisfactory anesthesia. He found that although the action of tropacocain was less prompt than that of cocain, it had the advantage over the latter in being less poisonous and dangerous.

Rydygier: *Przeglad lekarski*, 1904, No. 7.

This author reported on the success which attended the application of tropacocain as an anesthetic for the spinal cord by Kozlowski's method in 49 cases treated at the Lemberg Hospital.

Stolz: *Archiv f. Gynäkol., 73,* No. 3.

Stolz summarized the results of his large experience in connection with the anesthesia of the spinal cord as applied to gynecology and obstetrics.

Bellandi: "L'Analgésie chirurgicale par voie rachidienne au moyen de la tropacocaine," Alexandrie, 1903.

Levy: *Deut. zahnärztliche Woch.*, 1904, No. 18.

Matthes: *Ibid.*, 1904, No. 11.

Preindlsberger: *Versammlung deut. Naturforscher und Aerzte in Meran*, 1905; *Allg. med. Zentral-Ztg.*, 1905, No. 42, 808; and *Wiener klin. Woch.*, 1905, No. 26.

Trautenroth: *Deut. med. Woch.*, 1906, 253.

The last two authors described tropacocain as preferable to stovain in connection with the anesthesia of the spine.

Franceschi: *Allg. med. Zentral-Ztg.*, 1905, No. 42, 809, and No. 43, 827. *Klin.-therap. Woch.*, 1906, No. 41; *Münch. med. Woch.*, 1906, 1933.

Koder: *Wiener med. Woch.*, 1905, No. 37, 1781.

Colombani: *Wiener klin. Woch.*, 1905, No. 21, 538.

Foster: *Beitr. zur klin. Chir.*, 1905, *46,* No. 1.

Zahradnicky: *Wiener med. Ztg.*, 1905, No. 5, 55.

Karas: *Wiener med. Woch.*, 1905, Nos. 20 and 21.

Völker: *Monats. f. Geburtshilfe und Gynäkol.*, 1905, No. 4; *Münch. med. Woch.*, 1905, No. 33, 1612.

Ribolla: *Stomatologia*, 1905, No. 3.

Ribolla secured excellent results by the use of tropacocain as a local anesthetic in dental operations.

Becher: *Dissertation*, Giessen, 1905.

Becher demonstrated the remarkable efficacy of tropacocain in medullary application to animals.

Slajmer: *Wiener med. Presse,* 1906, Nos. 22 and 23.

This author was of the opinion that even anesthesia by inhalation could not compete with tropacocain anesthesia. His operations included 1,200 cases.

Schwarz: *Wiener klin. Woch.,* 1906, No. 30; *Presse méd.,* 1906, No. 64.

Arlt: *Münch. med. Woch.,* 1906, No. 34.

Baisch: *Deut. med. Woch.,* 1906, No. 38.

Baisch combined tropacocain anesthesia with scopolamin-morphin hypnosis for gynecological operations, and the method was found to present various advantages.

Müller: *Monats. f. Geburtshilfe und Gynäk.,* 1905, No. 2.

Dönitz: *Münch. med. Woch.,* 1906, No. 28.

Kocher: *Wiener med. Presse,* 1906, 1039.

Kümmell: *Med. Klinik,* 1906, No. 43, 1120.

According to Kümmell, tropacocain proved, in the Eppendorf General Hospital of Hamburg, to be the best and the least poisonous, easy to sterilize, and a constant anesthetic.

Bier (*ibid.*) expressed the opinion that the dangers of spinal analgesia were due to the selection of unsuitable drugs. In 1906, he announced that he considered that tropacocain was the most suitable preparation.

Ach: *Münch. med. Woch.,* 1907, No. 33, 624.

Ach described the results of lumbar anesthesia in 400 cases. He concluded that, of the drugs recommended for lumbar puncture, the least harmful, namely, tropacocain, should be selected.

Thorbecke: *Med. Klinik,* 1907, No. 14, 386.

Gallatia: *Gynäkol. Rundschau,* 1907, No. 11.

Bosse: *Deut. med. Woch.,* 1907, No. 5.

Goldschwend: *Wiener klin. Woch.,* 1907, No. 37, 1098.

This author had very satisfactory results with tropacocain, even in the most serious laparotomies.

Masotti and Angeletti: *Revista Veneta di scienze mediche, 47,* Nos. 8 and 9; *Deut. Med. Ztg.,* 1908, No. 14, 149.

Remenar: *Wiener klin. Woch.,* 1907, No. 45, 1397.

Gilmer: *Münch. med. Woch.,* 1907, No. 38, 1904.

Baum: *Ibid.,* 1905.

Seitz: *Ibid.,* 1905.

Preindlsberger: *Wiener klin. Rundschau,* 1907, No. 46.

Valenta: *Gynäkol. Rundschau,* 1908, No. 1.

The eight authors last mentioned gave favorable accounts of tropacocain and its lumbar use.

Bloch: *Heilkunde,* 1906, No. 2.

Bloch reported on the employment of tropacocain in general medical practice. He found it to be a never-failing remedy in ophthalmic and dental practice.

Erhardt: *Woch. f. Tierheilk.*, 1908, Nos. 27 and 28; *Münch. med. Woch.*, 1908, Nos. 19 and 26.

Erhardt found that the addition of 3 per cent gum acacia to a 1 per cent solution of tropacocain diminished the toxicity of the anesthetic in lumbar anesthesia. See *Erhardt's Solutions.*

Dönitz: *Münch. med. Woch.*, 1908, No. 32.

Strauss: *Med. Klinik*, 1908, No. 6.

Masotti and Angeletti: *Revista Veneta di scienze mediche*, 1908, No. 6.

Saggini: *Giornale di medicina militare*, Apr., 1908.

Hartleib: *Münch. med. Woch.*, 1908, No. 5.

Valenta: *Gynäkol. Rundschau*, 1908, No. 1.

Remenar: *Wiener klin. Woch.*, 1908, No. 45.

Tomaschewski: *Deut. med. Woch.*, 1908, No. 51.

Klein: *Münch. med. Woch.*, 1908, No. 47.

The last eight contributions relate to the use of tropacocain in spinal anesthesia.

Colombani: *Wiener klin. Woch.*, 1909, No. 39, 1336.

Colombani gave a detailed report of 1,100 cases of spinal anesthesia, showing that tropacocain afforded excellent results.

Slajmer: *Med. Blätter*, 1909, No. 47.

Rieck: *Zentralb. f. Gynäkol.*, 1909, No. 41, 1429.

Klose and Vogt: *Mitteil. aus den Grenzgebieten der Med. und Chir.*, *19*, No. 5; *Zentralb. f. innere Med.*, 1909, 965.

The last paper was the result of an experimental investigation on spinal anesthesia.

Heinz: *Wiener med. Woch.*, 1910, No. 37.

Slajmer: *Beitr. zur klin. Chir.*, 1910, 67.

Arlt: *Münch. med. Woch.*, 1910, No. 28.

Morrison: *Lancet*, Sept. 10, 1910.

The last four papers relate to lumbar anesthesia induced with tropacocain.

Budde: *Deut. militärärztl. Z.*, 1911, No. 4, 168.

Gros: *Riedel's Mentor*, 1911, 44.

Tropein or Tropeine.—See *Tropacocain.*

Turpentine.—Turpentine oil was proposed as an anesthetic by Nunneley in 1849. It has been used in emergencies with success; it has also been added to chloroform to prevent collapse. Richardson (*Sci. Am. Suppl.*, No. 516, 8240) found that the vapor of turpentine was irritating at first and difficult to breathe, but that it was productive slowly of deep anesthesia, accompanied with convulsive rather than tetanic movements. Recovery was slow, as if from deep intoxication. Richardson regarded its anesthetic value as indifferent. See *Wachsmuth's Mixture,* and also *Apinol.*

Udrenin.—A local anesthetic containing beta-eucain and adrenalin. According to "Riedel's Mentor," 1912, 208, udrenin contains, per c. c., 0.01 gm. beta-eucain hydrochlorid and 0.00003 gm. adrenalin hydrochlorid in physiological salt solution, with the addition of 0.5 per cent chloretone as a preservative. This combination is mentioned by Coblentz ("The Newer Remedies," 4th ed., 128), but he unmistakably refers to *Eudrenin, q. v.*

Urea Hydrochlorid.—See *Quinin and Urea Hydrochlorid* and *Thibault's Local Anæsthetic.*

Urethane.—Urethane (Ethyl Carbamate; Ethylurethane),

$$CO\begin{cases} NH_2 \\ OC_2H_5 \end{cases}$$

is well known as possessing a rapid hypnotic action, although not sufficiently powerful for use in cases where there is pain or distress. Hübner and Sticker tried urethane on man, and Mairet and Combemale on animals, but were unable to show that it possessed a reliable hypnotic action. Nerking and Schürmann (*Med. Klinik,* 1908, No. 46) subsequently tested the preparation to ascertain its value as an anesthetic, assuming that urethane was split up in the organism into urea and the ethyl group. The intravenous application of 5 to 10 c. c. of a 20 per cent solution of urethane gave no positive result in rabbits, and it consequently seemed doubtful whether anesthesia could be obtained by the aid of urethane alone. Satisfactory results were obtained, however, with the combination of urethane and chloral hydrate. Nerking and Schürmann used a 20 per cent solution of urethane and a solution of chloral hydrate 5:10, suitable doses being injected intravenously. *These trials effected a quiet, safe anesthesia,* with complete abolition of sensation; but so far, to our knowledge, trials of this method have not been made on man. Hauckold (*Z. f. exper. Path. u. Therap.,* 1910, 7, No. 3, 743) studied the effect of scopolamin on the action of urethane, and ascertained by experiments that scopolamin, which does not by itself produce anesthesia in rabbits, had a considerable effect in enhancing the anesthetic properties of urethane. Small quantities of urethane, which would not by themselves produce anesthesia, showed a narcotic action by means of a minimal dose of scopolamin. The latter was also found to possess a similar action in combination with morphin.

Urosemin.—This local anesthetic is a 1 per cent solution of uric acid in 2 c. c. of water, with the addition of 1 c. c. of *Ensemin* (*q. v.*), and 0.00005 gm. of adrenalin hydrochlorid.

On urosemin, see Mannich and Schwedes: *Apoth.-Ztg.,* 1912, 351; Wolfer: *Med. Klinik,* 1912, 1581.

Valerene.—See *Amylene.*

Vanodrin.—This dental anesthetic contains 0.015 gm. novocain and 0.0001 gm. adrenalin hydrochlorid in 1 c. c.

Vienna Anesthetic.—A mixture of alcohol, 12 parts by weight; chloroform, 77 parts by weight; and ether, 11 parts by weight.

Vienna Elizabeth Hospital Mixture.—See *Wertheim's Mixture.*

Vienna General Hospital Mixture.—Alcohol, 9 parts; chloroform, 30 parts; and ether, 9 parts. On this mixture, see Potter: "Mat. Med. Pharm. and Therap.," 10th ed., 88.

Vienna Mixture.—A mixture, introduced about 1856, of 8 parts of ether and 1 part of chloroform in hot weather; and 6 parts of ether and 2 parts of chloroform in cold weather. See *Sci. Am. Suppl.,* No. 516; also, Richardson: "Asclepiad," 1885, 274. According to Hewitt "Anæsthetics and Their Administration," 3rd ed., 466), Vienna mixture is composed of chloroform, 1 part, and ether, 3 parts. According to Müller ("Narkologie," 492), Vienna mixture is composed of chloroform 3 parts and ether 1 part.

Viferral.—See *Polychloral.*

Vinyl Trichlorid.—See *Ethylene (monochloro-) Chlorid.*

Vinyldiacetonalkamin.—Schering (Eng. Pat., 20,697, 1896) claimed that the vinyldiacetonalkamin of Fischer was a mixture of two bases, and that its derivatives might be employed as anesthetics.

Wachsmuth's Mixture.—A mixture of chloroform, 4 parts, and oleum terebinth., 1 part. "To prevent syncope." Müller, "Narkologie," 1, 493. See *Turpentine,* and cf. *Apinol.*

Waite's lokaler Schmerztöter.—An anesthetic for minor operations, said to be a water solution of cocain, iodin, thymol, and glycerin, containing only cocain and creosote in glycerinized water (*Gehe's Codex,* Nov., 1910, 382).

Water.—On water as a local anesthetic, see Wyeth: *N. Y. Med. J.,* Jan. 6, 1906. Water has been employed as a local anesthetic (pressure anesthesia) in dentistry and in certain minor surgical cases. It is no doubt true that the anesthetic action of certain compounds is solely attributable to the pressure anesthesia produced by hypodermic injection of the solution.

Welt-Anæsthetikum (Universal Anesthetic).—A dental local anesthetic containing adrenalin hydrochlorid, sodium chlorid, chloretone, cocain hydrochlorid, menthol, eucalyptol, and distilled water.

Wertheim's Mixture.—This is a mixture of chloroform, 1 part; ethyl ether, 2 parts; and benzin or canadol, 1 part. It is a modification of Schleich's mixture and is often referred to as *Vienna Elizabeth Hospital Mixture.* Wertheim's solution or mixture was used by Williams (*Trans. Soc. Anesth., 4,* 98). Silk's experience (*Ibid., 5,* 138) led him to believe that the petroleum ether contained in it was inoperative, so that the solution was practically one of ether and chloroform. As such he considered that it had some merits.

"Westron."—See *Tetrachlorethane.*

Wigger's Anesthetic Ether.—See *Ethyl Chlorid Polychlorated.*

Wilson's Local Anesthetic.—A water solution, of which 100 parts contain 7.5 per cent alcohol, 0.05 per cent boric acid, 0.05 per cent benzoic acid, 0.75 per cent cocain hydrochlorid, 1.0 per cent nitroglycerin solution (1:100), 0.05 per cent naphthol, and 2 drops of a mixture of equal parts of oils of eucalyptus, peppermint, gaultheria, and thyme.

Yohimbin.—This is claimed to be a local anesthetic for eye and nose practice. It is, however, best known as an aphrodisiac. Yohimbin hydrochlorid ($C_{22}H_{28}O_3H_2.HCl$) is a white crystalline powder, having a melting point of + 288-290° C. For a full study of the pharmacodynamic properties of yohimbin, see Müller: *Archives internat. d. pharmacol. et d. thérap.*, 1907, 65; *Archiv f. Anat. und Physiol.*, 1907, 391; Franz: *Med. Klinik*, 1907, No. 34, 1027. Müller showed that the action of yohimbin depended chiefly on its influence on the walls of the vessels, and that, even when applied locally, the action was vasodilating and anesthetic. Large doses were found to produce a continued fall of blood pressure, and lethal ones to paralyze the heart also by injuring the cardiac muscle. Holterbach (*Berl. tierärztl. Woch.*, 1907, No. 32; *Deut. tierärztl.* Woch., 1907, Nos. 13 and 14) points out that the anesthetic action of yohimbin may be said to be recognized. On the comparative effects of yohimbin, protoveratrin, and veratrin on isolated muscle and nerve, see Waller: *Proc. Physiol. Soc.*, 1910, xi-xiv; *J. Physiol.*, 41, xi.

On the anesthetic action of yohimbin, see the following papers:

Löwy and Müller: "Zur Kenntnis der anästhesierenden Wirkung des Yohimbin," *Münch. med. Woch.*, 1903, No. 15.

Magnani: "Zur anästhesierenden Wirkung des Yohimbin," *ibid.*, 1903, No. 5.

Magnani: "Un nuovo alcaloide anestetizzante la congiunctiva e la cornea," *La clinica moderna*, 1902, No. 35.

Oberwarth: "Ueber Yohimbin," *Virchows Archiv, 153*, 292.

Yohydrol.—"Yohydrol" is a proprietary name for a *Yohimbin Hydrochlorid* (*q. v.*) of German manufacture.

Zeuner's Halspastillen; Zeuner's Hustenpastillen. These contain *Anesthesin* (*q. v.*).

Zykloform.—See *Cycloform.*

CHAPTER XXI

STATISTICS

INTRODUCTION.

COLLATERAL INFORMATION: Local Anesthesia; Nitrous Oxid Alone or with Air; Nitrous Oxid with Oxygen; Anesthol-Ether Sequence; Chloroform-Ether Sequence; Nitrous Oxid-Ether Sequence; Anesthol; Ether, Drop or Vapor; Ethyl Chlorid-Ether Sequence; Ethyl Chlorid; Chloroform-Oxygen; Chloroform, Drop or Vapor; Intratracheal Anesthesia; Oil of Bitter Orange Peel-Ether Sequence; Comparison of American Statistics for 1905-1911 with Those for 1892; Comparison of American with European Statistics; American Statistics, 1905-1912, Inc.

CONCLUSIONS.

INTRODUCTION

In March of 1911, circulars were sent out to all the public hospitals with not less than ten beds in the United States, Canada, Cuba, and the Canal Zone. Ninety-nine hospitals, widely separated (in forty States, Canada, and the Canal Zone), furnished the facts on which these statistics are based. The data given by these ninety-nine hospitals may be considered as fairly representative of statistics from American hospitals in general. In New York City two large hospitals (St. Luke's Hospital and the German Hospital) had statistics from an anesthetic standpoint immediately available. We feel that hospital administration should require that accurate data as to the anesthetics used should be kept on file, as well as other information.

The Army and Navy officials sent replies by return mail, showing that these statistics are kept on file as are others.

A careful study of the Army and Navy statistics will amply repay one. (Page 842.)

It is a remarkable fact that the only two fatalities that occurred in the naval service were under ether.

The location of the four chloroform fatalities mentioned in Table 2 is unknown.

The third table on page 843 includes the Army and Navy statistics. The anesthetics are placed according to their value as regards life. The

TABLE 1.—THE UNITED STATES NAVY FOR THE YEARS 1908–1910

Anesthetic	Number	Deaths
Ether	2,218	2
Ether (rectal)	2	..
Ether, morphin and scopolamin	40	..
Ether and nitrous oxid	140	..
Ether and chloroform	2	..
Ethyl chlorid (general)	16	..
Ethyl chlorid and ether	24	..
Ethyl chlorid and chloroform	2	..
Chloroform	365	..
Cocain	91	..
Cocain and ethyl chlorid (local)	3	..
Cocain and epinephrin	3	..
Beta-eucain and epinephrin	4	..
Eucain	1	..
Novocain	4	..
Novocain and epinephrin	4	..
Schleich's solution No. 2	2	..
Total	2,921	2

TABLE 2.—ANESTHETICS USED IN SURGICAL OPERATIONS PERFORMED ON OFFICERS AND ENLISTED MEN OF THE ARMY FOR THE YEARS 1904–1910

Year	Chloroform No.	Ether No.	Chloroform and Ether No.	Spinal No.[1]	Local No.
1904	835	878	....	....	1,096
1905	713	806	83	60	1,070
1906	684	861	73	....	1,234
1907	571	831	37	29	1,270
1908	497	965	67	9	1,652
1909	335	1,326	100	....	1,873
1910	296	1,513	55	....	1,793
Total	3,931	7,180	415	98	9,988

[1] The agents used in spinal analgesia were tropacocain and beta eucain. Four deaths were due to the anesthetic (chloroform) in all the cases.

number to the left of each anesthetic refers to the relative frequency of their administration.

These statistics speak for themselves. The following remarks are based upon collateral information obtained with the numerical data.

The total number of administrations from the ninety-nine hospitals was 278,945.

