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TIME

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HEALTH
DOUBLE
ISSUE

THIS BABY COULD LIVE TO BE 142 YEARS OLD

Dispatches From the Frontiers of Longevity

LIVING LONGER

THE NEW AGE OF MUCH OLDER AGE

EVERYONE WANTS TO LIVE LONGER, AND SCIENCE IS STARTING TO MAKE THAT HAPPEN. BUT LIVING BETTER WILL BE THE REAL CHALLENGE—AND OPPORTUNITY

BY LAURA L. CARSTENSEN

WE LIVE IN EXTRAORDINARY TIMES. AND THANKS TO medical and scientific advances that even a generation ago would have sounded like science fiction, our lives are getting longer. An American born today has a projected average lifespan 20 full years longer than one born in 1925, and we are, as a society, growing old. For the first time in U.S. history, the number of people over 60 exceeds those under age 15.

Long life is a remarkable achievement. But our aging society presents challenges every bit as fundamental and pervasive as climate change and globalization. If we address the reality of longevity, we will avoid a crisis—and improve the quality of our lives at all ages.

Even as we look forward to more years ahead, the idea of a long life can also trigger anxiety. The unease we experience has to do with how quickly the age structure in the global population has been reshaped. In less than a century, more years were added to life expectancy than all years added across all prior millennia of evolution combined. Long-lived societies appeared so suddenly that culture—the crucible that holds science and technology along with wide-scale behavioral practices and social norms—has not caught up.

The challenge we face today is converting a world built quite literally by and for the young into a world that supports and engages populations that live to 100

Photo-illustration by Evan Kafka for TIME

years and beyond. This is no small feat. Consider, for example, that parks, transportation systems, staircases and even hospitals presume that users have both strength and stamina; suburbs across the country are built for two parents and their young children, not single people, multiple generations or elderly people who may be unable to drive. Our education system serves the needs of children and young adults and offers little more than recreation for experienced people.

Indeed, the very conception of work as a full-time endeavor ending in the early 60s is ill suited to long lives. Arguably most troubling is that we fret about ways that older people lack the qualities of younger people rather than exploit a growing new resource right before our eyes: citizens who have deep expertise, emotional balance and the motivation to make a difference.

Science and technology are the reasons for the increase in life expectancy, and looking forward, science and medicine will be responsible for how we extend life even further. But to get a handle on where we're going—the potential for a life longer than any of us can imagine—it helps to think about how we got here.

Prize-winning economist Robert Fogel and his colleague Dora Costa describe a phenomenon called "technophysio-evolution," that is, biological changes due largely to technologies that ensured a steady food supply. But this explosion wasn't limited to agriculture. Electricity was discovered and made widely available; refrigeration improved the safety of food; pasteurization and water purification contributed further to health; the systematic disposal of waste greatly reduced the spread of contagious disease; and medical science led to dramatic reductions in premature death thanks to vaccination programs that effectively wiped out lethal viruses from large parts of the developed world.

Although we were and remain little different genetically from our ancestors 10,000 years ago, the working capacity of our vital organs has improved greatly. Average body size has increased. We have grown taller, and our brains have come to process information faster.

Longer lives and the fact that we're having fewer kids, in combination, began a global process by which population pyramids—with many at the bottom and a tiny proportion of old people at the top—are being transformed into rectangles. If you're the type of person who can get chills from population statistics, these are the numbers for you. What they mean is that for the first time in history, the majority of babies born in the developed world have the opportunity to grow old.

As much as we may fancy ourselves freethinking, the crux of the longevity challenge is, quite frankly, that humans are creatures of culture. The culture that guides us today—that tells us when to get an education, marry, have children, buy a house, work and retire—is profoundly mismatched to the length of the lives we are living. Today's culture offers little in the way of cures or even treatments for the chronic diseases that afflict older people, nor does it offer guidance about how to finance decades-long retirements. And so individuals worry they will succumb to dementia, run out of money, lose their relevance. But it needn't be so. Instead of hand-wringing about productivity falling and infirmity rising, we need to change the course, both biologically and socially, of long life.

With sufficient financial support, the potential of scientific advances is breathtaking. Biologists are beginning to understand, at a molecular level, the processes by which aging increases the risk of a whole range of diseases and, importantly, how to slow and even reverse some of these processes. The very nature of chronic, degenerative diseases is being revealed, which paves the way for therapies and possibly even cures that were scarcely imagined a generation ago.

Meanwhile, technological advances have made available devices that can compensate for a wide range of age-related problems, such as difficulties with hearing, balance and mobility, just as eyeglasses rendered presbyopia no more than a minor inconvenience more than a century ago. And with an investment in social science we can develop methods that help people better envision and plan for their futures, improve fitness, remain cognitively sharp and, in some cases, reverse diseases rooted in lifestyles.

We can apply science so that the youngest children among us today live happy and healthy lives as centenarians. In partnerships with businesses and industries, products can be developed that help people age well. Examples include cars that brake before impact, smart homes that improve the safety of occupants, mobile devices that influence behavior and financial products that allow people to effectively finance long lives.

We might also trade retirement for new models of working longer, so that parents spend more time with young children, sabbaticals become commonplace and—imagine this—workers experience periods of leisure before they reach old age.

An essential first step is to change the way we think about our suddenly longer lives.

Thirty or more extra years of life also means we can improve the way we live. To the extent that we can build a world where people arrive at old age mentally sharp, physically fit and financially secure, the problems of individual aging will recede. And finally, we can change the ongoing conversation about a crisis on the horizon to one about long life and new opportunities. ■

LONGEVITY GURU:

Laura L. Carstensen, director of the Stanford Center on Longevity
Age: 61

AGING INTERVENTION

"Oddly enough, I don't think much about chronological age. I do think a lot about physical and psychological health. I keep my priorities clear. Exercise and persistently trying to solve big problems is what keeps people sharp and makes life satisfying."

Carstensen, professor of psychology and director of the Stanford Center on Longevity, is the author of A Long Bright Future: Happiness, Health and Financial Security in an Age of Increased Longevity

ILLUSTRATION BY GRAPEFUL FOR TIME

AGE DISRUPTERS

A DRUG FROM DIRT AND SOME SIAMESE MICE HAVE RESEARCHERS INCHING TOWARD THE SEEMINGLY IMPOSSIBLE: A CURE FOR AGING

BY ALICE PARK

IF THERE WERE GUINNESS WORLD RECORDS DEDICATED to high-achieving rodents, Mouse UT2598 would deserve a mention. The average life span for a mouse is 2.3 years—so at age 3 and still going strong, Mouse UT2598 has a shot at beating the record for longest-lived, which stands at about 4. Translating that to a human life span, he's hovering around the centennial mark, but on the outside, he looks no different from his much younger brethren. His fur is glossy black, he's lean, and while he's a bit on the small side, he's scrappy and surprisingly active as he explores, sniffs and pokes around his cage at the University of Texas Health Science Center at San Antonio.

