DHEA: A Master Hormone in Search of Its Identity

At sixty-seven, Amy Woolfe found that even getting out of bed in the morning took almost as much energy as she had. "I've gotten used to feeling bad," she told me. "It becomes a way of life." Amy, a mild diabetic, was so tired that I considered diagnosing her condition as Chronic Fatigue Syndrome. But, when I tried her out on DHEA, in less than thirty days she came back and told me, "I've never had so much energy in my life. I feel like I'm twenty-five again." That was three or four years ago, pretty early in my career as a doctor who prescribes hormones. I was amazed then; nowadays I hear similar stories from other men and women and am not surprised.

Growth hormone certainly has a more obvious and visible effects on the human body, but it may turn out to be DHEA that is the more interesting of the pro-longevity hormones, primarily because of its ready availability, low cost, and absence of significant side effects at replacement doses. It has the advantage of being good, to a greater or lesser extent, for almost everything. A claim like that ought to arouse your skepticism. When it comes to dehydroepiandrosterone—that's its full, formal, chemical, tongue-twisting title—a look into the medical literature tends to defuse skepticism rather quickly.

I expect that not all of you will have heard of this hormone, and I know for a fact that few doctors have given it much thought since the days when they read a paragraph or two about it in Basic Endocrinology. Yet our adrenal glands produce more DHEA than all the other adrenal hormones combined. If it doesn't have a profound significance, then your body is guilty of profligate excess in its secretion. Which is inherently unlikely, for the human body runs a tight ship.

Our only problem has been figuring out what vital purposes this important hormone serves.

We do find that when people take it, they feel emphatically younger. Ask Joan Baldick, one of the participants in a University of California study. For six months she took a DHEA pill not knowing whether it was the real thing or a placebo. But: "My body knew. I slept less, but I slept better. I felt eager to get out of bed in the morning. And there's

no question I felt more feminine, more sensuous. I sure did notice the difference."

If DHEA makes a difference it's not surprising, for some researchers to call it "the most reliable biomarker of aging," and certainly from a lab technician's point of view, it's a superb measuring rod of age. At twenty, you have extraordinary quantities of DHEA in your body. By the age of eighty, you have about 10 percent of that original abundance. And during the intervening six decades, the graph of loss will be a steady declining line with very little in the way of eccentric bumps or dips. Is this coincidental or do youth and vigor go down as DHEA goes down—perhaps, to a significant extent, because DHEA goes down?

Since DHEA can be readily converted into other hormones, including cortisone, progesterone, estrogen, and testosterone, scientists originally thought this richly supplied adrenal hormone was simply a transition substance, a reservoir upon which the body could draw when it needed to manufacture other steroids. Further research demonstrated, however, that most cells in the body contain specific DHEA receptors, the sole function of which is to bind DHEA. This is as clear an indication as we can get that DHEA has essential functions of its own in the human body.

What are those functions? We're going to speculate as the chapter continues, but I'II tell you now, we won't reach any hard and fast conclusions. DHEA is still a thorny biomedical enigma. But if the precise mechanisms of its action remain elusive, its ultimate effects are crystal clear.

We now know that low levels of DHEA are strongly associated with heart attack risk. We have abundant evidence that high levels of DHEA protect against cancer. We've found that it helps in treating and preventing diabetes. We've seen in animal studies and in double blind studies on humans that it aids memory, eases depression, and causes a striking improvement in an individual's sense of psychological and physical well-being. Finally, we know that it so strongly supports the immune system that many scientists have become convinced that a shortage of this very hormone contributes significantly to the immune system’s collapse in old age. If this were not sufficient, there is also evidence that DHEA can help in the treatment of osteoporosis, rheumatoid arthritis, obesity, and chronic fatigue. It mediates stress, improves sleep, and appears to ginger up the sex drive in some folks.

Perhaps, after all, the body knows what it's doing when it provides the vigorous and active twenty-year-old with copious quantities of DHEA.

FIXING WHAT AILS YOU? SOMETIMES IT SEEMS THAT WAY

We can all see that, on the face of it, DHEA is a model pro-longevity hormone. It is a normal part of our metabolism, something the body produces daily. Yet it becomes radically depleted as we grow older. Most important of all, when it is replaced, the body accepts that replacement and shows emphatically positive effects.