TABLE 3.—American Statistics

Anesthetic	1905	1906	1907	1908	1909	1910	1911	Total	Deaths	Percentage
5. Local anesthesia	1,422	1,882	1,881	2,462	2,458	2,611	2,092	14,878	0	0–14,878
6. Nitrous oxid with oxygen	144	175	335	881	1,619	2,130	3,301	8,585	0	0– 8,585
10. Anesthol-ether anesthesia	152	406	435	584	559	772	919	3,827	0	0– 3,827
13. Ethyl chlorid-drop sp	67	102	133	97	115	136	255	905	0	0– 905
14. Nitrous oxid with air	51	90	......	40	90	......	290	561	0	0– 561
15. Spinal analgesia	66	43	86	64	34	63	165	521	0	0– 521
18. Anesthol-ether-chloroform	......	17	52	27	18	39	......	153	0	0– 153
19. Anesthol-chloroform	......	......	......	67	28	28	......	123	0	0– 123
20. Nitrous oxid, ether-anesthol	......	......	75	16	14	9	.....	114	0	0– 114
21. Oil orange-ether seq	......	......	......	......	......	......	100	100	0	0– 100
22. $A_1C_2E_3$ or C_2E_3 mixture	2	2	......	......	......	6	85	95	0	0– 95
23. Ether-chloroform, sequence	3	18	10	1	15	13	34	94	0	0– 94
24. Nitrous oxid anesthol	......	32	8	......	3	2	......	45	0	0– 45
25. Ethyl chlorid-anesthol	......	25	2	......	......	14	......	41	0	0– 41
26. Anesthol-oxygen	15	......	16	......	......	4	2	37	0	0– 37
27. Ethyl bromid-anesthesia	12	8	......	......	......	......	......	20	0	0– 20
28. Ethyl chlorid-oxygen	......	......	......	......	1	2	10	13	0	0– 13
29. M-H-C- anesthesia	......	......	9	......	......	......	......	9	0	0– 9
4. Chloroform-ether sequence	756	1,374	1,770	1,641	3,022	3,804	3,687	16,054	2	1– 8,027
2. Nitrous oxid-ether sequence	2,359	2,576	4,147	4,991	11,274	6,703	9,385	41,435	6	1– 6,905
7. Anesthol	1,132	880	956	1,271	782	648	470	6,139	1	1– 6,139
1. Ether, drop or vapor	7,523	12,279	15,154	19,322	23,049	26,145	53,981	157,453	28	1– 5,623
8. Ethyl chlorid-ether sequence	199	169	467	477	872	1,135	1,012	4,331	1	1– 4,331
9. Chloroform-oxygen	401	472	664	673	461	660	678	4,009	1	1– 4.009
3. Chloroform, drop or vapor	3,048	2,557	2,532	2,339	1,910	2,080	1,924	16,390	8	1– 2,048
11. Nitrous oxid	111	84	203	216	198	203	296	1,314	2	1– 657
16. Rectal anesthesia	......	......	......	60	129	152	175	516	1	1– 516
12. Intratracheal insufflation	......	......	......	......	......	......	1,000	1,000	4	1– 250
17. Nitrous oxid - ether - chloroform anesthesia	4	......	......	7	12	20	140	183	1	1– 183
								278,945		

COLLATERAL INFORMATION

Local Anesthesia.—It will be noted that local anesthesia is first in the list, with a total of 14,878 administrations with no deaths. It is safe to presume that very few of these were for major operations. We have knowledge of two deaths from local anesthesia, both occurring in private practice. In one case, a laparotomy, the patient died of pneumonia within four days of the operation; in the second, external urethrotomy, the patient died from psychic shock. The latter accident was an avoidable one. If the patient had been properly prepared, and had been given a preliminary hypodermic of morphin, the psychic element would in all probability have been removed.

Local anesthesia deserves more consideration, both for major and minor operations.

Nitrous Oxid Alone or with Air.—Nine-tenths of the small mortality under nitrous oxid has occurred when the gas was administered either alone or diluted with air. Hewitt gives a list of thirty reported deaths between 1860 and 1900. No statistics are to be had as to the number of administrations during that time, but the proportion of deaths is given by different writers as from one in 100,000 to one in 500,000. We are inclined to believe that both of these estimates are wrong. One death in 20,000 would be more nearly correct. Even if this statement is true, it would still make nitrous oxid the safest pulmonary anesthetic now in general use. All deaths noted were reported as resulting from asphyxiation, the patient exhibiting some one of the following characteristics: (1) Narrowed air passages by enlarged tonsils, deformed jaw, or fixed morbid growth. (2) Very strong, having good muscular control. (3) Obesity, or enlarged, fixed tongue or uvula. (4) Alcoholic.

Twenty-two of the thirty were dental operations and four surgical. The other cases were indefinite. All of these patients were predisposed to asphyxial symptoms. The athletic alcoholic is the most difficult of all patients with this form of anesthesia.

Nitrous Oxid with Oxygen.—Nitrous oxid with oxygen has 8,585 administrations in the foregoing table, with no deaths. This combination rightfully holds its place as the safest of all pulmonary anesthetics, not only according to American statistics, but also in all other available statistics. That it is not totally devoid of danger is attested by the deaths following its administration reported from time to time in the medical press.

The statistics for dental administrations should not be combined with those of general surgery. We have no hesitation in stating that one death in a million cases, as reported by Hare, will not hold for surgical cases. One death in ten thousand is a fair estimate for this combination in America.

While nitrous oxid with oxygen is unquestionably the safest anesthetic now known, the only likelihood of death being by asphyxiation, yet there are patients who will reach the asphyxial stage before reaching surgical anesthesia; or, surgical anesthesia having been induced, the asphyxial point is so very near the plane of surgical anesthesia that, with some subjects, it is an ever-present danger. The same patients that are pronounced difficult or dangerous with nitrous oxid and air, while easier to anesthetize with nitrous oxid and oxygen, form the most dangerous and difficult class of patients for this combination.

No deaths attributable to the anesthetic were reported for a long while, but as nitrous oxid and oxygen became more commonly used for long operations, deaths have been and are being reported from time to time. Unfortunately, surgeons and anesthetists make use of this anesthetic without studying its previous history, its peculiarities, indications, and contraindications. It is known that few surgeons have the courage to report deaths under anesthesia, especially those occurring in private practice. This was not the case with Lydston,[1] of Chicago, who made the first report of death by nitrous oxid and oxygen. The mistakes in this case should be helpful in enabling others to avoid similar errors in the future.

The first mistake was in not giving preliminary medication.

The second, in commencing the operation before full surgical anesthesia had been established long enough to insure obtunding of the reflex mechanism.

The third, in the surgeon or anesthetist not being prepared for a tracheotomy in case of accident.

The following case is reported by Teter. He gives a detailed report showing that the anesthetic was not the primary cause of death, but, if the theories of Yandell Henderson and Gatch are correct, this death may have been due to too much aeration of the lungs.

"*Case 7. Patient*—Mrs. M., aged 60, had been vomiting for over a month and was in an exhausted condition from starvation. The cause of her trouble was very obscure and symptoms were lacking. Gall-stones were finally diagnosed. Owing to her extremely exhausted condition an operation was considered hazardous but imperative. The persons interested were aware of the likelihood of a fatal termination, so were prepared in a way for what followed. I found a very weak, thready, irregular pulse, running at the rate of 150, and hardly perceptible in the radial artery.

"*Anesthesia.* The anesthetic was started with 95 parts nitrous oxid and 5 parts oxygen. The oxygen was increased rapidly up to 10 parts.

[1] Lydston, Frank: *Med. Rec.*, Nov. 12, 1910; Feb. 11, 1911.

The patient was found to be fully anesthetized after she had taken about eight inhalations. It was necessary to increase the oxygen to 20 parts or more to prevent too deep anesthesia. There was a peculiar livid appearance in the face, but there was no cyanosis or any indication of anoxemia. The respiration being unhampered and regular, the pulse was about as rapid as at the beginning, but was of better tension and more regular.

"*Operation.* This was begun within two minutes. There was no noticeable alteration in either respiration or circulation when the incision was made. The corneal reflex was abolished from the time anesthesia was noticed to be present. It was necessary to increase the oxygen and diminish the nitrous oxid greatly to prevent an overdose of the anesthetic. By the continued application of the phonendoscope the heart was found to be acting fairly well. Everything was going along nicely until work was begun in the cystic duct and gall bladder; then respiration became uneven and forced, and the heart sounds were barely discernible. The operation had been in progress for fifty-five minutes. There was no cyanosis present in the face and oxygenation seemed to be perfect, but it was noticed that the fingers of the patient were blue. This blueness gradually crept up the hands and arms, and as a large increase of oxygen and the discontinuance of the nitrous oxid did not remedy the condition, we at once used pure oxygen, atropin, strychnin, but with no results, as the pulse and respiration ceased.

"Artificial respiration and lung inflation with pure oxygen and other resuscitating measures were carried out for forty minutes without a sign of reanimation. This death was due to shock and primary cardiac failure. The anesthetic was blamable only in so far as it added its influence in bringing about a lower resistance of the organism."

Crile reported one death (the third) six hours after the operation, and attributed the death partly to the anesthetic and partly to imperfect technique and administration.

The fourth case was reported from Johns Hopkins University.

One of the authors was told of a death occurring when nitrous oxid was administered by a reliable dentist in New York City, but in such a way that it is impossible to make a detailed report upon this case.

Unquestionably deaths occur under this anesthetic, as with others, that are never reported. These statistics are compiled only from reliable data given from hospitals.

Albert Miller, of Providence, R. I., has collected references to eighteen deaths under nitrous oxid with oxygen. The list given below includes those just reviewed:

Teter: "Shock and Primary Cardiac Failure," *J. Am. Med. Assn.*, Aug. 7, 1909, 643; Crile: "Myocarditis, Six Hours after Operation," *Southern Med. J.*, Jan., 1910, 29; Lydston: "Anesthetic," *Med. Rec.*, Nov. 12, 1910, 866; Allen: "Uremia," *Boston Med. and Surg. J.*, Oct. 19, 1911, 589; Allen: *Ibid.*, no details; Gatch: "Hyperthyroidism," *J. Am. Med. Assn.*, Nov. 11, 1911, 1593; Gatch: "Pericardial Effusion," *Ibid.;* Gatch: "Lymphatic Diathesis," *Ibid.;* Olow:[1] "Diseased Arteries," *Beitr. klin. Chir.*, Dec., 1911; Boys: "Anesthetic," *Surg. Gynec. and Obstet.*, Apr., 1912, 388; Miller: "Suffocation from Inspired Vomitus," *J. Am. Med. Assn.*, Nov. 23, 1912, 1847; Flagg: "Anesthetic," *N. Y. J. Med.*, Nov., 1912; Teter: "Impure Gas," *J. Am. Med. Assn.*, Nov. 23, 1912, 1861; Salzer: "Anesthetic," *J. Am. Med. Assn.*, Nov. 23, 1912, 1872; Collins: "Impure Gas," *J. Am. Med. Assn.*, Nov. 23, 1912, 1862; Buchanan: "Anesthetic," *J. Am. Med. Assn.*, Nov. 23, 1912, 1860.

Anesthol-Ether Sequence.—Anesthol-ether is the next safest combination, no deaths being recorded in 3,827 administrations.

Chloroform-Ether Sequence.—Chloroform-ether comes next in the point of safety, having one death in 8,027 administrations.

As these two sequences are practically identical, we will consider them together.

Anesthol-Ether and Chloroform-Ether Sequences.—The anesthol-ether statistics were taken principally from the German Hospital, in New York City, where morphin and atropin, or some similar combination, is administered. The fact that 59 per cent of the hospitals in the United States give preliminary medication before all anesthesias suggests the possibility that the majority of the chloroform-ether anesthesias reported were preceded by morphin also. This preliminary medication is here an important point. It is a factor of safety that should never be omitted when the anesthesia is started in this way. If we precede the anesthol or chloroform with a few drops of the oil of orange, as outlined in the practical part of this volume, another factor of safety is added. That these two sequences are so comparatively safe, is readily understood when the physiology of this method of initiation is considered. Bearing in mind the two factors of safety just mentioned, and continuing the narcosis drop by drop, the blood pressure and pulse are kept more nearly normal than when the nitrous oxid-ether sequence or ether by the drop is used.

When the excitement stage (which should be evidenced only by deep breathing) is passed, a switch being then made to ether by the open

[1] The case reported by Olow in *Beitr. z. klin. Chir.*, Dec., 1911, seems to have been reported by him again as another case in *Surg. Gynec. and Obstet.*, April, 1912. Of the other cases to which he refers in the same article, that of Adams (*Lancet*, Mar. 24, 1894) is included in Hewitt's list of deaths under nitrous oxid ("Anæsthetics," 2nd ed., 228, *Case 10*), and that of Owen (*Brit. Med. J.*, Dec. 17, 1914) was a death under nitrous oxid for a dental operation, and not under nitrous oxid with oxygen.

drop method, there is very little likelihood of plunging the patient into the danger zone, and it is a comparatively easy matter to maintain an even plane after anesthesia is induced in the manner outlined.

Nitrous Oxid-Ether Sequence.—The nitrous oxid-ether sequence comes next with one death in 6,905 cases. While both blood pressure and pulse are enormously raised with this method of initiation, the principal danger seems to be from asphyxia. In the hands of one who has acquired the technique, and in selected cases, it is an ideal initiatory anesthetic. In the hands of inexperienced internes, and as a routine, it is *not* a pleasant sight to witness.

Anesthol.—While anesthol is comparatively safe, as shown by the table, it is being rapidly discarded as the *terminal* anesthetic. The physiological action of both chloroform and ethyl chlorid upon the tissues fully warrants this.

Ether, Drop or Vapor.—Ether, drop or vapor (principally drop), while coming next in point of safety with one death in 5,623 administrations, is first in the total number of administration.

When we consider these two factors, together with the rapid and steady increase in its administration and its wider latitude of safety as compared with all other anesthetics, we are justified in stating that if other anesthetics were used proportionately and as indiscriminately this anesthetic would probably take the first place as regards immediate safety.

Ethyl Chlorid-Ether Sequence.—The ethyl chlorid-ether sequence comes next with one death in 4,331 administrations. The use of this sequence is on the increase, but it showed a slight loss from 1910 to 1911. It does not compare in point of safety with the nitrous oxid-ether sequence, according to these figures, and yet it is almost unanimously conceded to be safer for children than "gas-ether."

Ethyl Chlorid.—The statistics of ethyl chlorid, used alone, present widely divergent figures. One author gives the death rate as 1 in 17,000 administrations, another as 1 in 12,000, while others, reporting "considerable experience," have seen no deaths from its use. No one places this agent above nitrous oxid in safety; many question its rank as compared with ether and chloroform; while others enthusiastically predict the displacement of the two last-named agents by ethyl chlorid for long surgical operations.

Perhaps the most formidable array of figures concerning ethyl chlorid are the statistics compiled by Wood,[1] covering over 51,507 cases, with a mortality of 1 in 5,710. In statistics covering over 1,000,000 cases, Wood found a mortality of 1 in 15,000 with ether, and 1 in 3,000 with chloroform. If these statistics are accepted, ethyl chlorid falls between chloroform and ether. Wood considers ethyl chlorid as being

[1] Wood, A. C.: *J. Am. Med. Assn.*, 1910, *55*, 2229.

two hundred times as dangerous as nitrous oxid, this estimate being based upon the statistics of nitrous oxid, which are given as 1 death in 1,000,000 cases. This computation, doubtless based largely upon the use of nitrous oxid in dentistry, thus involving a much larger proportion of very short operations than enters into the estimates of others, cannot be accepted at the present time as a basis of comparison with ethyl chlorid used for both dental and surgical operations. The probable death rate for nitrous oxid and oxygen for surgical cases (conceded to be safer than nitrous oxid alone) is 1 in 10,000, this rate being fixed from the number of deaths reported to the authors.

Peterka [1] collected from the literature the following figures concerning the use of ethyl chlorid:

Haeker	11,000	Mather Sill	500
Malherbe	5,248	Neuenborn	400
Herrenknecht	3,000	Kulenkampff	200
Eotel	5,575	Behr	300
Ware	12,436	Lotheissen	500
Seitz	15,150	Lop	420
Grobon	16,000	Murray	150
McCardie	2,620	Bad Hall and S. Pelagio	286
Paris	5,000	Daniell	100
Benn	2,000	Pollosom	200
Reboul	1,500	Bossart	200
Elhs Morgan	1,000	Severeann	100
Stieda & Zander	1,000	Vicol	109
Krupp's Dental Clinics	1,500	Stepinoki	170
Roux	1,000	Brodtbuk	550
Camns	1,500	Billeter	150
Novi Losserand	2,000	Helsted	120
Van Stockum	3,000	Chaminade	200
Barton	2,000	Rabejac	300
Luke	2,000	Varia	687
Hornsbrook	800		
		Total	100,971

Dividing the collected figure of 100,971 narcoses by the nine deaths contained therein, these narcoses yield a mortality rate of 1:11,219. Including the five deaths reported as occurring in the Graz clinics, the figure amounts to 1 in 8,414.

[1] Peterka, H.: "Die Aethylchlorid-bei (?) Kelennarkose." *Bruns' Beitr. zur klin. Chir.*, 81, 436, 1912.

Estimated Mortality-Rate from Ethyl-Chlorid as a General Anesthetic (A. H. Miller)[1]

Observer	Death-Rate	Observer	Death-Rate
Hare	1 in 2,000	Lotheissen	1 in 12,000
McCardie	1 in 3,000	Ware	1 in 12,436
Luke	1 in 8,000	Seitz	1 in 16,000
Hewitt	1 in 10,000	Lotheissen	1 in 17,000
McCardie	1 in 10,000	Luke	1 in 36,000
Ware	1 in 11,207	Luke	1 in 150,000

Series of Ethyl-Chlorid Anesthesias Reported from Personal Knowledge[2] (A. H. Miller)

Observer	Cases	Deaths	Observer	Cases	Deaths
Soullier	8,417	0	Luke	2,000	0
Lotheissen	2,550	1	Tuttle	230	0
Ware	2,000	0	Herrenknecht	3,000	0
Cumston	197	0	Leighton	79	0
Newman	1,867	1	Greene	12,000	0
Koenig	40	0	Lee	5,575	1
Malherbe	170	0	Dodge	300	0
Wiesmer	400	0	Webster	1,880	0
Allen	60	0	Miller	6,648	1
Murray	350	0	Hornabrook	3,500	0
McCardie	1,000	0	Stieda and Zander	1,000	0
Barton	200	0			
Total				53,463	4

[1] Read in the Symposium on Anesthesia in the Sections on Pharmacology and Therapeutics and Pathology and Physiology of the American Medical Association, at the Sixty-Third Annual Session held at Atlantic City, June, 1912; *J. Am. Med. Assn., 59,* 1847.

[2] References:

Soullier: *Bull. méd.,* Paris, 1895, 417.

Buxton: "Anæsthetics," Blakiston, 1900, 297.

McCardie: *Birmingham Med. Rev.,* Jan., 1900.

Hewitt: "Anæsthetics," Macmillan, 1901, 228, 384.

Seitz: *Cor.-Bl. f. schweiz. Aerzte,* 1901.

McCardie: *Lancet,* London, March 9, 1901, 698.

Ware: *Med. Rec.,* Apr. 6, 1901, 533.

Ware: *Med. News,* Aug. 3, 1901, 168.

Chaldecott: *Lancet,* London, Sept. 13, 1902, 743.

Anesthetic Society: *Brit. Med. J.,* Nov. 22, 1902, 1654.

Ware: *J. Am. Med. Assn.,* Nov. 8, 1902, 1160. (*Continued on p. 851*)

Chloroform-Oxygen.—Chloroform-oxygen comes next with one death in 4,009 operations. It is safe to conclude that all of these were major cases, as this combination is seldom used for short operations. The use of this combination is justifiably on the increase.

Chloroform, Drop or Vapor.—Chloroform, drop or vapor, is next with one death in 2,048 cases. A glance at the table shows a decrease in its use from 1910 to 1911 as a "straight anesthetic," that is, used from start to finish, and this is also in conformity with laboratory experience and theoretical teaching.

