



Pills, Patches, and Shots: Can Hormones Prevent Aging?

Tips from the National Institute on Aging

We could not survive without hormones. They are among the most common and vital chemical messengers in the body. From head to toe, each moment of life, they signal cells to perform tasks that range from the ordinary to the extraordinary. Among their many roles, hormones help regulate body temperature, blood pressure, and blood sugar levels. In childhood, they help us “grow up.” In the teen years, they are the driving force behind puberty. But what influence, if any, the natural decline in some hormones has on the aging process in middle and late life is unclear. Although a few proponents are convinced that hormone supplements can favorably alter the aging process and have advocated their widespread use, the scientific evidence supporting this premise is, for the most part, sketchy.

For more than a decade, the National Institute on Aging (NIA), a component of the Federal Government’s National Institutes of Health, has supported and conducted studies of replenishing hormones to find out if they may help reduce frailty and improve function in older people. These studies have focused on hormones known to decline as we grow older:

- Dehydroepiandrosterone (DHEA)
- Growth Hormone

- Melatonin
- Testosterone
- Menopausal hormones, such as estrogen and progesterone

The results from these NIA-sponsored studies and other research projects likely will improve our understanding of the pros and cons of hormone supplementation. Until the results of these studies are compiled, analyzed, and a consensus among scientists is reached, recommendations to use supplemental hormones and hormone-like molecules to influence the aging process and health problems associated with aging should be viewed with skepticism. It is not yet known, for instance, how much is too much or too little, and when or whether hormone supplements should be taken at all. This tip sheet provides information about what is known so far and what researchers are doing to find out more.

What Is A Hormone?

Hormones are powerful chemicals that help keep our bodies working normally. The term hormone is derived from the Greek word, *hormo*, which means to set in motion. And that’s precisely what hormones do in the body. They stimulate, regulate, and control the function of various tissues and organs.

Made by specialized groups of cells within structures called glands, hormones are involved in almost every biological process including sexual reproduction, growth, metabolism, and immune function. These glands, including the pituitary, thyroid, adrenals, ovaries, and testes, release various hormones into the body as needed.

Levels of some hormones like parathyroid hormone, which helps regulate calcium levels in the blood and bone, actually increase as a normal part of aging and may be involved in bone loss leading to osteoporosis. But the levels of a number of other hormones, such as testosterone in men and estrogen in women, tend to decrease over time. In other cases, the body may fail to make enough of a hormone due to diseases and disorders that can develop at any age. When this occurs, hormone supplements—pills, shots, topical (rub-on) gels, and medicated skin patches—may be prescribed.

Unproven claims that taking hormone supplements can make people feel young again or that they can slow or prevent aging have been “hot” news items for several years. The reality is that no one has yet shown that supplements of these hormones prevent frailty or add years to people’s lives. And while some supplements provide health benefits for people with genuine deficiencies of certain hormones, they also can cause harmful side effects. In any case, people who have diagnosed hormone deficiencies should take them only under a doctor’s supervision. *Remember:* More is not necessarily better. The right balance of hormones helps us stay healthy, but the wrong amount might be damaging.

Heed The Warnings

The NIA recognizes that some hormone-like products are available over the counter and can be used without consulting a physician.

The Institute discourages individuals from self-medicating with these products for a number of reasons. First, these products are marketed as “dietary supplements”, and therefore are not regulated by the Food and Drug Administration (FDA) in the same way as drugs. This is an important distinction because the requirements for marketing a dietary supplement are very different from those that apply to hormones marketed as drugs. Unlike drug manufacturers, a firm selling dietary supplements doesn’t need FDA approval of its products and doesn’t need to prove that its products are safe and effective before marketing. Also, there is no specific guarantee that the substance in the container is authentic or that the indicated dosage is accurate. Because of these differing standards, hormone-like substances that are sold as dietary supplements may not be as thoroughly studied as drug products, and, therefore, the potential consequences of their use are not well understood or defined. In addition, these over-the-counter products may interfere with other medications you are taking.

