

DHEA

Dehydroepiandrosterone

DHEA has been shown to improve neurological function (including memory, mood enhancement, and EEG readings), immunity and stress disorders. DHEA replacement therapy has become popular as an anti-aging regimen and offers aging patients help in preventing diseases such as osteoporosis, fatigue, depression, atherosclerosis, and cancer.

DHEA is a precursor building block that allows our bodies to more easily create hormones that may be in decline because of age, disease, prescription medications, or other factors. Hormones such as testosterone and estrogen as well as serum DHEA levels begin to decline between 25 and 30 years of age and may be reduced by 95% of youthful peak levels by age 85.

The most remarkable finding about DHEA came from a human study by S. S. C. Yen and associates at the University of California, San Diego, in which 50 mg a day of DHEA over a 6-month period restored youthful serum levels of DHEA in both men and women. Dr. Yen showed that DHEA replacement was associated with an increase in perceived physical and psychological well being for both men (67%) and women (84%).

DHEA (50 or 100 mg a day) was also shown to significantly elevate insulin-like growth factor (IGF). Aging causes a decline in IGF levels that contributes to the loss of lean body mass, as well as to excess fat accumulation, neurological impairment, and age-associated immune dysfunction.

DHEA has been shown to protect against heart disease and atherosclerosis. A study using coronary artery angiography showed that low DHEA levels predispose people to more significant coronary artery blockage. Another study showed that DHEA inhibits abnormal blood platelet aggregation, a factor in the development of sudden heart attack and stroke. In contrast, some studies on DHEA do not show the cardiovascular disease protection.

In the journal *Drugs and Aging* (Oct. 1996), an analysis of previous studies on DHEA showed that:

In both humans and animals, the decline of DHEA production with aging is associated with immune depression, increased risk of several different cancers, loss of sleep, decreased feelings of well-being, and increased mortality.

- DHEA replacement in aged mice significantly improved immune function to a more youthful state.
- DHEA replacement has shown a favorable effect on osteoclasts and lymphoid cells, an effect that may delay osteoporosis.
- Low levels of DHEA inhibit energy metabolism, thus increasing the risk of heart disease and diabetes mellitus.
- Studies in humans show essentially no toxicity at doses that restore DHEA to youthful levels.
- DHEA deficiency may expedite the development of some diseases that are common in the elderly.

Depression Responds to DHEA Treatment

Depression is a broad term for a host of unpleasant feelings, including emotional numbness, lack of energy, lack of motivation, feeling like a failure, and feeling undesirable. These feelings frequently show up for the first time in middle-aged people who feel like they're "over the hill." Elderly people, too, frequently get depressed, and they are particularly at risk of suicide.

Doctors have long known that giving estrogen to women and testosterone to men during mid-life can avert symptoms of depression. Reports are stacking up that DHEA works better. DHEA turns into both estrogen and testosterone. And it just so happens that it declines about the time people start thinking about being "over the hill." DHEA has consistently been linked with depression. It was studied as far back as the 1950s as an antidepressant. Back then, researchers reported that it gave people energy and confidence, and made them less depressed. While it seemed to work great, no one followed up on the studies.

Researchers have different theories about how DHEA alleviates depression. DHEA can cross the blood-brain barrier and interact with the brain directly. DHEA can affect serotonin, GABA receptors, and other brain factors. In addition, DHEA is the precursor for estrogen and testosterone, which have been reported to enhance mood.

DHEA also has anti-stress effects that may be part of its antidepressant action. Research shows that cortisol, the stress hormone, is elevated in major depression. DHEA counteracts cortisol. Calmness appears to be associated with higher levels of DHEA. People who practice transcendental meditation have higher levels of DHEA than those who don't. People who took part in a stress reduction program were able to increase their DHEA by 100%. At the same time, they reduced their stress hormone by 23%.

Exercise has been reported to enhance mood. This mood-enhancing effect may in part be due to DHEA. Exercise raises levels of DHEA, which also positively affects the heart. In a study published in the American Journal of Cardiology, depression and heart attack went together: women with depression are at greater risk of heart attack, and vice-versa. Exercise elevates DHEA, which, in turn, benefits the heart.

DHEA Inhibits Cancer Cell Proliferation

DHEA may be effective in preventing and treating cancer. In one study, DHEA inhibited tumor proliferation of rat liver cells by blocking the cancer cell promoting enzyme glucose 6-phosphate dehydrogenase (G6PDH). The human equivalent dose of 600 mg a day suppressed breast tumors in mice by 70%, yet these scientists showed that even human equivalent doses of 25 to 120 mg showed striking cancer prevention benefits, with no evidence of toxicity.

DHEA has been shown to inhibit chemically induced cancers in the colon, lung, breast, and skin. When DHEA is applied directly to the skin, DHEA prevented chemically induced skin cancer. DHEA had this effect by blocking the binding of carcinogens to skin cells and by inhibiting the enzyme G6PDH.

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DHEA Protects against Brain Aging

Acetylcholine is a neurotransmitter that transmits nerve impulses from one brain cell to another. Acetylcholine is crucial for short-term memory and to protect brain cells against age-associated atrophy. Aging causes a decline in the release of acetylcholine into regions of the brain where it is needed for learning and memory.

In a study in Brain Research (Sept. 16, 1996), DHEA was administered to rats in order to measure the effect it produced on acetylcholine release into the brain. DHEA significantly increased acetylcholine release above pretreatment levels in all doses tested. At the highest dose, DHEA caused a fourfold increase in the release of acetylcholine compared to the control group. The scientists concluded that this was the first study to demonstrate a direct effect of DHEA in promoting the release of acetylcholine from brain cells.

A study in Life Sciences (Oct. 4, 1996) showed that DHEA could help protect against the precursor changes in brain cells that result in the pathological alterations associated with Alzheimer's disease.