It is universally conceded that it is unjustifiable to draw conclusions from statistics of less than 1,000 anesthesias. We refrain from further remarks on the comparative value of the remaining nineteen sequences and combinations.

No better illustration of the fact just stated could be given than the nitrous-oxid-ether-chloroform sequence. The statistics of the private cases of the professional anesthetists who use this combination are

(*Continued from page 850*)

Cumston: *Boston Med. and Surg. J.*, Jan. 1, 1903, 12.
Allen: *Am. J. Med. Sc.*, Dec., 1903, 1014.
Erdmann: *Med. News*, May 28, 1904, 1024.
Owen: *Brit. Med. J.*, Dec. 17, 1904, 1635.
Hilliard: *Practitioner*, London, Feb., 1905, 203.
Seelig: *Ann. Surg.*, Aug., 1905, 185.
McCardie: *Lancet*, London, Oct. 7, 1905, 1023.
Luke: *Brit. Dental J.*, Nov. 1, 1905.
Murray: *Lancet*, London, Nov. 25, 1905, 1542.
McCardie: *Brit. Med. J.*, March 17, 1906, 616.
Luke: *Lancet*, London, May 5, 1906, 1233.
Patton: *Anesthetics*, Cleveland Press, Chicago, 1906, 159.
Leighton: *St. Louis Med. Rev.*, Feb. 16, 1907, 158.
Rugh: *N. Y. Med. J.*, Aug. 10, 1907, 262.
Barton: *Practitioner*, London, Sept., 1907, 391.
Herrenknecht: *Münch. med. Woch.*, Dec. 3, 1907.
Gibbon: *Ann. Surg.*, Nov., 1908, 795.
Greene: *Items of Interest*, Cons. Dent. Mfg. Co., New York, Sept., 1908.
Lee: *Ann. Surg.*, Nov., 1908, 641.
Dodge: *Boston Med. and Surg. J.*, Feb. 25, 1909, 234.
Webster: *Surg., Gynec. and Obst.*, Apr., 1909, 402.
Miller: *Boston Med. and Surg. J.*, May 20, 1909, 643.
Teter: *J. Am. Med. Assn.*, Aug. 7, 1909, 451.
Crile: *Southern Med. J.*, Jan., 1910, 20.
Allen: *Boston Med. and Surg. J.*, Oct. 19, 1911, 589.
Hornabrook: *Australasian Med. Gaz.*, Nov., 1911.
Gatch: *J. Am. Med. Assn.*, Nov. 11, 1911, 1593.
Lydston: *Med. Rec.*, Nov. 12, 1910, 866.
Boys: *Surg., Gynec. and Obst.*, Apr., 1912, 388.
Olow: *Beitr. z. klin. Chir.*, Dec., 1911.
Stieda and Zander: *Med. Klin.*, Mar. 24, 1912.
Hare: "Keen's Surgery," Saunders, 1910, 1038.

naturally not included in this list, but that the combination fell into bad hands is observed from the record of one death in 183 cases.

Hewitt[1] states of this sequence that he has now employed it for several years, and, while admitting that it is hardly suitable for those who have had but little experience, he confidently recommends it to all others.

The senior author fully agrees with this statement, having used it in thousands of cases with only the most satisfactory results.

Statistics given for chloroform vary greatly. Lawrie[2] reports 30,000 chloroform anesthesias without a death. In some of the British hospitals the deaths are reported as high as one in 250. The German statistics give a mortality of one in 2,200. The statistics of Lawrie quoted above would confirm Gwathmey's experiments as regards temperature in the administration of chloroform.

Charles Prevost Grayson,[3] of Philadelphia, in 1912 reported that during the last eight years he had used it 3,800 times in adenoid and tonsil operations without mishaps of any kind.

The United States Army reports four deaths in 3,931 operations. In the statistics gathered from the different hospitals in the United States we have two deaths in 1,314 administrations, an average of one in 657 operations.

In the United States Navy no deaths have occurred in 365 administrations of chloroform.

Hewitt reports 214 deaths in 676,767 administrations of chloroform, making a death rate of one in 3,162.

Intratracheal Anesthesia.—The statistics of intratracheal anesthesia show that administrations by this method are rapidly running into the thousands and that no recent deaths have been recorded. This is now considered by those whose judgment is impartial as an absolutely safe procedure, the four deaths reported under this method being entirely avoidable, and not apt to be repeated.

Oil of Bitter Orange Peel-Ether Sequence.[4]—The oil of bitter orange peel-ether sequence by the closed method (first accomplished by Woolsey, of Brooklyn) was an important discovery. It showed that the administration by the closed method of a non-anesthetic agent followed by ether, producing an absolutely safe anesthesia while abolishing the second stage of excitement entirely, gives a resultant anesthesia sufficiently deep for all surgical work requiring absolute relaxation.

[1] Hewitt: "Anæsthetics," 1912, 501.

[2] *Bull. Johns Hopkins Hosp.*, Jan., 1895.

[3] At the meeting of the American Laryngological, Rhinological, and Otological Society, 1912.

[4] For a full discussion of the use of the oil of bitter orange peel in anesthesia, see Chapter II, "General Physiology."

Comparison of American Statistics for 1905-1911 with Those for 1892.—That progress has been made in America is shown by comparing these statistics with those gathered in 1892 as reported in the tenth volume of the *Medico-Legal Journal* of that year.

Sixty-two operators reported 109,196 cases, with thirty-nine fatalities, or one death in approximately 2,800.

	Narcoses	Deaths	Ratio
Chloroform	94,123	36	1–2,614
Ether	9,431	..	0–9,431
Ether and Chloroform	2,891	1	1–2,891
Ether and Alcohol	1,381	..	1–1,381
Bromoform and Ethyl Bromid	2,151	1	1–2,151
Pental	201	1	1– 201
	110,178	39	1–2,825

Post-mortems were held in many of these and in twenty-five some form of cardiac disease was found.

The present statistics give one death in approximately 5,000 cases. The safety to the patient has almost doubled since 1892. This comparison would also seem to show that preliminary medication, combinations, and sequences of anesthetics are potent factors of safety.

Comparison of American with European Statistics.—There seem to be no late statistics available. Hewitt gives a number gathered by Sir B. W. Richardson in 1892 as follows:

	Administrations	Deaths	Ratio
Chloroform	35,162	11	1–3,196
Ether	8,431	1	1–8,431

If we gather statistics according to climate, they present an entirely different aspect. For instance, Dastre [1] reports one death in 11,448 administrations of chloroform during the Crimean War, and Lawrie [2] reports 30,000 chloroform anesthetizations without a death.

These statistics would seem to support the contention of the authors

[1] Dastre: "Les Anesthésiques," 115.

[2] Lawrie: *Bull. Johns Hopkins Hosp.*, Jan., 1895.

that warmth, when applied to anesthetics, is a distinct factor of safety. It will thus be seen that chloroform, when given under favorable circumstances, is equal to ether in regard to immediate safety.

If we should administer the chloroform with oxygen in a Southern climate the probability is that we might have an anesthetic practically free from danger. In the Southern States chloroform immediately rises in value as regards life. When chloroform is administered by a closed method and oxygen, and rebreathing is used as in the Roth-Dräger apparatus, it seems to be equally as safe as nitrous oxid and oxygen, but, when used in a crude way without regard to rebreathing, warmth, and moisture, ether immediately rises in value from 2 1/2 to 8 times the safety of chloroform.

By combining Juilliard's and Ormsby's statistics, Hewitt gives the following table:

Anesthetic	Administrations	Deaths	Ratio
Chloroform	676,767	214	1–3,162
Ether	407,553	25	1–16,302

"Ether is, roughly, more than five times as safe as chloroform," according to these statistics.

Probyn Williams[1] gives the following:

Ether	Chloroform
1 in 16,000	1 in 2,500

Luke and Ross[2] report twenty-five deaths under nitrous oxid, and thirty under ethyl chlorid.

The statistics for 1912 are now completed. The figures have been combined with those of 1911, all duplicates being omitted.

Number of States and Territories 45
Not including
Manila, P. I., Halifax, N. S., Honolulu, H. I., Montreal, Quebec, Cape Breton, Ancon, C. Z.
Number of Hospitals 386

The following is the result:

American Statistics[3]—1905-1912, Inc.—The supplementary list of 439 "experiments" follows:

[1] Williams, Probyn: "A Practical Guide to the Administration of Anesthetics," 1907, 176.

[2] Luke and Ross: "Anesthesia in Dental Surgery," 1910, 207.

[3] "American" here refers in fact to the United States.

	1905	1906	1907	1908	1909	1910	1911	1912	Total	Deaths	Ratio
3. Local Anesthesia	1,546	1,999	2,112	2,811	2,863	3,674	9,549	6,292	30,846	0	0–30,846
6. Ethyl Chlorid, Drop or Vapor	560	594	848	779	1,157	2,837	2,620	2,866	12,261	0	0–12,261
7. N_2O with Oxygen	144	175	335	881	1,619	2,130	3,316	2,487	11,087	0	0–11,087
11. Anesthol-Ether (or Somnoform)	152	406	435	584	559	772	964	835	4,707	0	0– 4,707
14. N_2O with Oxygen and Ether	......	......	......	......	......	......	......	1,358	1,358	0	0– 1,358
16. $A_1C_2E_3$ or C_2E_3	2	2	......	......	......	6	338	817	1,165	0	0– 1,165
18. Spinal Analgesia	66	43	86	64	34	63	165	139	660	0	0– 660
19. Essence of Orange-Ether	......	......	......	......	......	......	100	475	575	0	0– 575
21. Nitrous Oxid-Oxygen-Ether-Chloroform	14	8	5	3	7	6	2	254	299	0	0– 299
24. Anesthol-Ether-$CHCl_3$	......	17	52	27	18	39	......	......	153	0	0– 153
25. Anesthol-Chloroform	......	......	......	67	28	28	......	11	134	0	0– 134
26. Nitrous Oxid-Ether Anesthol	......	......	75	16	14	9	......	......	114	0	0– 114
5. Chloroform-Ether	792	1,420	1,839	1,707	3,107	3,885	4,215	3,050	20,015	2	1–10,007
8. Anesthol	1,132	880	956	1,271	782	648	470	684	6,823	1	1– 6,823
2. Nitrous Oxid-Ether	3,293	3,473	5,271	6,342	13,050	8,141	12,156	12,516	64,242	10	1– 6,424
10. Chloroform and Oxygen	441	502	710	702	535	767	837	520	5,014	1	1– 5,014
1. Ether	12,995	18,304	22,234	27,044	37,461	40,614	76,578	59,423	294,653	65	1– 4,533
9. Ethyl Chlorid-Ether	199	175	477	541	950	1,240	1,281	318	5,181	2	1– 2,590
4. $CHCl_3$, Drop or Vapor	3,422	3,197	3,208	3,009	2,727	2,521	2,842	1,587	22,513	14	1– 1,608
13. N_2O with Air	51	90	......	40	90	......	290	1,089	1,650	2	1– 825
17. Intravenous Anesthesia	......	......	......	......	......	......	......	792	792	1	1– 792
20. Rectal Anesthesia	......	......	......	60	131	152	178	27	548	1	1– 548
12. Nitrous Oxid	11	84	203	216	198	206	296	567	1,881	5	1– 375
15. Endotracheal. Insuff.	......	......	......	......	......	......	1,006	318	1,324	4	1– 331
23. N_2O-Ether-$CHCl_3$	4	......	......	7	12	20	140	......	183	1	1– 183
22. Ether-Chloroform	3	18	10	1	15	13	34	155	249	2	1– 124
27-41 Inc. Supple'tary List, P. 50.	......	......	......	......	......	......	......	......	439	0	0– 439
Grand Total of all Anesthetics, Combinations and Sequences for 1905–1912, Inclusive									488,866	111	1– 4,404

Statistics—Supplementary List (Combined), 1905–1912, Incl.

	1905	1906	1907	1908	1909	1910	1911	1912	Total	Deaths	Percentage
27. H-M-C	......	......	9	......	......	......	44	34	87	0	0– 87
28. Endopharyngeal	......	......	......	......	......	......	......	67	67	0	0– 67
29. Anesthol-Nitrous Oxid	......	32	8	......	3	2	......	20	65	0	0– 65
30. Ethyl Chlorid-Anesthol	......	25	2	......	......	14	......	......	41	0	0– 41
31. Anesthol-Oxygen	15	......	16	......	......	4	2	......	37	0	0– 37
32. Ethyl Chlorid-Oxygen	......	......	......	......	1	2	11	20	34	0	0– 34
33. Local Anes-Ether	......	......	......	......	......	......	......	30	30	0	0– 30
34. Nitrous Oxid with Air and Ether	......	......	......	......	......	......	......	21	21	0	0– 21
35. Ethyl Bromid	12	8	......	......	......	......	......	......	20	0	0– 20
36. H-M-C and Ether	......	......	......	......	......	......	7	12	19	0	0– 19
37. Somnoform and Local	......	......	......	......	......	......	12	1	13	0	0– 13
38. Pharyngeal Insufflation Ether	......	......	......	......	......	......	......	2	2	0	0– 2
39. Somnoform	......	......	......	......	......	......	......	1	1	0	0– 1
40. Somnoform-Chloroform	......	......	......	......	......	......	......	1	1	0	0– 1
41. Somnoform-Ether-Chlorof	......	......	......	......	......	......	......	1	1	0	0– 1
Total, 27–41	......	......	......	......	......	......	......	......	439	0	....

CONCLUSIONS

The statistical tables coincide remarkably with the principles advocated in these different chapters. Bearing in mind the pharmacological action and clinical history of each anesthetic as well as the statistical tables, we make the following deductions and recommendations:

(1) Nitrous oxid with oxygen (with or without ether) is the safest inhalation anesthetic we know of at present; (a) Nitrous oxid should not be used alone; (b) Nitrous oxid should not be used with air, if oxygen is available; (c) The nitrous oxid-oxygen-ether sequence is safer than the nitrous oxid-ether sequence; (d) The statistics bear out the principles given in Chapter II concerning oxygen as a factor of safety.

(2) Anesthol alone should not be used. A study of the tables will show that a steady decrease in the use of this agent alone has taken place since 1908. (a) Anesthol as a preliminary to ether gives a safe sequence, and has steadily increased in favor from 1905 to the present time; (b) The combination of anesthol and chloroform has steadily decreased in use, showing that it is unsatisfactory; (c) Anesthol, alone or with any other agent, should not be given by the closed method.

(3) Ethyl chlorid should not be used as a terminal anesthetic on account of its physiological action. It is not safe, according to these statistics, as a preliminary to chloroform, nitrous oxid, or anesthol.

(4) Chloroform alone should not be used except in emergencies, or in cases in which it is specially indicated. Its use has steadily decreased from 1905 to the present time. (a) The chloroform-ether sequence, as shown by the table, is relatively safe, ranking higher than the nitrous oxid-ether sequence, or ether alone; (b) As the majority of the hospitals of the United States use preliminary medication, we may conclude that this factor of safety has been employed when the chloroform-ether sequence was used; (c) The combination of chloroform and oxygen, according to these statistics, is safer than ether alone.

(5) Ether alone is more generally used, according to these statistics, than any other agent, combination, or sequence, comprising nearly half of the 488,000 administrations reported. (a) Ether alone is not as safe as is generally believed; (b) Ether is materially safeguarded by oxygen; (c) Chloroform-ether, nitrous oxid-ether, and anesthol-ether are relatively safe sequences, ether being the terminal anesthetic.

(6) Sequences and combinations, when properly used, are safer than any known single anesthetic.

APPENDIX I[1]

ETHYL ETHER

History of Ethyl Ether.

Manufacture of Ether: Ether from "Methylated" Alcohol; Ether from Ethylene; Theories of Etherification.

Purity of Ether: The Commercial Purification of Ether; Verified Tests for Proving Purity of Anesthetic Ether; Rôle of Water in Anesthetic Ether; Explanation of Changes Liable to Occur in Ether Improperly Stored; The Purification of Ether Remnants with the View of Removing Aldehyd in Particular; Acidity of Ether and Effect Thereon of the Container; Physiological Consideration in Reference to Small Amounts of Impurities; The Degrees of Purity of American Ethyl Ethers Used for Anesthesia.

HISTORY OF ETHYL ETHER

Raymundus Lullius,[2] in the thirteenth century, and Basilius Valentinus,[3] in the fifteenth century, investigated the action of sulphuric acid upon spirit of wine, and consequently it is possible that these alchemists were acquainted with ethyl ether.[4] It is to Valerius Cordus, however, that we owe our first exact knowledge of the existence of the compound.[5] The process of Cordus for the preparation of ethyl ether was published by Conrad Gessner in 1552,[6] and it occurs in the later editions of the first legal pharmacopœia of Germany.[7]

[1] Much of this appendix is taken from a paper by Baskerville and Hamor, *J. Ind. Eng. Chem.*, *3*, Nos. 5 and 6.

[2] "Epistola accurtationis lapidis benedicti; libelli aliquot chemici," 1600, 319.

[3] This alchemist refers to a spirit obtained in this way which has a "subtle, penetrating, pleasant taste, and an agreeable smell." See Kopp's "Geschichte der Chimie," 1847, *4*, 299.

[4] This is, in fact, generally assumed, and one would be inclined to accept it as correct, were the authenticity of their writings established.

[5] "Dispensatorium pharmacorum omnium," 1535.

[6] "Thesauro Euonymi de remediis secretis," 1552.

[7] This recipe is as follows: Equal parts of spirit of wine which has been rectified three times and sulphuric acid are allowed to remain in contact for two months, and then the mixture is distilled from a water- or sand-bath; the distillate consists of two layers of liquid, of which the upper one is the oleum vitrioli dulce verum.

Ether is mentioned by Libavius,[1] Oswald Cross,[2] and Willis;[3] but at the commencement of the eighteenth century, the details of its preparation seem to have been almost entirely lost, even though a mixture of spirit of wine and ethyl ether was employed in medicine at this period. This mixture was, however, introduced into commerce by Martmeyer, an apothecary of Halle, under the name of *Panacea vitrioli.* It was recommended by Friedrich Hoffmann, and under the name of *Liquor anodynus Hoffmani,* or *Hoffman'sche Tropfen,* it became well known, but the preparation of this medicine was kept secret for a considerable period, and the positive presence of ethyl ether—for that matter, its existence—was not demonstrated until it was first prepared "free from spirit of wine."

In 1730 August Siegmund Frobenius[4] described, in general terms, the preparation of *spiritus vini æthereus,* but without publishing any details.[5] On November 18, 1731, Frobenius made experiments with ether and phosphorus before a meeting of the Royal Society,[6] and in his second contribution to the Royal Society he gave his method for the preparation of ether in more detail, but this description was not made public until after his death in 1741, when a detailed receipt was published by the secretary.[7]

The method of Frobenius was soon widely adopted, and several Ger-

[1] "Alchemia," 1595.

[2] "Basilica chymica," 1608.

[3] "Pharmaceutice rationalis," 1675.

[4] *Phil. Trans., 36,* 283.

[5] He manufactured the ether in Hanckewitz's laboratory and sold it at a high profit. He forwarded some of the new substance to St. F. Geoffroy, and wrote (1730) as follows, after extolling the valuable properties of the compound: ". . . . . . Paratur ex sale violatili urinoso, plantarum phlogisto, aceto valde subtili, per summam fermentationem cunctis subtilissime resolutis et unitis."

[6] See Mortimer: *Ibid.,* Abst., *9,* 372.