I started giving DHEA to my patients a decade ago, using it cautiously, in limited amounts. I made careful laboratory measurements of their blood levels to ensure that what I gave them brought them only up to what was normal in a healthy young adult. The response was pretty striking. Men and women who had noticed they were slipping and sliding into age, into a place they didn't want to be yet, came back to my office two or three weeks later and said, whatever you do for me, please don't stop giving me DHEA.

Some were people who had absolutely nothing wrong with them. George Bloom was only forty-one years old, but his blood level of DHEAS (DHEA Sulfate, the form in which the hormone is measured) was low for his age. George is a take-vitamins-and-exercise sort of person, determined to slow the aging process before it even begins. He asked me for DHEA, and I prescribed it in appropriate doses. After a few months on the hormone, he noticed that his energy level was markedly higher, his skin was thicker and moister, and he was sleeping six and a half hours a night instead of eight and waking rested. George says he feels six or seven years younger, and, as he puts it, "When you're on DHEA, it feels as if every cell in your body is humming." That's not an uncommon observation of people taking this pro-longevity hormone. George has also noticed that his sex drive has ratcheted upward.

Carol Constance was forty-seven, and she had more immediate reasons for replacing hormones. I suppose it would be fair to say Carol was going through a pretty serious mid-life crisis with everything hitting at once. Her menstrual cycle had been going haywire for about a year. Each month she had terrible migraines around the time of her period. And for her that was really twice a month since her cycle now went for only ten to fifteen days. It was winter, and Carol was suffering terrible depression. As she told me, "I kept thinking of my

wasted life, of all the things I thought I would do when I was nineteen that I'd never done. I would lie in bed and wail during the night."

If Carol needed more problems, asthma provided them. It had surfaced in her life in 1988, and over the next decade it had gotten markedly worse. Carol slept with her cats, and I told her she really shouldn't. She told me bluntly that as she was now divorced, she certainly wasn't going to kick her cats out of bed.

And then DHEA came on the scene, and, to my astonishment and hers, somewhat miraculously, almost everything turned around.

"Within an hour after taking my first capsule, I suddenly found I could breathe again. That month my periods went back to normal—I was on my old regular twenty-seven day cycle-and my headaches disappeared. My depression lifted within the first few days. Two months after I started DHEA I joined a dance class. It had always been a childhood dream to dance. I feel like a teenager, as if I were renewing myself."

It has been over a year since Carol Constance went on DHEA. She's had one or two minor asthma attacks in that time, but not a trace of her other problems. The only side effect she's noticed has been a mild outbreak of acne, which went away when she interrupted her DHEA for a few days. I've found that acne only occurs in patients who are quite clearly deficient in DHEA, as Carol was. The problem soon disappears after normal levels are maintained for a while, apparently an adjustment of the oil glands in the skin to the restoration of youthful quantities of DHEA.

George and Carol's results are typical of the wide range of apparently unconnected positive effects that this powerful adrenal hormone produces in the human body. Therefore is it surprising that scientific studies have shown a real statistical relationship between how much DHEA you have at any given age and how healthy you are? We've all seen people who at fifty, sixty, or seventy-five still seem to possess what other folks have lost. In a word: Youth. I think as more research is done, we're going to find that most of these lucky individuals have more of the juice of life in their hormonal tanks than the rest of us.

Your Basic Feel-Good Hormone

The folks at the University of California have been among the most vigorous investigators of DHEA. In 1994 **Samuel Yen, M.D., the**

head of one team on the La Jolla campus, published a double-blind study on healthy people that was charming in its simplicity. Thirteen men and seventeen women ranging in age from forty to seventy were given a "replacement dose" of DHEA—enough to bring the body's levels to the level of a vigorous young adult—for three months and a fake pill (placebo) for another three. No one knew who was receiving which until a code was broken at the study's end.

Since the thirty subjects were all healthy, there was never any question of curing illness. What happened, however—measured by answers to lengthy questionnaires—was startling enough. An overwhelming majority (67 percent of the men and 84 percent of the women) reported a "remarkable increase in perceived physical and psychological well-being" during the period in which they were on DHEA.

