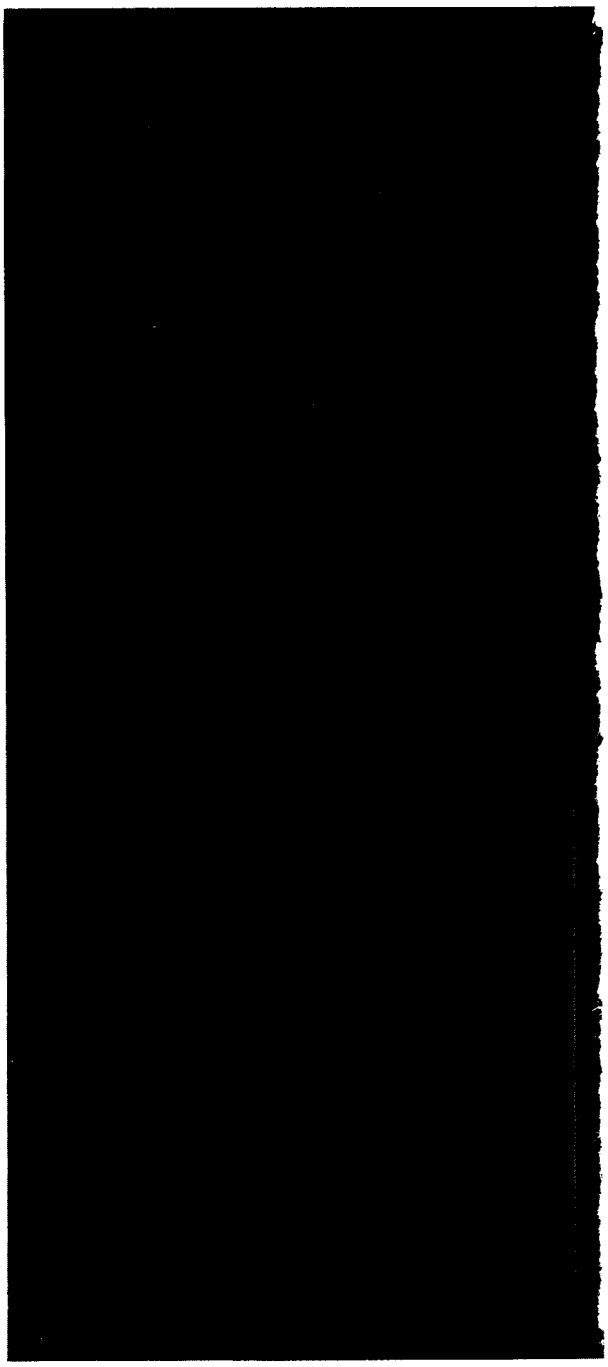
In the twenty-first century antiaging substances will revitalize our skin, our organs—and our genes

BY ANN GIUDICI FETTNER AND PAMELA WEINTRAUB

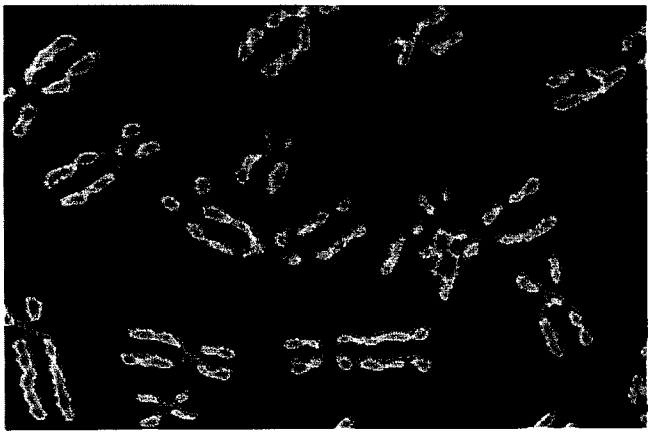


During Prohibition Mama and her friends used to ride out into the still-rural area surrounding Atlanta to buy bootleg whiskey from Pop Adams. In the Southern mode they would sit on the porch drinking buttermilk while Pop's daddy, who was one hundred one, tossed a shovel across his shoulder and nipped down through the piny woods to disinter some fruit jars of white lightning and outwit the Feds. Mama said the liquor was so raw it'd take the enamel off your teeth. But it must have been doing something right because the old men swore by it. "We have a little toddy now and then through the day, yessiree," Pop's daddy said, a Home Run cigarette dangling from his mouth. "Good corn likker's the secret to long life; wouldn't miss a day."