[7] *Phil. Trans.,* Abridg., *9,* 380. This may be thus stated in abstract: "Take 4 lbs. in weight of the best oil of vitriol, and as much in weight of the best alcohol, or the highest rectified spirit of wine. . . . First, pour the alcohol into a chosen glass retort, then pour in, little by little, one ounce of oil of vitriol; then shake the retort till the two liquors are thoroughly mixed, when the retort will begin to grow warm; then pour in more of the spirit of vitriol, and shake it again." The mixture was then placed on a sand bath, and gradualy heated, "that the drops may fall so fast that you may count five or six between each . . . continue this heat as long as they emit the scent of true marjoram. As soon as the smell changes to an acid . . . take out the fire. . . . There remains behind an *eleum vini.* . . . The second day, when your glass is cold, infuse the remainder with half as much alcohol, and distil again as before, and you will have the same; the third day again with as much, and proceed as at first, it gives it again. Go on as long as you can obtain any (of the ethereal spirit) till all turns to a *carbo;* then separate it, and alcalize it with spirits of *salt armoniæ* made without spirits of wine, till all effervescence ceases, and distil once more *e Balneo Mariæ;* so is it ready for experiments."

man and French chemists studied the preparation of ethyl ether. In 1757 Antoine Baumé published his *"Dissertation sur l'æther,"* in the first 26 pages of which he gave an historical discourse on *æther vitriolique.* On account of its inflammability ethyl ether was termed at this time *naphtha,* but was also called "vitriolic ether," "sulphuric ether," and "vitriol-naphtha," since it was prepared by the action of sulphuric acid on alcohol.

MANUFACTURE OF ETHER

Valentin Rose,[1] in the year 1800, demonstrated that the name "sulphuric ether" was a misleading one, since this substance, when pure, does not contain any sulphur or sulphuric acid. Fourcroy[2] propounded the idea that ether is formed from alcohol by the withdrawal of the elements of water. However, a number of facts contradicted this view; for example, Frobenius had observed that the residue in the preparation of ether may again be employed for a future conversion of alcohol into ether, a fact which had met with confirmation in the hands of other chemists, particularly Cadet (1774).[3]

The discovery of the continuous process now employed for the manufacture of ether is generally attributed to Boullay.[4] Squibb[5] stated that 360 pounds of concentrated sulphuric acid sufficed to etherify 120 barrels of clean spirit; the acid charge must be then changed, as the mixture will have become dark and tarry, and liable to froth in the still.[6]

Ethyl ether was first manufactured on a large scale in this country

[1] *Allg. J. Chem.* (Scheerer), *4,* 253.

This savant in conjunction with Vauquelin [*Allg. J. Chem.* (Scherer), *6,* 439] made attempts to experimentally establish this view, the results of which were confirmed in 1807 by Saussure and in 1815 by Gay-Lussac; both of whom analyzed ether. Then it was thought that the action of sulphuric acid on alcohol could be accounted for by the fact that this acid removed from the alcohol either the elements of water or water already present in the compound.

[2] *Éléments d'histoire naturelle et de chimie,* 1789.

[3] Cadet and Baumé had a discussion concerning the manufacture of ether; and the former stated that, while Baumé sold the compound at twelve livres per ounce, he charged only forty sous for the same quantity. Quite pure ether was prepared by Lowitz in 1796 by means of chlorid of lime (?) (*J. Pharm. Chim.*, *1,* 97).

[4] This process depends on the fact that a small quantity of sulphuric acid is sufficient to convert a large quantity of alcohol into ether; in fact, theoretically, one portion of sulphuric acid will convert an unlimited quantity of alcohol into ether, but in practice some of the sulphuric acid is reduced, and not only is there loss of acid and alcohol, but, in consequence of this reduction, the ether becomes contaminated with sulphur dioxid and must be purified before use.

[5] "Ephemeris," *2,* 590.

[6] See *U. S. Patent* 516, 766, of 1894, of Kraft and Roos. The production of sulphur dioxid in the process may be prevented, it is claimed, by using benzene-sulphonic acid in the place of sulphuric acid in the still.

by Rosengarten & Sons at Philadelphia in 1823, and by Carter and Scattergood of the same city in 1834.

Ether from "Methylated" Alcohol.—One of the strong arguments in advocating the enactment of denatured alcohol laws was cheaper ethyl alcohol for the manufacture of ether. Ethyl alcohol denatured with ten per cent methyl (wood) alcohol was first authorized. "Methylated" alcohol was then used for the manufacture of ethyl ether. Ether made from methylated spirit contains, according to some authorities, a considerable quantity of gaseous methylic ether in solution, which lowers the specific gravity and boiling point of the preparation.[1] Ten per cent of methylated ether may be detected by the mixture commencing to boil at a lower temperature than ether prepared from rectified spirit.[2]

Three grades of ether prepared from methylated spirit are used in Great Britain.[3] Hewitt[4] states that, while it may be regarded as

[1] Abraham: *Chem. and Drug.*, *41*, 520.

[2] Jones (*Pharm J. and Trans.*, *16*, 663) obtained the following results with various British ethers:

100 c.c. taken.	*c.c. obtained.*	*Remarks.*
Rect. ether, 0.720	0	
Rect. ether, 0.730	0	
Meth. ether, 0.717	60	Boiled freely at 74° F.
Meth. ether, 0.720	54	
Meth. ether, 0.730	23	

[3] Allen ["Commercial Organic Analysis," *1908*, *1*, 181] has pointed out that, owing to the extreme volatility of methylic ether, ether made from methylated spirit would be practically pure ethyl ether, were it not for the presence in it of other constituents of wood spirit. This is undoubtedly true from a general standpoint, but nevertheless methylic ether has usually been considered to exist in solution in ether prepared from methylated spirit, as determined by an observation of the commencement of boiling. Williamson (*Ann.*, *81*, 79; see also Norton and Prescott: *Am. Chem. J.*, *6*, 244) found that methyl ethyl ether is formed together with methyl and ethyl ethers by the etherification of a mixture of methyl and ethyl alcohols by sulphuric acid; and since methyl ether boils at 34° C., and methyl-ethyl ether between 10° C. and 13° C., the latter is likely to occur in larger amounts than the former in ether prepared from methylated spirit.

Ether of the specific gravity 0.735 has been official in Great Britain for many years, but foreign pharmacopœias only recognize the fluid which is official in the British Pharmacopœia as "Æther Purificatus." The latter is identical with the "Æther pro narcosi" of the German and Swedish Pharmacopœias. In 1893 Dott (*Pharm. J. and Trans.*, *23*, 617) suggested that the specific gravity of the official ether of the British Pharmacopœia should be altered to "not exceeding 0.724." The following ethers are used in Great Britain: (1) From Pure Rectified Spirit: (a) æther (off.). Sp. gr., 0.735. "Ordinary medicinal ether." Occasionally employed as an anesthetic, but is not so suitable for inhalation as (b) "æther purificatus" (off). Sp. gr., 0.720-0.722 (*British Pharmacopœia*, 1898, 26); (2) from Methylated Spirit: (c) "absolute ether." Sp. gr., 0.717-0.719. Said to be not adapted for general anesthesia; (d) "rectified ether." Sp. gr., 0.720. Reported as being adapted for producing general anesthesia; (e) "methylated ether." Sp. gr., 0.730. Employed for common purposes.

[4] "Anæsthetics and Their Administration," 1907, 22.

highly probable that the purer ether possesses slight advantages over the methylated, the latter, if carefully prepared by a recognized manufacturer, is certainly quite suitable for hospital use. Richardson [1] decided in favor of "methylic ether" for rapid anesthesia.

Ethers on the American market—that is, those manufactured in the United States from rectified spirit or from denaturant formulas authorized by the Commissioner of Internal Revenue [2]—are, so far as we have been able to ascertain, free from methylic ether, methyl-ethyl ether; and American ethers are not contaminated with these substances, formaldehyd, or formic acid.

Ether from Ethylene.—Fritsche [3] devised a method for the preparation of ether free from alcohol. In this method, gas containing ethylen is treated with sulphuric acid,[4] and the ethyl-sulphuric acid so obtained is converted into ether and sulphuric acid by means of water. This process was operated on a commercial scale in this country for some time,[5] but the industry was finally destroyed by the Denatured Alcohol Act.

Theories of Etherification.—Mitscherlich [6] proposed the "catalytic hypothesis" to account for the action of sulphuric acid on alcohol, and Berzelius adhered to the same view. Neither of these chemists noted, however, that the first action of sulphuric acid on alcohol, in the manufacture of ether, is the production of "sulphovinic acid," or hydrogen ethyl sulphate, an observation which was made by Hennell. This subject was investigated quite carefully by Liebig.[7] He concluded that ethyl sulphuric ether was first formed, and that this decomposed at a temperature of + 126° C. to + 140° C. into ether, sulphuric acid, and sulphur trioxid, this latter combining instantly with the water formed in the reaction; the sulphuric acid again formed ethyl sulphuric acid

[1] *Med. Times and Gaz.*, April 9, 1870.

[2] Alcohol to be used in the manufacture of ether in the United States may be denatured with ether. See Regulations No. 30, Supplement No. 1, *United States Internal Revenue;* and *Bulletin No. 130,* Bureau of Chemistry, 1910, 163.

[3] *Chem. Ztg., 33,* 759. See also Pierre: *Ann. chim. phys., 15,* No. 3, 360, 400.

[4] *Z. anal. Chem. 36,* 298; *U. S. Patent* No. 475,640, Jan. 19, 1897.

[5] *Bull. 92, U. S. Dept. of Commerce and Labor, Bureau of the Census,* 1909, 96. Vaporized petroleum was used as a source of ethylene, and natural gas was suggested later, but it was not available in the locality of the plant and it was not considered economical to move the plant. Monroe proposed erecting a by-product coke plant at the locality, since this furnishes comparatively large amounts of ethylene, but such a step was not taken owing to the inability to secure encouragement from the firm controlling the most suitable by-product coke oven. It is likely, however, that a similar industry may be revived, as natural gas might serve as a suitable material from which to prepare ether (cf. *French Patent,* 352,687, of 1905, of Lance and Elworthy).

[6] *Pogg. Ann., 31,* 273; *53,* 95; *55,* 209.

[7] *Ann., 23,* 39; *30,* 129; *60,* 31.

with the alcohol, which was being continually added, and thus Liebig accounted for the continuous nature of the reaction.[1]

Williamson [2] adopted the views of Laurent and Gerhardt, and therefore gave ethyl ether the molecular formula $C_4H_{10}O$, whereas those using the equivalent weights adopted the formula C_4H_5O. However, according to the theory of types, alcohol is derived from water by the replacement in it of one atom of hydrogen by ethyl, and hence ether, according to Williamson's view, must be regarded as alcohol, in which the hydrogen of hydroxyl is replaced by ethyl. By a new synthesis he was enabled to prove the correctness of this conception, not only for ethyl ether, but for ethers in general. His method was the transposition taking place between sodium ethylate ($NaOC_2H_5$) and ethyl iodid (C_2H_5I); and the formation of ethyl ether from alcohol and sulphuric acid Williamson explained by a continuous breaking down and reformation of ethyl sulphuric acid, made possible by the contact of alcohol with the acid at + 140° C.

Further confirmation of the views of Williamson was afterward given by Berthelot.[3] Chancel,[4] who really preceded Williamson in publication, independently arrived at the same conclusions, by heating a mixture of potassium ethyl sulphate and potassium ethylate. The objection that ethyl ether, because of its low boiling point, could not contain the double number of carbon atoms in its molecule Chancel removed by citing the boiling point of ethyl acetic ester.

[1] The simultaneous production of water and of anhydrous sulphuric acid was accounted for by the assumption that the latter only combined with the water in its immediate neighborhood, while, in the other parts of the mixture, the passage of the ether vapor carried away some water vapor. Heinrich Rose explained the curious fact that ethyl sulphuric acid should be formed and decomposed at the same time and in the same liquid by the suggestion that a diminution of temperature sufficient to permit of the formation of ethyl sulphuric acid occurred at the point where the alcohol flowed in, but that the other portions of the mixture were sufficiently hot to result in the decomposition of this acid. Mitscherlich rendered this hypothesis untenable (*J. Chem. Soc.*, *3*, 24), by demonstrating the continuous formation of ether under conditions in which no such local diminution of temperature could occur. Graham, like Mitscherlich and Berzelius, assumed the existence of contact action, but shortly afterwards the investigations of Williamson placed the true theory of the continuous etherification process on an experimental basis. Prior to his work no completely satisfactory theory of the formation of ether could be established, due to the lack of complete experimental evidence and owing to the general use of the equivalent weights.

[2] *Brit. Assn. Repts.*, 1850, 65; *Phil. Mag.*, *37*, No. 3, 350.

[3] *J. Pharm.*, *26*, No. 3, 25.

[4] *Compt. rend.*, *6*, 369.

PURITY OF ETHER

The Commercial Purification of Ether.—The ether distillate resulting from the reaction between sulphuric acid and alcohol is usually treated with either milk of lime or sodium hydroxid, to remove the sulphur dioxid and to absorb any "oil of wine,"[1] and then further rectified.[2] The rectified ether is usually run into tin cans provided with a neck and the cap is sealed by soldering.[3]

Verified Tests for Proving Purity of Anesthetic Ether.—Specific Gravity of Anesthetic Ether.—The specific gravity of ether intended for anesthesia should not exceed 0.720 at 15° C., providing an ether containing minimum quantities of alcohol and moisture is required; however, an ether which shows a specific gravity of 0.7215 (2 per cent absolute alcohol), 0.7228 (3 per cent absolute alcohol), or even 0.724 (4 per cent absolute alcohol), providing the sole "impurity" is ethyl alcohol, is acceptable for anesthetic purposes, according to various pharmacopœias. The specific gravity may be best determined by means of a pyknometer.

A convenient form of pyknometer is that devised by Squibb[4] and also described by Rosengarten,[5] the use of which is described on page 865.

Boiling Point.—The fractionation should show that at least 97 per cent of the sample distils over between + 34° C. and + 36° C. (at 760

[1] The term "heavy oil of wine" is held to signify the oil which passes over if the temperature is raised after the preparation of ethyl ether. Liebig (*Handw. d. Chem.*, 1857, I, 223), who found that it passes over when sulphur dioxid and olefiant gas are given off, regarded "heavy oil of wine" as an ethyl sulphate of "etherol." According to Claesson (*J. prakt. Chem.*, *19*, II, 259) and Serullas (*Ann. chim. phys.*, *39*, II, 152) it consists of ethyl sulphate mixed with olefines. The composition varies materially, and the phrase is indefinite and rather vague; but it is considered that the yellowish oil of a penetrating odor (sp. gr., 1.095 to 1.13) procurable in the manufacture of ethyl ether is a possible contaminant of the latter, and the term "heavy oil of wine" is therefore used by way of distinction.

[2] In rectification the apparatus devised by Mohr has had extensive use. This consists essentially of a still from which the vapor is conducted through a vessel kept at + 35° C. by warm water. Here most of the alcohol and water vapors are condensed and the ether passes over to be condensed in a suitable, well-cooled worm.

[3] It sometimes happens that a small amount of zinc chlorid, used as a flux in soldering ether "tins" by manufacturers, is introduced accidentally into the ether. This constitutes one of the real difficulties in being sure that an unopened tin of ether is uncontaminated.

[4] "Ephemeris," 1897, 1773.

[5] *J. Ind. Eng. Chem.*, 1911, *3*, No. 11.

mm.), and none of it should come over above + 37° C.;[1] after the fractionation to this temperature no residue should remain in the fractionating vessel.

Residue (Extractive Matter, Odor, and Acidity).—(1) When

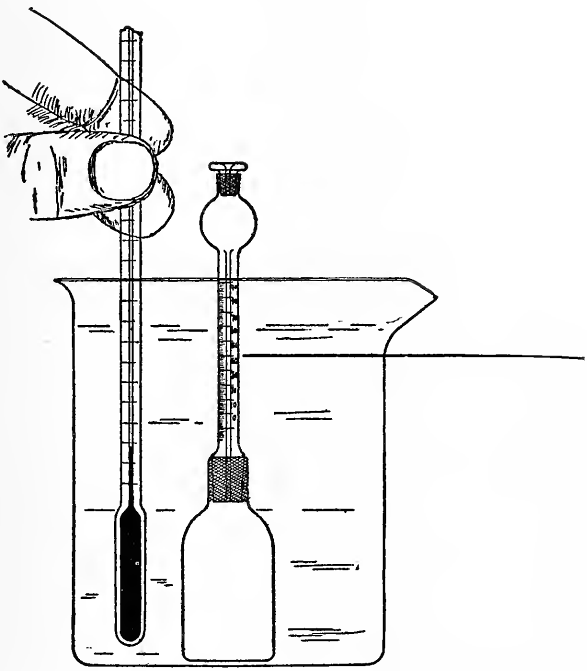


Fig. 283.—A Calibrated Pyknometer of 25 c. c. Capacity. To determine its volume the pyknometer is first weighed with water at 25° C., choosing a convenient mark on the stem, say 30 or 40, whichever may be more convenient, as indicated in the sketch by a line. The pyknometer is then filled with ether to a little above the mark at which the weight of water has been determined and placed in a 1,000 c. c. beaker containing water which is carefully kept at 25° C. and constantly stirred with a thermometer. When the volume of ether becomes constant in the pyknometer, the excess of ether is drawn off by means of a capillary pipette until the desired mark is exactly reached. The pyknometer is then quickly dried with filter paper and weighed. A capillary pipette for this purpose is easily made by drawing out an ordinary eyedropper.

25 c. c. of the sample are allowed to evaporate spontaneously in a clean, dry glass dish, the moist residue must possess no odor, and must neither

[1] Although the boiling-point of pure ether is + 34.6° C. at 760 mm., there are no ethers of anesthetic grade on the market which comply fully with this requirement, owing to the mutually opposing influence of water and alcohol on the boiling point, and only ether distilled over sodium closely approximates it. Since, therefore, these influences render the constancy of the boiling point as ordinarily determined of little or no use as a criterion of purity, it is sufficient to require that ether shall commence to distil at a temperature not under + 34° C., and that it shall possess a boiling point of + 34°-36° C.

redden nor bleach blue litmus paper; this residue must evaporate completely on a water bath, that is, there should be no fixed residue.

(2) 100 c. c. of the ether under examination are allowed to evaporate spontaneously in a flask until about 15 c. c. remain in the vessel. This residue should be free from color and foreign odor, and should comply in full with the following tests:

(a) When 5 c. c. are allowed to evaporate at room temperature after the addition of 2 c. c. of water, the residue should neither redden nor bleach sensitive light-blue litmus paper.

(b) When another portion of 5 c. c. is allowed to evaporate on a 9 cm. filter paper contained in a porcelain dish, no foreign odor (amyl compounds, empyreumata, pungent matters, etc.) should be perceptible as the last portions disappear from the paper, and the latter should be left odorless. The ether should be added to the paper in portions in such a manner as to completely moisten it each time.

(c) On the addition of the remaining 5 c. c. to 5 c. c. of concentrated sulphuric acid, kept cool during the test and contained in a glass-stoppered tube previously rinsed with concentrated sulphuric acid, there should result no perceptible coloration.

Anesthetic ether should comply in full with these tests.

Acidity.—When 20 c. c. of pure ether are shaken with 10 c. c. of pure water and 2 drops of phenolphthalein, the same depth of color should result on adding an equal amount of N/100 potassium hydroxid solution as in a test using pure water alone.[1] When more than 1 c. c. is required the ether should be rejected for anesthetic purposes.