My own experience with patients has shown over and over how frequently they come back after taking DHEA for a while and tell me—in vague but glowing terms—that their life has somehow just improved. This is an interesting response, certainly different from conventional methods of measuring physical well-being (not to mention actuarial life expectancy.)

The actual perception of increased vitality that patients report when they take DHEA may seem modest in health terms. But it indicates to me that, when one supplements with the hormones that youth has returned abundantly, a certain reversal to youthfulness is part of the package.

A few of the conditions I haven't mentioned yet that have been reported to improve when DHEA is administered include allergies, Alzheimer's, arthritis, chemical sensitivities, chronic fatigue, elevated cholesterol, Epstein- Barr syndrome, herpes, liver disorders, lupus, menopause, recurrent infections, and senility.

The Difference Between Life and Death?

DHEA is clearly good for the healthy as well as the ill. As I look at the tremendous body of research that's been done on this adrenal hormone over the past ten or fifteen years, it has occurred to me that what it certainly seems to be doing for healthy folks is preventing them from getting sick.

Among well-conducted scientific studies in this area, the eye-opener came in 1986, when **Elizabeth Barrett-Connor, M.D., head of epidemiology at the University of California at San Diego, published a report** that tracked heart attacks and deaths over a twelve-year period in 242 men aged fifty to seventy-nine. In this group, men with higher DHEA levels had a 36 percent reduction in mortality from all causes and a 48 percent reduction in mortality from heart disease.

The heart disease reduction was particularly striking being so specific to one illness, and it's particularly interesting because of some confirming animal studies that have been done since. Animal studies have had singular importance in DHEA research because of a basic fact of economics. DHEA is a natural substance, unpatentable and unprofitable. Research has to be done the cheap way—on animals. No drug company will spend hundreds of millions of dollars conducting major clinical trials on humans. But animal research can be very suggestive.

There is a breed of rabbit called the New Zealand White that has been used in cardiovascular research since 1914. It inherits the trait of extremely high cholesterol levels and consequently tends to rapidly form arterial plaque and die of narrowing of the arteries. Scientists at Johns Hopkins took twenty of these New Zealand Whites and, using catheters, caused slight irritations to the intima (the inner-most lining) of the aorta in order to even further promote plaque formation. Some of the rabbits then received DHEA in their chow over the next three months, while the rest did not. In those receiving DHEA, t**here was an almost 50 percent reduction in plaque size, and the degree of protection was directly related to the final blood level of DHEA achieved.**

That study was conducted in 1988. In 1993 scientists at the Medical College of Virginia tried another variation on high-cholesterol rabbits. Both in humans and in rabbits, heart transplantation tends to cause a dangerously accelerated rate of atherosclerosis in the coronary arteries. John Nestler, M.D., and his associates did heart transplants on forty-five rabbits and then using light microscopy observed the progressive development of arterial narrowing in these hearts. **When DHEA was administered on a regular basis to these rabbits, there was a 45 percent reduction in the number of significantly narrowed vessels.**

Will what works in rabbits work in humans? Barrett- Connor's original study at the University of California would tend to make me believe so.

Stress and Your Aging Immune System

I wonder if the most powerful benefit of DHEA isn't going to turn out to be immune enhancement. As you can read elsewhere on this website, relative to growth hormone, I place great importance on this issue. Failure of immune function is one of the most important factors that can kill you as you get older. The benefits of hormones can perhaps somewhat simplistically be divided into two parts. There are the benefits that make life in an aging body more pleasant, more fulfilling, more like what we enjoyed in youth. And then there are the benefits that actually extend life expectancy.

I believe that much of the longevity benefits of the pro-longevity hormone team will ultimately turn out to revolve around immune enhancement. If you live to be 120, it will be largely because your immune system demonstrates a superb capacity to deal with the insults of daily living.

