

# *the* **Secret** *to a long life*

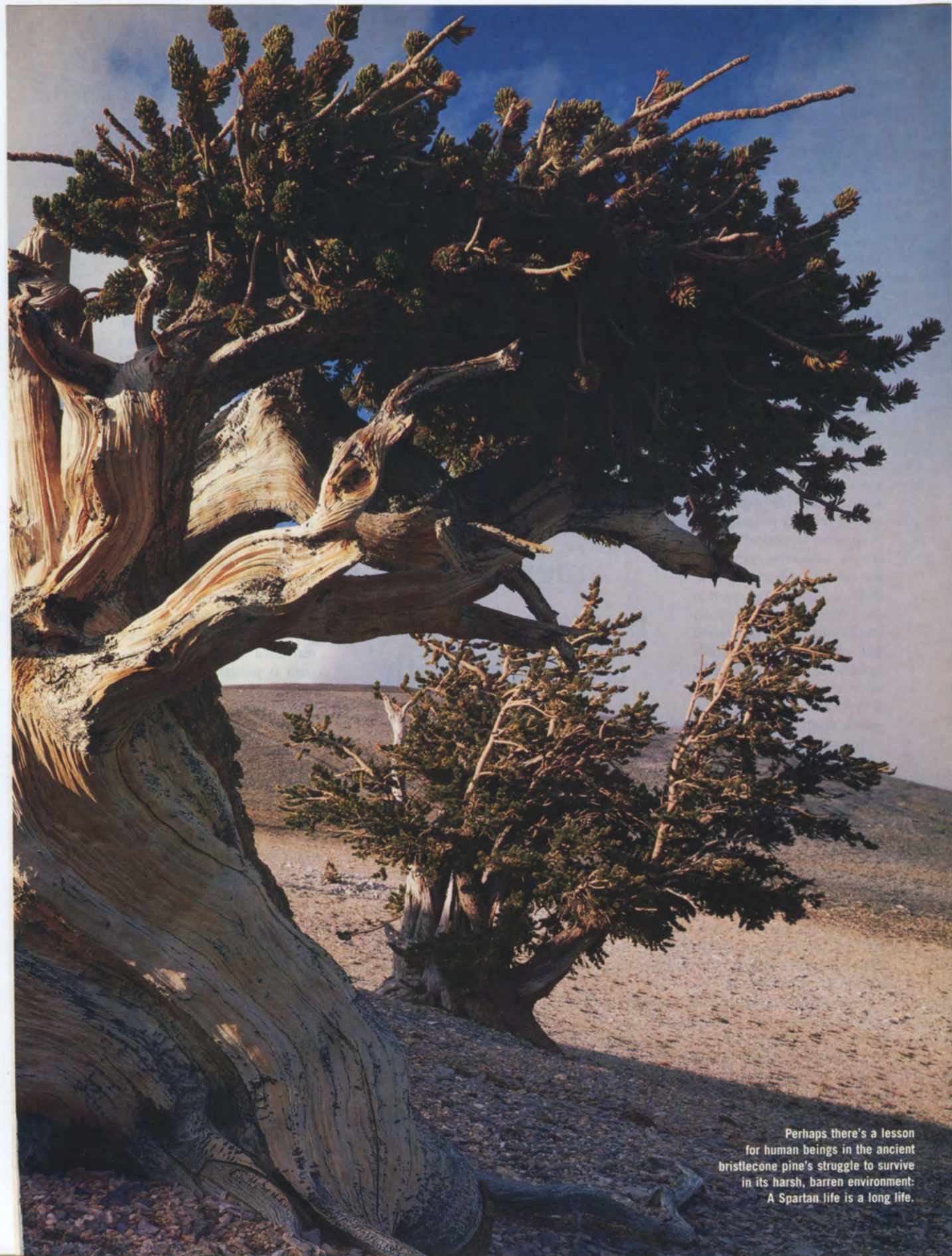
Juan Ponce de León hunted for the secret to eternal life in the wilds of Florida; Faust made a pact with the Devil for it; and a Harvard professor named Charles Édouard Brown-Séquard proclaimed in 1889 that he had found it in a potion of mashed dog's testicles. Longevity may have long been the stuff of folklore and quackery, but in the past few years the search for the Fountain of Youth has finally become "a legitimate subject of scientific inquiry," in the words of Richard Cutler, Ph.D., a gerontologist at the National Institutes of Health's Gerontology Research Center. Instead of a wizard with a bubbling caldron, there is a flock of learned scientists employing electron microscopes and bio-engineering techniques to peer into cells that lie at the heart of the mystery of aging.