Acetaldehyd.—On covering solid potassium hydroxid (two clean, freshly broken pieces about 2 cm. long will answer) with 40 c. c. of the same in a 50 c. c. glass-stoppered vessel and allowing this to stand for three hours, tightly closed and protected from the light, and shaking occasionally, the potassium hydroxid should not acquire a yellowish color, and no yellowish or brown-colored substance should separate. This is recommended as the exclusion test for anesthetic ether.[2]

[1] When 0.5 c. c. of a 1: 100 alcoholic solution of phenolphthalein is added to 100 c. c. of water, 0.5 c. c. of N/100 KOH is necessary to produce a distinct red color. In this connection see Trommsdorff's table in Bockman's "Chemisch-technische Untersuchungsmethoden der Grossindustrie," 3rd ed.; Cohn's "Indicators and Test Papers," 220; and A. A. Noyes: *J. Am. Chem. Soc.*, *32*, 815. It appeared from the last mentioned investigation that thymolphthalein might be advantageously substituted for phenolphthalein as the indicator in estimating the acidity of ether. It was found, however, that, when the former is employed, the color change is less distinct, and that it is less sensitive.

[2] In order to determine the value of this test experimentally, 5 gm. of potassium hydroxid were added to the following samples of ether, 30 c. c. of each being used in the tests:

(1) Ether distilled over sodium, and containing mere traces of acetaldehyd; (2) an ether containing 0.5 per cent of hydrogen dioxid but otherwise pure;

Peroxids.—When 2 c. c. of a 10 per cent cadmium-potassium iodid solution are well shaken with 10 c. c. of the sample there should result no liberation of iodin within one hour. This may be easily determined by adding starch solution, although the yellow color which results in the presence of the merest traces of peroxids is easy to distinguish.

Rôle of Water in Anesthetic Ether.—The presence of excess moisture should be guarded against in the storage of ether, since ether in contact with water or moist air for any length of time gives rise to various impurities of an objectionable nature. Thus anesthetic ether may develop impurities to be avoided quite as much as if they had been introduced in the original materials or later produced in the manufacture or unintentionally added in the preparation for distribution in commerce.

Ether, when freshly distilled over sodium, possesses a specific gravity of 0.7178 to 0.719 at 15°/4° C.; but if it is not, immediately after its rectification, drawn off into vessels, which are at once sealed and carefully stored, the specific gravity increases in a short time. The purest ether procurable on the market is of 0.718–0.719 specific gravity at

(3) an ether intended for analytical purposes; this ether contained small amounts of the moisture; (4) No. 3 after the addition of 3 per cent of absolute alcohol; (5) No. 3 after the addition of 0.05 per cent of acetaldehyd; (6) No. 1 after the addition of 0.05 per cent of acetaldehyd; (7) No. 3 after the addition of 0.05 per cent of acetaldehyd; (8) No. 3 after the addition of 0.10 per cent of acetaldehyd; (9) No. 8 after the addition of 3 per cent of absolute alcohol.

After standing 30 minutes, Nos. 6, 7, and 8 possessed a brown color, and No. 9 had assumed a yellow color. At the end of 24 hours the following results were observed:

(1) Nil; (2) clear, uncolored, separate; potassium hydroxid and ether colorless; (3) very small amount of a brownish substance; (4) brown solution; no colored substance on the potassium hydroxid as in No. 3; (5) clear, uncolored, separate; no brownish substance; (6) yellow solution and considerable "aldehyd resin"; (7) as in No. 6; (8) much more considerable in amount than in No. 6; (9) red-brown solution.

From these experiments it was concluded that the yellow or brownish separate is only caused by the presence of acetaldehyd, and, in cases where the ether is tinted yellow or brown, this is often due to the presence of alcohol, as well as aldehyd, the former dissolving the resin formed by the latter. Peroxids may produce a turbidity, but no coloration or colored separate.

There is a source of error in the potassium hydroxid test, however. Just as spirits stored in casks made of wood containing tannin show a coloration with potassium hydroxid, so do samples of ether containing pieces of cork, the latter being introduced from the stoppers. The coloration in this case is probably due to the presence of quercitannic acid and resinous matter extracted from the cork through contact with ether. An ether containing mere traces of acetaldehyd—that is, aldehyd not detectable by the potassium hydroxid test—may thus become colored when the test is applied, providing it has remained in contact with cork or contains pieces of broken cork, the latter being by no means unusual owing to the form of the neck of the tin containers in use.

+ 15° C., but this absorbs water on exposure to the atmosphere and rises to 0.720-0.721 specific gravity, when it becomes fairly constant.

Explanation of Changes Liable to Occur in Ether Improperly Stored.—Baskerville[1] has conducted an extensive investigation on the changes which occur in ethyl ether during storage, and the experimental data obtained lead to the conclusion that the oxidation of ether in the presence of moisture is productive of a series of complex conversions, initiated, however, by the formation of hydrogen dioxid. The slow combustion of pure ether in the presence of water, and under such conditions as exist when it is improperly stored, as, for example, varying temperature and in sunlight, in colorless glass vessels, or in badly stoppered tin containers, would appear to occur in the following stages:

(1) The formation of hydrogen dioxid from water and oxygen of the air. This is particularly likely in cases where there is direct exposure to light, and it is more or less activated by contact action.

(2) Dissociation of hydrogen dioxid into water and oxygen, which latter then exerts a direct oxidizing action, resulting in the formation of the following: acetic peroxid, acetaldehyd, and acetaldehyd peroxid, and eventually acetic acid. The formation of acetic peroxid facilitates a series of oxidations, and, by its hydrolysis alone, acetic and peracetic acids are formed. The peracetic acid then becomes converted into acetic acid and hydrogen dioxid. Therefore, it is reasonable to conclude that a continuous cycle of changes occurs in ether during its oxidation and that such changes result in the simultaneous formation and occurrence of peroxidized compounds, intermediate (aldehyd) and ultimate (acetic acid) resultants.

The Purification of Ether Remnants with the View of Removing Aldehyd in Particular.—Several methods have been devised for the removal of aldehyd from ether. Some are secret. Although it is exceedingly difficult to eliminate this impurity completely, yet it has been done commercially and the anesthetist should insist upon his ethers being free from aldehyd.

Treatment with potassium hydroxid or metallic sodium serves to remove not only water, but also aldehyd, and an ether so treated contains mere traces of the latter impurity. Lassar-Cohn[2] has found that ether may be most satisfactorily freed from alcohol and aldehyd, however, by boiling it with a reflux condenser for twenty-four hours with an alloy of potassium and sodium. The application of any method should not be undertaken by any except an experienced chemist.

Acidity of Ether and Effect Thereon of the Container.—It has been

[1] Assisted by Hamor, *J. Ind. Eng. Chem.*, *3*, Nos. 5 and 6.

[2] *Ann. 284*, 226. This alloy is fluid at low temperatures, and is superior to metallic sodium in that it is not liable to become encrusted with a protective layer of hydroxid and resin.

only within the last twenty-five years that serious attention has been given to the detection of acidity in the various anesthetic ethers. None that we have examined contained acids (sulphurous, sulphuric, acetic) in what may be termed injurious amounts, since the amount present never exceeded 0.002 gm. of acetic acid per 100 c. c. of the sample in any instance. The degree of acidity is liable to vary more or less in both directions in short intervals during storage in glass vessels, just as in the case of the oxidation of ether itself. The variations in acidity —theoretical, but not in general sensible—may be due to differences between the rapidity of the oxidation and the saturation of the acids by the bases of the glass. In fact, the nature of the ether container is of vast importance in the light of the oxidation changes which are possible. The extent of the oxidation—or, for that matter, any oxidation at all—is dependent upon the quality of the glass used in bottles for storing ether; and in the case of metallic containers, in view of some recent researches, it is probable that all metals which show anomalous anodic conductivity are likely to develop free hydrogen dioxid in contact with water and oxygen. The presence of such metals should, therefore, be guarded against.

Physiological Consideration in Reference to Small Amounts of Impurities.—The presence of small amounts of substances has oftentimes been the cause of a chemical reaction proceeding in a particular direction by virtue of a so-called "catalytic" or other kind of action. So the presence of even traces of certain substances, as peroxidized compounds, aldehyd, etc., may have caused some reactions to be incorrectly explained, or to follow an unusual, or unaccounted for, route. This is certainly true of the animal body, wherein the courses of the myriad chemical reactions coincident with life processes, if they be not really such, are affected by the presence of the anesthetic and undoubtedly made to take queer directions by the simultaneous presence, even in small amounts, of an unsuspected constituent.

The Degrees of Purity of American Ethyl Ethers Used for Anesthesia.—The main impurities contained in American ethers are, beside alcohol and water, acetaldehyd and acids. As previously noted, the presence of small amounts of alcohol is permissible or may even appear necessary; but anesthetic ethers should contain but mere traces of moisture, and, as has been indicated, it is desirable that they should be absolutely water-free. This would undoubtedly increase the cost of production; however, so long as ether is supplied in small tins of such a size that the contents are used completely at an operation or that, not used, being little, may be discarded, and not stored, it is only necessary that the amount of moisture present be reduced to very low percentage.

The following table will serve to show the comparative purity of three samples of anesthetic ether, purchased in the open market by Gwathmey and submitted to Baskerville, numbered, and without the latter knowing the name of the manufacturer:

Test	D	E	F
Sp. gr. at 25°	0.7162	0.7189	0.7161
Odor	No foreign odor	Id.	Id.
Ether distillate	98.50%	97.00%	97.50%
Distillate above 36°	0.5%	2.00%	1.50%
"Organic impurities"	None	Id.	Id.
Relative acidity in gm. acetic acid in 100 c.c.	0.0006	0.00015	0.00165
U. S. P. litmus test	Negative	Id.	Id.
Residue	None	Id.	Id.
Water	Present[1]	Id.	Id.
Alcohol	Present in permissible amount	Excessive	As in No. D
Relative total impurity (Allen's approximate method)	5.00%	6.00%	5.50%
Peroxids	None	Id.	Id.
Aldehyd	Present in permissible amount	Id.	Excessive as compared to others

[1] In all three samples the amount of water present was not excessive providing the ether would be properly stored or at once consumed completely by the user. All the samples were properly canned. The samples of "D" examined possessed a relatively higher degree of uniformity than the samples "E" and "F."

The American product is universally recognized as of high grade; however, not sufficient attention has been given to the storage of ether by the user, and until the latter coöperates with the manufacturer, fully and intelligently, the results obtained may continue to be variable, and rigid requirements on the part of the producer are useless. However, the purer the product to begin with the better results are to be expected. Ether freed from moisture and all but traces of aldehyd by means of sodium or other methods is not required in this country for anesthetic purposes, and it is generally considered satisfactory if no "after-effects" are observed.

APPENDIX II[1]

CHLOROFORM

History of Chloroform.

Preparation of Chloroform: From Ethyl Alcohol; From "Methylated Spirit"; From Acetone; From Methane; From Carbon Tetrachlorid.

Varieties of Chloroform of European Make: Chloral Chloroform; Chloroform Pictet; Chloroform Anschütz.

Purification of Chloroform.

The Decomposition of Chloroform: The Changes Which Chloroform Undergoes Upon Exposure to Air.

Verified Tests for Purity of Anesthetic Chloroform: Odor; Residue; Specific Gravity; Organic Impurities; Acetone; Acetaldehyd; Acidity; The Decomposition Products of Anesthetic Chloroform.

Degrees of Purity of American Chloroforms.

History of Chloroform.—Silliman[2] confused chloroform with ethylen dichlorid, stating that it had been "long known to chemists under the name of 'oil of the Dutch chemists' and 'Dutch oil,' from its discovery in 1796 by an association of Dutch chemists."

In 1831 Liebig[3] obtained chloroform by the action of a water solution of potassium hydroxid on chloral and by treating acetone with bleaching powder. Almost at the same time, however, Soubeiran[4] obtained chloroform by the action of bleaching powder on dilute alcohol, terming the product "ether bichlorid," and he was regarded as the discoverer of the compound until Liebig[5] advanced his claim as having been the first to prepare it, although he originally believed the substance to be a new chlorid of carbon.

According to some writers,[6] Samuel Guthrie discovered chloroform

[1] Much of this appendix is taken from a paper by Baskerville and Hamor: *J. Ind. Eng. Chem.*, 1912, *4*, Nos. 3, 4, 5, 6, 7.

[2] *Am. J. Sci.*, *5*, No. 2, 240.

[3] *Pogg. Ann.*, *23*, 444; *Ann.*, *1*, 31, 198.

[4] *Ann. chim. phys.*, *48*, No. 2, 131; *Ann.*, *1*, 272; Soubeiran and Mialhe: *Ann.*, *71*, 225.

[5] *Ann.*, *162*, 161.

[6] *E. g.*, Wurtz.

simultaneously with Liebig and Soubeiran, and it has also been stated[1] that his discovery antedates that of Liebig by several months. Silliman[2] stated in 1848 that "the production of 'chloric ether,' so-called, by the action of alcohol with bleaching powders, was discovered almost simultaneously and without conference by our ingenious countryman, Samuel Guthrie, of Sackett's Harbor, New York, and by M. E. Soubeiran in France."

Liebig considered that he had prepared carbon trichlorid, whereas he actually obtained chloroform, and Guthrie confused his own product with ethylene chlorid; in both cases the investigations were made in 1831 and published in the early part of 1832. Guthrie prepared chloroform without knowledge of the work of Liebig or Soubeiran, and is fully entitled to be credited with its independent discovery.[3]

Dumas,[4] in 1834, showed that chloroform contains hydrogen, and later he determined its true formula.[5] Dumas obtained chloroform by boiling tri-chloro-acetic acid with aqueous alkaline solutions, and it was

[1] *Pop. Sci. Mon., 12,* 738.

[2] *Loc. cit.*

[3] The attention of Guthrie appears to have been directed to the preparation of "chloric ether" by reading a passage in a work by Silliman ("Elements of Chemistry," *2,* 20), wherein it was stated that the alcoholic solution of "chloric ether" is of medicinal value. By the term "chloric ether" Silliman referred unmistakably to ethylene chlorid, which Guthrie considered he had prepared in "spirituous solution" by the action of chlorid of lime on alcohol of density 0.844, whereas he actually obtained an alcoholic solution of chloroform (*Am. J. Sci., 21,* No. 2, 64). Silliman, commenting on Guthrie's original contribution (*ibid.,* 408), stated that "we cannot say precisely what takes place during the distillation of alcohol from chlorid of lime. It is, however, worthy of notice, that, as alcohol is believed to be composed of olefiant gas and water, . . . and as chloric ether has been heretofore produced by the combination of chlorin and olefiant gas, it seems hardly to admit of a doubt, that in distilling alcohol from chlorid of lime, the latter gives its chlorin to the olefiant gas of a part of the former, and thus produces chloric ether, which passes over, in solution, in another portion of the alcohol, while the water of that portion of the alcohol which afforded the olefiant gas, or the water which may be supposed to be produced by a combination of the elements, is detained by the lime." The question was raised, "Can any method be devised by which the alcohol can be detached from the chloric ether, and the latter obtained concentrated and in quantity?" Guthrie later (*ibid., 22,* 105; see also, Hayes: *Ibid.,* 163) found that this could be accomplished by distillation over sulphuric acid, and obtained an "ether" possessing a density of 1.486 and boiling at 166° F. In a communication to Silliman, he stated that "as chloric ether is said to have a specific gravity of only 1.22 at 45° F., a boiling point at 152° F., and to be decomposed by sulphuric acid, evolving chlorin, you may have good reason to doubt the purity of my product, or the accuracy of my estimate, but you can very readily verify the first, and I shall be found to be very near the truth with the latter."

[4] *Ann. chim. phys., 56,* No. 2, 115; *Ann., 32,* 113.

[5] *Ann. chim. phys., 71,* No. 2, 353.

he who gave the compound its present name.[1] Regnault[2] proved that chloroform is the second substitution product of methyl chlorid; he termed it "éther hydrochlorique de methylene bichlorure." Berzelius referred to chloroform as "formylsuperchlorid," and Mitscherlich as "chlorätherid."

Preparation of Chloroform.—FROM ETHYL ALCOHOL.—Soubeiran showed that chloroform is made by the action of "bleaching powder" on dilute ethyl alcohol.[3] When ethyl alcohol of various strengths is poured upon "bleaching powder" and distilled, the distillate affords an oil which may be separated by fractionation.[4] A small amount of ethyl chlorid is also formed.[5]

According to the process of Schering,[6] chloroform is produced when halogen salts of the alkalies or alkaline earths are electrolyzed in the presence of alcohol, acetone, or aldehyd in a warm aqueous solution.[7]

Although ethyl alcohol was formerly used for the production of chloroform, it is now largely, or almost entirely, replaced by acetone. Recently carbon tetrachlorid has become an important source of chloroform.

FROM "METHYLATED SPIRIT."—Pure methyl alcohol does not yield chloroform when treated with bleaching powder, although it is formed from commercial methyl alcohol.[8] "Methylated chloroform," at one time extensively used in England, is chloroform prepared from wood

[1] *Ibid.*, *56*, No. 2, 120. To quote Dumas: "La formule . . . correspond à une chlorure d'hydrogène carbone, qui est l'équivalent de l'acide formique anhydre . . . C'est ce qui m'engage à la designer sous le nom de chloroforme."

[2] *Ibid.*, *71*, No. 2, 377; *Ann.*, *33*, 328; *J. prakt. Chem.*, *19*, 210.

[3] See also, Bechamp: *Ann. chim. phys.*, *22*, No. 5, 347.

For papers on the manufacture of chloroform from alcohol and "chlorinated lime," see *Am. J. Pharm.*, 1862, 25, 42; 1868, 289.

In *Chem. Ztg.*, *10*, 338, is described the process in use in Germany in 1886; see also Frerichs: *Am. Inst. Chem. Eng.*, 1911; *J. Ind. Eng. Chem.*, *4*, No. 5.

On the preparation of chloroform from alcohol, see, in addition, Goldberg: *J. prakt. Chem.*, *132*, 111; Soubeiran: *Compt. rend.*, *25*, 799; Meurer: *Chem. Centr.*, 1848, 154; Carl: *Ibid.*, 1848, 236; Larocque and Hurault: *N. J. Pharm.*, *13*, 97; Siemerling: *N. Br. Arch.*, *53*, 23; Kessler: *N. J. Pharm.*, *13*, 162; Ramdohr: *N. Br. Arch.*, *83*, 280; and Hirsch: *Ibid.*, *107*, 137. The alcohol used should not contain fusel oil [Regnault and Hardy: *J. pharm. chim.*, (4), *30*, 405] or higher alcohols.

[4] Dott (*J. Soc. Chem. Ind.*, *27*, 6, 271) gives the reaction: $3C_2H_5OH + 8Ca(OCl)_2 = 2CHCl_3 + 3CaCO_3 + CO_2 + 8H_2O + 5CaCl_2$.

[5] Finnemore and Wade: *J. Chem. Soc.*, *85*, 938.

[6] *German Patent 29771*, 1884; *Ber. 17*, 624; also Dony-Hennault: *Z. Elektrochem.*, *7*, 57.

[7] Kempf (*Eng. Pat. 8148*, 1884) invented a process for the manufacture of chloroform by electrolyzing suitable halogen compounds of the alkalies and alkaline earths in alcoholic solution with constant heating; and Trechinski (*J. Russ. Phys.-Chem. Soc.*, *38*, 734; *Pharm. Ztg.*, *51*, 523) prepared chloroform by the electrolysis of an aqueous alcoholic solution of calcium chlorid.

[8] Belohoubek: *Ann.*, *165*, 349.

spirit ("methylated spirit").[1] It is incorrect to suppose that "methylated chloroform" has received an actual addition of methyl alcohol, but such chloroform is liable to be much less pure than that obtained solely from ethyl alcohol. According to Allen,[2] chloroform prepared from "methylated spirit" is more difficult to purify than that made from ethyl alcohol alone; but a product has been manufactured in England from the former source which appears to be equal in all respects to that prepared from straight ethyl alcohol.[3]

From Acetone.—The preparation of chloroform from acetone was referred to by Liebig in 1832. Böttger, in 1848, showed how to prepare chloroform from acetates and from acetone. The process was not quickly followed probably, as indicated by Squibb,[4] on account of the erroneous statements of Siemerling (1848) and Wackenroder, adopted by such authorities as Gmelin and Watts.[5] Orndorff and Jessel [6] found that the products formed by the action of bleaching powder on acetone are chloroform, calcium hydroxid, calcium chlorid, and calcium acetate. Numerous patents [7] have been granted.