Pop himself had no patience for Mama's shudder as she gagged down the white-corn squeezings and longed for something bottled in bond. "That government whiskey? Why, 'tain't nothing but a little water and a double handful of chemicals that'll kill ya surer'n hell." Pop's professional bias notwithstanding, it's likely that *some* double handful of chemicals—produced internally or consumed in the course of everyday life—enabled the Adams men to survive in exceptional health and vigor to great old age.

The search for this double handful of chemicals—a magic potion to stave off death and postpone the ravages of age—is as old as man. The myth of Shangri-la, for example, comes from the Greek tale of the Hyperboreans, who—after living 1,000 years—simply plunged into the sea. The promise of gold wasn't the Spaniards' only quest in the New World: They genuinely thought they would find the Fountain of Youth on the shores of Florida. Had the Spaniards recognized Aztec and Inca ritual snake paintings as symbols of rebirth, though, it would probably have tipped them off: The Indians were looking, too.

But now, after millennia of



ELIXIRS OF YOUTH

PHOTOGRAPHS BY DAN McCOY

frustration, youth elixirs may be at hand. What's more, the dozen or so substances on the horizon stem not from the commercial aspirations of a health-food chain or the twisted imaginings of a crank but from a new and profound understanding of how we age.

To scientists in the forefront of longevity research, aging is the tragic side effect of life. The hormones released during puberty and as a result of stress slowly erode the body's organs. The food we eat and the air we breathe generate highly reactive free radicals, which make subtle but deadly changes in DNA. And environmental hazards, from ordinary sunlight to industrial toxins, infiltrate the cells, helping to grind their engines to a halt. Some scientists have even found compelling evidence for an aging clock in the brain. As that clock winds down, they say, it alters the levels of hormones and other biological substances, slowly lowering the effectiveness of the heart, lungs, immune system, and just about everything else that keeps the body healthy and strong.

Increased comprehension of the problems, however, may soon yield what amounts to an aging cure. Within the next decade we might use hormones to bolster our immune systems, viruslike vaccines to slow the death of cells, and uric acid to prevent the destruction of our genes. Such supplements could help us maintain our health and vigor throughout much of our current maximum life span of 115 years. What's more, in the twenty-first century these potions will be dwarfed by a new, more potent generation of "longevity pills." Enzyme drinks will endow us with the ability to repair each new nick in our armor of DNA, and synthetic neurohormones will literally reset the aging clock in our brains. Instead of simply keeping us healthier longer, these new drugs will push the outside of the aging envelope, eventually increasing our life span by dozens of years.

The first longevity drugs to reach the market *could* be the thymosins, a family of hormones produced by the thymus, the master gland of the immune system. "The immune system is the bubble that protects us from a dangerous, hostile environment," says biochemist Allan Goldstein, chairman of the biochemistry department at George Washington University. "And the immune systems of superhealthy people are unusually effective. The thymosins play a key role for these people. Our goal is to learn how. Then we'll put the thymosins into stay-healthy pills, to be taken once a day like vitamin supplements. The pill could add perhaps a dozen years to the maximum human life span of one hundred fifteen. But even if it doesn't, it should help us live out in health the years to which we are genetically entitled."

Twenty-five years ago no one even knew what the thymus gland was. Indeed, because the thymus is the first gland in the body to atrophy—it weighs 200 to 250 grams at birth, begins to shrink at puberty, and has shriveled to a three-gram, grizzled clump of cells by the sixth decade of life—scientists always believed it had no function at all. But in 1961 researchers from the University of Minnesota removed the small, pink organ from a group of newborn mice. Much to their surprise the mice failed to grow and then died of overwhelming infection. The suggestion: that the thymus gland was crucial to the immune system *and,* quite apart from that, to the growth of the whole organism.

Enter Goldstein, a brilliant young postdoctoral student at Albert Einstein College of Medicine in New York. The year was 1964, and Goldstein was lucky enough to be working under the late biochemist Abraham White. When asked by White to conduct a needle-in-a-haystack search for a thymus hormone, Goldstein agreed.

