Your great-grandchildren may live twice as long as you do, says this eminent longevity researcher. You don't have to rebuild the body or redesign the brain. The secret is just to retune a few key genes

INTERVIEW

RICHARD CUTLER

Stringy gray hair, long on one side, covers the expanse of his scalp. His face is lined, his hands rough-hewn. His kids, almost grown, just wear him thin. "They mostly need money," he says of the two at expensive universities. "The days when I could play with them, nurture them, teach them are gone." Richard Cutler, age fifty, is prey to the inexorable passage of time. But like a cancer researcher who charts the course of his own malignancy, Cutler, pioneer in the field of human longevity, is cursed with the knowledge of truth. His diminishing strength: the unrelenting onslaught of oxygen, hormones, and nutrients. His loss of zest: molecules of hemoglobin pulsing ever outward from deregulated neurons in his brain. "I can *see* the process of aging," Cutler says. "I can see it all coming on."

Cutler accepts the certainty of his *own* short life and ultimate death. But, declares this preeminent advocate of scientific life extension, "there's not one shred of evidence for any bottleneck on the evolution of human longevity. How can we keep building new and wonderful machines while *we've* stayed the same for a hundred thousand years? Our first priority must be to control man's aging process, and from that all other things will flow."

Cutler's dream of longevity flowed from the lonely Colorado town that was his childhood home. Born a Mormon among Mormons, he was brought up to think of life as a testing ground for the reward of heaven beyond. "The Devil was always here tempting you," he explains. "For that reason your best bet was *not* to stick around too long." Cutler had his doubts, of course, but as a boy whom parents and teachers had pigeonholed as intellectually slow, he didn't feel equipped to protest.

Cutler, still a teenager, was catapulted out of the oppressive dominion of his past by an unbelievable, explosive series of

PHOTOGRAPH BY MIKE MITCHELL

events. One minute he was a backwoods boy on his way to vocational school; the next, the brilliant, quirky Cutler found himself head of a corporation funded by one group of millionaires while yet another millionaire sent him through school. "It was really wild," Cutler reflects. "Almost like coming out of a cave."

Cutler eventually found his way to graduate school in biophysics at the University of Houston and to prestigious posts at the Brookhaven National Laboratory on Long Island and the University of Texas at Dallas. All the while, he pursued the question that had gnawed at him ever since his youth: Why do we *have* to age and die, and what could be done?

Approaching the problem with his broad and eclectic intelligence, Cutler scrutinized anthropology, evolution, comparative physiology, molecular biology, and more. And in the interstices of the disciplines, buried in data from thousands of reports, he saw the pattern: No more than six tenths of a percent of all human genes could possibly be involved in the evolution of longevity. Aging—the field that *seemed* to require a complete understanding of every organ, system, and cell type in the human body—might be reduced to common denominators. And those denominators might be comprehended, harnessed, and even changed. Human longevity might be extended not just by 20 years, Cutler declared, but by 200 years or more.

Cutler's radical theories have thrust him into the biomedical spotlight, bringing both songs of praise and scathing attack. Although his theories derive from tight, deductive reasoning, they're just too unconventional for many mainstream scientists. Many of his colleagues in gerontology, already troubled by the economic burden of the infirm aged, are philosophically opposed to his work. He has been accused of plagiarism. And his two most loyal benefactors have recently been forced to limit their support. To make up for the loss, his medical technician wife, Edith, works in his lab gratis from ten in the morning to four in the afternoon. (Then she goes to her job as a *paid* lab technician from 4:30 to midnight.) "I sometimes feel bad that my wife still has to come in and help me," Cutler declares. "Her presence reminds me that I'm struggling. She's there to save the day. Without her I simply couldn't go on."

Despite his troubles Richard Cutler has prevailed. He has secured a tenured position at Baltimore's prestigious Gerontology Research Center, part of the National Institute on Aging. And though his support has been limited, he has conceived perhaps the most sweeping theory of human longevity to date. His elegant ideas, rooted in the ancient axioms of evolution and the driving logic of DNA, may one day yield up the reward of prolonged life. They may also point the way toward vast increases in intelligence and creativity, ultimately aiding the future evolution of man. Richard Cutler was interviewed in his office and over lunch at Baltimore's quaint European Cafe by *Omni* senior editor Pamela Weintraub.

Omni: What initially lured you into life extension research?

Cutler: Disappointment with religion. The first thing I learned was how lucky I was—a white male in the right church in the USA. All I had to do was work hard, follow the rules, and heavenly immortality would be my reward. I was uneasy about that point of view from the start, but I went along.