The inquiry has not yet produced any Methuselahs, but the efforts are paying off in a dramatic reshaping of the prevailing views in the field. "Gerontologists are starting to recognize that life span can be greatly, possibly infinitely, expanded," says Caleb Finch, Ph.D., professor of neurobiology and gerontology at the University of Southern California. While most scientists are reluctant to put a number on the ultimate limit, Dr. Cutler believes that humans might someday count their allotted time not in decades, but in centuries. Scientists have already added years to the life expectancy of many other mammals, and they have doubled the life span of the fruit fly, which is as complex among invertebrates as humans are among vertebrates.

There are two approaches to the question of aging. The more conservative one might be called the nicks-and-scratches school: We die because our body simply wears out like a '62 Chevy. This school seeks to postpone the body's degradation through ways that are now well understood—through better nutrition, regular exercise and adjustments in the body's chemistry. Such a program is not meant to extend life, but rather to increase the health and vitality of the years one does live.

BY JOHN SEDGWICK

*Scientists now  
believe that the  
human life span can be  
doubled or even tripled.  
But does anyone want  
to live 200 years?*



Perhaps there's a lesson for human beings in the ancient bristlecone pine's struggle to survive in its harsh, barren environment: A Spartan life is a long life.

## LONG LIFE

The other approach is truly radical, almost breathtakingly so. It regards the human life span as a species trait determined by our genes. Thus, to produce longer life, geneticists are working to actually change the body's essential blueprint. While no one has come close to doing this yet, the payoff is potentially vast. Life spans might be increased two- or threefold, allowing humans to live more than 200 years. The geneticists' plans are so ambitious that they will probably take decades to be realized.

More impressive still, scientists seem to be avoiding the mistake a Greek goddess made when she petitioned Zeus to grant her mortal husband eternal life—but forgot to ask for eternal *youth*. Scientists are contemplating a future in which every phase of human life—youth, middle age and old age—is equally extended, a concept Dr. Finch calls the “biology of extended time.”

### How to extend life beyond 120 years

Because no one has ever been known to survive past 120 years, many researchers believe human life expectancy to be genetically programmed. In apparent support of this notion, a pioneering gerontologist named Leonard Hayflick, Ph.D., professor of anatomy at the University of California, San Francisco, has discovered that some of the body's cells (specifically, fibroblast cells) automatically shut down after 50 replications, as if obeying a genetic death wish.

Recently, another piece was added to the puzzle when Calvin B. Harley, Ph.D., a biochemist at McMaster University in Hamilton, Ontario, uncovered a mechanism that might explain how these cells are able to count to 50. Each chromosome strand within each cell turns out to trail a kind of ribbon of genetic material, and every time the cell divides, a little more of this tail is trimmed off. When the last of it is gone, the cell loses viability and dies. While at first blush this line of research appears to confirm the view that life span is genetically limited, Dr. Harley himself has taken it to mean only that a centralized command governs the behavior of individual cells.

These governing agents, called longevity assurance genes (LAGs) by researchers, have become the Holy Grail of gerontology. Without such a master-control system, the possibility of markedly extending life would be hopeless, because the only way to recalibrate a human's life span would be to reengineer each of his 10 trillion cells. With a limited number of master controls, scientists would have to reset only a few switches.

Unfortunately, no one has actually proved that these longevity assurance genes could be adjusted to extend life. In

fact, there is an inherent paradox that makes altering them troublesome. It seems that cell immortality can spell death to the cell's possessor. “When cells become immortal, what you have is a cancer,” explains Richard Sprott, Ph.D., associate director of the National Institute on Aging. Only cancer cells keep replicating indefinitely, so the mechanism for clamping down on the number of cell divisions may have evolved as a way of warding off tumor growth.

