How Long Is the Human Life-Span?

Perhaps longer than we thought. New data from humans and fruit flies are challenging the notion that the body necessarily falls apart at, say, age 85

WHAT IS THE BIOLOGICAL LIMIT TO THE HUman life-span? That question is, of course, riveting to all us of us as we contemplate our own approaching mortality. But it also has some very practical medical and economic consequences—particularly in a "graying" society. Knowing how long our species is capable of living would influence strategies for combating the diseases of old age; it would also allow estimates of the future strain on social and medical programs expected to take care of the burgeoning number of older—and likely sicker—people.

But for the moment the question of whether there is a biological limit on the human life-span—and, if so, what that limit is—is very much a matter of debate. That debate may take a new turn next week when proponents of two distinctly different points of view come face to face over some new data at a session of the annual meeting of the Gerontological Society of America in San Francisco. One of the two, Stanford rheumatologist James Fries, is the leading current proponent of the notion of inborn limits; he thinks they kick in around age 85. Presenting the opposing viewpoint will be University of Minnesota demographer James Vaupel, who is currently a visiting professor at the Odense University Medical School in Denmark. Vaupel has been putting Fries' ideas to the test using Scandinavian population studies as well as data from fruit flies. His preliminary results, he says, show Fries to be wrong.

Fur may fly when Vaupel and Fries—who is widely known for his rhetorical skills—take the stage. "I can't predict what is going to happen when you get these two people up there, one saying [the limit to life] is 85, and the other saying there is no limit," says demographer Jay Olshansky of the University of Chicago, whose own work is in trying to estimate the practical limits to human life expectancy. But whether the symposium proceeds politely or not, it will surely provide a window onto a field that is now in a state of intellectual ferment.

Some of the parameters of the current debate were set 30 years ago when Leonard Hayflick, then of the Wistar Institute in Philadelphia, showed that cultured cells undergo a limited number of divisions. Hayflick extrapolated from this test-tube work to assert that the organs and tissues of the human body also run out of gas after some biologically predetermined time limit. This general notion, which Hayflick based on such findings as the fact that cells from older people undergo fewer doublings than those taken from younger people, became the central assumption in much of aging research.

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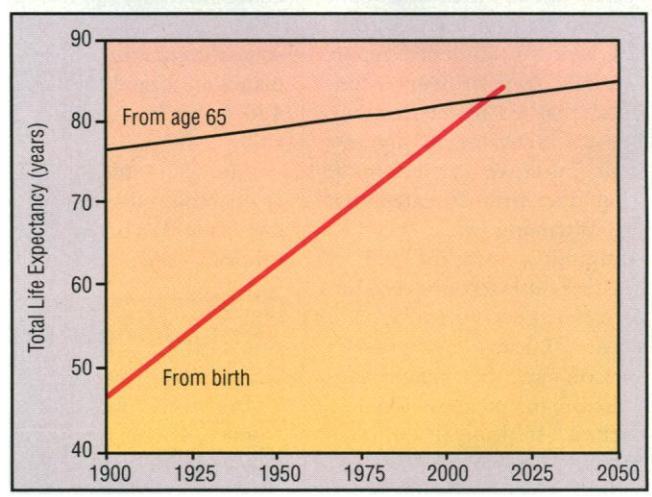


Aging opponents. *James Fries* (left) *thinks senescence sets in around 85. He bases his conclusions partly on the fact that the curves describing life expectancy from birth or from age 65 intersect at about age 88. James Vaupel questions this reasoning.*

Fries picked up what Hayflick began, with an article in 1980 in *The New England Journal of Medicine*, in which he argued that the human body is biologically destined to fall apart at about age 85, give or take a few years. "It is frailty, rather than disease," that kills people at very old ages, Fries told *Science*. "I think that by and large most people sort of sense this."

The concept of natural death is self-evident, says Fries, to anyone who has watched the gradual decline, or senescence, of older people, to the point where the tiniest insults—a fall that would have been trivial at age 20, a spell of hot weather, or a minor case of the flu—are enough to cause death. An elderly person may survive one insult only to succumb to another equally minor one. "I use the analogy of a sun-rotted curtain," adds Fries. "Try to sew up a tear in it and it just tears someplace else."

