THE ULTIMATE BABY BOTTLE

Are artificial wombs in our future? Was Aldous Huxley right? **By Tabitha M. Powledge**

NOBUYA UNNO brings up the nightmarish novel *Brave New World* himself, marveling at Aldous Huxley's accurate prediction that the kids are likely to be anemic after they emerge from their artificial wombs. Actually, Unno's little ones are not quite kids yet. They're fetuses. Goat fetuses.

Raising the ticklish subject of Huxley's 67-year-old novel is pretty cheeky for a scientist who has devoted a decade to developing an artificial womb. But Unno, an obstetrician-gynecologist and researcher at the University of Tokyo, might simply be acknowledging the inevitable. The novel's clever and even now slightly shocking vision of human kids fostered in jars always lurks beneath any talk of artificial wombs.

It's hard to dismiss Huxley, even though the purposes of the artificial wombs being developed at several institutions around the world differ from those described in his book. They are not the government's way of breeding a citizenry specialized for particular chores, most of them menial. Quite the opposite. They are born of consumer demand for fertility treatments and better babies.

NOT YOUR AVERAGE SIBLING RIVALRY

Today's assisted-reproduction technologies, such as in vitro fertilization, have resulted in a boom of cases of a womb with a two—or a three or a four. Indeed, it is not so rare for five, six or even more fetuses to be jammed together in a berth that was really designed for just one. One consequence has been more babies born far too early. Their tiny lungs are not ready to breathe air, so we plunk them into incubators and hook them up to respirators. The result is what doctors delicately term iatrogenic injuries, meaning damage arising from medical intervention. To wit: brain damage, blindness, intestinal damage, delays in development, mental retardation and other lifelong handicaps. So the hunt is on for safer ways to help fetuses through the transition to becoming air-breathing creatures.

Hence the artificial womb. Unno and his colleagues at the University of Tokyo call their version the Extrauterine Fetal Incubation system, or EUFI. Although incubation is its middle name, EUFI is quite different from a conventional incubator. It attempts to simulate the fetal universe.

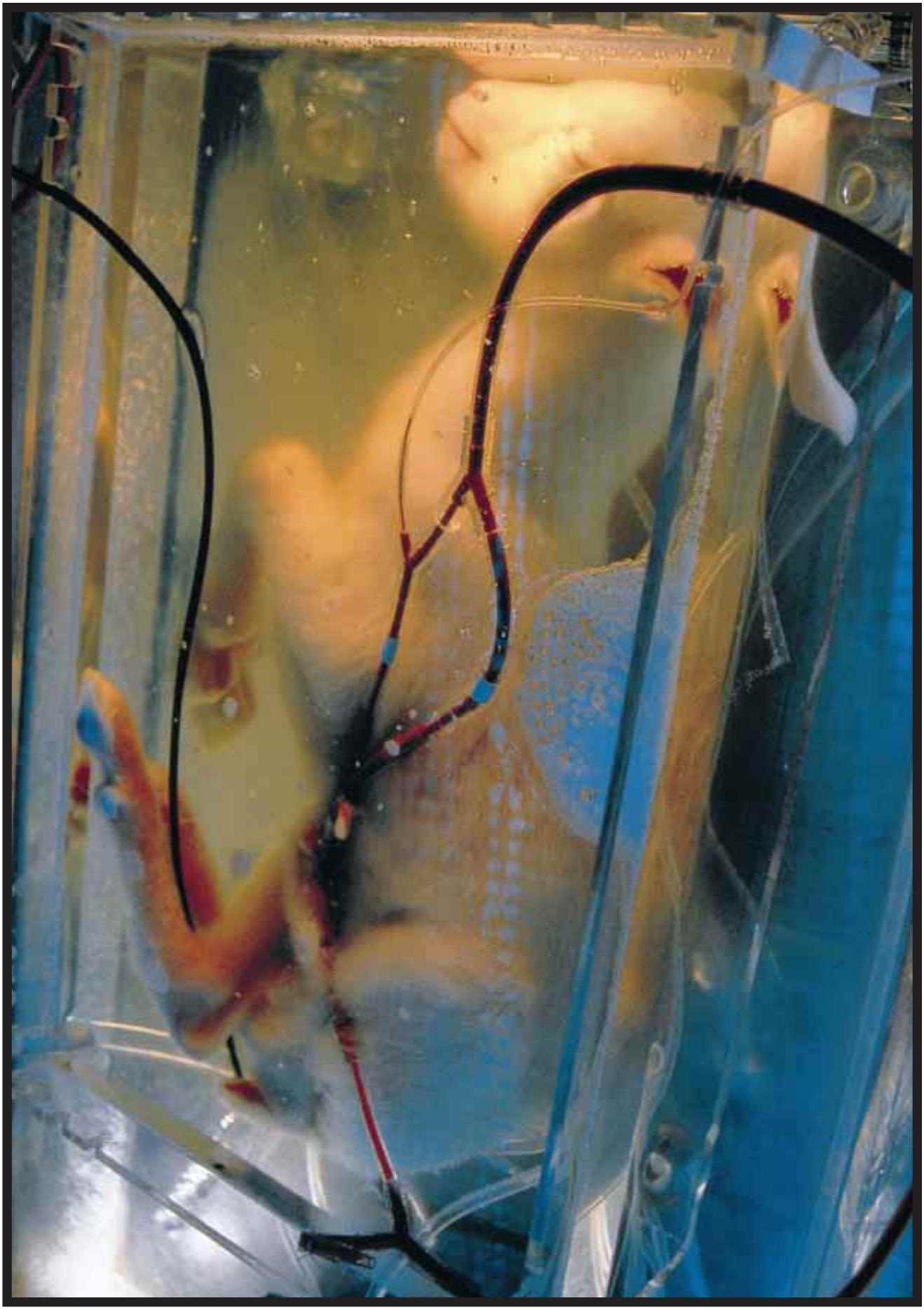
EUFI is a double-walled, vertical acrylic box filled with artificial amniotic fluid warmed to just under 40 degrees Celsius (104 degrees Fahrenheit), the normal temperature of a nanny goat's own. The furry fetus floats in the fluid and need not breathe air. The truly critical component of the artificial womb, however, is not the container itself but its substitute for the placenta.

