

## **DHEA INFORMATION PAGE**

### **Introduction**

A growing body of research suggests that DHEA can prevent or reverse the diseases that anti-aging experts have identified as the most prominent markers of accelerated aging: atherosclerosis (hardening and clogging of the arteries), cancer, diabetes, and reduced immunity. Moreover, mounting evidence indicates that the level of DHEA in a person's blood is an excellent predictor not only of these age-related health problems but also of aging itself. "DHEA is undeniably one of the most crucial predictive factors in diagnosing aging-related diseases," according to Ronald Klatz, D.O., president of the American Academy of Anti-Aging Medicine.

There is no question that DHEA extends the life spans of animals and holds promise as a defense against the degenerative diseases of aging. But can the hormone actually extend human life span? While the research literature strongly supports this claim, it remains unproven.

The definitive answer should come soon. Formerly relegated to a position of minor importance by the scientific establishment, DHEA has become the subject of intense scrutiny. A flurry of research is underway, underwritten by the National Cancer Institute, the National Institutes of Health, the National Institute on Aging, and the American Cancer Society. These and other major agencies are investigating DHEA as a potential treatment for chronic fatigue syndrome, depression, Epstein-Barr virus, herpes, lupus and other autoimmune diseases, menopausal symptoms, osteoporosis, and even AIDS.

What can the average healthy person expect from DHEA? Although everyone's experience differs, people report that they have more energy, handle stress more easily, think more clearly, and generally feel better. Other benefits include enhanced immunity (stronger resistance to colds, flu, and the like) and lower cholesterol.

### **The Age-Old Question**

Your adrenal glands are responsible for manufacturing DHEA. Actually, the cascade of adrenal hormones starts with cholesterol, from which the brain hormone pregnenolone is made. Pregnenolone is then transformed into DHEA. And DHEA serves as the raw material from which all other important adrenal hormones--including the sex hormones estrogen, progesterone, and testosterone and the stress hormone cortisol--are synthesized.

DHEA is the most abundant hormone in your body. But production peaks at around age 20. From then on, your DHEA level decreases with age. By the time you reach 40, your body makes about half as much DHEA as it used to. By 65, output drops to 10 to 20 percent of optimum; by age 80, it plummets to less than 5 percent of optimum.

Because DHEA has such broad-spectrum effects, declining production makes itself known in every system, every organ, and every tissue of your body. The immune system is especially sensitive to diminishing DHEA output, opening the door not just to viruses, bacteria, and other microbes but also to free radicals and the Pandora's box of degenerative diseases they cause.

If levels of DHEA decline with age, can replacing the hormone reverse aging in humans? Nobody knows for sure. In studies, laboratory animals given DHEA supplements live up to 50 percent longer than normal. But we humans metabolize DHEA differently than animals, so these results don't necessarily apply to us.

A host of studies suggest that the lower a person's level of DHEA, the greater his risk of death from age-related disease. DHEA levels in 242 men between the ages of 50 and 79 were tracked for 12 years in a study by noted hormone researcher Elizabeth Barrett-Connor, M.D., professor and chairperson of the department of preventive medicine at the University of California, San Diego. The study found a close correlation between higher DHEA levels and reduced risk of death from all causes. The men who survived had three times the DHEA levels of the men who died.

Research has pinpointed low DHEA levels as a marker for many degenerative diseases and accelerated aging. The hormone has been implicated as a contributing factor in a host of health problems, including Alzheimer's disease, autoimmune disease and other immunological disorders, cancer, chronic fatigue syndrome, diabetes, heart disease, high cholesterol, memory problems, obesity, osteoporosis, and stress disorders.

What's more, the collective indirect evidence from more than 5,000 published studies overwhelmingly supports DHEA's anti-aging role. Scientists now have proof that DHEA:

\* Enhances immunity

- Decreases the risk of heart disease
- Defends against some cancers
- Improves blood sugar control, decreasing the risk of diabetes
- Reverses the age-accelerating effects of the stress hormone cortisol
- Prevents and reverses osteoporosis

How could any substance that protects us from virtually every major degenerative disease not protect us from aging as well?

### **Living Better Than Ever**

Whether or not DHEA extends life span, it undoubtedly improves quality of life. Most people who take DHEA do so because the hormone helps them deal better with stress, gives them more pizzazz, and makes them feel young again. My patients on DHEA almost invariably report that they just plain feel better. This is not a placebo effect.

Research has shown that DHEA levels in the bloodstream correlate highly with general health and vitality, sense of well-being, and increased stress tolerance.