The thymus and its hormones, Goldstein eventually learned, control production of the white blood cells known as T cells, the brain and brawn of the immune system. He found that the thymosins work their magic by aiding in the activation of three types of T cells: *killer* cells, which attack foreign organisms and cancer cells directly; *helper* cells, which aid in the production of antibodies; and *suppressor* cells, which prevent the immune system from attacking one's own tissue. "It was obvious," Goldstein says, that "any imbalance in the numbers of various T cells could lead to poor health. The further implication: that we could increase a person's immunological response by manipulating the amount of thymosins in the blood."

"Enzyme drinks will endow us with the ability to repair each new nick in our armor of DNA. And synthetic neurohormones will literally reset the aging clock in our brains."

Finally, in the early Seventies, Goldstein put his theories to the test with a five-year-old girl named Heather, who was suffering from a condition known as thymic hypoplasia. "Her body didn't make enough T cells," Goldstein explains. "She should have weighed sixty to seventy pounds, but she weighed only twenty-six pounds. She had all sorts of severe infections. In truth, her condition was terminal. But five days after we started her on thymosin, her T cells were multiplying, her infections had decreased, and she was gaining weight."

Today, Heather is a healthy junior high school cheerleader living a normal life. "I have a beautiful picture of Heather on my wall," Goldstein says. "And I think that what was true for Heather will be true for the great majority of the aged. Right now the shriveled thymus glands of the elderly produce only small amounts of T cells. Instead of suffering from the acute disease that Heather had, they go into gradual decline. But for them and for Heather, the solution will be the same. If we can give them enough thymosin to keep the T cell level high, we should be able to enhance immunity throughout old age."

Rejuvenating the immune system with thymosins would add perhaps a dozen years to life by fighting off cancer, arthritis, pneumonia, and many other diseases to which the aged are prey. But Goldstein's most recent work, suggesting that the thymosins regulate an aging clock in the brain, should *revolutionize* the longevity field.

According to Goldstein, the idea that the thymus regulated more than the immune system came to him in the mid-Seventies as a result of a series of experiments done by endocrinologists like Sandra Michaels at the State University of New York at Binghamton.

Michaels found that removing the thymus gland in female mice not only decreased resistance to infection—a sign of impaired immunity—but also distorted the ovaries and altered the vaginal opening. What's more, when Michaels gave the mice thymosin supplements, the conditions were corrected. Strange as it seemed, the thymosins—in addition to the normal array of sex hormones—were affecting sexual development, usually under the control of two glands at the base of the brain: the hypothalamus and the pituitary.

Goldstein decided to study the relationship between sexual development and the thymosins, too. Under normal circumstances, he knew, the hypothalamus secretes hormones that trigger a second platoon of substances in the pituitary—the sex hormones—that take us through puberty and ultimately make us mature.

Goldstein and Robert Rebar, now at Northwestern University Medical School, found that when they removed the hypothalamus and pituitary from mice and kept them in solution, the glands *still* released the full cascade of hormones—as long as *thymosin* was added to the solution as well. Thymosin, it seemed, could trigger the release of hormones in the brain.

In subsequent experiments Goldstein learned that thymosins were directly linked to other brain systems as well: They could stimulate the brain's production of adrenocorticotrophic hormone (ACTH), normally associated with fight-and-flight reactions; beta endorphin, the "feel-good" chemical; and prolactin, a growth hormone. Stimulation of ACTH, for instance, caused the adrenal gland to pump out the hormones of stress. Even more interesting, he found, the stress hormones traveled full circle back to the thymus gland. They shrank the

gland, turning production of thymosins—and thus release of stress hormones—down.

According to Goldstein, these elaborate feedback loops between the thymus and the brain are the key to aging itself. "As we grow older," he says, "there are changes in brain chemistry. These changes alter hormone levels, causing deterioration throughout the body. And our studies place the thymosins at the center of this process. It's even possible that the whole range of brain hormones falls off from optimum levels as soon as the thymus begins to shrink, before the onset of puberty. The suggestion is that it's the deterioration of the thymus that leads to deterioration of the brain—and ultimately of the body itself. By adding the thymosins back, much of that decay should be set in reverse."

Goldstein still recalls that when he first developed an interest in the field of aging, his mentor, Abraham White, said, "Allan, whatever you do, don't pursue it until you're at least forty-five because it's sure to ruin your reputation. People will think you're a crackpot." Now forty-eight, with the discovery of the thymosins behind him and pictures of powerful political friends on his office wall, Goldstein can *afford* to dream: We know for sure that thymosins prime the levels of brain hormones involved in reproduction, growth, and development, he says. Thus we should be able to use them to maintain a whole complement of characteristics associated with youth: fertility, razor-sharp cognitive skills, facile memories, fast reflexes, potent wound-healing abilities, and even that most intangible of traits, a youthful zest for life. Because these restorative hormones also bathe our skin, muscles, and bones, these body parts should retain their youthful structure and appearance as well.