A biological placenta adds oxygen and removes carbon dioxide from the fetus's circulating blood, just as its lungs will do once they are fully developed. Artificial-womb scientists must mimic that ability, building a detour into the fetus's circulation so that blood passes from umbilical artery to umbilical vein, exchanging gases as it goes. The Japanese design passes the blood through a membrane oxygenator made of hollow silicone fibers; the unit looks like a thick, clear plastic tube full of straws.

Unno and his co-workers have maintained a fetal goat in EUFI for more than three weeks. (Because goat gestation is about half as long as a human pregnancy, three weeks for a goat fetus is roughly comparable to six weeks for a human one.) But none of the kids the scientists have kept in EUFI for long periods have survived

TOM WAGNER *SABA*

Goat-in-a-box? Using goat fetuses as guinea pigs, researchers at the University of Tokyo have developed the world's most advanced artificial uterus technology. They say their plastic box filled with synthetic amniotic fluid is almost ready to nurture a human fetus.



after they were "born," even with mechanical respirators to help them breathe. The researchers have had better success removing kids from their dams for several hours or a day and then replacing them: three have been nurtured temporarily this way. Unno's theory is that his current setup doesn't allow the fetuses adequate nutrition, a problem he claims can be corrected.

"I believe, technically, we are ready to apply the concept of our system to human fetuses, although of course we need to redesign the whole system to maximize safety before actual clinical use," he says. But even at its present technical level, he suggests, the apparatus might be ready for preemies born at 25 or 26 weeks. Eventually the system could be applied as early as 23 weeks, the present record for a premature baby to be born and still survive.

The Japanese success appears to have provoked interest elsewhere. At least two other EUFI-like projects are in the works. A Spanish artificial womb, still in the design and very early testing stages, resembles Unno's. Pediatric surgeon Vicente Martinez Ibañez and his colleagues at Hospitals Vall d'Hebron in Barcelona are planning to set a sheep fetus adrift in a small transparent pool. Outside will be two fluid filters and a pump that also performs the task of an oxygenator. This pump will be connected to the umbilical blood vessels, and it will act as an artificial placenta as well.

If grant money is forthcoming, Martinez Ibañez foresees that the womb could be ready in three to five years. "Our main problem is the financial issue, but we are optimistic," he says.

HELLO, JELL-O BABY

There's also a new collaborative effort among several laboratories at Harvard University and the Massachusetts Institute of Technology to invent what researchers there call minimally invasive medical technologies. Support for the extremely premature infant is its first project, which is still very much on the drawing board. For competitive reasons, Joseph P. Vacanti, a surgeon at Harvard Medical School and a pioneer in the new field of tissue engineering, declines to discuss the group's plan for gas exchange except to say that it, too, will mimic the placenta.

"Our concept," he says, "is that we would probably have to put the baby into a semiaqueous environment in a sort of Biosphere." By "semiaqueous" he means one of the new hydrogels that can be either very liquid or fairly solid, with the degree of jelling adjusted to cushion the fetus and permit gas exchange. (But try not to think of the Boston Baby Biosphere as a bowl of Jell-O.)