Therefore, the NIA does not recommend taking any supplement, including DHEA and melatonin, that is touted as an “anti-aging” remedy because no supplement has been proven to serve this purpose. The influence of these supplements on a person’s health is unknown, particularly when taken over a long period of time.

Talk to your doctor if you are interested in any form of hormone supplementation. In fact, you might want to show this fact sheet to your doctor to help explain your concerns.

How Hormones Work

Most hormones exist in very low concentrations in the bloodstream. Each hormone molecule travels through the blood until it reaches a cell with a receptor that it matches. Then, the

hormone molecule latches onto the receptor and sends a signal into the cell. These signals may instruct the cell to multiply, to make proteins or enzymes, or to perform other vital tasks. Some hormones can even stimulate a cell to release other hormones. However, no single hormone affects all cells in the same way. One hormone, for example, may stimulate a cell to perform one task, while the same hormone can have an entirely different influence over another cell. The response of some cells to hormonal stimulation also may change throughout life.

Hormone supplements, particularly if taken without medical supervision, may adversely affect this complex system. These supplements, for instance, may not behave exactly the same way as our own naturally produced hormones have because the body may process them differently. In addition, natural hormone production isn't constant, so circulating blood levels may vary significantly over a 24-hour period. Hormone supplements can't replicate these fluctuations. As a result, high doses of supplements, whether pills, shots, gels, or skin patches, may result in excessive and unhealthy amounts of hormones in the blood. Hormone supplements also may compound any negative effects caused by hormones naturally produced by the body.

Finally, most of the processes in the body are tightly controlled and regulated. Too much stimulation can elicit natural responses to inhibit a hormone's action. The body's system of checks and balances is complicated and the notion that hormone supplements can improve function may be an oversimplification.

DHEA

Dehydroepiandrosterone or DHEA is made from cholesterol by the adrenal glands, which sit on top of each kidney. Production of this substance peaks in the mid-20s, and gradually declines with age in most people. What this

drop means or how it affects the aging process, if at all, is unclear. In fact, scientists are somewhat mystified by DHEA and have not fully sorted out what it does in the body. However, researchers do know that the body converts DHEA into two hormones that are known to affect us in many ways: estrogen and testosterone.

Supplements of DHEA can be bought without a prescription and are sold as "anti-aging remedies." Some proponents of these products claim that DHEA supplements improve energy, strength, and immunity. DHEA is also said to increase muscle and decrease fat. Right now there is no consistent evidence that DHEA supplements do any of these things in people, and there is little scientific evidence to support the use of DHEA as a "rejuvenating" hormone. Although the long-term (over 1 year) effects of DHEA supplements have not been studied, there are early signs that these supplements, even when taken briefly, may have several detrimental effects on the body including liver damage.

In addition, some people's bodies make more estrogen and testosterone from DHEA than others. There is no way to predict who will make more and who will make less. Researchers are concerned that DHEA supplements may cause high levels of estrogen or testosterone in some people. This is important because testosterone may play a role in prostate cancer, and higher levels of estrogen are associated with an increased risk of breast cancer. It is not yet known for certain if supplements of estrogen and testosterone, or supplements of DHEA, also increase the risk of developing these types of cancer. In women, high testosterone levels can cause acne and growth of facial hair.

Overall, the studies that have been done so far do not provide a clear picture of the risks and benefits of DHEA. For example, some studies in

older people show that DHEA helps build muscle and reduce fat, but other studies do not. Researchers are working to find more definite answers about DHEA's effects on aging, muscles, and the immune system. In the meantime, people who are thinking about taking supplements of this hormone should understand that its effects are not fully known. Some of these unknown effects might turn out to be harmful.

Growth Hormone

Human growth hormone (hGH) is made by the pituitary gland, a pea-sized structure located at the base of the brain, and is important for normal development and maintenance of tissues and organs. It is especially important for normal growth in children.