In 1994, the Journal of Clinical Endocrinology and Metabolism published the first placebo-controlled human study examining the therapeutic effects of DHEA replacement therapy. ("Placebo-controlled" means that some participants received DHEA, while others received fake pills.) The DHEA-takers had more energy, slept better, and handled stress better than the placebo-takers. The researchers concluded that "DHEA will improve the quality of life over a longer period and will postpone some of the unpleasant effects of aging, such as fatigue and muscle weakness."

In another study, researchers at the University of California, La Jolla, gave people 50 milligrams of DHEA every day for six months. Sixty-seven percent of the men and 84 percent of the women reported improvements in energy, sleep, mood, feelings of relaxation, and ability to handle stress--overall, a remarkable increase in subjective experience of physical and psychological well-being.

### **Maximizing Immunity**

Does DHEA rejuvenate immune function? You bet. It boosts antibody production; enhances the activity of monocytes, immune cells that attack cancer cells and viruses; activates natural killer cells, immune cells that attack and destroy viruses and other foreign invaders; and maximizes the anti-cancer function of immune cells known as T lymphocytes. In aging laboratory animals, DHEA restores youthful levels of cytokines (immune chemicals involved in protection and healing) and reduces the production of autoantibodies (antibodies that attack healthy tissues). When administered concurrently with a flu vaccine, DHEA dramatically improved the effectiveness of the vaccine in aging mice and in older humans.

DHEA's power to invigorate the immune system is closely linked to its potential to fight aging. Remember, heightened immunity translates directly into protection against oxidation, which in turn translates directly into protection against degenerative disease. So anything that strengthens your immune system also has the capacity to lengthen life. Immune deterioration with age is accompanied by increased incidence of atherosclerosis, autoimmune diseases, cancer, cataracts, and infections--all evidence of accelerated aging.

An important study conducted by leading DHEA researcher Samuel Yen, M.D., of the University of California, San Diego, underscores the hormone's age-opposing activation of immune function. After measuring baseline immune parameters in healthy older men (average age 63), Dr. Yen put the men on a program of 50 milligrams of DHEA per day. After 20 weeks, the men showed dramatic improvement in all markers of immune function, including an average of 45 percent increases in monocytes, 29 percent increases in antibody-making B lymphocytes, 20 percent increases in T lymphocyte

activation, 40 percent increases in T lymphocyte anti-cancer response, and 22 to 37 percent increases in natural killer cells.

Perhaps most significant of all, DHEA increases production of insulin-like growth factor-1 (IGF-1), a hormone-like molecule that is used to measure levels of another potent anti-aging compound called human growth hormone. (Because it is not yet widely available, is administered by injection, and is very costly--\$10,000 a year--human growth hormone exceeds the scope of this book.)

### **Stopping Stress in Its Tracks**

DHEA protects your body from the hormone cortisol and the stress that triggers its production. Like DHEA, cortisol is secreted by the adrenal glands. If over-secreted, cortisol injures your body's tissues. When you're under stress, your adrenal glands release large amounts of cortisol. People under chronic stress have high cortisol levels (unless their adrenal glands have already burned out, in which case their cortisol levels are low). The presence of too much cortisol leads to age-accelerating damage. As stress accumulates over decades, cortisol levels tend to rise as well. Many people over age 40 have elevated cortisol.

DHEA and cortisol have an inverse, or adversarial, relationship. When you're faced with prolonged stress, your cortisol/DHEA ratio--a measure of health status and aging--can rise by a factor of 5. This means that the excess cortisol is battering DHEA's protective shield. DHEA supplementation increases your stress tolerance, lowers your cortisol/DHEA ratio, and protects you against cortisol-induced cellular damage.

### **Mending a Broken Heart**

The cardiovascular research community is abuzz about DHEA's potential to conquer America's number one killer, heart disease. Several studies examining the role of DHEA in heart disease have produced intriguing findings.

Research has shown that depleted DHEA is a more accurate predictor of heart attack than elevated cholesterol. DHEA levels were significantly lower in men who died of heart attacks than in men who were healthy.

DHEA level was shown to correlate with the degree of atherosclerosis in 200 men and women undergoing coronary angiography, in a study by David Herrington, M.D., of Bowman Gray School of Medicine of Wake Forest University in Winston-Salem, North Carolina, which was published in the Journal of the American College of Cardiology. He found that as DHEA levels went up, coronary artery disease (as measured by the frequency and severity of arterial lesions) went down.

A follow-up study showed that the degree of development of atherosclerosis in 63 heart transplant patients was inversely correlated with DHEA levels. In other words, the higher the heart recipient's DHEA level, the lower his likelihood of developing post-transplant atherosclerosis. What's more, the heart recipients with high DHEA had a much better five-year survival rate (87 percent) than the heart recipients with low DHEA (65 percent).