In high school my family moved to Anaheim, California. I wasn't considered too bright. After I took an aptitude test, my guidance counselor suggested I forget college and go to vocational school for welding. As a senior I found my way to the machine shop and constructed a helicopter of unusual design, with engines in the tips of the blades. I flew it in my backyard and created quite a ruckus. There was a lot of noise and wind, and with fire streaming out of the top, people thought there was an explosion. Police and newspapers arrived, and a reporter wrote a long story about me in the Sunday edition of the *Santa Ana Bulletin*. He took me under his wing, and I ended up at a two-year college—the Electronic Engineering Institute in Englewood, California. I met some people there belonging to the Los Angeles Philosophical Society and began to think about things—psychokinesis, levitation, UFOs. I was just nineteen years old, and after my Mormon upbringing this was like coming out of a cave. I began to question the notion of immortality and realized, in the face of aging and death, just about every religion offered hope of salvation in a world beyond. It just seemed like a cop-out. I even went to UCLA and asked some professors what we could do to increase our life span, and they said, "Nothing at all. The aging process is too complex." That's when I decided increasing longevity was something I'd like to attempt.

Omni: What was your plan?

Cutler: About that time the accountant at the electronics institute saw the article in the *Santa Ana Bulletin*. He put together a group of four millionaires and convinced each to invest about a quarter of a million dollars in what we called the Cutler Helicopter Corporation. The idea was that I would design a light, cheap craft affordable to the masses. I had several machinists and welders in a building in Pasadena helping to make the helicopters. Once I made my millions, I planned to set up my own laboratory and do aging research. The whole thing was crazy. My parents thought it was totally wild, and in fact I was lucky to escape with my life. The first time we tested our engine at the Van Nuys Airport, it blew completely apart. First it tore up the test stand, then it flew off altogether, wiping out several large airplanes. I had constructed a tower from which I conducted the experiment—that collapsed, too. I was left dangling by my arms. We were insured by Lloyd's of London, thank heavens.

Omni: Were your backers upset?

Cutler: No, they were delighted. The experiment proved that the engine was really powerful. The work went on until eventually I was contacted by *another* millionaire who had also read the article in the *Santa Ana Bulletin*. This man had made his fortune in hydraulic valves, and had recently lost his son in the Korean War, so he set up a foundation in his honor. After questioning me for about half an hour, he told me he'd help me through college. I walked out with a five-thousand-dollar check. Though I never saw him again, he sent me several thousand dollars a year for five years, until my undergraduate education—I majored in physics—was complete.

Omni: How did you switch from physics and helicopters to longevity?

Cutler: The helicopter company folded, and I began scouring the country for a place to pursue my true interest, longevity. Finally I found a program in biophysics at the University of Houston. It was a totally new field with two main goals: to reveal the impact of physical phenomena such as light or X rays on organisms and cells; and to explain complex living systems through basic forces or laws, much as physicists try to explain the universe. Biologists told me that aging was too incredibly complex to ever understand. You'd first have to understand every system in the body—heart, lung, skin, brain—and then alter each one. I wanted to find some underlying principle that might control aging no matter *what* the animal, organ, or cell. The time was ripe—Watson and Crick had just discovered the underlying mechanism for heredity in the structure of DNA. So I took off for Houston in my little hot-rod car. For the first time in my life I was heading far from home.

Omni: What did you do there?

Cutler: I found a way to make all the cells in a single bacterial culture divide at once so that they passed through all the stages of life literally in synchrony. *This* study made it possible to map the bacterial genome. But none of it would have happened if I hadn't been taking organic chemistry at night with this girl named Edith. I'd rarely been out with girls. Always helicopters, you

"Some of our greatest scientists and musicians were exceptionally neotenous. People don't realize that being like a child is what made them great."

know. But now I was kind of lonely, and this girl looked nice, so I asked her out to see *West Side Story*. As it turned out, she was also real good in chemistry. She turned out to be a medical technologist and a superb bacteria counter. She could just look at cells and tell me what they were like! I'm half blind, so I could hardly see the cells, but with her expertise, she just executed the bacteria-culture concept I'd come up with, and it worked. We got married three months after that first date, and she's been helping me ever since.

On the basis of that work and many letters, I finally got a fellowship with Howard Curtis of Brookhaven National Laboratory. Curtis was the only American studying aging from a molecular perspective. He gave me my own lab and assistant—I was in heaven. I decided to devote myself to determining how complex the biology of aging really was. If it was too complex to unravel within the context of twentieth-century science, I would leave the field. But if I could find some indication that understanding—and perhaps slowing—the aging process was possible with current knowledge, I would devote my life to the quest.

Omni: How did you proceed?

Cutler: Curtis showed that as animals age, their chromosomes acquire aberrations. So he postulated that with increasing age DNA accumulates mutations that destroy the basic information used to run a cell. That leads to aging. Being right there, I picked up something about his work that most everybody missed. He experimented on three species: the beagle, with a life span of about twenty years; the guinea pig, with a life span of eight years; and the mouse, with a life span of three years. He found that the rate of chromosomal aberration correlated well with the aging rate. Longer-lived species acquired mutations at a slower rate. Thus longevity appeared to be regulated by factors *within* the cells. Because the cells making up dog, guinea pig, and mouse are extraordinarily similar, this suggested that the cellular differences contributing to longevity must be simple, despite the complexity of the aging process itself.