Studies have shown that injections of supplemental hGH are helpful to certain people. Sometimes children are unusually short because their bodies do not make enough hGH. When they receive injections of this hormone, their growth improves. Young adults who have no pituitary gland (because of surgery for a pituitary tumor, for example) cannot make the hormone and they become obese. When they are given hGH, they lose weight.

Like some other hormones, blood levels of hGH often decrease as people age, but this may not necessarily be bad. At least one epidemiological study, for instance, suggests that people who have high levels of hGH are more apt to die at younger ages than those with lower levels of the hormone. Studies of animals with genetic disorders that suppress growth hormone production and secretion also suggest that *reduced* growth hormone secretion may prolong survival in some species.

Although there is no conclusive evidence that hGH can prevent aging, some people spend a

great deal of money on supplements. These supplements are claimed, by some, to increase muscle, decrease fat, and to boost an individual's stamina and sense of well being. Shots—the only proven way of getting the body to make use of supplemental hGH—can cost more than \$15,000 a year. They are available only by prescription and should be given by a doctor. In any case, people in search of the “fountain of youth” may have a hard time finding a doctor who will give them shots of hGH because so little is known about the long-term risks and benefits of this controversial treatment. Some dietary supplements, known as human growth hormone releasers, are marketed as a low-cost alternative to hGH shots. But claims that these over-the-counter products retard the aging process are unsubstantiated.

While some studies have shown that supplemental hGH does increase muscle mass, it seems to have little impact on muscle strength or function. Scientists are continuing to study hGH, but they are watching their study participants very carefully because side effects can be serious in older adults. These include diabetes and pooling of fluid in the skin and other tissues, which may lead to high blood pressure and heart failure. Joint pain and carpal tunnel syndrome also may occur. A recent report that treatment of children with human pituitary growth hormone increases the risk of subsequent cancer is a cause for concern. Further studies on this issue are needed. Whether older people treated with hGH for extended periods have an increased risk of cancer is unknown.

For now, there is no convincing evidence hGH supplements will improve the health of those who do not suffer a profound deficiency of this hormone.

Melatonin

This hormone is made by the pineal gland, a structure in the brain. Contrary to the claims

of some, secretion of melatonin does not necessarily decrease with age. Instead, a number of factors, including light and many common medications, can affect melatonin secretion in people of any age.

Melatonin supplements can be bought without a prescription. Some people claim that melatonin is an anti-aging remedy, a sleep remedy, and an antioxidant (antioxidants protect against “free radicals,” naturally occurring oxygen-related molecules that cause damage to the body). Early test-tube studies suggested that, in large doses, melatonin might be effective against free radicals. However, cells produce antioxidants naturally, and in test-tube experiments, cells reduce the amount they make when they are exposed to additional antioxidants.

Claims that melatonin can slow or reverse aging are very far from proven. Studies of melatonin have been much too limited to support these claims and have focused on animals, not people.

Research on sleep shows that melatonin does play a role in our daily sleep/wake cycle, and that supplements, in amounts ranging from 0.1 to 0.5 milligrams, can improve sleep in some cases. If melatonin is taken at the wrong time, though, it can disrupt the sleep/wake cycle. Other side effects may include confusion, drowsiness, and headache the next morning. Animal studies suggest that melatonin may cause some blood vessels to constrict, a condition that could be dangerous for people with high blood pressure or other cardiovascular problems.

These side effects are important to keep in mind since the dose of melatonin usually sold in stores—3 milligrams—can result in amounts in the blood from 10 to 40 times higher than normal. What long-term effects such high

concentrations of melatonin may have on the body are still unknown. Until researchers find out more, caution is advised.

Testosterone

Ask an average man about testosterone, and he might tell you that this hormone helps transform a boy into a man. Or, he might tell that you that it has “something” to do with sex drive. Or, if he has read news stories in recent years, he might mention “male menopause,” a condition supposedly caused by diminishing testosterone levels in aging men. In reality, there is scant evidence that this controversial condition, also known as “andropause” or “viropause,” exists.