Fries supports his view with U.S. census statistics showing that the amount of expected life remaining for those who have reached age 65 has been constant in the United States for the past decade: 18.6 years, on average, for women and 14.7 years for men. He also plots U.S. life expectancy from birth and from age 65 for the past century and finds that the extrapolated lines converge at about age 85, suggesting, he says, that 85 is the biological limit to life. "I think that [85] is generally accepted," says Fries. "You can arrive at it in several different ways."

But Fries' conclusion isn't really as "generally accepted" as all that. Indeed, his view that most deaths of older people are due to biological senescence puts him at one end of a continuum that makes up today's debate on aging. Others take quite different views. For example, mathematical demographer Kenneth Manton of Duke University argues that many old people die from causes—such as osteoporosis or atherosclerosis—that were once considered the inevitable hallmarks of old age but that can now be prevented or delayed. Senescence, he says, is a catch-all term for those causes we don't yet understand or can't control. "If you approach and deal with a number of the major causes [of death]," says Manton, "you are incrementally dealing with what we had previously called senescence." Life expectancy, he argues, can and will continue to increase as medicine chips away at the diseases of old age.

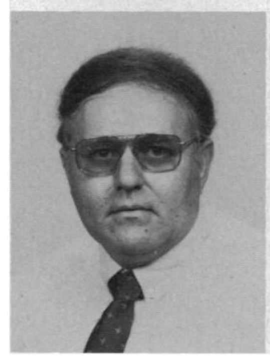
As for the collection of U.S. statistics Fries uses to buttress his case, Manton argues that they are misleading: The plateau cited by Fries, Manton claims, was an artifact caused by changes in Medicare reimbursement policy introduced in the early 1980s that apparently decreased access to medical services for people over 85. Mortality rates for those over 65 have in fact resumed a downward trend in the last 3 years, he says. Moreover, both Manton and Chicago's Olshansky argue vehemently that Fries' intersecting lines make no sense. "The point at which those lines cross is influenced by things like infant mortality rates, which have nothing to do with the biological limits to life," Olshansky says.

Olshansky also laments that his own work has been misinterpreted as supporting Fries' conclusions, when in fact it does not. Olshansky and his colleagues showed that even if we were to eliminate most heart disease, cancer, and diabetes—the major causes of death in aging adults—life expectancy in the United States would not advance much beyond 85. But, says Olshansky, "we are talking about a practical limit, not a biological one." The point, he says, is not that you can't reduce death rates for 85-year-olds, but rather that even if you do, you won't change overall life expectancy figures, because there are too few people over 85 to influence the overall statistics.

Into this quagmire of arguments and counter-arguments steps Vaupel, who hopes to clarify matters with an infusion of new data. "In the past, this field has been characterized by debate," says Vaupel. "It's really time for science in this area to move beyond debate and start looking at evidence and models." Vaupel and his colleagues have been doing just that, and their findings, he says, are likely to produce, in his words, "a paradigm shift" away from the idea of biologically programmed death, at least at ages younger than 110 or so.

One problem with the present debate over lifespan, says Vaupel, is the poor quality of the data. Many of the arguments are based largely on U.S. figures. But Vaupel says these data for people over age 85 are notoriously flawed, citing studies by Gregory Spencer of the Census Bureau and Ansley Coale of Princeton showing that age exaggeration and misreporting make the numbers highly unreliable. Vaupel decided to turn instead to Swedish vital statistics—which have been kept with impeccable accuracy by the Lutheran church since 1750—to test Fries' claim that mortality rates at age 85 have barely changed since the turn of the century.

ROBERT DREA



DUKE UNIVERSITY

Jay Olshansky (top), *Kenneth Manton.*

Vaupel and Swedish demographer and statistician Hans Lundstrom have been computerizing the records to look at trends in life expectancy for people 85 and older. What they have found, says Vaupel, is that the mortality rates for 85-year-old Swedes have dropped dramatically in the last 50 years. "Since World War II, death rates for 85-year-old Swedish females have been cut by more than one-third," says Vaupel; for men the progress has been half of that. Moreover, he says, the same is true for 90-, 95- and 100-year-olds as well.

Vaupel says his project is the first systematic examination of thousands of humans over age 85—a group called the "oldest old." But he didn't want to stop with humans. "The dispute [over the existence of a biological limit on lifespan through senescent death] is not a dispute that holds only for humans, it's a dispute that holds for all different kinds of animals," he says. "And virtually nothing is known about mortality rates at very old ages among any species except humans."