Omni: Did you see any other evidence for the theory that relatively simple factors were contributing to longevity?

Cutler: What struck me most was that the increase in longevity across species seemed to be accompanied by increases in intelligence. Humans, for instance, have a particularly long life span. In the wake of that observation, I came across George Sacher's work. A radiation biologist at Argonne National Laboratory, Sacher had dedicated much of his life to understanding the biology of longevity. He realized that the larger the brain-to-body-size ratio, the slower a species will age. Sacher even came up with a formula relating maximum life span potential [MLSP]—the maximum number of years that an individual of any given species could possibly live—to brain size and body weight. Just knowing the brain and body sizes of any mammal would enable you to plug into the formula and crank out the MLSP.

Omni: Did he explain the phenomenon?

Cutler: Because shorter- and longer-lived species had essentially the same cell biology, Sacher decided longevity-control mechanisms had to reside in the brain. Bigger brains, with their superior processing, could better maintain the body. He even tried to find a longevity-controlling center in the brain but never did.

Omni: Where did you fit in?

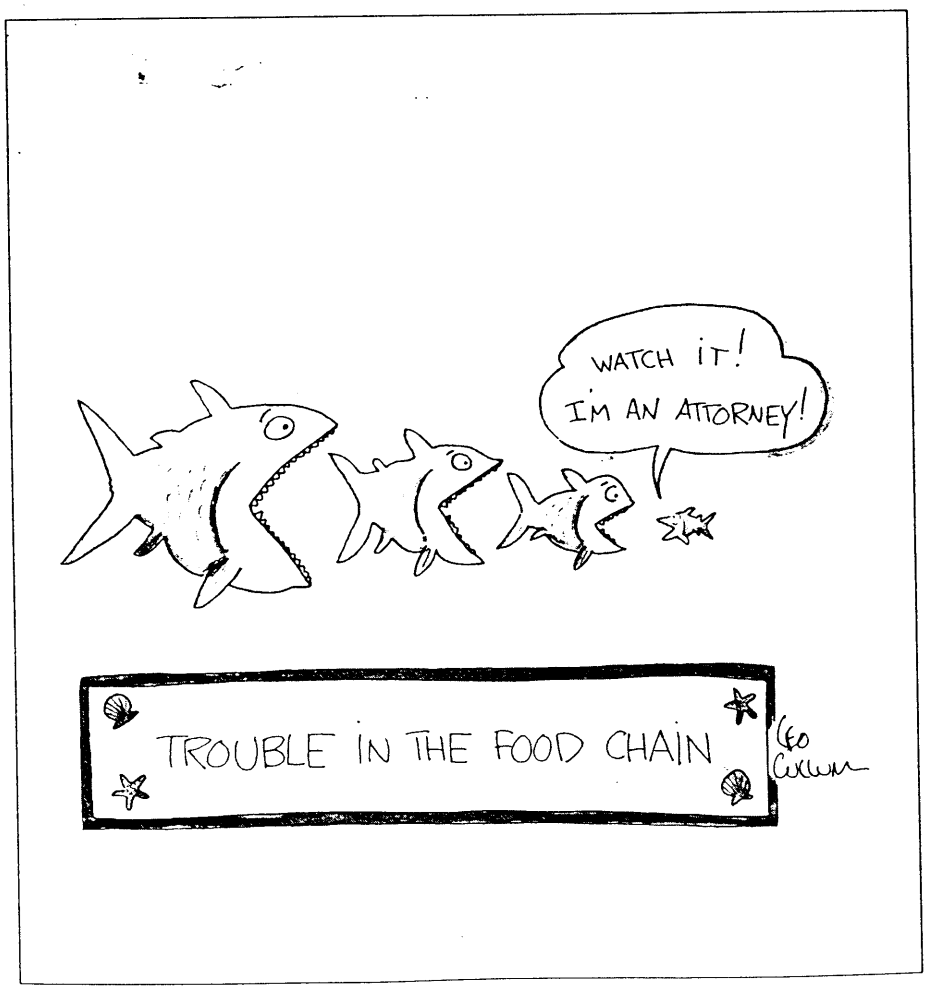
Cutler: I reinterpreted his results. Even though different species had essentially the same biology, I nonetheless thought that basic biology, not brain size, had the primary role. The correlation between brain size and longevity, I said, was there by virtue of evolution. If larger-brained mammals have longer life spans, it's because a longer life span confers an evolutionary advantage to those with sizable brains. Life span and brain size coevolved.

Omni: If the brain doesn't control longevity, what does?