"In five to ten years even healthy people will be taking the thymosins on a daily basis," Goldstein declares. "Those supplements should help to push the average person's vigorous years upward of eighty or ninety simply by boosting the immune system. Because we'll also increase the level of vital brain hormones, the impact will probably be greater still."

While Goldstein wants to reset the aging clock in the brain with thymosins, other substances may also prove to be potent antiaging agents. As it turns out, it might be possible to tap into the feedback loop of aging at any point along the way. And one of the most promising youth elixirs to emerge from the brain–thymus feedback loop has the jawbreaking name of *dehydroepiandrosterone,* or DHEA. One of the most common steroid substances secreted by the adrenal gland, DHEA has recently been shown to protect the thymus gland, increasing the number of T cells available to fight off infection and disease.

The first chapter of the DHEA story, though, started more than a decade ago, when Temple University cancer researcher Arthur Schwartz stumbled upon a study of 5,000 women on the British island of Guernsey. The study found that those women who eventually developed breast cancer had abnormally low levels of DHEA. It seemed to Schwartz that if low levels of DHEA were associated with the presence of cancer, high levels might keep cancer away.

Schwartz went on to add DHEA and powerful carcinogens to animal cells in culture. The carcinogens alone would have resulted in high rates of mutation and cell death. But with the addition of DHEA, the culture continued to grow in perfect health.

To try to understand these results Schwartz went back to the literature for clues. And two things stood out. First of all, the amount of DHEA in the body was highest at age twenty-five or thirty. From that point on it decreased until, at age seventy, it was at about 5 percent of its peak.

Even more interesting, DHEA altered metabolism. Excess glucose, Schwartz explains, is normally stored in the body in the form of fat. But when DHEA was added, the fat pathway was blocked. The glucose instead traveled down the only other metabolic pathway available—the energy-yielding pathway, where it was converted to the body's ultimate form of fuel, ATP.

Significant weight loss resulted.

Studies had long shown that low-calorie diets prevented some forms of cancer. Now it seemed as if a mysterious cancer preventive, DHEA, acted just like a low-calorie diet, promoting weight loss. Perhaps DHEA and low-calorie diets worked in much the same way.

If so, Schwartz knew there was a tantalizing tie-in with aging. Thus far, the only proven means of extending life had been fasting: Anecdotal evidence came from the Himalayan Yogis, known for their long lives and subsistence diets. And experimental evidence came from Cornell University nutritionist Clive McCay, who in 1935 doubled the average life span of rats by limiting their food intake. Not only did McCay and other researchers eventually use the technique to stretch the average life span in a large number of mammalian species, the researchers also found they could increase what's known as *maximum* life span—the age reached by the oldest survivor of a population. The implication: Something basic to the very mechanism of aging had been changed.

Schwartz set out to see if that mechanism, whatever it was, could be affected by DHEA as well. And after eight months he achieved remarkable results. Untreated mice "were coming down with cancer right and left," while those injected with DHEA had no tumors at all. But the absence or presence of cancer was just the beginning: The untreated mice seemed old. They couldn't move as quickly, and their coats were coarse and gray. The DHEA mice ran around like pups—and their coats were sleek and black. Says Schwartz, "Without a doubt they were aging at a slower rate."

Today Schwartz is working with a safer, synthetic analogue of DHEA that he says is ten times more potent. He still hasn't received Food and Drug Administration approval to test the analogue on humans, but he expects to receive the go-ahead in a couple of years. And when he does, he hopes he might see some of the same life extension effects in people that calorie restriction has in the mice. If animal results can be carried over to humans—a distinct possibility—then the DHEA analogue might extend our life spans by as much as 50 percent. In other words, when treated with the supplements a sixty-year-old would resemble in every respect the forty-year-old of today. At age one hundred the treated individual would resemble a healthy person at sixty-five.

"The goal right now," Schwartz adds, "is to understand the mechanism by which DHEA seems to promote weight loss *and* longevity. Once we understand what's happening during calorie restriction, which seems to be the same thing that's happening when DHEA is consumed, we might develop a host of DHEA-like substances that can help us lengthen life—without reducing a person's weight."