Testosterone is indeed a vital sex hormone that plays an important role in puberty. In men, testosterone not only regulates sex drive (libido), it also helps regulate bone mass, fat distribution, muscle mass and strength, and the production of red blood cells and sperm. But contrary to what some people believe, testosterone isn’t exclusively a male hormone. Women produce small amounts of it in their bodies as well. In men, testosterone is produced in the testes, the reproductive glands that also produce sperm. The amount of testosterone produced in the testes is regulated by the hypothalamus and the pituitary gland.

As men age, their testes often produce somewhat less testosterone than they did during adolescence and early adulthood, when production of this hormone peaks. But it is important to keep in mind that the range of normal testosterone production is large. It is unclear how much of a decline or how low a level of testosterone is needed to cause adverse effects. The likelihood that an aging man will ever experience a major shut down of hormone production similar to a woman’s menopause, is very remote.

In fact, many of the changes that take place in older men often are incorrectly blamed on decreasing testosterone levels. Some men who have erectile difficulty (impotence), for instance, may be tempted to blame this problem on lowered testosterone. However, in many cases, erectile difficulties are due to circulatory problems, not low testosterone.

Still, some men may be helped by testosterone supplementation. These FDA approved products are prescribed for men whose bodies make very little or no testosterone—for example, men whose pituitary glands have been damaged or destroyed by trauma, infections or tumors, or whose testes have been damaged. For these few men who have extreme deficiencies, testosterone therapy in the form of patches, injections, or topical gels may offer substantial benefit. Testosterone products may help a man with exceptionally low testosterone levels maintain strong muscles and bones, and increase sex drive. However, what effects testosterone replacement may have in healthy older men without these extreme deficiencies requires more research.

The NIA is investigating the role of testosterone therapy in delaying or preventing frailty. Results from preliminary studies involving small groups of men have been inconclusive, and it remains unclear to what degree supplementation of this hormone can sharpen memory or help men maintain stout muscles, sturdy bones, and robust sexual activity.

Many other questions remain about the use of this hormone in late life. It is unclear, for example, whether men who are at the lower end of the normal range of testosterone production would benefit from supplementation. Some investigators are also concerned about the long-term harmful effects that supplemental testosterone might have on the aging body. It is not yet known, for instance, if testosterone

therapy increases the risk of prostate cancer, the second leading cause of cancer death among men. In addition to potentially promoting new prostate cancers, testosterone also may promote the growth of those that have already developed. Studies also suggest that supplementation might trigger excessive red blood cell production in some men. This side effect can thicken blood and increase a man's risk of stroke.

The bottom line: Although some older men who have tried testosterone therapy report feeling “more energetic” or “younger,” testosterone supplementation remains a scientifically unproven method for preventing or relieving any physical and psychological changes that men with normal testosterone levels may experience, as they get older. Until more scientifically rigorous studies are conducted, the question of whether the benefits of testosterone replacement outweigh any of its potential negative effects will remain unanswered. The NIA is planning to expand its research to gather more evidence on the risks and benefits of testosterone supplementation in aging men with low testosterone levels.

Estrogen and Progesterone

Estrogen and progesterone are hormones produced in a woman's ovaries before menopause. They play an important part in the menstrual cycle and pregnancy, but estrogen also helps maintain bone strength and might prevent heart disease and protect memory before menopause.

For more than 60 years estrogen has been used by millions of women to control the hot flashes and vaginal dryness that frequently occur with menopause. It is also used to prevent or treat osteoporosis, the loss of bone strength that often occurs after menopause. However, over time experts realized that estrogen could cause a thickening of the lining of the uterus

(endometrium) and an increased risk of endometrial cancer. Doctors then began giving progestin, a synthetic form of progesterone, to protect the lining of the uterus. Using estrogen alone (in a woman whose uterus has been removed) or with a progestin (in women with a uterus) to treat the symptoms of menopause is called menopausal hormone therapy (MHT), formerly known as hormone replacement therapy.