Cutler: I found part of the answer in studies on *speciation*—the mechanism by which different species form. One of the first things scientists studying speciation did was compare primates that had all presumably evolved from a single ancestor about sixty-five million years ago. They found extraordinary similarities from one group to the next. When researchers compared humans, with an MLSP of one hundred years, to chimpanzees, with an MLSP of fifty years, they found that ninety-nine percent of the genes were same. Chimp and human livers worked the same. Food and energy metabolism was similar. Studying the two species, from the skeleton to the muscles to the cells, there are no new structures. So what the heck was the difference? Structures and functions are just differentiated to different degrees. From species to species some genes are *expressed* more strongly than others. And that difference in expression is all you need to create new species. Evolutionary biologists went on to estimate that the one percent genetic difference between human and chimp resided in *regulatory* genes—genes that act like switches to turn other genes on and off. *My* concept was that slowing the aging process might be accomplished by altering these few genes.

Omni: Armed with evidence that altering life span might *not* be that complex, you plunged into the longevity field.

Cutler: Yes, and I *still* burn with excitement when I think of how it all came together for me. I'd gotten a job at the University of Texas at Dallas. Edith and I already had three kids—one right after another. I had a little Datsun 240 Z, and one day I piled my kids in the back and took off into the desert for Anaheim. Every so often I'd stop and write down notes, until I had road maps covered with scribbles. One thing made



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sense, then another, and I knew I was onto something. Aging *rate*, I reasoned, varied from species to species, but the *process* of aging was the same. No matter what the species, once aging set in, everything—eyes, ears, reflexes, muscles—seemed to go more or less at once. Every tissue of the body, in essence, was run by the same aging clock. Comparative physiology suggested some common master gene of regulation, altered slightly among species. To increase longevity we didn't need to invent new body processes or genes. It had to be a small number of control genes turning the volume, the quantity of certain longevity biochemicals, up or down. We might already possess the basic genetic makeup for a life span of four hundred years. I couldn't wait to test these ideas.

Omni: How could you prove that notion?

Cutler: One way was through a technique commonly used in evolutionary biology: To learn how many genes determine a characteristic, you ask how long it took the characteristic to evolve. If, for instance, a hundred thousand genes are involved in human longevity, a longer life span would take longer to evolve than if two hundred genes were involved. That's just the way evolution works. I needed to learn human longevity had actually evolved.

Omni: You'd have to measure the life span of extinct species—and they're already extinct!

Cutler: George Sacher had the key when he showed that you could calculate MLSP by comparing brain size to body weight. Well, I checked out his formula for a whole range of species, from recently evolved primates to the opossum, which has been around in its present form for millions of years. This doggone formula seemed to work across the board. I didn't see why it shouldn't work for completely extinct species as well. So I went back to the literature, digging up the anthropologists' measurements of fossils. They had calculated the brain size and body weight of primate species as they'd evolved over millions of years. I discovered that longevity generally increased during primate evolution, but at different rates, depending upon the lineage, be it squirrel monkey, ape, or baboon. But for hominid lineage, the rate kept going up faster and faster the closer you got to modern man. The line on my graph went almost straight up. For the last few million years longevity could only change at that pace if it involved no more than six tenths of a percent of the entire genome, roughly six hundred genes.

Omni: Then longevity is evolving still?

Cutler: Not at all. Evolution of longevity, like the evolution of brain size, has come to a total halt. I found that Neanderthal men, for instance, had longer MLSPs than *Homo sapiens*. Researchers also found the remains of hominids with superbrains and, according to my calculations, superlong life spans. They probably looked like men from Mars, but the trait didn't prevail.

I calculated that hominid longevity increased an astounding fourteen years over the last hundred thousand years. But about fifty thousand years ago the rate at which longevity increased fell to zero because of the specific way we evolved. Our ancestors lived in small, traveling communities generally led by a single chief with superior traits. Because he passed on more of his genes than anyone else, these were the ones that took. If another individual, with yet more potent traits, arrived on the scene, *he* would take over, and his genes would propel evolution further still. With the advent of civilization, these traveling bands disintegrated; because everyone had a more or less equal chance to reproduce, selection for superior traits, including increased longevity, stopped.

Another factor that probably played a role is a process known as neoteny. *Neoteny* means the retention into adulthood of early developmental features. Individuals take on increasingly childlike features—greater brain-to-body ratio, larger eyes, sparser hair. The larger brain necessitates a longer period for learning, so neotenous species spend more time in childhood; development is essentially stretched out so that every phase of the life cycle expands. As generations passed, individuals simply became increasingly neotenous until eventually we had modern man. A normal adult *Homo sapiens* has the same brain-to-body ratio as a baby chimp. He takes twice as long as the chimp to reach adolescence, spends twice as much time in

the prime of adulthood, and takes twice as long to die.