Chloroform is now made by electrolysis of sodium (or other) chlorid in acetone.[8] A strong prejudice in the pharmaceutical trade against

[1] "Methylated spirit" is a mixture of rectified spirit with 10 per cent of wood alcohol (methyl alcohol); it has been used in the manufacture of chloroform owing to its being obtained duty free (Thorpe).

[2] "Commercial Organic Analysis," 1908, *1*, 235. "Methylated chloroform" is not on the American market.

[3] Allen is also authority for the statement that imperfectly purified "methylated chloroform" is specifically lighter than the pure substance, has an empyreumatic odor, and produces disagreeable sensations when inhaled. In some cases, we are told, such chloroform appears to be actually poisonous, and produces general and rapid prostration. Such chloroform contains several units per cent of a chlorinated oil, lighter than water and boiling at a much higher temperature than chloroform. A similar but different oil (heavier than water) has been detected in much smaller quantity in chloroform prepared from alcohol containing no methyl compounds; these oils may be totally eliminated by purification of the crude chloroform.

[4] *J. Am. Chem. Soc.*, 1896, 231.

[5] *A Dictionary of Chemistry*, *1*, 918; also Siemerling: *Arch. Pharm.*, *53*, No. 2, 23.

[6] *Am. Chem. J.*, *10*, 366. Dott (*Pharm. J.*, *81*, 54) found that there are also considerable amounts of calcium carbonate and chlorate in the residual liquor obtained in preparing chloroform from acetone.

[7] Michaelis, U. S., 322,194 (1885); Michaelis and Meyer, England, 8523, (1880) and Germany 36,514 (1886); Rumpf, U. S., 383,992 (1888); Porsch, U. S., 573,482 (1896); Chute, U. S., 893,784 (1908).

[8] *Rev. Prod. Chim.*, *3*, 309; *Klar. Chem. Ind.*, *19*, 159. Teeple (*J. Am. Chem. Soc.*, *26*, 536) found that the conditions necessary for the successful preparation of chloroform by the electrolysis of a chlorid in the presence of acetone are: A temperature below +25° C., absence of alkali, a high current density at the cathode and a low one at the anode.

chloroform from this source doubtless had something to do with causing manufacturers to be reluctant about divulging any information concerning the process.

From Methane (Natural Gas).—Pennsylvania natural gas contains 50-95 per cent of methane,[1] and, bearing in mind the demonstration of Regnault[2] that chloroform is formed by the action of chlorin on methane in daylight and quickly in sunlight, several investigators have sought to effect a chlorination in order to obtain substitution products. So far, although numerous patents have been secured, no process for making chloroform from methane has been operated commercially with success.[3]

From Carbon Tetrachlorid.—Geuther found that chloroform results from the action of nascent hydrogen (from zinc and sulphuric acid) upon carbon tetrachlorid.[4] It was not until successful commercial processes for the production of carbon tetrachlorid had been developed, however,[5] that it was ascertained that chloroform might be advantageously prepared from carbon tetrachlorid.

In 1902 A. W. Smith devised a process of making chloroform from carbon tetrachlorid, which process consists of the following steps: The action of heated sulphur upon heated carbon, so as to produce carbon disulphid; the action of chlorin upon sulphur, so as to produce sulphur chlorid or dichlorid; the action of sulphur chlorid or dichlorid upon carbon disulphid, so as to produce carbon tetrachlorid; and, finally, the reduction of carbon tetrachlorid, so as to produce chloroform. It has been stated that "technically pure" chloroform produced from disulphid-tetrachlorid may be recognized by its small content of carbon disulphid and carbon tetrachlorid, and that such a grade also possesses a higher refractive index than other varieties. "Anesthetic chloroform" made from carbon tetrachlorid conforms in full with the required pharmacopeial standards. From chemical evidences, any prejudice at-

[1] Pennsylvania natural gas contains from 50 to 99 per cent total paraffins; Ohio gas, 90 to 93 per cent; and West Virginia gas, 80 to 87 per cent.

[2] *Ann. chim. phys., 71*, No. 2, 380.

[3] These processes are summarized in the paper by Baskerville and Hamor, *loc. cit.*

[4] *Ann., 107*, 212.

[5] As early as 1834 it was learned that carbon disulphid may be converted into carbon tetrachlorid by chlorination (Kolbe: *Ann. 45*, 41; *54*, 146; see, also, Hofmann: *Ibid., 115*, 264; Klasow: *Ber., 20*, 2376; Mouneyrat: *Bull. soc. chim., 19*, No. 3, 262; and Serra: *Gaz. chim. ital., 29*, 353). Muller and Dubois (*Eng. Patent* 19,628, 1893) devised a process for the production of carbon tetrachlorid by the addition of a finely divided iron to a mixture of carbon disulphid and sulphur chlorid; cf. *Eng. Patent* 13,733 of 1901, of Urbain, wherein practically the same process is claimed; and *U. S. Patent* 753,325, dated March 1, 1904, of A. W. Smith.

tached to such chloroform is without foundation, and there should be no hesitancy in disclosing the source.

Varieties of Chloroform of European Make.—Considerable quantities of chloroform are produced in Germany by special purification processes for domestic and foreign consumption.[1] Some of these are on the American market.

In addition to anesthetic chloroform prepared by the action of bleaching powder on alcohol and acetone (Chloroform *Gehe, Riedel, Merck, Kahlbaum, de Haën, König* and *Cotta*), "chloroform e chloral," "chloroform Pictet," and "chloroform Anschütz" are found on the German market.

Chloral-Chloroform.—Liebig found that chloroform may be prepared by distilling chloral with excess of aqueous potassium hydroxid, sodium hydroxid, or baryta, or with milk of lime, repeatedly agitating the oily distillate with water, separating from the water as completely as possible by decantation, and then distilling with 6 or 8 times its volume of strong sulphuric acid in a perfectly dry apparatus. In 1870 chloral-chloroform was sold under the name "English Chloroform" in Germany, and Hager, after an examination, expressed the opinion that chloroform from chloral was the purest then obtainable.[2]

The invention of Liebreich[3] for preparations for the production of chloroform relates broadly to a product consisting of a dry mixture of chloral hydrate and alkali, which may be compressed into any convenient shape; on treatment with water chloroform is produced. The product of this process has been known as "chloroform Liebreich," and "chloroform Schering," now on the American market, is prepared from Liebreich's crystallized chloral hydrate.

Langgaard[4] examined the eight principal brands of chloroform obtainable in Germany, and found that chloral-chloroform was the purest.

[1] In 1910, for example, 161,900 kg. of chloroform and chloral were exported, 19,000 kg. of which went to the United States; the average price was from 170 to 180 marks per 100 kg.

[2] *Year-Book of Pharm.*, 1870, 119. Hager found that "English chloroform" was really chloral-chloroform containing 0.75 to 0.80 per cent of alcohol. The addition of pure sulphuric acid to this chloral-chloroform caused no coloration, while it was found to color slightly the ordinary grade of chloroform then in use. Evaporation of some of the substance on a watch-glass in the air was found to afford another means of testing the substance. When all but a few drops had disappeared, the ordinary chloroform residue was found to possess a disagreeable odor, while the other retained its pleasant odor. Versmann (*Pharm. J.*, *2*, No. 3, 63) also found that the residue of chloral chloroform possessed no foreign odor.

According to a later writer, however (Arends: *Pharm. Ztg.*, 1891, 263), German chloroform is generally superior to that manufactured in England. The *British Pharmacopœia* is considerably less stringent than that of Germany.

[3] *Eng. Patent* 15,930, 1904.

[4] *Therap. Monatsch.*, May, 1902.

As a general rule, however, all of the German chloroforms of anesthetic grade are of good quality,[1] and the grade at present prescribed by the *Arzneibuch* is, at least in most cases, equal to chloroform prepared from chloral. It has also been claimed that chloral chloroform does not undergo decomposition, but this has been shown to be incorrect;[2] in fact, like all the other pure preparations, "chloroform e chloral" decomposes if not preserved by the addition of a little alcohol.[3]

Chloroform Pictet.—This preparation is obtained by crystallization at a low temperature, followed by fractional distillation (referred to again later). Schacht has shown that, although the Pictet chloroform is a good preparation, that obtained from the purest crystallized chloral hydrate is quite equal to it, and, like the latter, it requires a preservative to keep.

Chloroform Anschütz.—More recently a special preparation under the name "Anschütz salicylid chloroform" or "Salicylchloroform" has been placed on the German market; it is obtained from a crystalline compound of salicylid, and was first prepared by Anschütz.[4]

Purification of Chloroform.—The crude chloroform prepared by the action of bleaching powder on alcohol; by the action of bleaching powder on acetone;[5] or by the electrolysis of solutions of chlorids of the alkalies or alkaline earths in alcohol or acetone,[6] is not of so high a degree of purity as that obtained by the action of alkalies on previously purified chloral, and requires more careful purification before it is suitable for anesthetic purposes. The extent of the purification necessary is dependent upon the purity of the materials used as well as upon the process employed.

[1] The results obtained by Baskerville and Hamor in the course of an examination of the principal German products may be found in their paper, *loc. cit.*

[2] See *Am. J. Pharm.*, *42*, 409.

[3] See Schacht: *J. Soc. Chem. Ind.*, *1893*, 543.

[4] *J. Soc. Chem. Ind.*, 1893, 782. According to the patented process of Anschütz, chemically pure chloroform is produced by decomposing by heat double compounds of chloroform and lactid-like condensation products, derived from orthophenol carbonic acids, as salicylid, and then condensing the pure chloroform; salicylid-chloroform is prepared by boiling salicylid in chloroform (*U. S. Patent* 535,270, 1895), and in this compound chloroform plays the same rôle as the water of crystallization in many crystalline salts, being obtained in a pure state by simple distillation therefrom (Anschütz: *Ann.*, *273*, 94; Arends: *Chem. Ind.*, *16*, 78). Salicylid-chloroform is said to be extensively used by anesthetists in Russia, it conforming to the pharmacopœia of that country, and is especially recommended for anesthesia by many.

The comparative prices of chloroform prepared from acetone by means of bleaching powder, chloroform from chloral by potassium hydroxid, "chloroform Pictet," and "chloroform Anschütz," are, respectively, taking the first as a basis, 1, 3, 6, and 9.

[5] See *Pharm. J.*, *20*, No. 3, 84.

[6] See *J. Soc. Chem. Ind.*, 1885, 243.

The earliest methods for the purification of crude chloroform consisted in washing the distillate with water to remove alcohol,[1] and then drying over calcium chlorid, or sometimes rectifying without having previously dried the product. In 1848 the crude chloroform was purified by shaking with potassium hydroxid, drying over calcium chlorid, and then rectifying; this method served to remove chlorin [2] and acids, but it only partially eliminated alcohol and other probable contaminants.

Gregory[3] purified chloroform by agitating it and leaving it in contact with sulphuric acid until the latter was no longer colored by it; then he removed the chloroform and placed it in contact with a small quantity of manganese dioxid to free it from "sulphurous acid." About 1860 the German custom was to rectify overconcentrated sulphuric acid.[4] At the present time treatment with sulphuric acid is generally resorted to, and forms the most important stage of the purification of crude chloroform prepared from alcohol or acetone. Pure concentrated sulphuric acid has no action on chloroform itself unless the operation is unduly prolonged,[5] but it decomposes some of the impurities which are commonly present, and removes others. In the next place, the

[1] When made from alcohol, crude chloroform contains considerable quantities of alcohol in solution, from which it may be separated by repeatedly washing with water. In order to wash a yield of 160 to 175 kg. of crude chloroform, about 800 liters of water are necessary to obtain anesthetic chloroform, although this washing forms only one stage of the purifying process.

[2] Kessler [*J. Pharm. Chim., 13,* (3), 162] found that chloroform may be freed from chlorin by agitation with potassium hydroxid, and suggested that it be further purified by drying over calcium chlorid and followed by rectification.

[3] *Proc. Roy. Soc. Ednb.,* 1850, 391. According to Abraham (*Pharm. J., 10,* 24) chloroform, when thus purified, quickly decomposes, and is afterwards found to contain hydrochloric acid and free chlorin.

[4] The *United States Pharmacopœia* of 1850 gave a process for preparing chloroform; this was transferred in 1860 to the *Materia Medica Catalogue.* "Chloroform venale," or commercial chloroform, was introduced and also a formula for purifying chloroform; this was dropped in the *Pharmacopœia* of 1890.

[5] Christison (*Pharm. J., 10,* 253) found that chloroform keeps well after being once treated with sulphuric acid; but that the continued action of that liquid, especially if it is contaminated with nitrous acid, exerts a decomposing action on it. Tilden (*ibid., 1,* No. 3, 623) stated that the sulphuric acid used to purify chloroform must be free from all traces of nitrogen oxids; and it was his opinion that the decomposition of chloroform may be attributed to contamination of this kind. Redwood (*ibid., 12,* No. 3, 734) was inclined to ascribe the improved quality of the British chloroform of 1882 to the care used in its manufacture, particularly to the attention paid to the purity of the sulphuric acid used in the purification. Clark, however, maintained that the presence of nitrous or nitric acid in the sulphuric acid was not the cause of the instability of chloroform. Both Clark and Dott considered "that the decomposition of chloroform is not probably due to the presence of nitric acid in the sulphuric acid" (*vide* Preston, *ibid., 12,* No. 3, 981).

product is brought in contact with sodium carbonate,[1] or it is washed with lime water and then dried over calcium chlorid.[2] In any case, it should be finally distilled at a temperature not above + 64° C.[3]

Various other methods have been proposed for the purification of chloroform, especially when it has become contaminated with decomposition products. We have, for example, the method of Gibbs, wherein lead dioxid is employed;[4] that of Mentin, according to which the chloroform is distilled over 2 per cent of paraffin at 61°;[5] and the recommendation of Shuttleworth[6] that agitation with a dilute solution of sodium thiosulphate be employed.[7]

[1] Shuttleworth (*Am. Chemist, 4,* 339) observed that in samples of chloroform imperfectly rectified, as that of the ordinary German manufacture of 1873, the impurities produced by the agencies of time, light, moisture, and atmospheric exposure are, after a lapse of some months, easily recognizable. Traces of sulphuric acid were found to quickly induce this change; and when that chemical has been employed as the purifying agent, and has not been completely removed by repeated washings and rectifications, the product will very soon give sharp indications of decomposition. The method of purification adopted by the *British Pharmacopœia* of that time consisted in mixing the chloroform after treatment with acid, with lime and calcium chlorid, and then rectifying at once. Shuttleworth considered that the keeping qualities of the product would be much improved by agitating the chloroform, followed by washing with water. Werner (*Arch. Pharm., 25,* No. 3, 1113) stated that his method of purification afforded a product found to be perfectly satisfactory for medicinal use during 10 years' experience. This method (*ibid., 12,* No. 3, 481) consisted in shaking the chloroform with one-fourth its volume of distilled water, removing the latter the next day, then agitating the chloroform with fused sodium carbonate, and allowing the mixture to stand for 24 hours. After removing the sodium carbonate the residual product was distilled on a water bath, the distillate coming over below + 64° C. being used.

[2] Thayer (*J. Physical Chem. 3,* 36) found that traces of alcohol remained in chloroform even after the latter had been allowed to stand over calcium chlorid for a long time. He purified chloroform by washing it repeatedly with water, then keeping it in contact with calcium chlorid for two days, and finally decanting and distilling over fresh calcium chlorid.

[3] See Werner, *loc. cit.;* Thorpe, *loc. cit.;* Remys, *Archiv Pharm., 5,* III, 31; and Michaelis and Mayer, *Polyt. J., 261,* 496.

[4] *Trans. N. Y. Acad. Med., 1,* 146. Gibbs suggested, in 1850, that chloroform possessing an acid reaction and probably containing chlorinated oils be treated with lead dioxid. Metcalfe (*ibid.*) found that such treatment served to remove any disagreeable odor characteristic of such chloroform.

[5] *Ann. chim. fran., 10,* No. 4, 32.

[6] *Am. Chemist, 4,* 339. Shuttleworth recommended that chloroform which has been injured by time exposure be restored by agitating well with a dilute solution of sodium thiosulphate, separating from the supernatant liquid and washing with water, then separating and passing the chloroform through filter paper to free it from traces of moisture.

[7] Although this method yielded an improved chloroform, Shuttleworth considered that, when a pure preparation is desired, the impurities not removable by thiosulphate, those of a more stable character and possessing a higher boiling point than chloroform, be removed by distillation or by treatment with sulphuric acid.

Yvon [1] stated that he was enabled to obtain an absolutely pure chloroform by treatment with an alkaline potassium permanganate solution; this procedure has not come into use. Useless also, providing the chloroform has been brought to the proper state of purity prior to fractionation, is the French practice of distilling over poppy oil.[2]

In the process of Pictet [3] commercial chloroform is cooled to — 80° C., and the solid bodies are removed by filtration; it is then cooled to — 82° C., and the non-crystallizable portions, which contain impurities, are removed; the solid chloroform is melted and then distilled at a very low temperature, under reduced pressure, and the middle 80 per cent of the product is taken as "chemically pure" chloroform.

On its introduction it was announced that "chloroform Pictet" had been experimentally proved to possess a capability of resisting the influence of sunlight for four days. Schacht and Biltz [4] therefore inferred that it contained alcohol, and their prediction that such was the case, without even having seen a sample, ultimately proved to be the case. Moreover, Schacht [5] found that "chloroform Pictet" suffers the usual de-

[1] *Mon. Sci.*, Mar., 1882, 262. Yvon found that chloroform prepared according to the *French Pharmacopœia* of 1866, by agitating with water, leaving in contact with potassium carbonate, drying over calcium chlorid, and finally rectifying, is sufficiently pure for anesthetic purposes. He pointed out, however, that a still purer product could be obtained by modifications of this method.

[2] The method official in the *French Pharmacopœia* of 1899 for the purification of commercial chloroform was modified by Masson (*J. pharm. chim.*, *9*, 568), according to whose process crude commercial chloroform is first washed with water, the aqueous layer separated, and the chloroform shaken with 2.5 per cent of its weight of sulphuric acid, and the operation being repeated with a fresh portion of acid, if necessary, the acid being left in contact with the chloroform for two or three days. The chloroform is then treated with 3 per cent of its weight of sodium hydroxid solution (sp. gr., 1.33) which is left in contact also for two or three days. It is then washed with water, dried over calcium chlorid, and 2.5 per cent of poppy oil added. Distillation is then conducted into graduated receivers containing 0.2 per cent by weight of alcohol for the amount of chloroform they are to contain. The important modifications of this process are: the prolonged contact of the chloroform with the sodium hydroxid solution; the final distillation over poppy oil (it was then employed in the official process for a preliminary distillation); and the presence of a trace of alcohol in the receiver.

The "Chloroforme Officinal" of the present *Codex* (1908, 148) is prepared from rectified commercial chloroform by agitating with distilled water, decanting and filtering; shaking with sulphuric acid, then allowing to stand over sodium hydroxid; drying over calcium chlorid, and finally distilling over poppy oil and adding alcohol (5/1000 part by weight of absolute ethyl alcohol).

See also, Maillard and Ranc: *Compt. rend. Soc. biol.*, *61*, 483.

[3] *U. S. Patent* 489,592, 1893; and *English Patent* 15,514, 1891; see also *J. Soc. Chem. Ind.*, *18*, 231. On some peculiar phenomena in the solidification of chloroform, see Pictet: *Compt. rend.*, *114*, 1245.

[4] *J. Soc. Chem. Ind.*, *12*, 543; see also, *Western Drug.*, 1891, 379.