Unlike other hormones described in this tip sheet, many large, reliable long-term studies of estrogen and its effects on the body have been conducted. These studies suggested that using estrogen after menopause could provide many important benefits.

But estrogen also is a good example of why it is important to wait until researchers have discovered both the benefits and risks of a hormone before it becomes widely used. While some women are helped by estrogen during and after menopause, others are placed at higher risk for certain diseases if they take it.

Early studies suggested menopausal hormone therapy could lower the risk for heart disease (the number-one killer of women in the United States) in postmenopausal women. But results from the Women's Health Initiative (WHI), an important study of menopausal hormone therapy funded by the National Institutes of Health, now suggests that using estrogen with or without a progestin after menopause does not protect postmenopausal women (ages 50 and older) from heart disease and may even increase their risk. In 2002, WHI scientists reported that using estrogen plus progestin actually elevates some women's chance of developing heart disease, stroke, blood clots, and breast cancer. But they also found health benefits—not as many hip fractures and fewer cases of colorectal cancer. In 2004, the same scientists reported that using estrogen alone

increased a woman's risk of stroke and blood clots, but protected women from hip fractures.

Some studies suggest that estrogen may protect against Alzheimer's disease, but this has not yet been proven. In fact, in 2003, researchers in a WHI substudy, the WHI Memory Study (WHIMS) reported that women age 65 and older taking a combination of estrogen plus progestin were at twice the risk of developing dementia as women not taking any hormones. Again in 2004, these WHIMS scientists reported that using estrogen alone could increase the risk of developing dementia in women age 65 and older compared to women not taking any hormones.

As a result of these studies, experts have concluded that the health risks of using menopausal hormone therapy may be greater than the health benefits. These risks may differ between women who have menopausal symptoms and those who don't. Nevertheless, the FDA has stated that women who want to use menopausal hormone therapy to control the symptoms of menopause should do so at the lowest effective dose for the shortest time needed.

But the question of these greater risks is still an important public health issue. Even small increases, when millions of women are using menopausal hormone therapy, could mean many more cases of heart disease, stroke, blood clots, and breast cancer.

So the decision whether to take estrogen is now far more complex and difficult than ever before. Questions about menopausal hormone therapy remain: Would using a different estrogen and/or progestin or another dose change the risks? Would the results be different if the hormones were given as a patch or cream, rather than a pill? Would taking the progestin less often be as effective and safe? Does starting menopausal

hormone therapy around the time of menopause compared to beginning years later change the risks? Can we predict which women will benefit or be harmed by using menopausal hormone therapy? As answers to these and other questions are found, women and their doctors should frequently review the pros and cons of menopausal hormone therapy in order to make an informed choice based on a realistic assessment of personal risks and benefits.

Many Questions, Few Answers

The NIA sponsors research that will reveal more about the risks and benefits of hormone therapies and supplements. One goal is to determine whether DHEA, melatonin, and other hormonal supplements improve the health of older people, have no effect, or are actually harmful.

It is important to remember that these studies may not yield immediate or final answers, especially in the cases of DHEA, melatonin, and hGH, since research on these supplements is fairly new. Some of these studies, for example, may simply provide researchers with more information about what kinds of questions they should ask in their next studies. Research is a step-by-step process, and larger studies may be needed to give more definitive answers.

Until more is known about DHEA, melatonin, and hGH, consumers should view them with a good deal of caution and doubt. Despite what advertisements or stories in the media may claim, hormone supplements have not been proven to prevent aging. Some harmful side effects already have been discovered and additional research may uncover others.

More is known about estrogen, progesterone, and testosterone, and people with genuine deficiencies of these hormones should consult with their doctors about supplements. Meanwhile, people who choose to take any hormone supplement without a doctor's supervision should be aware that these supplements appear to have few clear-cut benefits for healthy individuals, and no proven influence on the aging process.



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