After a while, though, our physiology forced the process of neoteny to a halt: We simply reached the point where it was impossible to give birth to more neotenous, larger-brained children without warping the female's pelvis, totally destroying her gait, and impeding her ability to walk. With increasing neoteny impossible, the evolution of longevity stopped.

Omni: What a sweeping theory. What was the response?

Cutler: It thrust me into the blackest period of my career. It was 1975, and the *Proceedings of the National Academy of Sciences* sent my paper to George Sacher for review. He claimed I'd stolen all the ideas from *him* and rejected it. I found that incredible because I'd been communicating with him all along. We even co-organized a meeting three months prior to this in which I'd presented a paper on the same data. And his only comment at the time had been "fascinating." The academy decided to publish my paper anyway but asked me to acknowledge that Sacher had arrived at similar data independently. But Sacher was bitter and acrimonious and even formed his own clique of supporters. Before he died, in 1982, he wrote one last chapter claiming *everything* I ever did as his own. The matter has not been resolved, and people still say, "Cutler stole the data because he had trouble getting grants." Or, "He did it because he was too ambitious." Being accused of that was terribly upsetting. It hounds me. It diminishes everything I've done. But I try to follow my wife's advice: "Just keep going. Just continue. People will *see* where the ideas are coming from."

I had political problems everywhere, but I was finally put in touch with Don Yarborough, a philanthropist who was interested in aging research. He and his friends ended up supporting me. Don eventually introduced me to another philanthropist, named Paul Glenn, who helped me pay the salary of a lab technician. This money was what scientists call *soft*, but at least I was generating enough of it to keep myself and my research going. A year after the Sacher furor, I left Dallas for what I thought would be a better opportunity—my current, tenured job at the Gerontology Research Center, part of the National Institute on Aging.

Omni: So things improved?

Cutler: Not at all. I'd been here for just a few months when the man who hired me left. As new man on the block with these far-out ideas, I received little support. But Yarborough and Glenn supplied money for technicians. And my wife is *still* here supplying her expert services.

Omni: Despite difficulties, you kept on?

Cutler: Yes, and my first goal was to figure out what actually *causes* aging. There were two points of view. The more popular notion was that we had aging genes that programmed the production of a death hormone—because aging and death benefited evolution by killing off the old to make room for the new. Proponents of this idea suggested a Disneyland explanation for the death of animals in the wild: As rabbits grow old, crippled, and weak, wolves kill them off. But that's not the way it is at all. There aren't enough enfeebled rabbits for all the wolves. Instead, wolves kill healthy rabbits in a mostly random kind of way. Most rabbits are killed by natural predators while very young. No wild animal lives long enough to get old. The problem in nature has never been that animals live too long—it's quite the opposite—to stay alive to a decent reproductive age. So there'd never be any pressure to evolve a hormone promoting aging and death.

Omni: You reject the dogma that aging is genetically programmed into all individuals for the good of the species?

Cutler: That's right. So let's consider the other alternative: Aging is the by-product of *normal* metabolic and biochemical processes necessary for survival. Look at the hormones we produce at puberty. When scientists castrated Pacific coast salmon, they found that the fish, never producing sex hormones or reaching sexual maturity, lived about twice as long. You must become sexually mature to survive, but there's a price to pay. Other examples are the highly reactive particles, free radicals, you produce in metabolizing oxygen. You have to breathe in order to function, but you pay a price—free radicals that damage DNA. In nature, where most creatures are killed by predators and other hazards, the harmful aspects of these processes never come into play, because animals simply do not live long enough. But for humans living in the civilized world, these by-products cause aging. Because our basic biochemistry is virtually identical to that of the chimp, we must have better ways of coping with the same toxic by-products, agents of DNA damage, aging, and death.

Omni: How does DNA damage, per se, result in aging?

Cutler: Through a process called dysdifferentiation, which is essentially development in reverse. We all start from a single fertilized egg that develops by dividing and differentiating so that many different types of cells emerge. We have blood, brain, muscle cells, and so on. Free radicals produced in a cell can alter the proper differentiated state of the cell. For instance, brain cells have been found to produce hemoglobin, a protein previously produced only by blood cells. As the brain cells continue to produce hemoglobin, the brain becomes just a bit less efficient. And other parts of the body undergo this process as well; kidney cells may begin to function a bit like liver cells, for instance, and stomach cells begin to produce proteins previously specific to the intestines. After a while you can't run the four-minute mile. Small and subtle departures from the optimum state occur over time, and very little change is required to account for the aging proc-

ess. My theory is that free radicals, along with other active chemicals, make the dysdifferentiation occur. Thus the mechanisms that keep a cell in its proper state of differentiation might be the very ones that determine the longevity of an animal.

If free radicals cause aging, then some species live longer because they have better ways of fighting them off. So you'd expect longer-lived species to have higher levels of *antioxidants*, substances that neutralize free radicals. Finding higher levels of protective antioxidants in the tissue of longer-lived species would be the acid test of this idea. That's what I set out to do.