Many have taken Schwartz's goal to heart. This past summer, when longevity researchers attended the prestigious Gordon Conference in the tiny college town of Plymouth, New Hampshire, the *big* news was that the diet-restriction mechanism—and the body chemicals that drive it—were on the verge of being found.

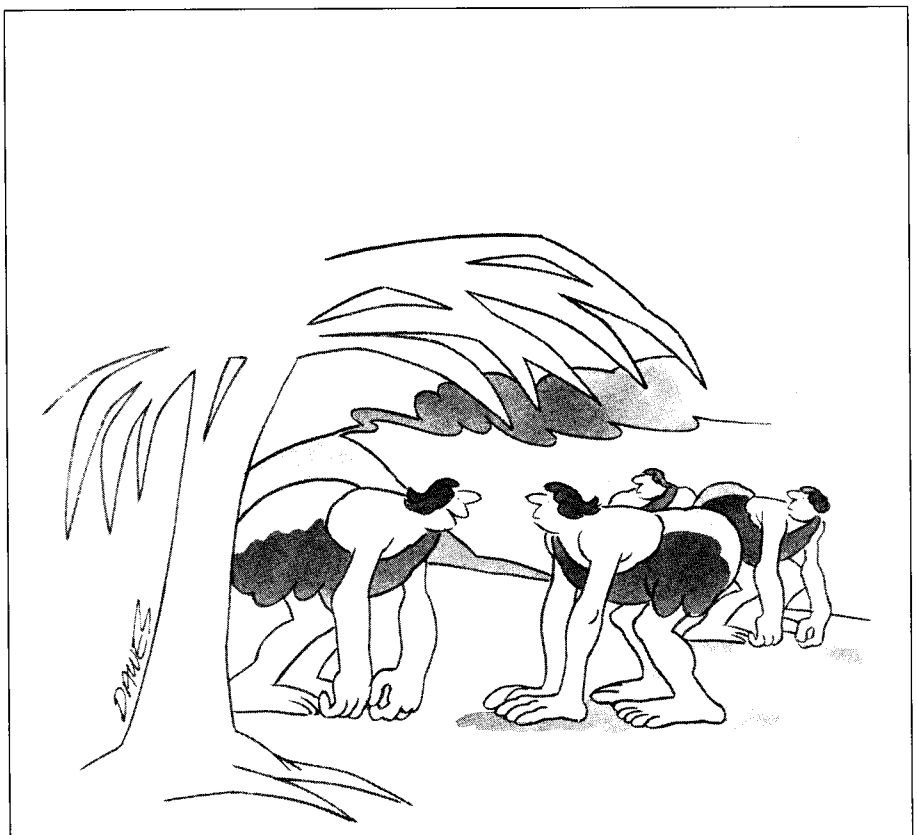
Gathered at the foothills of White Mountain, in the solemn lecture halls of the Plymouth State College, the world's top longevity researchers were unprepared for the weight of evidence that would mount. First German gerontologist Klaus Beyruther reviewed the life cycle of a cell. Ever since Leonard Hayflick published his classic paper in 1961 it has been known that human cells are mortal: They divide some 60 times over a period of years. Then they suddenly stop. Beyruther explained that the amount of time between each division cycle could be increased or decreased, depending on the nutrients present in the petri dish. The cells could divide at least 60 times in as little as a year; but if they were virtually starved, the 60 divisions would take three times as long. If diet-restricted mice stretched out their life spans because they had less food, perhaps diet-restricted cells did the same.

Also on the agenda was physiologist Edward Masoro of the University of Texas at San Antonio. When Masoro restricted the calorie intake of laboratory rats, he extended life spans by 50 percent.

Recently, Masoro reported, he had come to suspect that the increase in life span might be due not to a decrease in calories per se but rather to a decrease in a specific *component* of the diet. To test that notion he restricted elements of the everyday diet, one by one. But it was to no avail. He now believes that diet restriction itself seems to trigger the release of a neurotransmitter or hormone, and this, in turn, is what extends life. "I'm now preparing experiments with two guiding principles: What kind of hormonal change might cause life extension? And how can hormonal response be modified by calorie restriction? Once we find the answers to these questions, we may be able to home in on the specific biochemical mechanism. Then, and this is a very real possibility, we'll be able to intervene in that mechanism, actually extending life."