For some researchers, this has been more good news than bad. James R. Smith, Ph.D., codirector of the Huffington Center on Aging at Baylor College of Medicine in Houston, has found some of the specific genes responsible for turning normal mortal cells into immortal cancerous ones. Other researchers have actually succeeded in turning cancer cells on and off, thereby bringing science a step closer to actually controlling the cell's aging process through gene therapy. In the meantime, the research has important implications in understanding cancer formation.

Perhaps the most compelling evidence that life span is

genetically controlled is being compiled by Michael Rose, Ph.D., a geneticist at the University of California, Irvine. Dr. Rose is breeding fruit flies for longevity. He believes that life span is a genetic trait no different from superior milk production in cows or fungus resistance in potatoes, and as such is passed on in predictable patterns from parents to offspring. Just as cows can be selectively bred to increase milk production, longer-lived individuals can be culled and bred together to increase longevity. Eventually—and this is

the hard part—the critical physiological elements that underlie the trait can be isolated. Rose has already succeeded in doubling the life spans of fruit flies from 40 to 80 days and has started to isolate the stress-resistance factors he believes are responsible. With enough money, he could test his results on mice and then on humans. “It can be done,” he says forcefully. “I guarantee it.” All that is required, he says, is a substantial infusion of money, at least \$50 million a year.

Rose may be promising more than he can deliver, but he is right about one thing: If humans really want to live longer, they will have to pay for the privilege. Right now, gerontological research is seriously underfunded. While the U.S. spends \$1.5 billion for cancer research, \$1 billion for heart disease research and \$100 billion on treatment of both, it spends a paltry \$100 million on aging research, and much of that is targeted for specific diseases. “For every one thousand dollars spent on coronary heart disease and cancer,” writes Thomas J. Moore in his book *The Oldest Dream*, “less than a dollar goes to understanding the basic process that may underlie both

A group of elderly men were rejuvenated after treatment with human growth hormone.

disorders." This is a peculiar ranking of priorities. Even if scientists did find a cure for all cancers, the average human life span would be extended by only a scant two years, and the conquest of heart disease would yield only eight more. But if aging itself could somehow be put on hold, the possibilities are limitless.

#### **A free-radical idea**

Another group of researchers is proceeding from the supposition that aging is not genetically predetermined, that it is the result of gradual damage to the cell's DNA, which, like a master builder, directs the process of cell replication. With

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## *Vitamins: the real fountain of youth*

Should you start taking vitamin pills to ward off aging? For many years the idea was dismissed as quackery by mainstream gerontologists. But now, a surprising number of them are changing their minds.

"There is a great deal of compelling evidence that the antioxidants beta carotene, vitamin E and vitamin C may indeed help reduce the risk of contracting diseases associated with aging," says Jeffrey Blumberg, Ph.D., associate director of the USDA Human Nutrition Research Center on Aging at Tufts University. "I don't believe that any of them will extend the life span, but they may well extend the 'health span' by delaying the onset of cancer, heart disease, arthritis and cataracts."

Most of the diseases associated with the aged actually start to appear very early. Signs of atherosclerosis have been found in 10-year-old children, and cataracts can start forming at age 20. Antioxidants may slow the development of these diseases by fighting off the free radicals that help cause them at the cellular level. With a full complement of antioxidants at work, Dr. Blumberg believes, individuals may gain 10 full years of disease-free living, pushing the onset of debilitation from the mid-sixties, the current norm, into the mid-seventies.

Recently, a number of major studies have confirmed the beneficial effects of antioxidants on the nation's current number-one killer, heart disease. Charles Hennekens, M.D., of Brigham and Women's Hospital in Boston has completed three of them—one involving 87,000 nurses, another with 333 doctors, and a third with 1,300 elderly subjects. All showed consistently that those individuals with the highest intake of the antioxidants vitamin E or beta carotene had the lowest risk of contracting heart disease.