What gives Mouse UT2598 his edge is a compound called rapamycin, which seems to slow aging and the damage it can do, at least to certain cells. His liver and heart function as if they were far younger, and his tendons have more spring and flexibility than they should at his age. There's also less evidence of tumors in his organs than is considered normal, so he could be spared the effects of cancer for quite a while longer. Place him alongside other mice his age, and the contrast is unmistakable.

The experiments involving Mouse UT2598 and rapamycin are just one example of the kind of research into aging that's producing new findings—and raising new questions—every day. In labs around the world, researchers are testing all sorts of agents, some of which already exist as drugs to treat human conditions (rapamycin is given to transplant patients to prevent organ rejection

Photograph by Evan Kafka for TIME

after surgery) and some of which are purely experimental. Scientists are also toying with ways to manipulate genes and pull out aging cells, all in a race to find a way to extend longevity to its outer limits.

These efforts mark a new push to examine the basic mechanisms of aging and find ways to counteract—or "cure"—them. And they are anything but fringe. Longevity research is being conducted by respected scientists with sound reasons for staking their careers on the hubristic notion that it's possible to slow down aging and maybe even reverse it.

"When I got into the field, the notion that you could actually do something about the aging process was viewed as a crackpot idea," says Richard Miller, director of the Glenn Center for the Biology of Aging at the University of Michigan. "The argument that one can slow aging, and diseases of aging along with it, used to be fantasy, but now we see it like a scientific strategy."

Nobody is talking about living forever. But as these experts see it, aging is the single most powerful factor in the diseases that are most likely to cut our lives short: cancer, heart problems, immune disorders and degenerative brain conditions like Alzheimer's. "Everybody knows that the main risk factors for heart disease are high cholesterol, obesity and high blood pressure," says Dr. Felipe Sierra, director of the division of aging biology at the National Institute on Aging (NIA). "But even stronger than those factors is just being 70 years old."

And that's why staving off aging—or at least slowing it—has become such a central focus of research. "We're going at aging itself," says David Sinclair, a geneticist at Harvard Medical School. "We might take someone who is showing signs of aging and be able to do something about it, to treat that as a disease. That's something I didn't expect to be seeing in my lifetime."

LONGEVITY GURU:

David Sinclair, geneticist at Harvard Medical School
Age: 45

AGING INTERVENTION:
"I take resveratrol, alpha lipoic acid and fish oil, exercise to exhaustion once a week and skip dessert. I haven't gained more than a few pounds in 30 years. I live every day like it's my last and did more than I expected to in two lifetimes."

A Modern Antiaging Elixir

MOUSE UT2598'S LONGEVITY DIET LACED WITH RAPAMYcin traces its existence back to some dirt samples collected in 1964 on an expedition to Easter Island. Those soil samples became the basis for developing a new antibiotic, which was named rapamycin. Researchers noticed that mice that were given the drug tended to live longer—by about 20%, compared with those that weren't taking it.

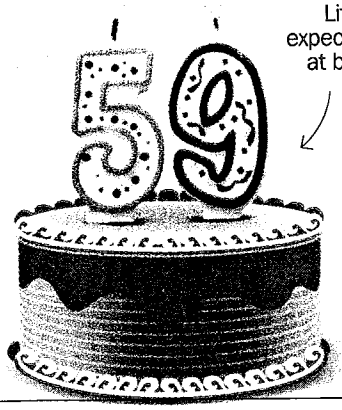
"Rapamycin is neat because it works in a wide variety of species, from yeast, worms and flies to mice," says David Harrison, who is studying the compound at the Jackson Laboratory, where scientists mine the genome for solutions to human diseases. He and Miller, along with Randy Strong—in whose lab Mouse UT2598 resides—are also testing other agents in a program sponsored by the NIA."Rapamycin is also neat because it works even when you start quite late in life."

Because of a delay in formulating rapamycin so it remained stable in mouse chow, the first animals to try it were already getting gray—they were 20 months old, or the equivalent of 60 years in people—but they still showed slower aging once they took the compound. If the research eventually leads to a human treatment, that could bode well for older people; they could potentially enjoy the same benefits that this lucky mouse is experiencing, even if they start in their 60s or 70s.

It turns out that rapamycin interrupts the function of a gene called mTOR, found in both mouse and man, which acts as a traffic signal for directing how cells take in and use energy. If there's plenty to eat, the

PUSHING THE LIMITS OF LONGEVITY

1925
Turn-of-the-century health regulations, requiring improvements such as clean water and better sewage disposal, curb outbreaks in the U.S. that are particularly deadly to children.



1955
Thanks to vaccines for smallpox, diphtheria, polio and other highly contagious—and often lethal—viruses, average life expectancy goes up.

1985
Public-health campaigns on heart health and the dangers of smoking reduce heart-disease deaths. Medical advances also help extend life.

gene is busy greenlighting cells to absorb nutrients and grow, grow, grow. When food gets scarce, the gene goes quiet, halting the cell-growing machinery until the next feeding time. While mTOR may explain, in part, the phenomenon of calorie restriction and its ability to prolong life—in the 1930s, studies in mice showed that cutting back on their daily diet could add nearly a year to their lives—there's also evidence that it taps into other energy-related pathways to longer life as well.

The more active state—the one in which cells are processing nutrients and growing—turns out to age cells considerably: as our cells are working hard to process our food, they also spew out toxic free radicals. The goal, then, is to keep mTOR as subdued as possible, preferably without requiring animals to starve themselves miserable. And that's what rapamycin appears to do.

So far it's the most promising compound under study, and Harrison and his colleagues are optimistic, though cautious, about its future. After all, resveratrol, a compound found in grapes and red wine, showed early promise in mice that gorged on high-fat diets, extending their lives, but it wasn't as impressive in helping animals on normal diets live longer. (Researchers aren't ready to give up on it yet, however, and it's still being studied at GlaxoSmithKline.)

While rapamycin dials up one antiaging circuit, it's clear that it is not yet a fountain of youth. "I'm 72, but I'm not popping rapamycin pills yet," says Harrison. Consider the downsides. In mice, it has resulted in a body size that is about 30% smaller than average, and mTOR-regulated mice were also more likely to develop cataracts and were more prone to diabetes. The males tend to experience gradual loss of testicular function—not exactly a selling point for a future longevity treatment.

20%

How much longer mice live when they eat chow spiked with rapamycin, compared with mice who nosh on normal chow

Human patients who took the drug after kidney transplants to lower their chances of rejecting the organ, for instance, also had slightly higher chances of developing diabetes, and the risk of cataracts requires more study before a broad application of the drug would be possible. Still, given the fact that rapamycin is already approved and safely taken by patients, antiaging researchers are hopeful that they'll be able to arrive at the right doses to tip the balance in favor of longevity while minimizing potential risks.