To Barbara Katz Rothman, author most recently of *Genetic Maps and Human Imaginations: The Limits of Science in Understanding Who We Are,* the stated mission of EUFI and the other womb designers sounds familiar—and ominous. Every technology for newborns, from infant formula to electronic fetal monitoring, follows the same path, she asserts. "It starts off as an alternative in a tragic situation and then becomes the more sophisticated, elite way to do it."

Eventually a woman who **wants a uterus** could place her order, donate her cells and **take delivery** of her **custom-made womb** in just six weeks.

She is concerned chiefly about the consequences of raising a baby without an attachment to another human being. A pregnant woman thinks constantly about her baby; long before birth, it is part of her life. "That is very different from putting in an order and having them give you a call when it's ready."

Katz Rothman, who is also a professor of sociology at the City University of New York, recalls once asking students how

PHOTOGRAPHS BY SAM OGDEN

Bioartificial bladders, such as the one now being grown at Harvard Medical School (*shown above and in incubator at left*), can serve as prototypes for a bioartificial womb. The main difference between the two organs is that wombs have thick, muscular walls for childbirth, whereas bladder walls are thinner and less structurally complex.

they would comfort a baby raised in a machine. "A guy in the back of the room said, 'Put it on top of the refrigerator!' "

She foresees—and she is not alone—that EUFI and its ilk will get better and better at helping increasingly young fetuses survive, eventually meshing seamlessly into the efforts of the assisted-reproduction technologists to get better and better at helping increasingly old embryos survive. When that happens, Huxley's imagined technology will no longer be fiction. "That will open all kinds of troubles: corporate babies and baby sales and babies being grown for God knows what purpose," she predicts.

WOMBS MADE TO MEASURE

Anthony J. Atala, a surgeon at Harvard Medical School's Children's Hospital, is taking a completely different approach to the artificial womb, one that doesn't trouble Katz Rothman at all. Atala is a tissue engineer whose idea is to grow transplantable organs from a patient's own cells. The patient's body would not reject such organs as foreign, and nobody else would have to part with a kidney or a nice piece of liver [see "Growing New Organs," on page 10].

Atala's report earlier this year about a tissue-engineered artificial bladder that works in beagles made a big splash. It took Atala and his colleagues 10 years to devise the right soup to nourish the bladder cells and to grow the bladder, which is basically a bag—a tough shape to grow in a lab.

Quick, what other well-known organ is also basically a (very muscular) bag? Guess what tissue Atala's lab is trying to engineer now? The bladder and the uterus have very different functions, of course, but Atala's plans for his womb grow out of his success with the beagle bladder. Already his lab is building the cell layers that compose uterine tissue: muscle and the spongy stuff called endometrium that lines the inside of the uterus. "We're doing very preliminary work: taking cells, placing them on a scaffold and creating small units of tissue," he explains.

Complex as it is, in a sense Atala's challenge is simpler than that of the Baby Biosphere researchers, because there's no placenta. Making its placenta is the baby's job. Atala's is just the container, one that would permit an embryo to implant and create its customary system for getting oxygen and getting rid of carbon dioxide and to provide housing until normal delivery time. "That's a long-term goal," he notes. "We are at a very elementary stage right now."

Atala wants to create a uterus that can be transplanted into women who are born without one or who have uterine abnormalities or scarring. Once the researchers know how to grow a uterus, the plan is for a woman who wants one to donate stem cells—early-stage cells that have not yet begun to specialize [see "Embryonic Stem Cells for Medicine," on page 18]. These will be grown in the lab into a uterus, which will then be surgically implanted into the woman, where it will work as if it were original equipment.

Atala predicts it might take as long as another 10 years to fashion his uterine bag because the uterus is more complex than the bladder. But eventually, he says, a woman who wants a uterus could place her order, donate her cells and take delivery of her custom-made womb in just six weeks.

"Nature does it best," Atala points out. "We can do some things in an incubator outside of the body. But during pregnancy there are so many things going on, so many hormones, such an interaction between the mother and the child. The best incubator is Mom."

Katz Rothman couldn't have put it better herself, which is why Atala's bag doesn't worry her one bit. "A uterus inside a woman's body, that's fine. To me that is not an artificial womb," she declares, suggesting instead that it's more like contact lenses or a prosthetic arm. "You're extending the body and making the body work. That is very different from pregnancy without a body."

Still, there's one possible use for Atala's bag that, while it might not bother Katz Rothman, would certainly discombobulate a lot of other people. To say nothing of transfiguring human culture, politics and the psychology of sex, reversing hundreds of millions of years of evolution, and giving birth to a new division of the fashion industry:

Welcome to the 21st century, when men can get pregnant.

ABOUT THE AUTHOR

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