Omni: What antioxidant did you look at?

Cutler: I chose superoxide dismutase [SOD], whose only known role is to protect against free radicals. It's present in all creatures from bacteria to man, and it's required for survival. We tested humans, chimpanzees, gorillas, rhesus monkeys, and a few short-lived species, including guinea pigs and mice. We found a beautiful linear correlation: Longer-lived species had more SOD to protect against a given quantity of free radicals than did shorter-lived species. When I repeated the experiment for other antioxidants, including vitamin E, beta carotene, and uric acid, the correlation held firm. What's so nice is that these findings fit into the control-gene theory. Just turn up the production of antioxidants, which all species have, and longevity increases.

Omni: Could I slow my aging by consuming some antioxidants?

Cutler: Not if you're already at the optimum level for your species. In that case raising the level of one antioxidant will probably lower the level of all others. That makes good biological sense—if life span is important to the evolutionary success of an animal, it won't be manipulated in a trivial way. It's going to have a set point of regulation, just like body temperature. And like body temperature, it will stay constant under a wide range of conditions. So the human MLSP is at most one hundred and ten years, no matter *what* the nationality, lifestyle, and nutrients consumed.

Omni: But if there's an optimum set point for humanity at large, certainly whole groups of people fall below.

Cutler: Indeed they do. If antioxidants play a role in life span, perhaps some individuals live longer than others because they just happen to have higher set points. Antioxidant protection might vary within our species, just like eye color or height.

The first spinoff of all my research will be a technique for diagnosis. People with abnormally low levels of antioxidants might age abnormally fast; with my technique they'll be diagnosed, and supplements will boost their antioxidants until the optimum level is reached.

We're developing a battery of assays to determine how much antioxidant protection you've actually got. For example, we analyze urine samples for thymidine glycol, a by-product of DNA damage. When-

ever a piece of DNA is damaged, thymidine glycol is removed. Because the molecule is stable, it's never degraded but simply finds its way into the urine. Knowing how much thymidine glycol you're peeing, I can calculate your total-body DNA damage load.

Omni: The more thymidine glycol I excrete, the more DNA damage I have?

Cutler: Yes. The solution is to prevent as much of that damage as possible. And that's what our assays will do. If urine analysis shows you have high rates of DNA damage, I'll take blood tests. I might find, for instance, that you have trouble absorbing vitamin E. The solution might be as simple as doubling your consumption of that vitamin. You'll come back in two weeks, and if lack of vitamin E *was* the major problem, then signs of excessive DNA damage in your urine sample should be gone. People could come to us early in their life, before signs of aging appear, and we might be able to readjust their system for a longer, more normal life span.

Omni: Can we increase our MLSP *beyond* one hundred and ten years?

Cutler: The next step is trying to increase the net levels of antioxidant protection in our cells: to change the set point to a higher level. Evolution itself continually increased the primate set point for longevity by increasing the production of protective substances. We have to understand the evolutionary process and push it still further.

Many different strategies have evolved to decrease the possible aging effects of free radicals. One might try, for example, to *trick* cells into thinking they were under more oxidative stress than they really were. When you exercise you burn more oxygen, produce more free radicals, and also generate more antioxidant protection. If you could trick the cells into thinking exercise was taking place when it wasn't, then you might increase production of more antioxidant while free-radical levels stayed the same. The question is, What's the mechanism by which the body recognizes that it's under oxidative stress? A particularly exciting possibility is the existence of a *central* coordinating factor. If it exists, one could identify and manipulate it without complex genetic engineering.

Omni: Have you narrowed in on this so-called factor? Have you ever tried to trick the cells yourself?

Cutler: We embarked upon such a program years ago. We started from a simple fact: Damaged DNA, one result of oxidative stress, produces molecules known as thymidine dimers. When the DNA is repaired, the dimers are removed, and you can detect their presence in the blood. The more dimers you find, the more DNA damage has occurred. We injected these dimers into mice, hoping their presence would cause the cells to think the damage was extreme and to respond with excess production of antioxidants and other protective substances. We had two groups of mice: one injected with dimers, the other with a placebo. Then we irradiated both groups of mice with X rays for twenty days. X rays, of course, produce stress, damage DNA. After a couple of weeks all the control mice were dead, but most of the thymidine-dimer mice were still alive. The thymidine-dimer mice ended up living about twice as long. This strategy seems to have worked, but we can't say for sure until more studies are done.

Omni: If this work pans out, could people perhaps inject themselves with thymidine dimers, trick their cells, and live longer?

Cutler: It's not likely. A better idea is to actually understand the mechanism, the central controlling factor. One possible factor triggering the genes that produce antioxidants is a messenger chemical known as cyclic GMP. When I injected cyclic GMP into mice, it protected them against radiation. Such experiments suggest that we might be able to artificially enhance our levels of protection without having to overhaul the body as a whole. We could well see pharmaceutical agents that intervene at the normal set points, actually expanding the MLSP.