To remedy that, entomologist James Carey of the University of California, Davis, is collaborating with Vaupel and directing the construction of the largest life table ever made for any species, using 1 million Mediterranean fruit flies, at a mass rearing factory in Tapachula, Mexico. "The standard life table is [based on] 25 white mice," Carey says. "A few get into a few thousand individuals, but nothing approaches this." The medflies are reared in cages segregated by hatching date, and each day every dead fly from every cage is logged. It is necessary to use huge numbers of medflies, says Carey, to get a population of "oldest-old" that will allow meaningful analysis. Even if only 0.1% of the 1 million flies live to 100 days (roughly equivalent to 100 years for humans) that is still 1000 flies—a substantial number for analysis.

Carey expects to have recorded the death of the 1 millionth medfly by December, but the preliminary results are already in and they are surprising: The probability of dying increases for the first third of the flies' lifespan and then appears to level off. "If you define senescence as the ever-increasing probability of dying," says Carey, "then the very oldest individuals are not senescing. It forces a complete re-think on the concept of senescence."

As if these two projects weren't enough, Vaupel and his colleagues have undertaken another pair of human-insect projects to address one of the underlying assumptions of the biological limit idea: the notion that senescence is determined, in Fries' words, by "the genetic characteristics of the species." That, says Vaupel, implies that individuals with identical sets of genes should begin to succumb to senescent death at roughly the same ages, provided they haven't succumbed to premature death.

To put that idea to the test, Vaupel turned again to Scandinavia, this time to lifespan statistics compiled by the Danish twin registry on about 4000 twins born in Denmark between 1870 and 1890. He and Danish genetic epidemiologist Niels Holm are applying computer modeling to determine whether the pattern of death among the twins suggests a role for senescent death. The model that fits best, says Vaupel, is one in which all the deaths are "premature"—that is, due to accidents or disease—rather than senescent. "When we forced the computer to estimate the parameters for the senescent-death factor," he says, "it turned out that the level of senescent death was very close to zero. And the mean age at which senescent death occurred was not 85 but some number greater than 110."

To supplement the twin study, University of Minnesota entomologist James Curtsinger is looking at the lifespans of 16 different genetically identical strains of fruit flies. "They are analagous to twins," says Vaupel, "except that instead of having two Danes, you have 1000 *drosophila*." If those 1000 identical *drosophila* share genetically determined maximum lifespans, and the first 900 die prematurely," Vaupel says, "then you would expect the last 100 to die very close to each other." But Curtsinger has found that only one strain, under the most harsh rearing conditions tested, shows that pattern. Summarizing the findings of all four projects, Curtsinger says: "The [probability of dying] seems to be leveling off at the oldest ages. We are seeing it in all the projects."

Reactions to the preliminary findings of the Vaupel study range as broadly as one might expect in such a divided field. "I think there is going to be tremendous pay dirt there," says gerontologist Caleb Finch of the University of Southern California. Finch, who is the author of *Longevity, Senescence, and the Genome*, a book that deals with aging and senescence in a wide range of species, is particularly intrigued by Carey's medfly results. The steady increase of mortality with age has been shown for humans and suspected for other species, says Finch, but "Jim Carey's data look convincing that under some circumstances medflies don't show this." As to what the final word will be on biological limits to life, Finch declares it "a wait-and-see situation."

Olshansky is a bit skeptical, not of Vaupel's results but of their practical importance. "Vaupel, I believe, has incontrovertible evidence to indicate that if there is a 'death gene,' it certainly [doesn't exert its effects] before the age of 110 in humans." But, he says, while that may have disproved Fries' extreme position, it doesn't mean life expectancy will soar into the hundreds, as long as there are multiple, theoretically but not practically preventable diseases that are likely to kill people sooner.

Fries would not comment in detail until he sees the Vaupel data for himself next week. He says, however, that any findings Vaupel might have would not alter his conclusions, unless they were to change the slope of his intersecting life expectancy lines and shift the crossing point to a higher age. "If he had a curve that extrapolated to age 100, that would be counter evidence," he says, "but he doesn't; I know he doesn't. We have done it for the United States and Japan, and I know that the life expectancy data for age 85 aren't any better in Sweden." Fries adds that if Vaupel is seeing a decrease in mortality for 85-year-old Swedes, it must be due to reduction in preventable deaths. "There are still preventable deaths at age 85," he says.

