

getting
ever older

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sign for living

BY POLLY SHULMAN

Jeanne Calment had the longest memory in human memory. As recently as 10 years ago, she recalled a trip she took to Paris where she saw an impressive new structure going up—the Eiffel Tower. Vincent van Gogh used to buy paint at her family’s shop in Arles, and the artist made a bad impression on young Jeanne: he was ugly, bad-tempered and reeked of alcohol, she told reporters years later. At 85 she took up fencing and at 120 gave up smoking—“It was becoming a habit,” she explained. She outlived all her descendants, including her grandson, a doctor, who died in 1963. Asked at 115 how she saw her future, she quipped, “Short. Very short.” But she was wrong: she lived seven more years, dying on August 4, 1997, at 122 years, five months and 14 days, the longest verifiable life span of any human being. She attributed her long life variously to olive oil, wine and a sense of humor. “I have only one wrinkle,” she said, “and I’m sitting on it.”

Most of us, of course, can never hope for longevity (or humor) to match Calment’s—she’s one in six billion, points out Thomas T. Perls, acting chief of gerontology at Beth Israel

Deaconess Medical Center in Boston. But the number of centenarians is rising every year. According to a July 1999 census report, there are about 72,000 people older than 100 in the U.S., a number expected to reach 834,000 within the next 50 years. Even

more important, says Richard M. Suzman, associate director for behavioral and social research at the National Institute on Aging, the rate of disability in all populations, including the oldest old, has been dropping since 1982. Demographers, geneticists and medical researchers hope that studying healthy people in their 80s, 90s, 100s and beyond—“the superstars of longevity,” as Perls refers to them—will yield vital clues to how all of us can live longer, healthier lives.

To Leonard W. Poon, principal investigator of the Georgia Centenarian Study, the secret to longevity is that there is no secret. Poon and his colleagues followed 144 cognitively intact, independently living centenarians, whom he calls “the cream of the crop.” Some were compared with groups of people in their 60s and 80s from similar backgrounds; others were interviewed and tested every six months for what remained of their lives. He believes the most important lesson of the study is the qualities that stood out among the oldest old.

For example, few of the centenarians in the study smoked, were obese or drank heavily. They remained active throughout life, ate breakfast regularly, and consumed plenty of vitamin A and carotenoids by eating fruits and vegetables. “In terms of psychology and attitudes, they’ve resolved whatever issues they have, they’re sure of themselves, and they want to have their way,” Poon says. “They would not take your word for anything—they want to find out for themselves. And they’re very protective of themselves.” Learning about the diversity of characteristics that centenarians share, he thinks, “isn’t a bad result, because anyone can find one factor rele-

FOR THE RECORD BOOKS: Jeanne Calment, whose life was the longest ever documented, here contemplates the world from the vantage point of 121 years, a year before her death in 1997.

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vant to their lives, one thing that's possible to change. The diversity gives all of us hope to be able to live longer."

Poon, a psychologist by training, considers motivation and attitude as important as genes. But Perls, director of the New England Centenarian Study and a co-author of *Living to 100*, believes there are genes that can guarantee their lucky recipients a better chance to live a long,

treme old age, such as a group of seven siblings, five of whom passed the 100-year mark. (Calment's family is another good example: her father died at 93, her mother at 86.) People in the past thought there were tens of thousands of genes that had a weak effect on longevity, but Perls and his colleagues believe there are probably just a few genes with very strong effects: "When you see the

The fact that members of such groups share large amounts of genetic material makes it easier to find relevant genes. The geneticists compare the genes of long-lived group members with those of members with short or normal-length lives. Because these people have so much genetic material in common, any genes found in the long-lived group but not in the short- or normal-lived group have a good chance of being the ones the scientists are looking for.

But once they find them, what good will it do the rest of us? If we're not blessed with lucky genes, should we throw up our hands and write our wills? Of course not, Barzilai says. The whole point is to find out what functions those genes perform, then develop medicines to mimic them. "If they have to do with oxidation, we'll try to manipulate oxidation. If they increase levels of HDL—that's the beneficial kind of cholesterol—maybe we can increase HDL. Here's another example: I had a 102-year-old who had a very high grade cancer, with a prognosis of two months, but she lived with it for five or six years. Maybe something in her genes protected her from this cancer," Barzilai notes.

If so, understanding how that protection worked could help doctors develop cancer-fighting drugs. The genes will also shed light on healthy behavior. If centenarians have genes that keep them slim, the rest of us could try to mimic that by cutting down on the excess calories, as Perls does (his work with the very old has inspired him to shed 15 pounds).

Although it's too soon for genetic results in their study, Barzilai and his team have been quizzing their centenarians for shared characteristics. Like Poon, they've found a lot of diversity. "No one of the centenarians is telling me that he did anything special to reach that age," Barzilai says. "Many of them ate what they shouldn't have eaten, or they smoked. But one thing they seemed to have in common was some form of flexibility. Many of them had very hard lives. They rolled with punches, got up and continued with a good attitude."