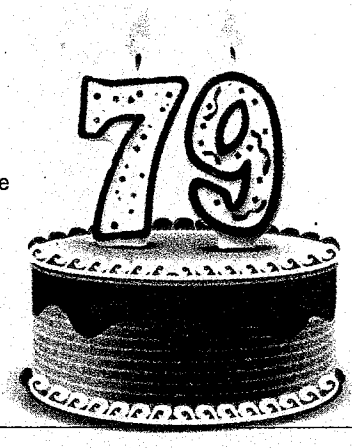
Find the Switches to Flip

FOR OTHER RESEARCHERS, THE KEY TO LONGEVITY MAY be in our genes. Telomeres are the timekeepers of a cell's life; each time a cell divides, it copies its chromosomes' DNA, and like a knot tied at the end of a thread, telomeres signal the end of the copying process. With each cell division, these little squiggles, which are the final segments of DNA at the ends of chromosomes, shorten—eventually disappearing altogether. And because certain things like exposure to UV light can cause telomeres to shorten at different rates, they're a target of lots of new antiaging research too. (For more on how telomeres are being studied, see page 80.)

In healthy people there is a balancing dance between the shortening of telomeres and the work of an enzyme called telomerase, which lengthens them just a little bit, to restore some of the DNA that's lost. But that doesn't happen in people with telomere-syndrome conditions—which includes some bone problems, liver failure and immune-system disorders. It's what makes those terrible conditions research gold for antiaging scientists.

2015

Improved drugs, diagnostic tests, surgeries, disease treatments and other medical advances reduce fatality rates for cancers and other illnesses.



2045

Regenerative medicine may interrupt aging. If not, conservative estimates put life expectancy at 81 as high obesity rates offset other gains.

Sources: CDC; NIH; SSA; S. Jay Olshansky, University of Illinois at Chicago

If they can figure out how to correct the misbehaving telomeres in those people, they may be able to correct them in normally—but inexorably—aging people too.

Twelve years ago, Dr. Mary Armanios met her first patient with such a condition while she was training with Carol Greider, a scientist who shared a Nobel Prize for the discovery of the enzyme telomerase. Through their lab at Johns Hopkins School of Medicine, Armanios met a college student with a blood disorder that required regular transfusions. He was in his 20s but had a shock of gray hair that had first appeared when he was 9. This alone was unusual, but his family history also intrigued her. Almost all his relatives on his father's side died young. His paternal grandmother, who had severe osteoporosis and bone disorders, died in her 60s. His father died at 59 while waiting for a liver transplant. His aunt and uncle died of pneumonia in their 60s. The young man, too, had been in and out of hospitals most of his childhood to treat infections. He eventually died, at age 31, of a staph infection.

"The cosmetic symptom was hair graying, but they all have a form of hair graying in other organs as well," says Armanios. It turned out that the family members all had dyskeratosis congenita, a rare condition with an extreme form of telomere dysfunction.

Armanios is confident she might learn something about how telomeres are supposed to work—and even how they might be manipulated and extended to halt aging-related problems, not just in those with dyskeratosis congenita but in healthy older populations as well.

One strategy may involve dousing cells with the right genetic ingredients to lengthen telomeres, as Helen Blau and her colleagues have done in petri dishes at Stanford University. "We turned back the clock on the cells by the equivalent of many years in human life," Blau says.

Even more encouraging, the cells didn't continue to divide indefinitely, which might raise concerns about uncontrolled growth, as occurs in cancer. "They start to [deteriorate] normally, and that bodes well for safety," she says. Eventually, Blau hopes the cells will be tested in the liver or lungs of patients with dyskeratosis congenita, where they can target the rapidly aging cells. If that is successful, the same techniques might turn back the clock on aging cells in the rest of us.

So Simple and So Strange

BUT THERE MIGHT EVEN BE A QUICKER—IF ODDER—WAY to defy aging that literally exploits the power of young blood. Relying on an innovative technique in which young and old mice can be conjoined, Siamese twin–style, to share the same blood system while keeping everything else separate, Amy Wagers at the Harvard Stem Cell Institute found something in the blood of younger mice that seems to rejuvenate an aging animal. The older mice that were yoked to the younger ones showed more new nerve-cell growth in their brains, their muscles were stronger, and in one study, some of the enlarging of the heart that comes with aging was reversed. "Their tissues are functioning more like younger tissues," she says.

What appears to be one of the secret ingredients here is GDII, a protein that's abundant in young animals' blood but is scarcer in older ones. Wagers is conducting more studies in both animals and people to see if longer-lived people have higher levels of GDII or whether people with low GDII might be more vulnerable to age-related diseases such as heart problems, cognitive decline and muscle atrophy.

And GDII isn't alone in showing such promise. At the University of California, San Francisco, neurobiologist Dena Dubal is investigating a hormone called klotho, named after the Greek fate responsible for spinning the thread of life for mortals. Increasing the klotho levels in mice helps animals live 30% longer, and 1 in 5 people also carries a version of the klotho gene that boosts its amounts. On average, those individuals live an extra three to four years. It's not the hormone of immortality, but it's a start.

Manipulating klotho, GDII, telomeres or any of the longevity genes could involve some invasive and high-tech interventions, including gene therapy and even cell transplants. But what if all those efforts are overthinking the solution, and it's possible to put the brakes on aging by simply removing aging cells, like plucking out gray hairs? That's what Dr. Jan Van Deuren and his team are pursuing at the Mayo Clinic. By seeking and pulling out dying cells in the muscle, fat and eyes of mice, he's helping them live longer than control animals. "We're getting rid of a cell type you don't have when you're born, something that accumulates over time that may not really be needed for survival," he says.

He is the first to admit that there is still plenty about that strategy—as well as other promising aging interrupters—that scientists don't understand. For example, are rapamycin-fed mice living longer because their cells are actually functioning like younger ones or because they're simply delaying aging conditions like cancer and heart disease? Are the old mice infused with young blood truly young again, or are their rejuvenated cells only temporarily acting more youthful? And while we know more every day about the roles telomeres play in the aging process, is the answer as simple as finding ways to safely lengthen them through drugs? They aren't easy questions to answer, but aging experts welcome them.

That's because what's happening in these labs is not just about extending a life indefinitely but rather extending a healthy life for a little bit longer. And researchers say they're truly optimistic that breakthroughs will come in their lifetime. After all, says Harrison, "It must not be all that complicated, or we wouldn't be having the success that we're having." ■

LONGEVITY GURU:

J. Craig Venter, co-mapper of the human genome
Age: 68

AGING INTERVENTION: "I do weight training at least three days a week to keep muscle mass up. Getting your genome sequenced will also be part of knowing the best way to stay healthier longer, but without the context of how it affects the way your body functions, it isn't helpful. In the next two to five years, we'll have more personalized information."

PORTRAIT ILLUSTRATIONS BY GRAFILU FOR TIME

WHERE IS THE BEST PLACE TO BE AN OLD PERSON?

BY JUSTIN WORLAND

AMERICANS HAVE BEEN RELOCATING TO ANY number of bucolic places, keen to spend their golden years away from it all. Mexico, Alaska, the Ozarks, small college towns all around the nation. But before you book a one-way ticket somewhere or clean out your bank account, think again. As it turns out, studies suggest that it may be best for you just to age in place. And for most people reaching old age in 2015, that means growing old in a city.