One of those insults—both mental and physical—is the inability to adapt in healthy ways to excessive stress. Beginning in the 1930s, scientists like Dr. Hans Selye started looking at just what stress does to us. I don't know if they were surprised, but they found that stress dramatically alters the kinds and quantities of hormones released by our bodies. One of the hormones that decreases rapidly under stress is DHEA. Others, like cortisone and adenalin, increase. The hypothalamus responds to stress by secreting a substance called corticotrophin releasing factor. This, in turn, signals the pituitary gland to produce a substance that instructs the adrenals to produce corticosteroids.

The corticosteroids suppress the immune system—which is why doctors often prescribe these powerful drugs (cortisone and prednisone are well-known examples) to the folks who are suffering from autoimmune diseases like rheumatoid arthritis, in which the body's immune system attacks the body itself. It's a well-attested fact that older people have particular problems adapting to stress. According to Dr. William Regelson of the Medical College of Virginia, older people's stress hormones rise to a higher level than young people's and remain there far longer. They are truly "stressed out," and the effect on their immune system is devastating.

It appears that one principal reason is their low levels of DHEA. In fact, many scientists now believe that one of the most important functions of DHEA is to act as a buffer hormone, a sort of normalizing hormone that de-excites and controls the activities of other hormones and enzymes in the body. This inhibitory function may explain DHEA's usefulness in controlling cancer, diabetes, and, to a certain extent, obesity. Specifically, with regard to stress, DHEA decreases corticosteroid levels, thus effectively functioning as an immune system stimulator and a stress buffer.

But stress management—vitally important though it is—appears to merely scratch the surface of DHEA's capacity to re-arm us immunologically.

Raymond Daynes, Ph.D., emminent DHEA researcher from the University of Arizona, has done a neat trick in the vaccination of mice. A crisply functioning immune system needs to be competent at making freshly designed antibodies to fight new diseases it has never met before. But old rodents aren't very good at this. (And neither are old people.) A seventy-five-year-old man or woman's immune system will still do a pretty good job at creating antibodies to combat an infection the body has been exposed to before. New diseases are quite another matter. Which is why vaccinations are markedly less effective for senior citizens than for young folks.

When Daynes took old mice and vaccinated them against diseases they had never had before, their immune systems proved almost totally ineffectual at creating the new antibodies required. He then gave the mice the virus the vaccine was designed against, and most of the unfortunate rodents died. So Daynes took another batch of old mice and carried out the same procedures but with the addition of DHEA. The old mice suddenly became almost as proficient at forming new antibodies as young mice, and almost all of them lived (personal communication).

For ethical reasons, one obviously can't give old people viruses, but two university studies have been under way to determine whether supplementation with DHEA will have the same effect on human ability to form novel antibodies as it does in mice. The results have not yet been published, but scientists involved in this research say that they appear overwhelmingly positive.

To return to animals, old mice that suffer burn injuries typically die. Supplementation with DHEA greatly increases the survival rate.

When rats were inoculated with a virulent West Nile virus and then subjected to the stress of immersion in cold water, two thirds of them died. **Treatment with DHEA significantly reduced the mortality rate.** It is now thought that DHEA stimulates the body's production of immune-related T-cells, B-cell lymphocytes, and macrophages. Our thymus gland, which is responsible for the production of T-cells, begins to shrink after we reach adulthood. One study now indicates that DHEA slows the rate of shrinkage. If more confirming evidence for that is found, then DHEA will fall into place alongside HGH and melatonin as a vital trio geared toward protecting the single most important organ of the immune system.

What Is DHEA?

A bit above waist level, a pair of small, yellowish organs rest on top of your kidneys. They're called the adrenal glands. The center of the glands produces adrenalin, your fight-or-flight hormone. The outer layer or cortex of the adrenals has as its prime production DHEA, a steroid out of which the adrenals manufacture a wide spectrum of other steroid hormones, including aldosterone, which preserves minerals in the body, and cortisone, which controls immune responses and affects energy and mineral metabolism. The adrenal glands also make both male and female sex hormones from DHEA but in much lower amounts than the reproductive organs do.

DHEA itself is made by the adrenals from cholesterol, an enormously useful substance, which has become a byword for cardiovascular danger to Americans (to an extent not readily supported by the facts). There is never any shortage of cholesterol even in old age, so DHEA's faltering production as the years pass is obviously the result of some difficulty in its manufacture rather than a shortage of raw material.