One tough problem is to separate



MARK HAVEN

WHAT'S HIS SECRET? Artist Harry Shapiro, who is 100 years old, is an Ashkenazi Jew, a group being studied in a search for longevity genes.

healthy life, and he means to find them. Siblings of centenarians in his study, he points out, have a five times greater chance than average of living to their early 90s and a 15 times greater chance of living to 100. Of course, siblings share environmental factors as well as genes. Could some of these be responsible? "Is it the chicken soup their mom makes?" Perls asks. "No, because their parents also live unusually long."

Along with medical and population studies, the New England Centenarian Study does genetic work with centenarians in collaboration with molecular geneticists. The scientists look for longevity genes in families with a high proportion of members who live to ex-

kind of clustering [of people] we're seeing, mathematically it's got to be only a few genes—maybe just 10 or so. In one family, you may find one or two." His team is very close to finding regions of chromosomes, he says, that contain such genes. Right now they're checking their results. "It's such a big-deal finding, we want to make sure we're correct. Once you find a region, you know everyone and his grandmother is going to be falling all over themselves to find the genes on that region."

Nir Barzilai, a gerontologist at the Albert Einstein College of Medicine who collaborates with Perls's group, is looking for longevity genes as well. He and his colleagues study "founder populations"—small, genetically isolated groups that gradually expanded to large numbers, all the while marrying within the community. One collaborator hunts through the genes of the Amish; Barzilai does the same with Ashkenazi Jews.

cause from effect. Did Barzilai's and Poon's centenarians live longer because they rolled with the punches, or did 10 decades of experience give them the wisdom to accept experiences that would have thrown them for a loop in their youth? Centenarian researchers would like to go back in time and interview their subjects at 20, 50, 80—but of course, they can't.

Butterfat for Couch Potatoes

Poon's centenarians got plenty of vitamin A and ate breakfast regularly. Well and good; Mom, your doctor and your cereal box would approve. But they also drank more whole milk and were less likely to avoid cholesterol than the 60- and 80-year-olds in the study. Is butterfat good for you? Or did they have genes that protected them from its deleterious effects, as Perls believes? "The centenarians in our study don't have a history of exercise, but the rest of us can't get away with this," he says. And what about Calment's cigarette habit? Do genes make smoking safe for some of us but deadly for others?

Such questions are important not only on an individual level but also demographically. Understanding and predicting changes in the general population and the health statistics of older people will be increasingly important to policymakers and health care providers as well as to aspiring centenarians.

The demographics of the oldest populations may yield some surprises. A study conducted at Odense University in Denmark, analyzing mortality data from 13 European countries and Japan, showed that after age 97 a person's chance of dying at a given age slowed from the expected exponential growth trend. Indeed, many diseases strike preferentially at earlier ages. Rates of many cancers decline after 85, as does the chance of developing Alzheimer's disease, particularly for the 25 percent of Americans who have at least one copy of a gene type predisposing them to it.

On the other hand, the incidence of other major diseases increases with age. And the very old, whose immune systems have weakened with age, are more susceptible to some common infectious diseases, such as pneumonia and flu. In

fact, for most of the elderly population, Suzman argues, mortality goes up, and the prevalence of disability and chronic diseases also increases with each additional year of age, although the rate of increase does seem to slow down sometime past 90.

One factor that sheds both light and confusion on the question of what the oldest Americans will be like in upcoming decades is the cohort effect. Groups born in different decades have very different patterns of mortality and survival, Suzman says, which can be difficult to tease out.

For example, levels of education that Americans attain have been rising with every generation. Increased education improves their life and health expectancy—although why is a big mystery. Part of the explanation is that education affects income level, which affects health.

Education may also encourage people to adopt healthier lifestyles. More highly educated people may end up in jobs that are less stressful, or education may allow people to deal better with the rigors of stress. "It may have an impact on the brain, and the brain may turn out to be the major arbiter of survival, rather than the coronary artery," Suzman observes. And education is only one of dozens of factors that vary dramatically from one decade to another, including nutrition, smoking, sun exposure and exercise.

How much, for example, does medical care affect mortality? "Oddly, that's never been effectively measured," Suzman says. Medical intervention will have an increasing impact, he believes, sometimes through information produced by medical research, rather than medical treatments. Convincing Americans to get off the couch and shed excess pounds, for instance, could have a huge impact. So could new methods of disseminating information, such as the



AND THE WINNER IS ... 114-year-old Eva Morris of England, who is currently the oldest person alive, according to the *Guinness Book of Records*.

Internet. "Life expectancy is the least of it," Suzman says. "More important is health expectancy."

Calment notwithstanding, most of us have genes that will take us to 85 or so, barring physical catastrophe. But our behavior can help reduce or eliminate chronic diseases that make the last years painful for many. And geneticists are planning to search the genes of centenarians for clues not only to killer diseases but also to diseases you can live with but may not want to—things like macular degeneration, Barzilai says, or hearing loss. "Sans teeth, sans eyes, sans taste, sans every thing," moaned Shakespeare, describing the last years of life. Thanks to centenarians, the future may not need to be like that.

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Further Information

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