Today, more than 80% of Americans and 54% of the population worldwide live in urban areas. The U.S. number includes more than 33 million people over 65. That's a good thing, aging experts say.

"It's the full panoply that make a city vibrant and great for all of its population, but particularly for older adults," says Paul Irving, who leads a group on aging at the Milken Institute, an economic think tank that recently ranked American metropolitan areas based on how suitable they are for growing old.

The criteria Milken's study assessed included access to health and wellness services, crime rates, weather, housing, job opportunities, transportation and suitability in terms of supporting social factors—including living arrangements, rates of volunteerism and availability of group enrichment programs, such as at a library or university or YMCA. Their verdict: of the 100 largest cities in the U.S., Madison, Wis., is the best in which to grow old.

'AS WE AGE, OUR WORLDS TEND TO SHRINK, MAKING OUR IMMEDIATE NEIGHBORHOODS ALL THE MORE IMPORTANT.'

MOVE TO MADISON? With 11 hospitals and senior access to university classes, it's the sleeper hit of senior-friendly cities

The traffic, expense and hassle of city life may not sound like the traditional vision of the golden years. But easy access to health care and cultural stimulation help tip the balance in cities' favor. In Madison, for example, seniors can take classes at the local university and receive care at one of its 11 hospitals, and when they don't feel like—or can't—walk around the pedestrian-friendly city, they can make use of an on-demand transportation system designed for those who need it.

Another advantage for cities: lots of other people. Academic research supports anecdotal evidence that staying connected has benefits. "As we age, our worlds tend to shrink, making our immediate neighborhoods all the more important," says Ruth Finkelstein, a longevity and health policy expert at Columbia University. "In addition to their social networks, people also have micro-relationships and connections—the people you're used to seeing, the sidewalks you're used to walking down, the shops you're used to frequenting. Those are relationships of reciprocity."

The urban option may grow even more attractive in the coming years. The World Health Organization launched an initiative in 2010 to push mayors around the globe to make their cities friendlier to older residents. And even though plans are still in the early stages, some mayors in the U.S. are working to increase affordable housing options, make transportation more accessible and find ways to engage older people in their communities. New York City, for instance, has something called Age-Friendly NYC, which works with the mayor's office to develop programs for the city's more than 1 million residents who are age 65 or older.

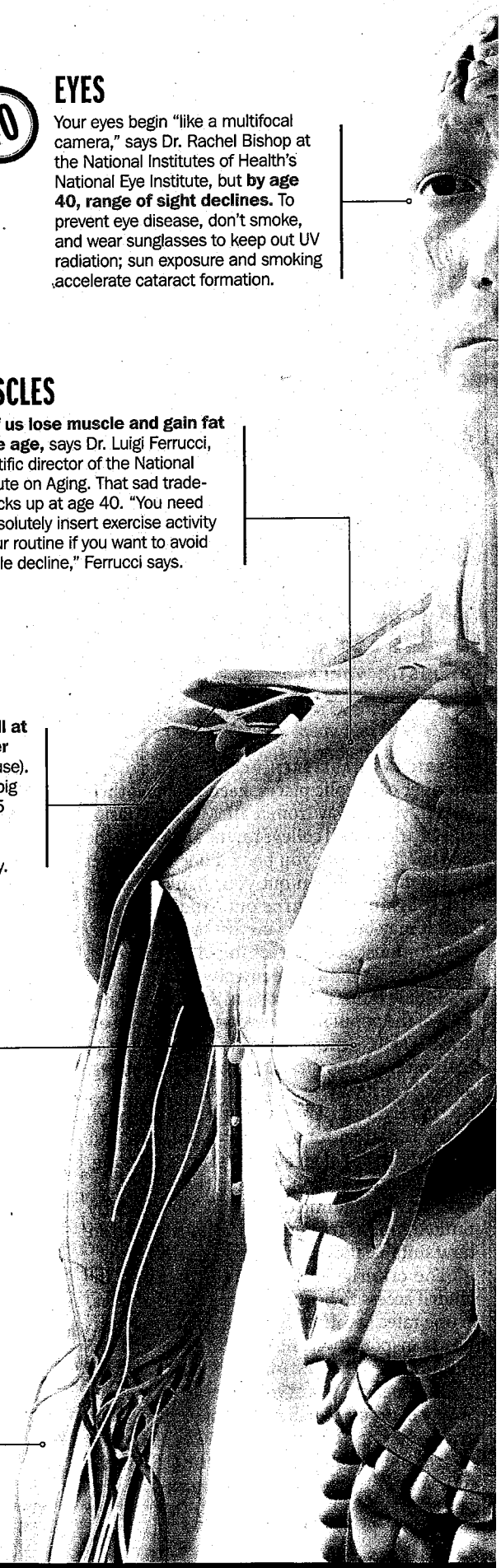
Similar programs in communities around the world are helping to prepare for a fast-changing reality, but cities may be aging quicker than public policy is evolving. Just a generation ago, swarms of retirees migrated to the warmth of Florida and the rest of the Sun Belt. Now, 71% of baby boomers say they want to grow older where they spent most of their adult lives, according to a recent survey by the AARP.

Finkelstein, who led New York City's initiative for older people, says she is among them. "I am speaking to you from my little teeny-tiny three-story wooden house in Brooklyn," says Finkelstein, 60. "They will carry me out of here in a wooden box." ■

STRETCH YOUR TIMELINE

BY MANDY OAKLANDER

AS SUDDEN AS AGING CAN feel, no one wakes up in a 90-year-old body without getting some warning signs first. But if you know what's coming, you can plan to give certain parts some extra care early on. Already in the throes of aging? (Trick question. We all are.) "You're never too old to do anything to help to maintain wellness of your body," says Dr. Ronan Factora, geriatric-medicine expert at Cleveland Clinic.



EYES

40

Your eyes begin "like a multifocal camera," says Dr. Rachel Bishop at the National Institutes of Health's National Eye Institute, but **by age 40, range of sight declines.** To prevent eye disease, don't smoke, and wear sunglasses to keep out UV radiation; sun exposure and smoking accelerate cataract formation.

MUSCLES

40

All of us lose muscle and gain fat as we age, says Dr. Luigi Ferrucci, scientific director of the National Institute on Aging. That sad trade-off picks up at age 40. "You need to absolutely insert exercise activity in your routine if you want to avoid muscle decline," Ferrucci says.

BONES

35

Bone mass tends to go downhill at a rate of up to 1% per year after age 35 (and faster after menopause). Weight-bearing exercise makes a big difference in bone density. A 2015 study found that simply jumping 20 times twice a day significantly improved hip-bone mineral density.

LUNGS

30

Lung function begins dropping 1% a year at 30 and declines more in people who are sedentary than in those who are active, says Dr. Thomas Perls, geriatrician and principal investigator of the New England Centenarian Study at Boston Medical Center. The antidote: exercise.