At around the same time, a highly publicized study of 1,900 Finnish men by Jukka T. Salonen, M.D., of the University of Kuopio suggested that men with the highest levels of iron were at the greatest risk for heart disease. While *The New York Times*, amazingly, drew the conclusion that individuals might want to reduce their blood iron by old-fashioned bloodletting, Blumberg points out that a more sensible interpretation is that Dr. Salonen's results confirmed the free-radical theory. Since iron is a notorious pro-oxidant, Blumberg

argues that it makes more sense to boost one's antioxidants than to reduce one's iron.

How many antioxidants should you take? That depends on whom you ask. Virtually all gerontologists believe that you should certainly get your full complement of recommended daily allowances. For women, that means 60 milligrams of vitamin C, which is found not just in oranges but also in broccoli, sweet and hot peppers, brussels sprouts, strawberries, potatoes, spinach and tomatoes; and 30 IUs of vitamin E, found in vegetable oil, margarine, shortening, leafy green vegetables, wheat germ, whole grain products, egg yolks, butter and liver. While there is no U.S. RDA for beta carotene, which is found naturally in carrots, leafy green vegetables, sweet potatoes, winter squash, apricots and cantaloupes, experts suggest at least five milligrams a day.

Many researchers are distrustful of dietary supplements that go beyond the U.S. RDAs, but quite a number of the gerontologists I interviewed for this story endorsed the idea and admitted, sometimes a little sheepishly, to taking extra vitamins themselves. Richard Cutler of the National Institutes of Health (NIH), for instance, takes 30 milligrams of beta carotene, 250 milligrams of vitamin C and 800 IUs of vitamin E; and Roy Walford takes 500 milligrams of C and 300 IUs of E. James Fleming of Eastern Washington University has taken 13 grams of vitamin C daily for the past 10 years and says he hasn't "come remotely close to getting sick" the entire time.

Taking extra pills would guarantee that you really are getting the U.S. RDAs, which otherwise can be extremely difficult to determine. But the recommended levels aren't very high; a single carrot, for instance, provides well over the recommended daily need for beta carotene. And there is little danger of overdosing on any of the antioxidants, although some vitamin pills can upset the stomach.

So, how much to take? Blumberg is reluctant to make across-the-board recommendations, since every individual is different, but he does offer the following guidelines: 15 to 30 milligrams of beta carotene, 250 to 1,000 milligrams of vitamin C, and 100 to 400 IUs of vitamin E. These quantities can be conveniently obtained in a single tablet.

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age, some cells lose what biologists call their "differentiation," or unique attributes. "It's what makes an eye cell an eye cell and a liver cell a liver cell," explains the NIH's Cutler. Over time, the cell's fundamental identity gets fuzzy. Cutler believes this explains why, as we age, hair starts to grow in unexpected places like our ears and noses, why intestinal cells are suddenly found lining our stomachs, calluses appear where they aren't needed, and moles start showing up everywhere. These cells seem to forget what they are supposed to be.

One theory holds that such slow degradation of the cell and its DNA is due to bombardment by free radicals. These renegade oxygen atoms have either one electron too few or one too many and can be produced in any number of ways: simply by breathing or by exposure to heat, radiation, air pollution, even sunlight. Their effects can be drastic. Alex Comfort, Ph.D., a respected gerontologist (and author of *The Joy of Sex*), has compared them to a wife-free conventioner eager to "combine with anything that's around." As they career around the body, they steal electrons from molecules wherever they can, leaving damaged cells in their wake. Some of this damage is never repaired, and research suggests that it can result in cataracts, emphysema, LDL, or "bad," cholesterol, heart attacks and diseases such as Parkinson's and Alzheimer's.