"If Fries is willing to admit that there is substantial premature death above age 85, that is something," Vaupel says. "That would mean we should be able to improve life expectancy." If this pre-symposium exchange is any indication, then the upcoming encounter may simply confirm what many in the field suspect: The debate over limits to lifespan is far from over. ■ MARCIA BARINAGA

ADDITIONAL READING:

J.F. Fries, "Aging, Natural Death and the Compression of Morbidity," *New England Journal of Medicine* 303, 130 (1980).

G.C. Myers and K.G. Manton, "Compression of Mortality: Myth or Reality?" *The Gerontologist* 24, 346 (1984).

J.F. Fries, "The Compression of Morbidity: Near or Far?" *The Milbank Quarterly* 67, 208 (1989).

S.J. Olshansky, B.A. Carnes, and C. Cassel, "In Search of Methuselah: Estimating the Upper Limits to Human Longevity," *Science* 250, 634 (1990).

The Sound of One Dune Booming

Space scientist David R. Criswell of the University of Houston still can't explain what he observed in the mid-1970s at an isolated sand dune, called Sand Mountain, about 20 miles east of Fallon, Nevada. The dune is no ordinary pile of sand, Criswell will tell you. When he and his co-workers dug into it with their hands or shovels, or even when they simply walked on it, they got "a sound like a strumming on a bass violin," he says. When they sat on its 300-foot crest and together pushed off a ripple of sand, the sound swelled to "a very loud and continuous booming" like a turbo-prop plane passing overhead at low altitude, complete with rumbles in their boots. "You had the sense that this shouldn't be happening," Criswell recalls. Now Sand Mountain's strange voices are wrinkling a few more brows.

"You had the sense that this shouldn't be happening."

—David Criswell

Last week, Criswell presented the first full report on his 15-year-old observations of Sand Mountain at a meeting of the Acoustical Society of America in Houston. His hope: that someone in his audience will be able to shed more light on the little-known phenomenon of booming dunes. Says Robert D. Finch, a University of Houston mechanical engineer who invited Criswell to speak: "Most people at the meeting had not heard of this [phenomenon] before."

If Criswell or his audience at the Acoustical Society meeting can understand Sand Mountain, they may have solved an acoustic mystery that is apparently common to many dry parts of the world. Reports of booming dunes, barking dunes, and otherwise vocally notable sand formations appear in folklore and literature as long ago as 1500 years. In Tunyang, China, for example, the Hill of the Singing Sound makes rumbles like "distant carts, drums, or thunder," according to published travelers' tales. Other "singing" dunes populate the Mideast, South Africa, Chile, California, and Hawaii.

Finch's interest in the phenomenon goes even further afield. He scheduled Criswell's talk for a session on the use of acoustics in space exploration—an odd context, you might think, for a booming dune. In fact, it was space exploration that first prompted Criswell, then at the Lunar Science Institute in Houston, to trek out to Sand Mountain. During the 1972 Apollo 17 lunar landing mission, a geophone placed in lunar soil by astronauts picked up mysterious vibrations, or "moonquakes," after every lunar sunrise. At the time Criswell learned of the moonquakes, he was pursuing an interest in how winds produce patterns in sand. In his reading, he happened onto an account of Sand Mountain's freakish acoustic behavior, which was known to Native Americans and Pony Express riders. Criswell thought that it might hold some clues to understanding the moonquakes.

To get to the bottom of the dune's behavior, Criswell's team used microphones for recording the low-frequency sounds and geophones to measure ground vibrations accompanying the louder ones. They also harvested sand samples, which yielded the strongest clues to the mechanism.

"Compared to normal beach sand," Criswell says, "the grains of the booming sand are very smooth on the micron level." He suspects this feature may be at the heart of the mechanism that transforms the tumbling motion of the grains into "very pure oscillations in the ground and in the air." The smoothness may enhance the grains' ability to remain dry or avoid latching onto one another. Either way, their tendency to dissipate energy soundlessly by sticking together would be reduced, Criswell thinks. But he hasn't gotten much further than that. "It still isn't clear what is producing the sound," Finch says.

Understanding terrestrial booming dunes may not solve the moonquake mystery, Criswell cautions—data about the quakes are too sparse. But it might have some arcane industrial spinoffs, he muses. He half-seriously imagines a way to improve earth-moving machines that rely on vibratory action: by redesigning them to act as booming dunes in reverse. ■ IVAN AMATO