The mechanism suggested by Masoro, it turns out, may have been found in what amounted to the most explosive life extension news in years. Molecular biologists James R. Smith of Baylor Medical College in Houston and Charles K. Lumpkin of the Veterans Administration Medical Center in Little Rock, Arkansas, and their colleagues said they were zeroing in on a senescence protein that inhibits DNA synthesis in skin cells, literally shutting down the cell.

As Lumpkin, a specialist on aging tells it, he began to suspect the existence of such a protein when he learned that old cells, infected with certain viruses, seemed



"We're going bi-pedal tomorrow. Pass it on."

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to revert to youth. If those old cells were damaged in numerous ways, he asked himself, how could a single virus restore them to vitality? It just couldn't. "I began to think," Lumpkin says, "that the virus simply repressed a protein that shut down the cell."

Then, in the early Seventies, Lumpkin discovered a paper by pathologists Tom Norwood and George Martin of the University of Washington in Seattle. The Seattle scientists took young and old cells and *fused* them to produce a cell hybrid—a single cell body with two nuclei in the center. (The cell nucleus contains the genetic material, the DNA.) In that single cell, neither the old nucleus nor the young nucleus was able to synthesize DNA. In other words, the fused cell took on the characteristics of the old cell. The implication: The old nucleus produced a protein that shut down its own replicative machinery and then traveled through the cell body to squelch the young nucleus as well.

Lumpkin was so impressed by the work that he went to Seattle to study with Martin. And it wasn't long before he'd used Martin's findings to help develop a potent theory of his own. Working with molecular biologist Jim Smith, Lumpkin proposed the existence of one or more cell proteins that turned DNA synthesis off.

Last year the two tested their notion in the lab. In essence they extracted genetic material from old cells, divided that material into segments, and injected each segment into a different young cell. Time after time, a specific bit of material from the old cell made the young cell age as well.

The present goal is to isolate and clone this genetic material—apparently the gene that codes for the senescence protein. Once the gene is found, Lumpkin says, we can find ways to turn it off. One suggestion might be a vaccine that instructs the body to produce antibodies against the protein. Another solution would be to override the protein with another natural substance—one that turns the cells on.

That may soon be possible, thanks to biochemist Vincent Cristofalo of the University of Pennsylvania and the Wistar Institute in Philadelphia. Cristofalo and his group have found proteins in the membrane that revive senescent cells. "There's a definite relationship," Cristofalo says, "between the balance of cell proteins and the rate at which organisms age."

As we get older, he explains, the proteins that prevent DNA synthesis become increasingly common in a larger proportion of our cells. As a result cells become less able to respond. Muscles, for instance, contract more slowly. And the cell receptors, which normally act as portals for everything from energy molecules to growth hormones, don't always recognize the substances they were designed to process and absorb. Without growth hormones, for example, wounds won't heal. And without sufficient energy the body can't function at all.

There's a strong correlation, Lumpkin says, between the life span of cells and the life span of the organism. "On the most basic level," he says, "the eighty-year-old would be able to heal his wounds as easily as if he were fifteen. Theoretically speaking, if we were to suppress the protein that inhibits DNA synthesis, our cells should be rendered immortal."

If all the body's organs, including the kidney and the liver, age in analogous ways, he adds, we might be able to surpass the current limit of one hundred and fifteen years in a sexually mature but youthful state, our bodies tight and our minds alert. "Once we understand the cellular pathways," Lumpkin says, "we might even be able to live three or four hundred years and keep on going from there."

Listening to the findings, gerontologist Richard Cutler of Baltimore's Gerontology Research Center suggested that the on/off proteins found by Smith, Lumpkin, and Cristofalo were the very substances responsible for extending the lives of lab mice placed on restricted diets. Mulling it over while in a canoe on Plymouth's placid Lake Squam, Cutler was reminded of a well-understood phenomenon known as heat shock response. "When heat becomes particularly intense, neurotransmitters in the brain stimulate a set of genes to produce a protective protein," he explains. "The protein literally cools the animal down, eliminating undue stress."

"The untreated mice seemed old. Their coats were coarse and gray. The DHEA mice ran around like pups. Their coats were sleek and black. They were aging at a slower rate."