That's not all. In people undergoing angioplasty (a procedure in which a balloon is used to open a clogged blood vessel), DHEA reduced the rate of restenosis--a treated vessel closes off again--from 68 percent to 28 percent. In healthy males given a clot-promoting substance (arachidonic acid, found in abundance in meat), DHEA blocked an increase in clotting. (An increased tendency to clot is a risk factor for heart attack and stroke.) In men, DHEA lowered total cholesterol and "bad" low-density lipoprotein cholesterol better than and more safely than the "statin" drugs such as clofibrate and gemfibrozil. DHEA is also nontoxic.

Animal studies are producing similar promising results. When researchers gave DHEA to rabbits with atherosclerotic arteries, the hormone produced a 50 percent decline in arterial plaques.

The bottom line in all of this: Age-related DHEA declines may leave us vulnerable to atherosclerosis, while DHEA replacement therapy appears to offer potent protection.

## **Beating Cancer**

Can DHEA prevent cancer? While scientists don't yet know for certain, the early reports are encouraging.

Low DHEA predicts breast cancer more accurately than any other known marker. Women with breast cancer consistently have lower-than-normal DHEA readings. DHEA may help protect against breast cancer by inhibiting glucose-6-phosphate dehydrogenase, an enzyme required for cancer growth. Also, because DHEA has antioxidant properties, the hormone probably defends against free radical cancer initiators.

In animal studies, DHEA has provided dramatic protection against tumors of the breasts, colon, liver, lungs, lymphatic vessels, prostate, and skin. Of course, what happens in animals doesn't necessarily translate to humans. This is especially true with DHEA because very little of the hormone is found in the bloodstreams of rodents.

So despite a general feeling among anti-aging experts that DHEA may well inhibit cancer formation, the jury remains out on the DHEA-cancer link--at least for the time being.

## **Good to Your Bones**

Osteoporosis is like a football game. Build a strong offense, and you're bound to gain yardage--that is, bone. Make do with a weak offense, and the opposing team will push you back for a serious loss.

Certain dietary and lifestyle factors give the opponent a distinct advantage: too little calcium; too much protein; preservative-rich processed foods; alcohol and other drugs; and lack of exercise. You can retain control of the ball by recruiting the following players for your bone-building team: regular exercise, a low-protein vegan diet, vitamins (A, B6, C, D3, K, and folic acid), minerals (boron, copper, magnesium, manganese, silicon, zinc--and, of course, calcium), and hormones.

Among the anti-aging hormones, DHEA stands out as a multitalented star with amazing ways of outsmarting osteoporosis. DHEA is the only hormone that can both inhibit bone breakdown and stimulate bone formation. Plus, DHEA is a precursor to estrogen, progesterone, and testosterone, all of which prevent bone loss in their own rights.

Bone cells convert DHEA to estrone, a type of estrogen that in turn increases the activity of bone-making cells called osteoblasts. DHEA's transformation into estrone depends on the presence of vitamin D3. (Likewise, D3 requires DHEA to stimulate osteoblasts. It can't do the job alone.)

Japanese researchers found a positive correlation between DHEA levels and bone density in women over age 50. The higher the women's DHEA, the denser their bones. When the same researchers gave DHEA to "postmenopausal" rats (actually, the animals had had their ovaries removed), the rats' bone density increased.

As DHEA levels decline with age, osteoporosis may appear. People with osteoporosis have significantly lower DHEA levels than people without the disease. When osteoporotic lab animals are given DHEA, their bones remineralize--that is, their bones become stronger. Although human studies have yet to be done, DHEA supplementation would in all likelihood increase our bone density as well.

## **Medicine for the Mind**

Don't be surprised if, in the next few years, you start seeing reports that DHEA is being used to treat Alzheimer's disease and other degenerative brain diseases. (You can say you read it here first.) While DHEA is no cure for Alzheimer's, strong evidence exists that the hormone is essential for maintaining healthy brain cells.

DHEA levels sink to markedly low levels later in life, when the incidence of degenerative brain disease is much higher. DHEA levels in people who have Alzheimer's are much

lower than in people who don't have the disease. Studies show that even very small doses of the hormone reduce amnesia while improving long-term memory.

When researchers gave 30 to 90 milligrams of DHEA a day to depressed middle-aged patients, they saw significant evidence not only of reduced depression but of improved memory as well.

## **The Lupus Link**

Systemic lupus erythematosus is a chronic autoimmune disease in which the immune system manufactures autoantibodies, which attack healthy tissues. In effect, the body turns on itself. Blood vessels, connective tissues, joints, kidneys, the nervous system, and skin may be affected.