[5] *Pharm. J.*, *22*, No. 3, 691.

composition, on washing to remove alcohol; and Biltz[1] regarded the decomposition of chloroform under the influence of light and air as a natural characteristic of chloroform, and not as a result of impurities.[2] However, DuBois-Reymond[3] stated that "chloroform Pictet" is affected less by sunlight than any other chloroform with even the addition of alcohol.[4]

J. F. Macfarlane & Co.[5] separated the following relative quantities of "impurity" from "chloroform Pictet" and a British product.

From domestic product	0 0000512	per cent.
" " "	0.0002050	" "
" "chloroform Pictet"	0.0008200	" "
" " "	0.0004100	" "

The "chloroform Pictet" examined by Baskerville possessed a density of 1.491 at 15/15° C., and all the tests for the presence of impurities and decomposition products gave negative results. Four other German products and one American anesthetic chloroform, all of which were purified by *chemical* treatment, were found to be fully as pure, however, which indicates that purification by cryogenic means is not necessary to secure chloroform of anesthetic grade.

DuBois-Reymond[6] has studied the physiological action of "chloroform Pictet" and of the residue of foreign substances obtained in the process of Pictet. He found that the shape of the pulse waves and the frequency of respiration are about equally affected by both substances, the rate of respiration varying freely; that the pulse rate, compared in nineteen cases, is higher at the close of the experiments with the residue than with those with the purified chloroform; that the blood pressure in by far the greater number of experiments at the moment respiration ceases is higher after inhalation of the purified chloroform than after inhalation of the impure residue; and, finally, that the residue causes stoppage of respiration much more quickly than does purified chloroform. DuBois-Reymond conducted hardly a sufficient number of physiological experiments to enable one to form a definite opinion of the physiological action of the commonly occurring impurities of commercial chloroform which are separated by means of the process of Pictet. In addition the variable nature of these impurities, owing to the various proc-

[1] *Ibid.*

[2] See also, Biltz: *Ber. Pharm. Ges.*, *2*, 76, 247; Schacht: *Ibid.*, *2*, 69; and Thilo: *Pharm. Ztg.*, *39*, 543.

[3] *Pharm. Centralh.*, *32*, 658.

[4] Had DuBois-Reymond made his comparisons of "chloroform Pictet" with properly purified samples of anesthetic chloroform, no such differences as he reported would have been observed.

[5] *Brit. Med. J.*, 1892, *1*, 525.

[6] *Brit. Med. J.*, 1892, *1*, 209.

esses of manufacture and the variability of the crude materials used therein, renders such an investigation of little value.

When acetone is used for the preparation of chloroform, it should be previously purified,[1] and this purification should be carefully executed in order to prevent the formation of condensation compounds.[2]

It has been stated that chloroform made from acetone is not nearly so good an anesthetic as chloroform made from ethyl alcohol;[3] but this opinion is based upon the findings of Wade and Finnemore;[4] that chloroform prepared from ethyl alcohol contains a very small proportion of ethyl chlorid. When chloroform is properly made from purified acetone careful purification will result in the production of pure chloroform.[5]

Gregory[6] found that the chloroform prepared from ethyl alcohol and wood spirit, when fully purified, is quite identical in all its properties, but that from the former is more easily purified. In fact, it may be asserted on the authority of Brown, Squibb, Schacht, and Biltz[7] that properly purified chloroform is the same from whatever source it is obtained; however, Cross and also Spilsbury[8] have expressed the opinion that chloroform made from ethyl alcohol is physiologically safer than that from methylated spirit and acetone. The latter opinion is a

[1] In *Am. J. Pharm.*, 1889, 321, is an account of a method for purifying acetone used in the preparation of chloroform.

[2] Dott (*J. Soc. Chem. Ind.*, *27*, 272) has called attention to the importance of the impurities which may be present in commercial acetone. He found that samples which indicated 99 per cent by the iodoform test and other methods gave about 7 per cent distilling above 58°. This was first thought to be due to the presence of higher ketones or other bodies yielding iodoform, but Gibson suggested that it might possibly be caused by the presence of even 1 per cent of a mixture of the condensation products of acetone (e. g., mesityl oxid, phorone, and mesitylene), which all have relatively high boiling points. It was found that, on mixing pure acetone with 1 per cent of the mixed condensation products, it behaved on distillation and in its iodoform yield, and otherwise, like the samples referred to. When purifying acetone, therefore, manufacturers should avoid treatment with mineral acids or other method which is likely to cause formation of the condensation compounds. On the purity of acetone, see also Guttman: *Dingler's Polyt. J.*, 1894, 96; Klar: *J. Soc. Chem. Ind.*, 1897, 722.

[3] Price: *Pharm. J.*, *23*, 89.

[4] *Loc. cit.*

[5] J. F. MacFarlane & Co. (*Lancet*, 1905, *1*, 747) have expressed the opinion that chloroform prepared from acetone is by no means generally accepted as inferior to chloroform prepared from alcohol, and consider that up to the present insufficient evidence has been adduced to establish the view that it is actually inferior.

We may state here that, from our experience, anesthetic chloroform manufactured from acetone has been found by American anesthetizers, to be fully as satisfactory as that from other sources.

[6] *Mon. J. Med. Sci.*, May, 1850; *Pharm. J.*, *9*, 580.

[7] *Pharm. J.*, *24*, No. 3, 811.

[8] *Ibid.*, *29*, No. 4, 660.

recent one (1909), and is substantiated, at least in part, by other evidence, but is totally incorrect when the chloroform is properly purified.[1]

The carbon tetrachlorid used is prepared from carbon disulphid (the electric furnace product), and manufacturers in the United States state that it is so free from sulphur compounds that "no part of the distillate separated from a batch of 5,000 pounds through a long fractionating column will show any sulphur compounds by the most delicate tests known." The presence of carbon disulphid in the chloroform produced is guarded against by means of a process for removing carbon disulphid from the carbon tetrachlorid used; when traces are present the tetrachlorid is fractionated in a high column still until the distillate will give no response with tests for the presence of carbon disulphid. The distillate is considered as commercial carbon tetrachlorid, which is usually guaranteed to contain 99.7 per cent of absolute CCl_4. The material remaining in the still is tested for the presence of carbon disulphid, and if found absent, then the material remaining in the still is used for the manufacture of chloroform.

The Decomposition of Chloroform.—THE CHANGES WHICH CHLOROFORM UNDERGOES UPON EXPOSURE TO AIR.—In order to secure a clear conception of this important matter it is desirable to compare the conduct of "pure" and "anesthetic" chloroform.

In 1848 Morson[2] found that "pure" chloroform undergoes decomposition in the presence of light and air, chlorin, hydrochloric acid, and probably other "chlorin compounds" being formed;[3] later he observed that the decomposition is variable in extent and rapidity, and that chloroform, when kept under water, does not decompose.[4] Maisch,[5] however, stated that chloroform containing moisture always showed the presence of "free chlorin" much sooner than dry samples.

[1] It has also been stated that headache frequently occurs among workmen while bottling chloroform made from methylated spirit, whereas the symptoms were not observed while manipulating chloroform derived from ethyl alcohol (*ibid.*, *18*, No. 4, 515). In this connection it may be noted that in one works where chloroform has been made from carbon tetrachlorid for eight years, according to a report from the officers, there has been not one case of accidental or other anesthesia among the workmen.

[2] *Pharm. J.*, *8*, 69.

[3] Therefore, Morson suggested the test with litmus paper and purification by repeated agitation with distilled water.

[4] *Ibid.*, 279. In 1850 (see *Trans. N. Y. Acad. Med.*, *1*, 146) it had been observed in this country that chloroform becomes acid and contains ''chlorinated oils'' through decomposition.

[5] *Proc. Am. Pharm. Assn.*, 1867. Chloroform of the density 1.492, dried by means of calcium chlorid, was kept in absolutely dry bottles and in bottles slightly moist, then both kinds were exposed to diffused daylight and to direct sunlight. Maisch concluded that the entire absence of water would not be sufficient to preserve the chloroform unaltered.

Hager,[1] investigating the question more extensively, concluded that "pure" chloroform is not decomposed by the action of light alone; but that, when chloroform is exposed to the action of the sun's rays, it becomes decomposed, exhibits an acid reaction to test paper, and there are found, among its products of decomposition, hydrochloric acid, "chloroxycarbonic acid,"[2] formic acid,[3] and free chlorin. Hager first pointed out that chloroform is decomposed when air has access to it, even in the dark, although very slowly.[4] Rump[5] made similar observations, having learned that protection from light does not prevent the decomposition of chloroform; he concluded that the smallest quantity of moisture and air will, in time, induce decomposition, and that this, once started, proceeds with increased rapidity. Under these conditions, by excluding the light, Rump found that carbonyl chlorid will result.

In 1882 Regnault[6] pointed out that carbonyl chlorid is the most dangerous impurity found in chloroform, and stated that it is produced in the presence of light by the action of air on chloroform.[7] In collaboration with Roux, Regnault demonstrated the formation of carbonyl chlorid from chloroform in several different ways: By the action of the spark from an induction coil on a mixture of chloroform vapor and air; by allowing air saturated with vapor of chloroform to circulate in an effluve apparatus;[8] and by the action of ozonized air. The last experiment showed that the production of carbonyl chlorid is independent of the thermal and electric phenomena of the other two, and, along with

[1] *Pharm. Z. Russland*, Sept., 1869.

[2] Personne found that samples of chloroform liable to decomposition always contain "chlorocarbonic ether." It has also been maintained that the change is attributable to the presence of allylene bichlorid.

[3] Kappeler ("Anesthetica," 173) stated that formic acid and aldehyd are products of the decomposition of chloroform.

[4] Hager found that chloroform, even if it does not exhibit an acid reaction, may be in a state of decomposition, and that this condition may be detected by the reaction such chloroform exhibits with ammonia, which then yields with it vapors of ammonium chlorid.

The results of Hager's investigations gave rise to the statement which has persisted in the literature till to-day, namely, that specimens of chloroform, originally of good quality, on keeping become impregnated with hydrochloric, hypochlorous, and formic acids.

[5] *Archiv. Pharm.*, Oct., 1874.

[6] *J. Pharm. Chim.*, *5*, No. 5, 504.

[7] Regnault considered the accidental presence of carbonyl chlorid common at that time.

[8] Regnault and Roux found that nitrogen charged with the vapor of chloroform also decomposes the chloroform in an effluve apparatus, the products being hydrochloric acids and a mixture of C_3Cl_6, and C_4Cl_6. Cf. the results of Besson and Fournier (*Compt. rend.*, *150*, 1118), on the action of the silent discharge on chloroform in the presence of hydrogen. Among the chlorinated derivatives separated were CCl_4, C_2Cl_4, C_2HCl_5, C_2Cl_6, and C_4Cl_8.

the work of Rump, established the formation of carbonyl chlorid during the oxidation of chloroform. Confirmation of this was later had from the investigations of Marty [1] and Stark.[2]

Just what are the other products of the decomposition of chloroform is a question which has received considerable, but only recently very careful, attention. Brown [3] found that, while chloroform is not decomposed by the action of sunlight in the absence of oxygen, it is so decomposed when oxygen is present, yielding as products chlorin, carbonyl chlorid, and water:

$$4CHCl_3 + 3O_2 = 4COCl_2 + 2H_2O + 2Cl_2:$$
$$2COCl_2 + 2H_2O = 2CO_2 + 4HCl.$$

These equations have been recognized as correct by Schacht and Biltz,[4] and by Adrian; [5] but Schacht and Biltz considered it necessary to add that they apply exclusively to the decomposition of chloroform which is perfectly free from alcohol. That the decomposition of chloroform is accelerated in an atmosphere of pure oxygen, is a fact which Schacht and Biltz were disposed to ascribe to the absence of nitrogen.

In regard to the ultimately recognizable results of the oxidation of chloroform in particular instances—for example, in the case of anesthetic chloroform—there is one circumstance which exercises a decided determining influence; but, as indicated by Schacht and Biltz,[6] it is not always sufficiently considered, and this fact has given rise to differences of opinion as to the nature of this decomposition and of its products. For instance, Ramsay [7] advanced the opinion that the only products of the decomposition of chloroform are carbonyl chlorid and hydrochloric acid, while Brown, Schacht and Biltz, and Adrian maintain that in addition to the formation of those products there is also an elimination of chlorin in the free state. Schacht and Biltz considered that this difference of opinion was doubtless to be ascribed to want of attention to

[1] *L'Union pharm.*, Nov., 1888. Marty found that "pure" chloroform did not remain unaffected more than two days in summer or 5 days in winter, when freely exposed to air. The same chloroform remained unaltered for 15 months in the dark, although in contact with air. With chloroform containing 0.1 per cent of absolute alcohol, no decomposition resulted even after an exposure of 15 months to continuous sunlight.

[2] *Pharm. J.*, *20*, No. 3, 407. Chloroform exposed to diffused sunlight for five months contained hydrochloric acid, carbonyl chlorid, and an "oily hydrocarbon." According to Stark, the alarming dyspnea produced by some samples of chloroform when inhaled is probably due to the presence of carbonyl chlorid.

[3] *Pharm. Soc. Ednb.*, March, 1893.

[4] *Pharm. J.*, 1893, 1005.

[5] *J. Pharm. Chim.*, *18*, 5.

[6] *Loc. cit.*

[7] *J. Soc. Chem. Ind.*, *11*, 772. The same view was held by Breteau and Woog: *Compt. rend.*, *143*, 1193.

the presence of alcohol in the chloroform experimented with,[1] and to the resulting misinterpretation of the chemical changes which occurred. They stated that they had succeeded in proving that the well-known influence of alcohol in preserving chloroform from decomposition [2] was due to the alcohol taking up and chemically combining with the deleterious products resulting from the decomposition, so as to render them innocuous. Later [3] they concluded that, though the direct products of the decomposition of "pure" chloroform were only chlorin [4] and carbonyl chlorid, in the case of chloroform containing alcohol the chlorin thus eliminated acted on the alcohol present, and so gave rise to the production of hydrochloric acid. In this way they accounted for the presence of hydrochloric acid in the first state of the decomposition of anesthetic chloroform,[5] and considered that they had explained the point which had given rise to dispute, namely, that the elimination of free chlorin is a primary feature of the alteration. These views led to a controversy with the Browns,[6] and the formation and presence of free chlorin as one of

[1] See *Preservation.*

[2] The correctness of this view, which has been generally favored, was considered in Chapter VII, p. 290.

[3] *Pharm. J.*, *22*, No. 3, 1041.

[4] Popov (*J. Russ. Phys.-Chem. Soc.*, 7, 1061) studied the influence of light on chloroform dissolved in linseed oil, finding that the iodin number of the oil was lowered, owing to the action of the halogen upon the unsaturated compounds of the oil. This work does not, however, prove that chlorin is a product of the photolytic decomposition of chloroform.

[5] Cf. Laurent (*Ann. chim. phys.*, 1837, 318) who found that chlorin acts on chloroform in the sunlight, forming hydrochloric acid and "C_2Cl_8." The opinions of Schacht and Biltz, variously expressed, seem to embody this general view: The gradual disappearance of free chlorin when chloroform is undergoing decomposition is an indication of its further action on the chloroform, producing hydrochloric acid and altering the relative proportions of carbonyl chlorid and hydrochloric acid so as to increase the latter.

[6] Schacht and Biltz (*Pharm. J.*, *23*, No. 3, 1005) stated that "decomposition cannot be detected in alcohol-reduced chloroform until all the added alcohol has been consumed." Brown (*ibid.*, *24*, 321) found that "pure" chloroform to which 0.077 per cent of alcohol had been added, when exposed to direct sunlight in colorless glass, began to decompose in 14 to 19 days. He found that after decomposition had been recognized by zinc iodid and starch, as well as by baryta water, reactions were obtained with 1:2000 potassium dichromate solution and the iodoform test, and these were ascribed to the presence of alcohol. Schacht (*Ber. pharm. Ges.*, Oct., 1894) defended his position, and stated that the reactions obtained were not produced by alcohol, but by "chloric ether" and "Phosgene alcoholide." The Browns (*Pharm. J.*, *25*, No. 3, 836) maintained that Schacht had not proved that ethyl chlorid and chloroformic ether are produced in the decomposition of alcohol-reduced chloroform, and that they give reactions similar to alcohol. On the other hand, they considered that they themselves had proved that at the time the decomposition is first recognized by means of zinc iodid and starch, chlorin has not been produced in sufficient quantity to combine with all of the added alcohol, and that ethyl chlorid, chloroformic ether, or carbonic ether do not give reactions which could be mistaken for those of alcohol.

the decomposition products of chloroform containing alcohol were by no means definitely settled.

Schoorl and Van den Berg[1] conducted quantitative experiments which seemed to indicate that, when chloroform is decomposed by the action of light in the presence of an excess of oxygen, carbon dioxid, water, and chlorin are formed in accordance with the following equation:

$$2CHCl_3 + 5O = 2CO_2 + H_2O + 3Cl_2$$

According to the same chemists, when insufficient oxygen is present—a condition usually obtaining in practice—carbonyl chlorid and hydrogen chlorid are produced in molecular proportions:

$$CHCl_3 + O = HCl + COCl_2$$

The equations given by Schoorl and Van den Berg were evidently intended to apply to the decomposition of pure chloroform, and the changes which occur in anesthetic chloroform were not, so far as we are aware, considered. Schoorl and Van den Berg[2] confirmed the observation that, in the absence of air or oxygen, chloroform is not affected by light exposure.

Finally Dott[3] has suggested that the formation of carbonyl chlorid in chloroform very probably occurs in accordance with the following equation:

$$CHCl_3 + H_2O_2 = COCl_2 + HCl + H_2O$$ [4]

Baskerville and Hamor concluded from their experimental results that:

(1) The products of the oxidation of pure chloroform are carbonyl chlorid and hydrochloric acid:

$$CHCl_3 + H_2O + O_2 = COCl_2 + HCl + H_2O_2;$$
$$CHCl_3 + H_2O_2 = COCl_2 + HCl + H_2O$$

They were convinced that oxidation would not occur if water were excluded, and the absolute exclusion of moisture appears to be impossible. Hydrogen dioxid is formed, although they were unable to detect it in chloroform undergoing oxidation, and therefore concluded that its existence is ephemeral, and oxidation of the chloroform continues throughout the period of exposure.

The decomposition of pure chloroform is favored by a degree of moisture, and is accelerated by light, as is shown by a comparison of the results obtained in the experiments wherein colorless glass was used with

[1] *Pharm. Weekblad.*, *42*, 877.

[2] *Ibid.*, *43*, 8. On exposure to air, in the absence of light, chloroform gave no precipitate with silver nitrate even after four hours, whereas bromoform and iodoform after one hour gave distinct indications of decomposition.

[3] *J. Soc. Chem. Ind.*, *27*, 272.

[4] Support to this view is had from the fact that conditions which favor the formation of hydrogen dioxid—a degree of moisture and direct sunlight—are also those which favor the decomposition of chloroform.

those in which anactinic glass containers were employed. Moreover, carbonyl chlorid is always formed with increased readiness in the presence of acids.[1]

The extent of the oxidation is dependent upon the nature of the container, the amount of air present, the purity of the sample, and the intensity of the light to which it is exposed. In light alone, when no air is present, no decomposition occurs for ordinary periods of exposure; and in cases where there is air contact alone, and no exposure to light, the oxidation is slow.

Free chlorin can only result from the photochemical decomposition of carbonyl chlorid:[2]

$$COCl_2 = CO + Cl_2$$

It is likely that in the cases where "chlorin" was identified as an indication of incipient alteration of chloroform hydrogen dioxid was the cause of the reactions observed. No chlorin was found by Baskerville when containers of anactinic glass were used.