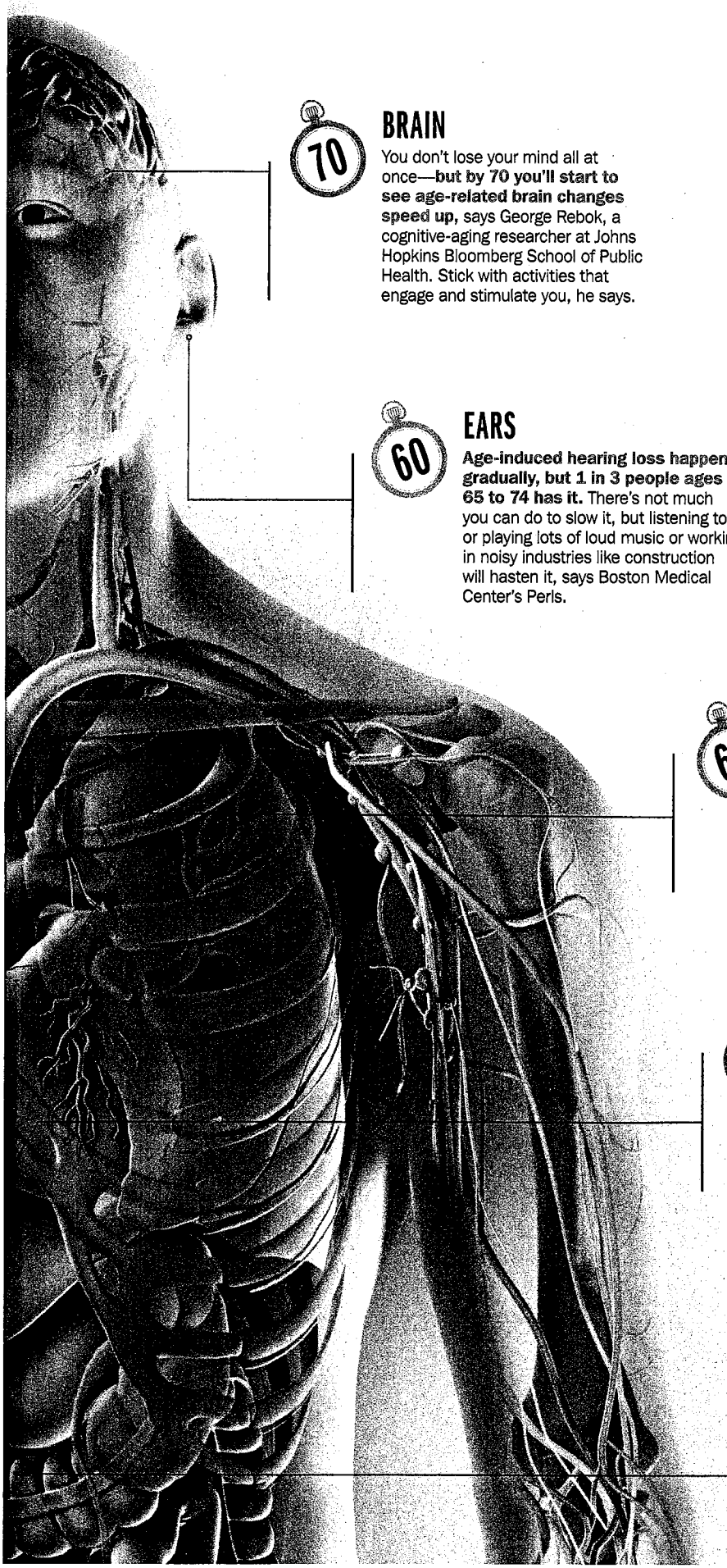
SKIN

18

From around 18, resilient collagen and stretchy elastin decline at about 1% per year. You can slow the process by not smoking, eating well and wearing titanium or zinc sunscreen every day—even if you're indoors. A 2012 study found that some compact fluorescent bulbs emit skin-damaging UV light.

?

Age when body part begins to falter



BRAIN

70

You don't lose your mind all at once—**but by 70 you'll start to see age-related brain changes speed up,** says George Rebok, a cognitive-aging researcher at Johns Hopkins Bloomberg School of Public Health. Stick with activities that engage and stimulate you, he says.

EARS

60

Age-induced hearing loss happens gradually, but 1 in 3 people ages 65 to 74 has it. There's not much you can do to slow it, but listening to or playing lots of loud music or working in noisy industries like construction will hasten it, says Boston Medical Center's Perls.

HEART

65

As you age, your heart-muscle cells shrink in number but expand in size, which makes your heart wall thicker. Your arteries tend to get stiffer too. Starting at age 20 to 30, peak aerobic capacity drops by about 10% per decade, and **heart disease typically kicks in around age 65.**

KIDNEYS

50

You won't necessarily feel it, but decline in kidney function starts around 50. The best thing to do is drink plenty of water. Since thirst decreases with age, you may have to remind yourself. One study found people who drank the most fluids were less inclined to kidney decline.

GUT

60

The hairs on your head aren't the only strands to go. **Villi in your intestine—tiny hairlike projections that absorb the nutrients in food—tend to flatten out around age 60,** says Cleveland Clinic's Factora, and the loss means you'll absorb fewer nutrients.

GET YOUR HEAD IN THE GAME

CUTTING-EDGE RESEARCH IS SHOWING THAT YOUR OUTLOOK CAN CHANGE HOW YOU AGE—AT THE CELLULAR LEVEL. HERE'S HOW

BY JEFFREY KLUGER

WE TEND TO FACE AGING WITH FEEL-GOOD SLOGANS, bringing platitudes to a knife fight. "I'm 70 years young!" we say, ignoring the fact that, going by average U.S. life expectancy, it won't be long before we're 78 years dead. "Fifty is the new 40," we tell ourselves, when the mathematical reality is no, it's not. Fifty will never even be the new 49½.

Then comes a bit of wisdom that, if anything, seems like the most shopworn of all: "You're only as old as you feel." As sentiments go, it has the twin flaws of being both banal and blaming—as if feeling old is your own fault. It turns out, however, that whoever coined that one may have been onto something big.

It's no secret anymore that the familiar mind-body divide, with your head home to the abstract and ethereal and your flesh home to the messy and mechanical, is nonsense. Your moods, feelings and thoughts all influence your physiology. Learn to relax and your blood pressure goes down; emerge from depression and your immune system picks up; take a pharmacologically useless sugar pill that you're told is a powerful drug for your headache or backache or infection and as if by magic, you get better.

The tantalizing question, then, has always been this: If the mind can heal the body, can it also rejuvenate it? Can it make it physically, measurably younger or, at the very least, slow the aging process? The people who research such things already accept that the way we

Photo-illustration by Evan Kafka for TIME

think and feel can increase the population of disease-fighting white blood cells and lower the level of the hormone that raises blood pressure, so why couldn't it help recalcify bones or reverse heart disease or preserve the brain cells that are lost with age? "You're only as old as you feel" may merely be part of the equation. Perhaps, within reason, you're only as old as you bloody well choose to be—because research is mounting that your outlook, your personality and, frankly, how upbeat you are have a profound impact not just on how you feel but also on how your cells age.