I should point out that, although, for the sake of simplicity, I refer to DHEA throughout the book, the hormone is actually most readily measured as DHEA Sulfate (DHEAS). DHEA levels can shift wildly from hour to hour. DHEAS, a more stable form of DHEA, which has storage depots in the bone marrow and the adrenals and fluctuates far less widely. Consequently, when lab tests are done, it corresponds very nicely with the total quantity of all forms of DHEA produced throughout the day. As for supplementation, both forms of the hormone are used, and there remains a controversy over which is more appropriate to use in supplementation. Both appear to be effective, but since DHEA has been more widely used and is proven both safe and effective, I would recommend it.

And, indeed, whatever the diverse mechanisms by which the pro-longevity hormones extend active immunological life, there seems to be no doubt now of their fundamental efficacy. Old animals regain the normal vitality exhibited by much younger animals when their supplies of HGH, DHEA, and melatonin are replaced. The considerable amount of research already done in people strongly supports the idea that we respond just as the animals do.

Cancer

If heart disease is catastrophic, cancer is fearful. Here, once again, the evidence is mainly in animals, but impressive nonetheless. DHEA has caused cancer to regress in studies on dogs and cats. In mice, it has inhibited both spontaneous breast cancer and chemically induced tumors of the lung and colon.

In humans, small studies have shown gastric cancer, prostate cancer, and bladder cancer to be associated with lower levels of DHEA. A much larger study conducted for nine years in the 1960s on the Isle of Guernsey and reported in Lancet in 1971 found only slightly lower DHEA levels in women who subsequently contracted breast cancer but **significantly lower levels of androsterone, a steroid hormone made from DHEA.** The jury is still out on whether DHEA supplementation will help prevent breast cancer, but it certainly does no harm.

MEMORY AND INTELLECTUAL ABILITY

Poorer memory in old age is one of the similarities of mice and men. Therefore, it's encouraging to report that old mice given DHEA in the course of training improved their ability to remember until they were almost as efficient at it as young mice. Memory difficulty is an aspect of aging that has been extremely hard to change positively.

Another indication that poor intellectual function among some older folks may be related to falling DHEA levels comes from a study by Daniel Rudman, M.D., showing that men in nursing homes had far lower blood levels of DHEAS than men of the same age who were living independently. Forty percent of the nursing home residents versus only 6 percent of the men who lived in their own homes had subnormal levels for their age. **Men who were senile or who were totally unable to care for themselves were even more likely to have low DHEAS.** Levels were subnormal in 80 percent of the latter.

Many scientists now believe that DHEA, which is six and a half times more abundant in normal brain tissue than in other bodily tissue, will prove to be important in the preservation of a vigorously functioning brain. Dr. Eugene Roberts added low concentrations of DHEA to nerve cell tissue cultures and found he could "increase the number of neurons, their ability to establish contacts between neurons, and their differentiation into highly functional brain cells."

HOW MUCH DHEA DOES ONE NEED?

DHEA conforms perfectly to the principle that this book adheres to. When it comes to anti-aging medicine, more isn't automatically better: The right amount is that which the body was made to handle. In practice, that often means that each individual should take a supplemental dose sufficient to bring his or her levels up to where they were when he or she was young. This is certainly the best procedure for prescribing DHEA, and, happily, we know roughly what normal levels are at different ages. (See the Table below.)

How much below the normal level for a twenty-year-old you may be depends on your age and also upon your individuality. Remember that, if used properly, DHEA is a very safe substance. However, it was, until recently, a prescription item. I think it's best if you still treat it as such and establish a bona fide doctor-patient relationship with a knowledgeable health care practitioner who appreciates the value of hormone replacement. He or she will be able to have your levels tested, as I describe below.

The Food and Drug Administration has decided to step back from regulating DHEA, and the Drug Enforcement Administration, which for a while was defining it as an anabolic steroid and, therefore, a controlled substance, has also backed off. You can now get DHEA without a prescription at most health-food stores and many drug stores. I can not guarantee the quality of all the products now marketed as DHEA.