The free-radical idea was first proposed by Denham Harman of the University of Nebraska more than 30 years ago and entered the national consciousness in 1983 with the publication of the bestselling book *Life Extension* by Durk Pearson and Sandy Shaw. Since then, millions of Americans have been ingesting a variety of nutrients, called antioxidants, that assist the body's natural defenses against the ravages of free radicals. Chiefly, these antioxidants are beta carotene and vitamins C and E. For a long time no broad, authoritative study had validated any of the claims. The evidence was particularly weak in support of the idea that antioxidants might reduce heart disease. Recently, however,

a study of 87,000 nurses by Charles Hennekens, M.D., at the Brigham and Women's Hospital in Boston has shown that those who took the most vitamin E and beta carotene had the lowest incidence of heart disease in the sample. Apparently, the antioxidant properties of the vitamins keep the free radicals from converting the cholesterol coursing through the bloodstream into artery-clogging fatty deposits.

### Human growth hormone: a magic elixir?

Another promising line of inquiry involves some extraordinary experiments by Daniel Rudman, M.D., a professor of medicine at the Medical College of Wisconsin. It has long been known that the levels of human growth hormone (hGH) decline dramatically after your mid-thirties. By injecting a dozen 60- and 70-year-old men with hGH for six months, Dr. Rudman was able to counter the usual decline. Some of the men found

To extend life, geneticists are working to change the body's basic blueprint.

themselves rejuvenated almost as astonishingly as the retirees in *Cocoon*. Their bodies rippled with muscles, and they felt newly energetic. Unfortunately, the effects disappeared as soon as the experiment was over, and it is doubtful that the hormone treatment had any lasting effects on longevity.

Other researchers are unsure about the safety of the drug. Cutler, for one, argues that there may be a good reason why hGH levels naturally decline with age—to inhibit cancer, for example. A cancer on the verge of metastasizing might need only a small kick of growth hormone to begin spreading. Such uncertainties point up the many complications in trying to isolate and address the aging process. In the view of most scientists, the body is like a Swiss watch, with a vast and intricate array of levers and gears that have to mesh perfectly to work. "If you change one thing," says Dr. Smith, "you might screw everything else up totally."

### Eat less and live longer

Although antioxidants and hGH seem to hold significant promise for warding off disease, increasing vitality and, by doing so, extending what have been called "health spans," neither of them has been shown to have any actual ability to increase life spans. Only one regimen has demonstrated that capability in mammals, and that is the low-calorie diet. When the diets of a wide range of animals and insects have been reduced by 30 to 50 percent of their normal caloric intake, their life spans have been routinely lengthened by anywhere from 20 to 100 percent. George Roth, Ph.D., is conducting a low-calorie experiment with rhesus monkeys at the NIA, and he notes that the restricted-diet monkeys act like "flyweight boxers," constantly hopping around their cages, while their mates who get all the food they want lie around like so many primate couch potatoes.

Roy Walford, M.D., a UCLA gerontologist and leading proponent of the low-calorie diet, is one of the few humans to actually try the diet himself. Now 68, Dr. Walford has restricted his caloric intake for the past six years, and he believes it will help him live to 120. Currently, he is the resident physician in Biosphere II, the futuristic enclosed environment in the Arizona desert.

Walford has no biological explanation of how a low-calorie diet would make him live longer. It may assist DNA repair, rejuvenate the immune system or limit the damage of free radicals. He believes that it makes use of an evolutionary adaptation that allows individuals to get through a period of food shortage by shifting their energy from what he calls "growth and development" to "maintenance and repair."

### Prosper and live longer

If, as Rose claims, the only thing standing between human beings and relative immortality is money, why have Americans happily expended \$24 billion to put a man on the moon, but shelled out only a few million to put off the prospect of dying? It may be that it seems somehow unbecoming, or even dangerous, to tinker with the fundamental facts of nature. As Richard Cutler puts it, "People seem to think it's okay to help the abnormal