"Let's treat *mind* and *body* as just words," says Ellen Langer, a professor of psychology at Harvard University who has been studying aging, mindfulness, decision-making and health since the late 1970s. "Let's put them together as one thing and say anywhere you put the mind, you also put the body."

Once you make that leap, the medical tool kit becomes a lot larger. It includes not just pharmacology and surgery but also things like meditation, optimism, resilience and social connections—all the stuff that's always been far outside medicine's visible wavelength but suddenly is finding a place comfortably within it.

Consider one study, for instance, showing that even a single day of a mindfulness meditation practice can down-regulate a gene that codes for inflammation—one of the greatest drivers of aging. Or the one showing that reducing stress can reduce the cellular damage from the highly reactive oxygen atoms known as free radicals. Or the research that found, most remarkably, that the telomeres within your cells—the little cuffs that cap chromosomes and erode over your lifespan—can actually be made to grow longer, provided your mind is in the right state to make it happen.

"It comes down to daily behavior and the choices we make," says Elissa Epel, a professor of psychiatry at the University of California, San Francisco (UCSF), who studies stress and aging. "We have a growing set of studies of people from around the world showing that aging is not just an aspect of genetics but of how we live." Deciding to live better, it increasingly seems, is the same as deciding to live younger.

Winding Back the Mind

IT WASN'T UNTIL THE LATE 1970S THAT RESEARCHERS began seriously thinking about using the mind to arrest the aging process, and it was Langer's landmark "counterclockwise" study that really got things started. In 1979, when she was just beginning her Harvard teaching career, she recruited a group of eight men in their 70s for a five-day stay at a retreat in New Hampshire. The men were in neither good nor bad health but what was considered age-appropriate health—which is to say slow, bent and easily fatigued. But Langer was determined to change that.

LONGEVITY GURU:

Ellen Langer, professor of psychology at Harvard University Age: 67

AGING INTERVENTION: "I don't get stressed about combatting age, which leads me to take care of myself naturally, without an agenda. I like to play tennis and take walks because it's fun to do so. When we nurture our minds, we're taking care of our bodies."

The retreat, as the men discovered when they arrived, was a former monastery designed to look as the world did to them in 1959. Vintage programs were showing on vintage TVs. Midcentury music played on midcentury radios. The men were treated too as they would have been back then—no one offered to help them with their bags or fetch them a blanket. They kept their conversation to the topics they would have discussed in 1959—the doings in the Eisenhower White House, say, or the Dodgers–White Sox Series face-off. And lest the men get a glimpse of themselves and break the spell, all mirrors were removed from the space.

At the beginning and end of the five-day span, Langer administered a series of physical and cognitive aptitude tests to the men, and the result was as she expected: on virtually every metric, their performance improved dramatically, and in many cases it was closer to what would be expected for men a decade or two younger.

"The study spoke volumes to the potential we have to change our health," Langer says. "At some point people just tell us we can't. If you're 20 and you hurt your wrist, you expect it to get better. When you're 70, you've bought into the mind-set that you're falling apart, and then you do."

Langer went on to test the same premise in other ways. After recruiting a sample group of hotel maids who were battling their weight, she told half the sample that studies showed the work they did every day was actually a vigorous form of calorie-burning exercise. The other women were given no such information. At the end of the study, the women who believed that their work was a workout lost more weight than those in the other group.

Langer's studies, compelling as they are, are not complete. They do a very good job of proving that thinking young appears to make the body young—or at least younger—but they don't say why. Langer herself is more philosophical than empirical on this. "The mechanism is the part that's so hard to get across to people," she says. "But when the mind and body are one, there's no mediator needed."

Maybe. But even if she doesn't need a mediator, other scientists do, and they're looking hard for it—starting inside human cells, at telomeres.

The Levers of Aging

OVER THE COURSE OF A LIFETIME, TELOMERES BURN down like a sort of candle wick, leaving the chromosomes vulnerable to damage and starting the aging process.

Investigators have understood the basics of telomeres since 1978, when then postdoctoral fellow Elizabeth Blackburn, now at UCSF, first mapped their structure and later, with her collaborator Jack Szostak of Harvard, their function. In 1984, Blackburn and her graduate student Carol Greider, now at Johns Hopkins

ILLUSTRATION BY GRAFILU FOR TIME

School of Medicine, discovered the enzyme telomerase, which repairs and maintains telomeres—at least when it's around at sufficient levels. When those levels fall, which happens as we get older, the aging process is kicked off. The discovery won all three of them the 2009 Nobel Prize for Medicine.

"When studies look at which individuals will die in the next three years," Blackburn says, "the chances are higher if your telomeres are shorter. Telomere shortening plays into cardiovascular disease, immune-system problems and maybe diabetes by affecting beta cells in the pancreas—though that one's been shown only in mouse models so far."

The question is, Are there ways to intervene to spare the telomeres and preserve your health? The answer—at least preliminarily—is yes, and stress reduction is one powerful method. In 2014, Epel and her colleague Eli Puterman, also of UCSF, studied 239 healthy, postmenopausal women over the course of a year. Many of the subjects were experiencing at least one of 13 major life stressors, which included unemployment in the family, financial woes, divorce and the illness of a child.

The length of their telomeres was measured at the beginning and end of the year, and the more life stressors these women experienced in that time, the more their telomeres shortened that year. But some of the women also practiced good health behaviors—they exercised, ate well and slept well. Consistently, the women who also practiced good health behaviors maintained their telomere length. "The question had always been whether the telomeres respond to daily lifestyle changes or if the system is chronic and proceeds at its own pace," Epel says. "In our study, it was lifestyle, with damage occurring mostly in people who were sedentary."

Worse, telomere-shortening stress is not confined to older people and does not even have to be experienced firsthand. Epel cites studies showing that when cord blood is drawn from newborns, the babies whose mothers had experienced more stress when they were pregnant showed shorter telomeres than those whose moms had easier pregnancies. "We replicated that original finding," she says, "and it suggests healthy telomere maintenance doesn't start when you're born but before you're born."

Some researchers believe that improvements in exercise and other healthy behaviors can increase the output of telomerase, and animal studies in test tubes show that increased telomerase may in turn make telomeres grow. Telomerase supplements, however—either synthetically produced or in the many herbal supplements that claim to include the enzyme—are not the answer. If telomeres never burn down, you get immortal cells—which is another way of saying cancer cells.

"Cancers love telomerase, and a number of cancers up-regulate it like crazy," says Blackburn. "But some cancers are also related to low telomerase because that makes telomeres less stable." Trying to boost telomerase through supplements is a very dangerous game to play—at least given the current state of medical knowledge. "We don't know how to strike some kind of balance. My feeling would be that if I take anything that would push my telomerase up, I'm playing with fire," says Blackburn.