Omni: How many years do you think we might gain through such therapy?

Cutler: It's hard to say, though the increase would probably not be radical because this technique imitates just *part* of the evolutionary process. To double or triple human longevity, we'd probably have to rely on neoteny itself. By slowing all stages of development and delaying production of sex hormones, we'd retain more of our fetal and early-childhood features into adult life. Neoteny as a mechanism for increasing longevity doesn't demand the development of new morphological forms, only the adjustment of the overall rate of the genetic program. Neoteny is an example of how a few regulatory genes can effect vast changes in overall morphology.

A neotenous version of *Homo sapiens*, with an MLSP of perhaps two hundred years, would be slightly taller and heavier than ourselves. But the head and the brain would be twice as large. The individual might reach sexual maturity at thirty, and that thirty-year-old would be proportioned just like an eight-year-old *Homo sapiens*. But the most fascinating characteristic of this *Homo futurus* might be the retention into adulthood of childlike *behavioral* characteristics. *Homo sapiens* already retains into later life some of the infantile traits of animals—curiosity, playfulness, the ability to learn. The new species will retain even more behavioral traits from the *human* childhood, such as the ability to learn spoken and mathematical languages and the intense urge to explore. Some of our greatest scientists and musicians, from Einstein to Mozart, appear to have been exceptionally neotenous. People always say, "He may be a great scientist, but he's like a child." They don't realize that perhaps being like a child *is* what made him great.

Omni: You've set your distant sights on the creation of this superneotenous race?

Cutler: My long-term goal is to contribute toward humanity's future evolution; this would probably occur along the same neotenous path we have already evolved. That would include not only extension of MLSP but all the other characteristics that went along with it: expanding the brain, slowing development, and enhancing neotenous behavioral characteristics. The goal is to coordinate a safe and balanced evolution in which all these characteristics emerge at once.

Omni: First you'd search for the regulatory genes responsible for primate evolution, and upon finding the right ones you'd regulate them to increase longevity?

Cutler: That's right. The first step is identifying these regulatory genes. Scientists currently mapping the entire human genome hope to complete that project within ten years. We'd compare the genes across the entire range of species. Those genes differing between primate species are maybe the ones propelling longevity. Perhaps creation of the new human species requires only a few changes in the regulatory genes.

Omni: If it's so simple, why don't we see these mutant humans *now*?

Cutler: One reason we haven't seen mutation in the direction of neoteny is that problem of the birth canal. With its larger head *Homo futurus* wouldn't survive its journey through the pelvis. And if *futurus* were born in a less mature state than the *sapiens* baby, it could never survive outside the womb.

Omni: How can such problems be solved?

Cutler: By sustaining them artificially outside the womb.

Omni: That would make the species *so* dependent on technology.

Cutler: You could say the same about sustaining a colony in space: What happens if the computer or the energy source shuts down? Whether we evolve into the species of *Homo futurus* or not, female pregnancy is likely to soon become a thing of the past. *All* babies would be conceived and raised outside the womb. By eliminating nine months of pregnancy, a woman would gain many advantages, even increasing her life span. Throughout history females *always* had shorter life spans than males because they spent much of their life pregnant, constantly stressed. They also produced pregnancy hormones that appear to accelerate the aging process. The female ultimately evolved a better cardiovascular system, stronger resistance to stress, and probably more protective antioxidants as well. With fewer children, the modern female not only lives longer than her historical counterpart but also longer than the male. The reason is that she's coasting on reserve capacity. Eliminating pregnancy altogether should boost female life span even further.

Omni: How will society cope with individuals who live two hundred or more years?

Cutler: Let's go back to primitive societies, which were societies of youth. Few individ-

uals survived much beyond thirty, with people dying of infectious disease and all the various, random natural hazards. The death of an individual depended not on how old he was but rather whether or not he happened to get caught. Civilization eliminated many of these hazards, substantially reducing the random component of survival. Suddenly people had a more uniform life span, limited by aging itself.

The preserve of aged people in our society today is an artifact of civilization. Senior citizens and the problems of caring for them are not natural to our species. Many people claim that increasing life span, including a longer period of decline, would only make the problem more extreme. But my studies show just the opposite to be true. Conferring even five or ten years of extra, healthy life on, say, a scientist or engineer would be an economic boon to society. Even more important, while random hazard has been drastically reduced, it still exists. People die via plane and car crashes every day. If people had the biological potential to live for six hundred years, according to insurance company statistics, there's almost a one hundred percent chance of meeting an accidental death. So with random hazards remaining as they are today, no one would worry about the problems of aging. We'd have returned to a society of youth. The closer society gets to that six-hundred-year life span, the less old age we'll have.