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## FASHION DETAILS & STORES

**PURE & PERFECT Page 78:** Taurus intaglio ring, \$500; star band, \$400; assorted bracelets, \$1,200 to \$1,500; all in brushed silver and gold by Laurence De Vries. At Bergdorf Goodman, NYC; Just Jewels, San Francisco; Maxfield, L.A.; Korshak, Dallas. Scoop-neck shirt by Calvin Klein Sport. **Page 79:** Antler bracelet, \$250; ibex cuff, \$330; deer bracelet, \$300; all in silver; gold love token rings, \$300 each; all by Gabriella Kiss. At Artwear, NYC; Ted Muehling, NYC; Bergdorf Goodman, NYC. Gray ribbed top by TSE Cashmere. **Page 80:** Gold and silver acrylic pendants, \$110 each, by Christina McCarthy. At Henri Bendel, NYC. Lurex gold sweater by Mary Jane Marcasiano. Woven gold and freshwater pearl earrings, \$150, and pendant, \$130; by Ally Tomi. At 66 On Seven, NYC. Gold disc belt, \$490; carved cross cuff, \$160; sculptural rings, \$40 each; all in gold from Robert Lee Morris, NYC. At Artwear, NYC. Studded foil bracelets, \$120 to \$180; pearl ball ring, \$70; gold-leaf oval earrings, \$85; all by Cynthia Rybakoff. At Body Sculpture, Boston; Henri Bendel, NYC. Gold cropped top and leggings by Michael Kors. Cable-knit sweater by TSE Cashmere. **Page 81:** Drop mesh earrings, \$150; silver disc bracelet, \$320; large mesh cuff, \$400; all by Jordan Schlanger at Artwear, NYC.

**SHIRT ALERT Page 108:** Men's printed silk tunic, \$245, by Timney-Fowler for Go Silk. At Bernini Inc., Las Vegas; I. Magnin, San Francisco; Neiman Marcus, select stores. Yellow silk trousers by Moschino Couture. Silver hoop earrings by John Iverson at Artwear, NYC. Cowboy shirt, \$125, by Ralph Lauren Country. At Polo Ralph Lauren, Beverly Hills and NYC; Saks Fifth Avenue, NYC. **Page 109:** *Top left*, striped tuxedo shirt, \$450, by Charvet. At Bergdorf Goodman Men, NYC. Suspenders by State of Claude Montana. Blue and gold cuff links by Kieselstein-Cord. Shirt studs by Sentimento. *Top right*, black silk organza shirt, \$245, by Equipment. At The Equipment Store, NYC. Capri pants by Moschino Cheap & Chic. At Bloomingdale's, select stores; Nan Duskin, Philadelphia. *Bottom right*, striped shirt, \$130, by Isani. At Bloomingdale's, select stores. *Bottom left*, classic white cotton shirt with illusion top, \$64, by Kenar Studio. At Dayton/Hudson; Nordstrom, select stores. Necklace by Gale Reiss at Showroom Seven. At Biba, Chicago; Ibiza, NYC.

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become normal, but not the normal become supernatural." By this reasoning, research money is for saving lives, not extending them.

But another reason may be that, for all the age-old fascination with the topic, human beings themselves are surprisingly lukewarm about the idea of living much longer than they do now. In one poll, only slightly more than half the respondents expressed a desire to live to be a hundred. This may be because they tend to regard long life as protracted old age, and old age—so deeply associated with debilitation and the death of loved ones—is currently not very popular. Or they may wonder how society could possibly support so many more elderly.

Curiously, even as the research on the biology of aging proceeds, there has been no authoritative study of its potential consequences for individuals or for society. Would life be improved by increased longevity? What about population pressures if people live longer? One of the social scientists who have considered the matter is Pulitzer prize-winning author Robert N. Butler, M.D. He is at work on a book called *The Longevity Revolution* in which he examines these very questions. Dr. Butler takes a hopeful view. He notes that average life spans have already been expanded by more than 60 percent in the past century (from the 47 years of 1900 to the 76 years of today), and "we have been able to deal with that very well." He notes that society has already started to adjust to the new longer life spans by passing laws against age discrimination in the workplace.

"There is no question that life extension would be a net positive," he says. "With increased longevity comes increased helpfulness and productivity." He expects that by the time truly long lives are possible, humans could alleviate pressures on the Earth's population by colonizing other planets. Whatever the ultimate consequences, we should start getting ready. "Like it or not, we are going to have time extension," says Butler. "The only question is, how are we going to adapt to it?" □

John Sedgwick wrote about the health care crisis in the December issue of SELF. His work also appears in GQ, The Atlantic and Esquire.

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