'THE REGULAR PRACTICE OF [MEDITATION] SEEMS TO BE ABLE TO ALTER THE TRAJECTORY OF AGE-RELATED CHANGES.'

—RICHARD DAVIDSON, NEUROSCIENTIST AT UNIVERSITY OF WISCONSIN, MADISON

Putting Out Fires

TELOMERES AREN'T THE ONLY BIG, STRESS-RELATED players in the aging game. Another is chronic inflammation. When you're anxious, the sympathetic nervous system—which is not known for thinking things through too clearly—assumes you're about to encounter a predator or some other life-threatening challenge. The brain thus sends a signal to the adrenal gland to start secreting the hormones epinephrine and cortisol; together, these hormones signal the immune system to release proteins known as inflammatory cytokines. These prepare white blood cells and other infection fighters to rush to the site of an anticipated wound.

That works quite well when there really is a wound, or when the danger is fleeting and you escape without injury. Either way, the system, thanks largely to cortisol, dials itself back down. But what if you're always braced for a battle of some kind—with your boss, your kids, your credit-card statements—and the body is always flooded with inflammatory chemicals? In those cases the body suffers from what's known as inflammation—and that's bad.

"There is no invader as there is with a wound, but we're reacting as if there is anyway," says Epel. "That creates a friendly environment for cancer, brain deterioration, cardiovascular disease." In other words, for many of the main killers of aging.

One of the best ways to battle this is with a settled psychic state, through meditation and mindfulness exercises. Increasingly, researchers are finding that a

particular form of meditation known as Mindfulness Based Stress Reduction (MBSR)—which, as its name suggests, includes paying close attention to feelings, thoughts and other stimuli while meditating—can calm an inflamed immune system in the same way it can calm an inflamed mood.

In 2013, Richard Davidson, a neuroscientist and the founder of the Center for Investigating Healthy Minds at the University of Wisconsin at Madison, conducted a pair of studies showing just how powerful an effect MBSR can have on the body. In one, he and his colleagues compared 40 subjects—21 of whom engaged in eight hours of a combination of guided meditation, meditative walks and lectures on meditation, and 19 of whom engaged in equally relaxing activities but without the meditation. At the end of even so brief a period as eight hours, the meditators showed a decrease in the expression of the very genes that regulate inflammation—meaning a decrease in inflammation itself too.

Another study replicated the findings over the course of eight weeks, and at the end, the experimenters used a suction device to raise a small blister on the arms of the subjects. When fluid was withdrawn, the meditators showed significantly lower levels of inflammatory cytokines—the same cytokines that do so much damage when they circulate in the body chronically.

"The regular practice of certain contemplative methods seems to be able to alter the trajectory of age-related changes," Davidson says. "Some studies even show that meditation can slow the age-related decline of gray matter in the brain."

On this last point, Davidson understates things. Exciting research published in February out of UCLA compared two sample groups of 50 people, ranging in age from 24 to 77—a good demographic slice since gray matter actually begins declining when we're in our 20s. One group was made up of people who did not meditate, the other of people who had been regular meditators for anywhere from four to 46 years. All 100 subjects' brains were scanned with magnetic resonance imaging, and the results were unmistakable: the meditators showed less gray-matter loss in several regions of the brain compared with the nonmeditators.

"We expected rather small and distinct effects located in some of the regions that had previously been associated with meditating," said Dr. Florian Kurth, co-author of the study. "Instead, what we actually observed was a widespread effect of meditation that encompassed regions throughout the entire brain."

The Optimism Effect

ALMOST AS POWERFUL AS MEDITATION—AND CERTAINly easier for people who would be perfectly happy to set aside time for solitary contemplation in a quiet place if they could find the hour and the place and the quiet—is simple optimism. Challenges and setbacks and even tragedies are nonnegotiable parts of life, but what is negotiable is how you face them.

Dr. Hilary Tindle, a physician and clinical investigator at Vanderbilt University, has produced a body of work on the connection between attitude and health, and all of it points to the improbable power of just being hopeful. In one massive 2009 study, Tindle analyzed data from 97,253 women who had filled out questionnaires for the National Institutes of Health's Women's Health Initiative, trying to correlate hopefulness and mortality. Women who had scored high on optimism—being hopeful about the future—the results showed, had significantly lower rates of heart disease, cancer and mortality than women who scored high on pessimism.

Tindle also studied cynicism, which can be described as feelings of pessimism about other people, expecting them to be untrustworthy and even harmful. Women with lower cynicism, compared with those who viewed most other people with suspicion, had lower risk of death.

In a 2012 study, she compared more than 430 people who had undergone coronary-bypass surgery—284 of whom were diagnosed with at least low-level clinical depression and 146 of whom were not. The subjects all took the same optimism survey that the sample group in the other study had. Within eight months after surgery, the depressed pessimists had more than twice the complication and rehospitalization rate than the optimistic group.

"As a doctor my goal is to help people understand this connection more than they do," Tindle says. "But they need to do so in a way that makes it actionable. In other words, how do we put all these new findings to work?"

That, ultimately, is the critical question. Researchers are divided on how possible it is for people who have made it to middle age cynical or stressed or sedentary to undo all the damage to their systems through outlook change and meditation alone. But the research is piling up that it can help—and it certainly can't hurt.

As with most matters involving health, it comes down in large measure to lifestyle—diet, exercise, adequate sleep and positive attitude. That's not sexy, but when it comes to longevity, take what works over what makes headlines. The fact is that the aging odometer never runs backward. The 70-year-old will always be 10 years older than the 60-year-old. But if you're talking about how many years both of those people have remaining, put your money on a happy, active 70 over a cynical, sedentary 60.

That, if nothing else, puts a sweet twist on the hard rule that all lives must end: enjoy the time you've got, and you just might get more of it. ■

LONGEVITY GURU:

Steven Austad, researcher on aging at University of Alabama at Birmingham
Age: 68

AGING INTERVENTION:
"I don't have a great relationship with relaxation. Exercise is one way I relieve stress. I find nothing more satisfying than going to bed at night and being so physically tired I can hardly lift my arms or my legs. If I died in a climbing accident at the age of 90, that would be perfect."

WHAT DIET HELPS PEOPLE LIVE THE LONGEST?

BY ALEXANDRA SIFFERLIN

WE'RE ACCUSTOMED TO THINKING ABOUT DIETS as a short-term fix for unwanted weight gain, but eating for a long, healthy life requires a different approach. The priority should be a diet that prevents illness—and especially heart disease, the No. 1 killer in the U.S. Many experts believe that means a diet high in vegetables, whole grains and some fat. But a meal plan for longevity might also mean cutting back on protein—and, some experts say, reducing calories overall.

Many experts look to Europe—to the Mediterranean, specifically—for dietary secrets to a long life. While some debate remains about what people in the region actually ate, there's near consensus about the benefits of fish, fruits and vegetables and extra-virgin olive oil.