Dietary restriction might work the same way. When the food supply is low, he notes, adult animals can't sustain a fetus or care for their young. In the face of this threat a hormone like the one suggested by Masoro probably switches on a special gene. The gene, in turn, probably generates the senescence protein found by Lumpkin and Smith. Under normal circumstances that protein would be produced only by very old cells, to trigger death. But in times of famine they might be switched on temporarily, delaying development—and the years of reproductive viability—until such time as nutrients would again abound. When food becomes plentiful, the protein found by Cristofalo comes into play. "Once we isolate the neurotransmitter or the proteins," says Cutler, "we might use them to enjoy the same antiaging benefits of diet restriction we see in the mouse."

A serum that inhibits the senescence protein might drastically increase the longevity of our cells, conferring infinitely more staying power on our organs and the body as a whole. But according to Cutler, the technique will add decades to life only if supplemented by a *third* sort of potion—one that prevents genetic damage caused by metabolism, environmental toxins, and the sun.

In the forefront of that research is the short, stiletto-thin Bruce Ames. A biochemist at the University of California at Berkeley, Ames is the controversial researcher who first declared that small amounts of man-made chemicals cause cancer by creating mutations in our genes.

In 1984, just as people were embracing the notion that cancer is caused by the toxins of our industrialized world, Ames came out with an even more radical sentiment. True, man-made chemicals are carcinogenic, he said. But most cancer-causing mutations come from the very food that we eat and the air that we breathe. Living is like being irradiated, he explained. Many fruits and vegetables produce natural pesticides that are as mutagenic as man-made ones. And the oxygen molecules we breathe tend to turn into highly reactive free radicals—particles that scavenge the body, voraciously consuming bits of DNA and damaging the cells.

As far as Ames was concerned, these same forces were responsible for aging. The genetic damage they caused was fairly constant throughout life, he theorized. Although DNA was always repairing itself, eventually the mutations would mount, resulting in aging and death.

He found support for his ideas in evolution itself. Indeed, as we evolved from our early primate ancestors to *Homo sapiens*, over a period of millions of years, our life span basically doubled while our metabolic rate was cut in half. "Perhaps we lived twice as long," Ames suggests, "because we were producing free radicals and other natural toxins at half the rate."

Ames was also aware of new research showing we could protect ourselves against the oxygen scavengers, at least to a degree, with another sort of natural substance—the *anti*oxidants. This group—including vitamin E, selenium, beta carotene (which provides carrots with their orange color), and superoxide dismutase—literally neutralized the free radicals before they had a chance to destroy DNA. "A major factor in the evolution of increasing life span," Ames adds, "might well be an increase in the presence of these protective mechanisms against free radicals."

Fascinated by this theory, Ames even discovered another, unlikely antioxidant—

uric acid, long considered nothing but a waste product. "I realized that at the beginning of primate evolution, we'd lost the enzyme that breaks down uric acid. What's more, the kidneys pump ninety-five percent of all uric acid back into our blood," he says. Thus unlike mice and rats, we have high levels of uric acid circulating throughout our bodies.

If antioxidants like uric acid and superoxide dismutase propelled the evolution of human longevity, then it only makes sense that raising their levels would extend life span even further. The problem with taking such supplements in pill form, however, is that increasing one antioxidant reduces the levels of all other antioxidants—unless the *total* antioxidant load is especially low.

If that load is low, DNA damage might pile up more rapidly than normal, and life span would be short. But if we could somehow *detect* that damage early in life, we would be able to *increase* antioxidant protection. DNA damage would be limited, and the potential for a normal life span would be restored.

Already Richard Cutler (see Interview, beginning on page 108) is developing a longevity kit to do just that. First he screens patients for high levels of thymidine glycol, a by-product of damaged DNA. "If someone excretes excessive amounts of thymidine glycol in the urine," Cutler says, "it's probable that free-radical damage is high—and that the antioxidant level is low. We'll keep adding different antioxidant supplements and retesting the urine for thymidine glycol. When the right combination of supplements has been found, thymidine glycol should be reduced to normal. Then we'll know that the aging is as low as possible and that antioxidant protection is prime."

Cutler, who takes supplements of beta carotene and vitamin E himself, says that his current technique may help those who now age abnormally quickly. But for the rest of us other tactics may be suitable. "What we've got to do is understand how evolution increased our antioxidant level, then use the same technique ourselves."

One of evolution's tricks may have been convincing the cells that extreme genetic damage had occurred. He explains: "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 that exercise or its equivalent was taking place when it wasn't, then you might *increase* the antioxidant levels while free-radical damage stayed the same."