DHEA Saves Skin

Estrogen's skin-enhancing effects are well known. It provokes collagen and a moisture factor known as hyaluronic acid. Aging decreases both estrogen and collagen. Enzymes that convert DHEA to estrogen also decline. Not surprisingly, women who take synthetic estrogen have scientifically proven thicker skin. Women who take both estrogen and testosterone have really thick skin-48% thicker than women who don't take either hormone. DHEA is converted to both estrogen and testosterone, providing the benefits of both hormones. DHEA is converted into estrogen and androgen-type metabolites found only in skin.

Immune Function and DHEA

DHEA levels decline 80 to 90% by age 70 or later. DHEA has demonstrated a striking ability to maintain immune system synchronization. Oral supplementation with low doses of DHEA in aged animals restored immune function to a reasonable level within days of administration. DHEA supplementation in aged rodents resulted in almost complete restoration of immune function.

Only limited human studies have been done to measure DHEA's effect on the immune system. In one study, scientists proposed that the oral administration of DHEA to elderly men would result in activation of their immune system. Nine healthy men averaging 63 years of age were treated with a placebo for 2 weeks followed by 20 weeks of DHEA (50 mg/day). After 2 weeks on oral DHEA, serum DHEA levels increased by three to four times. These levels were sustained throughout the study.

Compared to the placebo, DHEA administration resulted in:

- An increase of 20% in IGF-1. Many people are taking expensive growth hormone injections for the purpose of boosting IGF levels. IGF stands for insulin-like growth factor and is thought to be responsible for some of the anti-aging, anabolic effects that DHEA has produced in previous human studies.
- An increase of 35% in the number of monocyte immune cells.
- An increase of 29% in the number of B immune cells and a 62% increase in B-cell activity.
- A 40% increase in T-cell activity even though the total number of T-cells was not affected.
- An increase of 50% in interleukin-2.
- An increase of 22 to 37% in natural killer cells (NK) number and an increase of 45% in NK cell activity.
- No adverse effects noted with DHEA administration.

The scientists' conclusion: "**While extended studies are required, our findings suggest potential therapeutic benefits of DHEA in immunodeficient states.**" (Journals of Gerontology, Series A, 1997, 52[1])

DHEA Dosing and Safety Precautions

DHEA should only be taken under the direction of your physician. DHEA levels must be monitored throughout therapy. Over-the-counter DHEA supplements can vary widely in strength and quality. Prescription grade DHEA in sub-lingual form is the best choice.

Properly managed DHEA therapy can be useful for most men and women over 40 to increase energy, vitality and to foster an overall youthful feeling. However, there are guidelines that should be followed for safe long-term use of DHEA.

When taking oral supplements of DHEA, it is important that antioxidants are available to the liver because DHEA can promote free radicals in liver cells. Animal studies have shown that extremely high doses (from 2000 to 10,000 mg DHEA daily in human terms) caused liver damage in mice and rats. When antioxidants were given along with the DHEA, liver damage did not occur despite the massive doses of DHEA being administered to these animals. It should be noted that the amount of DHEA shown to cause liver damage is 20 times more than is necessary to produce anti-aging benefits. Alpha lipoic acid, vitamin E and N-acetyl-cysteine (NAC) are antioxidants that have been shown to be especially effective in suppressing free radicals in the liver.

A DHEA blood test should be taken three to six weeks after beginning DHEA therapy to help determine optimal dosing. Some people neglect to test their blood levels of DHEA and wind up chronically taking the wrong dose. When having your blood tested for DHEA, blood should be drawn three to four hours after the last dose.

Men

Before initiating DHEA therapy, men should know their serum PSA (prostate specific antigen) level and have passed a digital rectal exam. In some men, DHEA may convert into testosterone and other growth factors that could cause existing prostate cancer cells to propagate. In some

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men, however, DHEA will mildly elevate estrogen levels, which would theoretically be good for those with prostate cancer since estrogen is known to help suppress prostate cancer cell growth.

The preponderance of the published literature shows that higher DHEA blood levels do not cause prostate cancer. In fact, recent studies indicate that DHEA may confer a protective effect against prostate cancer. While some doctors still express theoretical concern that DHEA could cause prostate cancer, this theory loses credibility upon reading scientific studies showing that DHEA may protect against the development of prostate cancer.

Most prostate cancers develop in aged men that have extremely low levels of DHEA compared to when they were young. DHEA levels decline with age, yet prostate gland enlargement and cancers increase with age. Is it possible that DHEA, being a weak androgen, can actually attach to and block testosterone or DHT receptors on prostate tissue, thus preventing the influence by more powerful androgens? We do not fully know the answer to this question, which is why we advise prostate cancer patients to proceed cautiously in considering whether or not to use low-dose DHEA.

Women

DHEA can increase serum estrogen levels in women and eliminate the need for estrogen replacement therapy in some women. Women should consider estrogen and testosterone testing when they take their DHEA blood test in order to evaluate DHEA's effect on their blood levels of estrogens.

Women who have been diagnosed with an estrogen-dependent cancer should not take DHEA therapy. Some studies indicate that higher serum DHEA protects against breast cancer, but no adequate studies have been done to evaluate the effects of DHEA in breast cancer patients. If DHEA were to elevate estrogen too much, this could theoretically increase the risk of breast cancer.

Conclusion

If DHEA replacement sounds complicated, it is, compared to other preventive supplement programs. We suggest weighing the documented anti-aging benefits of maintaining youthful serum DHEA levels when deciding whether to embark on a DHEA replacement regimen. Or stated differently, review the degenerative effects of chronic DHEA deficiency to decide whether this program is worth your time and money.

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*Portions of this protocol have been excerpted from The Life Extension Foundation's "DHEA Protocol"