Lupus is commonly treated using immunosuppressive steroids and cancer chemotherapy agents. The treatment damages the immune system and thus undermines the healing process. Its side effects can be worse than the disease itself.

Aware of DHEA's immune-enhancing effects, researchers at Stanford University gave DHEA to 57 women with lupus. About two-thirds of the women reported some alleviation of their symptoms, including reduced frequency and severity of joint pain, headaches, rashes, and fatigue. Many also reported better exercise tolerance and improved concentration. Impressed with these findings, the Food and Drug Administration is supporting clinical trials to evaluate DHEA's efficacy as an alternative to conventional lupus therapy.

## **Taking DHEA**

DHEA replacement therapy offers powerful health benefits and is virtually risk-free. People have taken doses as high as 1,600 milligrams daily for a month with no adverse reactions.

In my practice, I test the DHEA levels of all of my patients over age 40. If the results indicate a deficiency (as they invariably do), I usually recommend DHEA replacement therapy. I provide informative articles about DHEA, and the patient and I reach a decision together.

The recommended daily dose range is 10 to 50 milligrams for women, 25 to 100 milligrams for men. (Women need less DHEA than men.) I usually start my patients--women and men--at 25 milligrams once or twice daily. The initial dose is determined by gender and baseline DHEA level (the lower the level, the higher the starting dose).

After one month, I retest. I increase the dose until the patient's DHEA level matches that of a 30-year-old of the same gender: between 200 and 300 micrograms per deciliter of

blood for women, and between 300 and 400 micrograms per deciliter of blood for men. Once the patient's DHEA level stabilizes within the desired range, testing can be done semiannually.

Though most people take DHEA without the benefit of knowing their blood levels of the hormone, routine monitoring is a really good idea. How else can you know whether you are taking the optimum amount? Many insurance plans, including Medicare, cover DHEA testing if it's ordered by a physician.

The ideal anti-aging strategy is to supplement both DHEA and its precursor, pregnenolone (which I'll discuss in a bit). Since your body will convert some of the pregnenolone to DHEA, any increase in the dosage of pregnenolone may result in a higher level of DHEA. (The opposite does not hold true, however: Your body doesn't convert DHEA to pregnenolone.) The rate at which pregnenolone is converted to DHEA varies from one person to the next. So monitor levels of both hormones every few months and adjust your doses until both are within their respective desired ranges.

Many hormones, including cortisol and thyroid hormone, are controlled by a feedback loop system that shuts off production when levels get high. Not so with DHEA and pregnenolone: Your body will keep right on making these hormones in the same amounts as before you began supplementation. In other words, taking supplements of DHEA and pregnenolone won't suppress your body's production of these hormones or cause adrenal atrophy.

For most people, the purpose of DHEA replacement therapy is to improve quality and quantity of life. But it may be prescribed for certain medical conditions, including Alzheimer's disease and other organic brain diseases, chronic fatigue syndrome, depression, diabetes, heart disease, immune deficiency syndromes, lupus and other autoimmune diseases, osteoporosis, and stress-related disorders. Patients who, because of family history or other factors, are at higher risk for any of these conditions can benefit from DHEA as preventive therapy.

Who shouldn't take DHEA? People under age 35 and people who have normal DHEA levels ("normal" being the level typical of a 29-year-old). They simply don't need it. Men with prostate cancer and women with reproductive cancers should consult their doctors before taking DHEA, even though no adverse effects have been reported.

DHEA does stimulate hair follicles and sebaceous (oil) glands, so it may cause facial hair growth in women or transient acne. (An article in the *New England Journal of Medicine* linked teenage acne to the rise in DHEA that takes place near puberty.) These side effects are rare. If they do occur, they'll disappear with dose reduction or discontinuation.

## **Beware the Wannabes**



Commercial DHEA products are made from diosgenin, an extract from the Mexican wild yam of the Dioscorea family. Biochemists can convert diosgenin to DHEA by engineering a series of chemical conversions.

The market is flooded with encapsulated yam products claiming to be "DHEA precursors" or "natural DHEA." Unfortunately, the human body--or any living system, for that matter--cannot convert diosgenin to DHEA. It happens only in the laboratory.

The ingestion of Dioscorea plant extracts can't possibly lead to the formation of DHEA in the body, according to prominent DHEA expert Seymour Lieberman, Ph.D., of St. Luke's - Roosevelt Hospital Center in New York City. Products containing Mexican yam or unconverted diosgenin may produce other beneficial hormonal effects, but they will not raise DHEA levels.

The research studies revealing DHEA's therapeutic effects were all done with real hormone, not yam extracts. Read labels and insist on 99 percent pharmacologically pure DHEA.