This view of the oxidation of pure chloroform is supported in full by the analogous case of the photochemical oxidation of iodoform,[3] the primary products of which are carbonyl iodid and hydriodic acid, free iodin resulting only from the decomposition of the carbonyl iodid and from the oxidation of the hydriodic acid.

(2) The products of the oxidation of anesthetic chloroform are primarily the oxidation products of alcohol, and no decomposition of chloroform itself occurs while the oxidation of alcohol proceeds. When the oxidation of alcohol reaches a maximum, decomposition of the chloroform goes on as in the case of pure chloroform, with the exception that chlorinated derivatives of the oxidation products of alcohol may result. The decomposition of the chloroform itself is retarded so long as oxidation of the alcohol proceeds, and the retardation is consequently dependent upon the amount of alcohol present, that is, the alcohol acts as a "negative catalyst" through its capacity for oxidation. The extent of the oxidation is, of course, subject to the conditions referred to as applicable to "pure" chloroform. It is important to note, however, that

[1] Lowry and Magson, *Trans. Chem. Soc.*, *93*, 121, who observed that the formation of carbonyl chlorid is evidently accelerated by the presence of acids.

[2] In this connection, see Coehn and Becker: *Ber.*, *43*, 130; and Weigert: *Ann. Physik*, 1907, *24*, No. 4, 55. The influence of light on the reversible reaction, $CO + Cl_2 \rightleftharpoons COCl_2$, is purely catalytic.

[3] See Plotnikow: *Z. physikal. Chem.*, *75*, 337, 385. According to this investigator the whole reaction is as follows: $CHI_3 + O = COI_2 + HI$; $COI_2 = CO + I_2$; $2HI + O = H_2O + I_2$.

In the light, under constant conditions, the iodin separated is proportional to the time, and if the illumination is removed the reaction still proceeds, but with reduced velocity. There is no separation of iodin in the absence of oxygen, and none in a benzene solution which has not been exposed to light.

anesthetic chloroform always contains water, the usual amount being about 0.05 per cent by volume, according to our experience.

Verified Tests for Purity of Anesthetic Chloroform.—Odor.—Pure anesthetic chloroform possesses a characteristic odor,[1] and such chloroform volatilizes entirely without disagreeable or foreign odor. The test may be carried out as follows: One hundred c. c. of anesthetic chloroform are slowly evaporated over a water bath until about 10 c. c. remain in the flask. This residuum should be colorless and possess no foreign odor; and, when it is allowed to evaporate on filter paper, there should result no odor of fusel oil, empyreumatic matter, or other substances than chloroform and ethyl alcohol, as the last portions disappear. If a decided odor is imparted to the filter paper after the evaporation of the residue, or if any foreign odor is observed during the course of evaporation, the chloroform should be rejected; but for further information may be tested for such impurities as fusel oil, chlorinated derivatives of alcohol, acetone or the higher alcohols, extractive matter, etc.

Residue.—When 100 c. c. of anesthetic chloroform are allowed to evaporate in a platinum dish at + 100° C., there should be left no weighable residue. In every case this should be determined gravimetrically, and not by vision.[2]

Specific Gravity.—The specific gravity gives a good indication of the strength of the preparation, that is, how much alcohol is present, and otherwise shows the purity of the drug to a much less degree. The determination should preferably be made with a pyknometer at + 15° C.[3] Chloroform is very sensitive to temperature variation. The Mohr-Westphal balance will serve to give a rapid approximate result, but should not be depended upon where any considerable degree of accuracy is desired.[4]

[1] Passy (*Compt. rend.*, *116*, 769) made comparative experiments on the odorous power of chloroform, bromoform, and iodoform, which afforded the following sharp results in millionths of a gram:

Chloroform	30.00
Bromoform	2 to 5
Iodoform	0.06 to 0.7

[2] White (*Pharm. J.*, *25*, No. 4, 540) proposed that when 10 mils of chloroform are allowed to evaporate in a clean glass beaker or dish, which is afterward heated on a water bath, there should be left no *visible* residue.

[3] The form of pyknometer designed by Perkin (*J. prakt. Chem. N. F.*, *31*, 486) is very suitable, although the Sprengel pyknometer is satisfactory.

[4] *Water.* When 10 c. c. of anesthetic chloroform are agitated with 10 c. c. of paraffin oil (sp. gr., 0.880) there should be perfect solution and no turbidity produced. This shows 0.1 per cent, but not traces, of water. The water *per se* is not objectionable, but its presence, provided air—that is, oxygen—is present, facilitates decomposition in storage. For the detection of smaller amounts of water, use calcium carbid. See Baskerville and Hamor: *Loc cit.*

Organic Impurities.—When 20 c. c. of *anesthetic chloroform* are mixed with 15 c. c. of concentrated sulphuric acid in a glass-stoppered vessel of 50 c. c. capacity which has been previously rinsed with concentrated sulphuric acid, no visible coloration should be imparted to the mixture after the addition of 0.4 c. c. of pure 40 per cent formaldehyd solution, and then shaking throughout a period of five minutes.[1]

Acetone.—Anesthetic chloroform should give a negative reaction in all cases when the following exclusion test is applied:

Ten c. c. of the sample are agitated with 5 drops of a 0.5 per cent sodium nitroprussid solution and 2 c. c. of ammonium hydroxid (sp. gr. = 0.925), and the mixture is then allowed to stand for several minutes. Chloroform containing up to 1 per cent of alcohol may impart a yellowish brown color to the supernatant liquid on agitation, but when acetone is present an amethystine color results. This test must be conducted in the cold. After application to the suspected chloroform direct, the first 10 per cent distillate and the 10 per cent residuum obtained by allowing 100 c. c.[2] of the sample to slowly distil should be tested.

Acetaldehyd.—When 10 c. c. of *anesthetic chloroform* are agitated with 10 c. c. of water and 5 drops of Nessler's reagent U. S. P., and the mixture is then allowed to stand for 5 minutes, there should result no precipitate, and the reagent should assume *no coloration,* although it may become opalescent or slightly turbid.

Acidity.—When 20 c. c. of *anesthetic chloroform* are thoroughly agitated with 10 c. c. of water and 2 drops of phenolphthalein solution, and then titrated with N/100 potassium hydroxid solution, added drop by drop, not more than 0.2 c. c. of standard alkali solution should be required to produce a faint but decided alkaline reaction permanent for 15 minutes, when the mixture is shaken 30 seconds after the addition of each drop of alkali. If the presence of free acid is indicated, the sample should be rejected, but for further information may be examined for the oxidation products of pure chloroform (carbonyl chlorid, hydrogen chlorid) and alcohol.

The Decomposition Products of Anesthetic Chloroform.—(a) The detection of *acetaldehyd* is referred to above;

[1] The reasons for this test are given in full in the paper by Baskerville and Hamor: *Loc. cit.*

[2] When the proportion of acetone to chloroform is 1: 500, the amethyst color is marked; but in the presence of 1 part in 1,000 the coloration is not distinct until the mixture of chloroform with ammonium hydroxid and sodium nitroprussid has been saturated with ammonium sulphate, shaken, and then allowed to rest for five minutes. It is advisable, in all cases, to run a blank test on pure anesthetic chloroform for comparison. Since acetaldehyd is generally present in fresh and properly stored samples of anesthetic chloroform in proportions greater than 1: 3300, usually the reaction is not interfered with by this substance; but in every case the sample should be examined for the presence of acetaldehyd.

(b) *Anesthetic chloroform* failing to comply with the above acidity test, and which contains no carbonyl chlorid or hydrogen chlorid, should be rejected, since then the indication is that *acetic acid* is present;

(c) When 20 c. c. of *anesthetic chloroform* are shaken during 20 minutes with 15 c. c. of concentrated sulphuric acid in a glass-stoppered tube of 50 c. c. capacity previously rinsed with sulphuric acid, and 2 c. c. are diluted with 5 c. c. of water, the liquid should remain colorless and clear, and should possess no odor foreign to anesthetic chloroform (chloroform and alcohol); and the liquid should still retain its transparency and colorless state when further diluted with 10 c. c. of water, and the transparency should not be diminished on the addition of 5 drops of silver nitrate solution. A positive result is indicative of the presence of chlorinated derivatives of the oxidation products of alcohol, etc.

Degrees of Purity of American Chloroforms.—The main impurities contained in American anesthetic chloroforms are, besides water, impurities decomposable by sulphuric acid and traces of the oxidation products of ethyl alcohol. The presence of small amounts of ethyl alcohol is necessary; but anesthetic chloroform should contain but mere traces of water, and it is desirable that it be absolutely water-free. The necessary precautions should be taken by manufacturers to guard against the presence of organic impurities as well as of extractive matter—a common contaminant of anesthetic chloroform contained in unprotected cork-stoppered bottles.

The table (p. 892) will serve to show the comparative purity of various samples of chloroform. Nos. 1–9 were samples of anesthetic chloroform, supposed to be of the present U. S. P. grade and such as are now being supplied to the trade;[1] No. 10 was a sample, stated to be of U. S. P. quality, contained in a tin and 17 months old; No. 11 was a sample of "Chloroform for Anesthesia" contained in a sealed tin, and 6 years old;[2] and No. 12 was an unopened tin of "chloroformum purificatum," manufactured in 1863 or shortly before.[3] The last two samples are of particular interest, since, so far as the authors are aware, they were the oldest samples of chloroform ever examined.

[1] All of these samples, with the exception of No. 6, were manufactured in the United States. These samples were obtained through the courtesy of the various manufacturers, to whom the authors desire to acknowledge their indebtedness.

[2] Sample, dated Nov. 1, 1905, supplied by Surgeon-General Torney, U. S. A.

[3] This sample was also furnished by Surgeon-General Torney who stated that this chloroform was taken out of a pannier of the variety issued during the Civil War, along with records, etc., which bore the date of 1863. To quote from his letter of transmittal, "I presume that the chloroform was made at that period, or before, and I may say that it is the last survivor, so far as I know, of the chloroform supplied at that period." It is important to note that this tin of chloroform possessed a smaller air space than No. 11, the container being almost full; this accounts for the difference in oxidation of the alcohol in the two samples.

COMPARATIVE PURITY OF VARIOUS SAMPLES OF CHLOROFORM

All samples gave tests for water present in permissible amounts; negative acidity tests, U. S. P.; negative tests for chlorides and for oxidation products of pure chloroform.

No.	Source.	Grade.	Density at 25/25°.	Odor.	Residue in gm. per liter.
1	Acetone	Anæsthetic	1.4827	Normal	......
2	Acetone	Anæsthetic	1.4730	Normal	None
3	....	Anæsthetic	1.4772	Normal	None
4	Acetone	Anæsthetic	1.4806	Normal	None
5	Acetone	Anæsthetic	1.4770	Normal	......
6	Chloral	Anæsthetic	1.4839	Normal	......
7	Acetone	Anæsthetic	1.4756	Normal	......
8	Acetone	Anæsthetic	1.4750	Normal	......
9	Carbon tetrachloride	Anæsthetic	1.4773	Normal	......
10	....	Anæsthetic	1.4751	Slightly pungent	0.0220
11	Acetone	Anæsthetic	1.4722	Normal	None
12	Alcohol	Anæsthetic	1.4747	Fruity	......
13	Acetone	Analytical	1.4752	Normal	0.0165
14	Acetone	Commercial	1.4846	Normal	0.0705

No.	Extractive matter.	Sulphuric acid test.	Formalin-sulphuric acid test.	Absolute ethyl alcohol in c. c. per 100 c. c.	Higher alcohols.
1	Present from cork	Faint	Faint brown	0.50	Not detected
2	Absent	Negative	Faint yellow	0.97	Not detected
3	Absent	Negative	Marked brown.	0.77	Not detected
4	Absent	Negative	Negative	0.56	Not detected
5	Absent	Negative	Brown color	0.70	Not detected
6	Present from luting	Marked	....	0.30	Not detected
7	Present from cork	Decided	....	0.80	Not detected
8	Indefinite	Faint	Very faint yellow	0.84	Not detected
9	Trace	Very faint	Faint yellow	0.74	Not detected
10	Trace	Faint	....	0.84	Not detected
11	Absent	Marked	....	0.83	Present
12	Present	Pronounced	....	0.60	Propyl
13	Present from cork	Faint	....	0.69	Not detected
14	Present	Marked	....	....	Not detected

No.	Acetone.	Acetaldehyde.	Acetic acid in gm. per 100 c. c.	"Odorous decomposition products."	"Chlorinated decomposition products."
1	Absent	....	0.0003	Absent	Absent
2	Absent	Trace	0.0001	Absent	Absent
3	....	Trace	......	Absent	Absent
4	Not detected	Trace	Absent	Absent	Absent
5	Not detected	....	Absent	Absent	Absent
6	....	Trace	0.00015	Faint reaction	Trace
7	Not detected	Trace	0.00015	Absent	Very faint reaction
8	Not detected	Trace	0.00030	Absent	Present
9	....	Absent	Absent	Absent	Absent
10	....	Present	0.00045	Absent	Present
11	Not detected	About 1 : 3300	0.0009	Absent	Present
12	....	1 : 2000	0.00045	Present	Absent
13	Not detected	Trace	....	Absent	Faint reaction
14	Not detected	Trace	....	Absent	Faint reaction

APPENDIX III

OXYGEN

History of Oxygen.
Methods of Manufacturing Medicinal Oxygen.
Impurities That May Be Present in Oxygen.
Purity of Commercial Medicinal Oxygen.
Standards of Purity That Should Be Required for Oxygen to Be Used in Medicine.

History of Oxygen.—The alchemists[1] were probably acquainted with oxygen, perhaps also the Greeks[2] in the fourth century, and the Chinese,[3] long before Priestley's experiments. In 1630 Jean Rey[4] knew that certain metals, when heated, fix a portion of the air, and in 1674 Mayow[5] prepared oxygen from niter. In 1771 Scheele[6] prepared a gas by heating several oxids, including the black oxid of manganese, and, at about the same time, Cavendish[7] studied oxygen. To Priestley,[8] however, has been given the honor of discovering oxygen as a constituent of the air. Davy[9] and Lavoisier[10] later studied the preparation and nature of this gas.

Methods of Manufacturing Medicinal Oxygen.—At the present time there are the following methods of preparation and manufacture of oxygen:[11]

[1] Bolton: *Am. Chem.*, *4*, 170.

[2] Hoefer: ''Histoire de la Chimie,'' *2*, 271.

[3] Duckwood: *Chem. News*, *53*, 250.

[4] Jean Rey: ''Essai sur la recherche de la cause pour laquelle l'airain et le plomb augmentent de poids quand on les calcine,'' Bazas, 1630.

[5] Mayow, Rodwell: *Chem. News*, *8*, 113.

[6] Scheele: ''Chemische Abhandlung von der Luft und dem Feuer,'' *Upsala u. Leipzig*, 1777.

[7] Cavendish: *Trans. Roy. Soc.*, *56*, 432; *74*, 119, 170; *75*, 372.

[8] Priestley: *Ibid.*, *62*, 147; *65*, 384; *73*, 398; *75*, 279; *78*, 147, 313; *79*, 7, 289; ''Experiments and Observations on Different Kinds of Air,'' London, 1775-1777, *2*, 29; *3*, 1; ''Experiments and Observations Relating to Various Branches of Natural Philosophy,'' London, 1779, *1*, 192.

[9] *Trans. Roy. Soc.*, *101*, 1.

[10] Crell: *Chem. Journ.*, *4*, 440; *5*, 125; *Chem. Ann.*, 1786, *1*, 33, 136; 1778, *1*, 354, 441, 528, 552; 1788, *2*, 55, 262, 431, 433; 1789, *1*, 145, 162, 260, 323; *2*, 68, 145, 433; 1790, *1*, 69, 518; 1791, *1*, 71; 1803, *1*, 29.

[11] Baskerville and Stevenson (*J. Ind. Eng. Chem.*, 1911, *3*, No. 7) made an elaborate investigation on this subject. For details of procedure and methods used, this paper should be consulted.

(1) Heating chlorates; (2) heating chlorates with various substances; (3) from hypochlorites, and reaction of chlorin and water; (4) heating sulphuric acid or sulphates; (5) heating various solids and mixtures (MnO_2, CuB_4O_7, etc.); (6) combustion of solid mixtures (chlorates with combustible material, alkaline peroxids with hydrated salts, etc.); (7) reaction of peroxids ("oxone") with water and aqueous solutions; (8) by electrolysis of water; (9) from the air by means of mercury, cuprous chlorid, barium dioxid; manganates, plumbates, or living matter; dialysis or absorption; (10) from liquid air.

For medicinal purposes oxygen is manufactured according to methods 2, 7, 8, and 10.

Impurities That May Be Present in Oxygen.—The following sorts of matter may be suspected to exist in a cylinder of oxygen gas:

(1) Solids; (2) liquids; (3) gases and vapors: H_2O; halogen acids, HNO_3, organic acids; O_3, NO_2, N_2O_3, SO_2; NH_3, organic bases; CO_2, halogens, oxids of chlorin; HCN, $(CN)_2$; PH_3, SbH_3, AsH_3, H_2S; H_2; CO_1CH_4, organic matter; N_2, N_2O, rare gases of the atmosphere.

If the method by which the oxygen has been prepared is known, a consideration of many of these impurities is unnecessary. For example, impurities which exert a distinctly injurious physiological action are not to be suspected in oxygen prepared by electrolysis, liquid air, or the decomposition of alkaline peroxids (Na_2O_2) by water. It is only necessary to know the percentage of actual oxygen present in the gas. This may be determined most conveniently, and with sufficient accuracy, by absorption in alkaline pyrogallate solution. Care should be taken to use an alkali produced electrolytically or Hempel's[1] precaution to prevent the production of carbon monoxid. Nitrogen and the inert noble gases of the air are determined by difference.

Purity of Commercial Medicinal Oxygen.—One of us (C. B.)[2] has devised elaborate methods for the examination of oxygen and determined the purity of "C. P." oxygen offered on the market for medicinal use. Below is given a tabulation of the results of analyses, according to these methods, of seven makes of oxygen.

No.	Source of oxygen	O_2	H_2O	CO_2	H_2	Organic Matter	N_2 etc.	All other impurities.
1	$KClO_3 + MnO_2$	93.20	0.30	0.11	0	0	6.39	0
2	$KClO_3 + MnO_2$	98.31	0.14	present	0	0	1.54	0
3	$KClO_3 + MnO_2$	92.82	0.26	trace	0	0	6.92	0
4	$KClO_3 + MnO_2$	97.13	0.23	present	0	trace	2.63	0
5	Liquid air	96.10	0.15	0.01	0	0	3.74	0
6	Electrolysis	99.23	0.35	9.03	0.14	0	0.25	0
7	$Na_2O_2 + H_2O$	99.20	0.50	trace	0	0	0.30	0

These were all medicinally pure.

[1] "Gas Analysis," English translation by Dennis, 1906, 149.

[2] In conjunction with Stevenson, *loc. cit.*

Standards of Purity That Should Be Required for Oxygen to Be Used in Medicine.—The gas should be neutral toward moist, delicate litmus paper (showing absence of irritating acid or alkaline gases); and, when passed through an aqueous solution of silver nitrate, it should produce no turbidity (absence of chlorin or chlorin oxids). Not more than an opalescence should be produced when 2 liters of the gas are passed slowly through an aqueous solution of barium hydroxid (showing minimum of carbon dioxid). This condition is to be modified when a mixture of oxygen and carbon dioxid (4 per cent of the latter) is deliberately used. See Chapter II. When 5 liters of the gas are passed slowly through an aqueous solution of sodium hydroxid, then over heated copper oxid, and finally through an aqueous solution of barium hydroxid, no turbidity should be produced (showing absence of organic impurities, as hydrocarbons). The gas should contain at least 95 per cent oxygen upon the dry basis. As supplied for use, the gas should contain no liquids and no solids.

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