In 2009 researchers randomly assigned 7,447 people at high risk for heart disease to one of three diets: the Mediterranean diet, with lots of olive oil; the Mediterranean diet, with extra nuts; and a low-fat control diet. Those who followed one of the versions of the Mediterranean diet, which was high in fat, had about a 30% lower risk of having a heart attack or stroke and a similar reduction in risk of dying of heart disease after five years. The findings were so impressive, the study ended early. (With results that strong, it's considered unethical to withhold the advantageous approach from the other groups.) The findings were published in 2013 in the *New England Journal of Medicine*.

It's impossible to parse which nutrients, exactly, produced the benefits. Many experts think it's the result of the foods in combination. And at odds with some nutrition trends, the healthy diet was also relatively low in protein, which provided on average just 17% of daily calories, compared with up to 35% in the standard American diet. Also raising questions about protein is a 2014 study in *Cell Metabolism*. It showed that middle-aged Americans who ate a lot of animal protein were more likely to die of cancer and other causes, compared with people who opted for more plant-based protein. Study author Valter Longo, director of the University of Southern California's Longevity Institute, recommends that people cut down on protein overall to live longer.

That advice may raise eyebrows, since many diets for weight loss, including the popular paleo diet, advocate high protein. "There's a misconception that it's O.K. to eat a lot of it," Longo says. "People don't understand it could lead to some major aging factors." One such factor is the impact of the growth hormone IGF-1 (insulin-like growth factor 1). While it's important for early development, getting too much from high-protein foods later may accelerate aging.

Longo and others were tipped off to the possibilities when studying a rural population in Ecuador with a genetic mutation that keeps their IGF-1 very low. They found that IGF-1-deficient people are typically short in stature but also rarely get diseases that tend to hit people as they age, like cancer or Type 2 diabetes. Limiting animal protein is a way to lower IGF-1 and keep aging effects at bay, says Longo.

A sizable camp of nutrition scientists also say we should cut back on how much we eat overall, with some recommending intermittent fasting—alternating between regular food consumption and short periods of eating almost nothing. Others say a diet with about 25% fewer calories than normal may extend life, as has been shown in many animal studies. In humans, studies have found that significantly reducing calorie consumption may reduce cardiovascular-disease risk—which could, in turn, impact longevity.

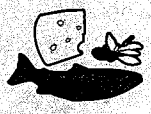
One thing experts can agree on is that we'd all benefit from less sugar, particularly added sugar in the form of fructose. A 2015 study in *Mayo Clinic Proceedings* pinpointed added fructose as the primary driver of Type 2 diabetes, which has reached epidemic proportions in the U.S.

For now, unsatisfying though it may be, the bottom line is that more research is needed before any one diet can be heralded as the key to a long, healthy life. But a diet low in sugar and high in plants, nuts, fruit, fat and some protein is a good bet. Just be sure to add the other secret ingredient too: exercise. ■

'MY LOW-PROTEIN DIET IS ALMOST COMPLETELY PLANT- AND FISH-BASED. I HAVE ONLY ONE MAJOR MEAL A DAY: DINNER.'

LONGEVITY GURU:

Valter Longo, director of the USC Longevity Institute
Age: 47



EAT WELL, LIVE LONGER: People who followed the modern Mediterranean diet had a 30% lower risk of heart attack than people on a low-fat diet

PORTRAIT ILLUSTRATION BY GRAFILU FOR TIME

IT'S TIME TO EMBRACE LIFESTYLE MEDICINE

BY DR. DEAN ORNISH

MEL LEFER'S CARDIOLOGIST TOLD HIM HIS heart disease was so severe he was unlikely to survive even a year. He was incapacitated by chest pain up to 30 times a day. More than 28 years ago, I treated him with a program focusing on diet, exercise, stress management and social support—and he has remained angina-free ever since. Tests showed that his heart disease was reversing. He's now 82 and leads a full life.

A convergence of forces has made so-called lifestyle medicine the most compelling trend in health care. Start with an aging population, and add an economic imperative to control spending and a political debate over how best to do it. Then throw in evidence that lifestyle changes can work as a treatment for some chronic diseases—either in combination with drugs and surgery or as an alternative—at a much lower cost and without side effects.

For almost four decades, my colleagues and I at the nonprofit Preventive Medicine Research Institute and at the University of California, San Francisco, have used science to test low-tech, low-cost lifestyle interventions. We landed on a simple prescription: a whole-foods- and plant-based diet; stress-management techniques, including yoga and meditation; moderate exercise; and social support. In short: eat well, move more, stress less and love more.

In randomized, controlled trials, we found that lifestyle changes alone can often reverse the progression of severe coronary heart disease. They may begin to reverse Type 2 diabetes and slow, stop or even reverse the progression of early-stage prostate cancer.

Tens of millions of Americans have been prescribed drugs to lower cholesterol, blood pressure or blood sugar. When the patient asks, "How long do I have to take these drugs?" the reply is usually "Forever." But when patients make changes, they can often reduce or discontinue medication under a doctor's supervision.

These studies helped persuade Dr. Kim Williams, the incoming president of the American College of Cardiology, to go on a whole-foods- and plant-based diet instead of committing to a lifetime of cholesterol-lowering drugs. As he wrote, "Wouldn't it be a laudable goal of the American College of Cardiology to put ourselves out of business within a generation or two? Improving our lifestyles with improved diet and exercise will help us get there."

The costs—both human and financial—of drugs and surgery are well documented. Randomized, controlled trials have shown that stents and angioplasties do not prolong life or prevent heart attacks in most stable heart patients. Only a small percentage of men who were treated for early-stage prostate cancer with surgery or radiation may benefit. Type 2 diabetes and prediabetes affect almost half of Americans over age 20, yet drug treatments to lower blood sugar do not prevent the onset and complications of diabetes as well as lowering blood sugar with diet and lifestyle does. And we found in a controlled study that lifestyle changes lengthen telomeres, thereby reversing aging on a cellular level.

Right now, 86% of the $3 trillion we spend each year on health care in the U.S. is for chronic diseases that can be treated through lower-cost interventions. That's one reason it was a goal of Obamacare to radically change the incentives for how doctors treat patients. In a fee-for-service environment, more operations and hospitalizations generate more revenue. Under the Affordable Care Act, new models of payment reward providers for better outcomes, reducing avoidable procedures by aligning incentives to encourage healthy lifestyles.

Lifestyle medicine is now reimbursable. Medicare and many private insurers are covering a lifestyle program for heart disease that my team and I developed. This is a game changer, because when reimbursement changes, so do medical practice and even medical education.

This kind of medicine is not just about how long we live but also how well. And because the mechanisms of health are so dynamic, you're likely to feel so much better, so quickly. It reframes the reason for making these changes from fear of dying—to joy of living. ■

LIFESTYLE MEDICINE IS NOT JUST ABOUT HOW LONG WE LIVE BUT ALSO HOW WELL WE LIVE

LONGEVITY GURU:

Dean Ornish is the founder and president of the Preventive Medicine Research Institute and a clinical professor of medicine at the University of California, San Francisco
Age: 61

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