Cutler is currently working on two ways to trick the cells so that excess antioxidant production occurs. In one experiment he's simply injecting mice with thymidine dimers, chemical by-products of damaged DNA. In another he's injecting them with cyclic GMP, a messenger chemical produced whenever free-radical damage has occurred. So far, he says, the cyclic GMP and the dimers seem to be ringing the alarm: Treated mice are more resistant to radiation. The extra protection, he adds, can be easily explained if we assume that excess antioxidants are produced.

If that turns out to be the case, Cutler says, then such supplements as thymidine dimers or cyclic GMP might eventually increase our protection against free radicals, expanding our maximum life span as much as a decade or two. But in the distant future there will be a far more powerful way of fighting off DNA damage—increasing the amount of enzyme available to literally *repair* our genes. Working on this technique is cell biologist and paramecia expert Joan Smith-Sonneborn of the University of Wyoming at Laramie. Someday, Smith-Sonneborn believes, "we'll be able to identify and clone the genes that make the different repair enzymes and transfer them into our cells."

Right now Smith-Sonneborn is attempting just that with her paramecia. She's chopping the paramecia's genome into sections and matching each section with a *known* repair gene from yeast. When she gets a match she'll know that the paramecia's repair gene has been found. Then she'll transfer cloned versions of the gene into the paramecia cells. "If the repair genes do what we think they should," she says, "the life span of the paramecia will increase." We might then use the same technique to create a gene-repair formula for consumption by man.

"Theoretically, once we suppress the protein that inhibits DNA synthesis our cells should be rendered immortal. If we understood the cellular pathways, we might be able to live 300 or 400 years."

Yet another formula might pry open our genes, Smith-Sonneborn believes. DNA, she explains, is tightly coiled. If we could relax the coils, the genes would open up, and we'd get in more repair enzyme.

One of the most important benefits, Smith-Sonneborn predicts, would be a boost for our immune system: Recent experiments lead her to suggest that some DNA-repair enzymes and the antibody-building enzymes may be one and the same. And, she adds, it's possible that an increase in these enzymes will offer a cosmetic advantage, too.

"Skin is wrinkled by ultraviolet rays from the sun," she explains. "What those rays do is damage DNA. But repair enzymes might fix the damage as fast as it occurs."

Finally, Smith-Sonneborn's experiments indicate that stimulating DNA repair can boost the life span of single-celled paramecia by 50 percent. "One thing's for sure. When we tap into the mechanism of DNA repair, we're tapping into a great many of the things that make us age," she says. "If we can increase repair, we'll help ameliorate any pathology associated with damage to our genes." Our immune systems should produce more antibodies, and we should be less prone to cancer and infectious diseases. We'll reach old age later, and we might be able to greatly exceed the maximum human life span of one hundred and fifteen years.

Many experts, of course, doubt that we'll be able to achieve drastic expansion of human life any time soon. Dr. Edward Schneider, deputy director of the National Institute on Aging, says, "I don't foresee a magic bullet, an antiaging pill that you could take to restore youth. But I do predict that our increased knowledge about the aging of different organs will enable us to prevent various body functions from deteriorating. We might be able to restore immune function, for instance, and even prevent short-term memory loss. In the next decade or so, we might see average life span increase from seventy-five to about eighty-five years for men and ninety years for women. Perhaps in the next few years someone will eventually live to be as old as one hundred and thirty. Barring some unforeseen breakthrough, though, I don't think we'll see people living to one hundred fifty in the near future."

But a lot of longevity researchers say Schneider may be erring on the side of caution. "There's no obvious bottleneck on the extension of life span," Cutler declares. "Today it seems probable that aging is caused by hormones and other molecules that alter the activity of genes. We should eventually be able to manipulate those hormones and molecules directly or through control sites in the brain. The result would be a slowing of the aging rate of virtually every organ and cell."

The impact would be profound. Once we fine-tune our engines we'll spend more time in the flush and energy of youth. Natural proteins will make us more vigorous. Enzyme supplements will restore smoothness to our skin and rigor to our bones. Hormone additives will add fight to our immune system, giving us powerful resistance to cancer, arthritis, lupus, and the array of infectious diseases. Viruslike vaccines will literally alter our genes, suppressing the chemicals that once wore us down and made us old.

After we extract the secret fuel of old Pop Adams and his hundred-year-old daddy, we'll fulfill the dreams of Ponce de León. In the twenty-first century the Fountain of Youth will be here. In one sense, Ponce de León was born 500 years before his time. But in another, the answers have always resided within him and us all.