Omni: Why is six hundred years the optimum human life span?

Cutler: There isn't a shred of evidence for any real bottleneck on the evolution of longevity. But there's a practical limit: A six-hundred-year-old would have to wait ninety years to become sexually mature.

Omni: I'd wait thousands of years if it meant I could live forever.

Cutler: But these longer-lived versions of man would probably be intelligent enough to come up with novel approaches to life extension. After we'd tripled or quadrupled our life span by enhancing mechanisms used during the natural increase of longevity, new means for increasing life span would evolve. In that instance you're talking about life spans of thousands of years. I can imagine the removal of all internal organs, from the liver to the spleen, because they generate toxic by-products. There'd be no need for a digestive system, only a mechanical heart to pump fluid through a "body." You'd "eat" a predigested medium full of all the critical nutrients and vitamins. Ultimately, because biological tissue can last just so long, you might eliminate the biological components for virtually everything but your brain. The brain itself would be enhanced by antioxidants and periodic transplants of new, healthy cells. But with life span extending beyond six hundred years, you'll start to see increasing anxiety over the possibility of accidental death. People would start trying to avoid accidents at any cost. You'd drop that sports car. Give up travel by plane. In fact, you might just hole up at home. You could build redundancy into your system, even isolate your brain in the equivalent of an iron vault and have it communicate with your body electronically. If the body were destroyed, well, that could always be cloned or reproduced.

Omni: What about you? On the cutting edge of life extension research, you have various options for increasing your own longevity. At fifty, do you ever consider injecting yourself with thymidine dimers, cyclic GMP, or anything else?

Cutler: Not yet; I'm afraid of it. These substances could turn out to be dangerous. My father will be eighty this December and is concerned about his aging, but I can't help him. I myself simply take vitamin E and beta-carotene capsules after every meal, hoping to reduce the possible mutagenic effects of food. I try to avoid particularly strenuous exercise. Though I know that the cardiovascular system can benefit from such exercise, I'm afraid that the gain may be more than offset by the extra oxygen metabolism and increased free-radical production. Right now there just isn't much we can do to extend life beyond the current MLSP.

Omni: Doesn't it bother you that you yourself might miss out on the increased life span you're helping to create and might die of natural causes at seventy or eighty?

Cutler: Sure, I feel real bad about it. I'm like a person who studies cancer and suddenly discovers he has cancer himself. He can do a self-diagnosis, make charts of it, watch it grow. That's what *I've* been doing in watching myself develop all the changes of age. But I also feel good because I'm contributing toward the ultimate extension of human life span. That's my replacement for immortality. Also, let's say you *could* live two hundred years. Then you'd feel bad because a six-hundred-year life span was just around the corner. Those with a six-hundred-year life span would feel bad knowing that just a few generations later, they could have lived forever. That might be the worst feeling of all.

The important thing is that people in general are becoming increasingly dissatisfied with short life spans. Most politicians and scientists are still resistant to the idea of life extension. But historically, most radical scientific movements started this way. You have a few investigators who are considered wild. They undertake a lot of hardships to produce some key experiments, triggering the interest of the general scientific community to go at it in a more careful way. Despite politics, I believe that humans will want to increase their natural life span. We already have the hypotheses as to how this might be done. Around the year 2000 some researcher may finally use genetic engineering to double the life span of a mouse. That will be the breakthrough. People will stop and say, "*This isn't quackery. This is real.*" Thousands of scientists might ultimately get involved. And that's when the bulk of the work will be done.

Here is the solution to last month's J & B puzzle.

1	1	1	■	2	1	3
1	■	1	1	9	0	4
2	1	8	4	■	5	3
■	4	8	■	1	0	■
4	3	■	3	7	4	4
4	3	9	5	6	■	2
6	6	7	■	4	3	5

ANSWERS ACROSS:

1. 54 + 50 + 8 – 1 = 111
3. 2130 ÷ 10 = 213
6. 1984 × 6 = 11904
8. 24 × (90 + 1) = 2184
10. 63 – 10 = 53
11. 42 + 6 = 48
12. 61 – 51 = 10
13. (6 × 8) – 5 = 43
14. 16 × 2 × 9 × 13 = 3744
16. 666 × 66 = 43956
18. 29 × 23 = 667
19. 1927 – 1492 = 435

ANSWERS DOWN:

1. 76 + 30 + 6 = 112
2. 12 × 11 × 9 = 1188
3. 16 + 2 + 8 + 3 = 29
4. 1313 × 8 = 10504
5. 7 × 7 × 7 = 343
7. 2156 ÷ 154 = 14
9. 1024 × 14 = 14336
12. 42 × (11 + 11 + 10 + 10) = 1764
13. (75 × 6) – 4 = 446
14. (14 × 5) ÷ 2 = 35
15. 17 × 25 = 425
17. 48 + 49 = 97