

science meets DHEA

DHEA AS A CURE FOR OBESITY, CANCER AND AGING? PERHAPS NOT. BUT THE FIRST LARGE-SCALE DHEA TRIALS SUGGEST THAT IT CAN HELP THOSE WITH LUPUS.

By William Wells

It all started with a viral infection. It seemed to be nothing really, just a persistent, beginning-of-winter annoyance. But by Christmas 1995, Kathleen Whitehurst knew it was something more than the common cold. "It was almost like someone had hit me with a baseball bat," she says, "but on every joint."

She was so exhausted that she could either shower or dry her hair, but not both. And the inflammation in her joints just got worse. "I was so crippled," she says, "that I couldn't open a refrigerator door, brush my teeth, or pick up a glass of water."

What began as a mild infection ended up as systemic lupus erythematosus (SLE), a largely mysterious auto-immune disease. Though lupus often begins with an infection of some kind, and the genes we inherit from our parents weigh in to some extent, the real cause of SLE is unknown.

What is known is that the immune system becomes over-enthusiastic, and starts to attack what it is supposed to defend. "The immune system is meant to produce a certain amount of antibodies," says Ronald van Vollenhoven, MD, an assistant professor of medicine and clinical chief of rheumatology. "In some instances the immune system goes overboard and produces antibodies that attack the wrong target." Initially lupus usually attacks connective tissue in the joints, but in its more serious form lupus can progress to organs such as the lungs, heart and liver.

In a series of clinical trials over the last few years, van Vollenhoven has been testing the natural hormone dehydroepiandrosterone (DHEA) on his patients, in an attempt to relieve their symptoms and reduce their reliance on corticosteroids.

DHEA — what some call "the mother hormone," because other hormones are made from it — comes with its fair share of hype, but van Vollenhoven is not looking at it as a wonder drug for lupus. Other treatments will remain in use, including the corticosteroid prednisone, immunosuppressants, and the anti-malarial drug plaquenil. These drugs have helped boost the five-year survival rate from 50 percent to a level almost indistinguishable from the

general population.

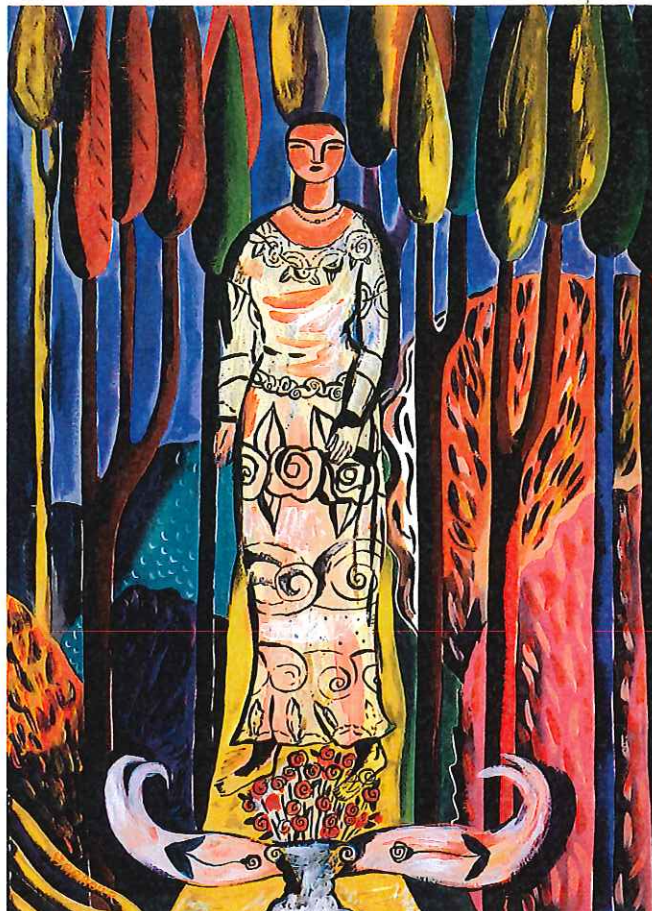
But there is a catch. "What is a real concern," says van Vollenhoven, "is that after 15 to 20 years, these patients have serious complications, mostly from the treatments."

Prednisone is a particularly serious culprit. It is the only drug that will rapidly reverse a lupus flare involving internal organs. But in the short term it causes weight gain, a bloated "moon" face and acne, and in the long term the worries include weak bones (osteoporosis), weak muscles, cataracts, high blood pressure and diabetes.

Thus, in an early trial at Stanford and in a later, multicenter trial including 200 patients, van Vollenhoven wanted to see if DHEA treatment allowed patients to cut down on their prednisone treatment. "The preliminary result," he says, "is that the DHEA patients could lower their prednisone much more successfully, provided their lupus was active at the start of the trial." (Patients whose lupus was mild at the beginning of the trial succeeded in lowering their prednisone dose whether or not they received DHEA.)

Promising results lead to more studies. Patient Whitehurst took part in the second multicenter trial, which was designed to gauge whether DHEA treatment leads to an improvement in lupus symptoms. The trial is nearing completion, but van Vollenhoven does not yet know all the results.

He has also coordinated smaller trials at Stanford to investigate whether the benefits of DHEA therapy continue to accrue with longer treatments (they do), if DHEA helps prevent the osteoporosis triggered by prednisone (not yet clear), and if patients with the severest forms of lupus benefit from



DHEA (they do, but to a lesser extent).

The decision to try DHEA for lupus was far from random, says van Vollenhoven. Lupus patients have abnormally low levels of DHEA. Also, DHEA looks promising in a mouse model of lupus. Additionally, since lupus is primarily a female disease, and since DHEA is counted as a male hormone (although both sexes make it to some degree), researchers suspect that DHEA may make the immune system behave in a less female manner and so become more resistant to lupus.

Work by Edgar Engleman, MD, professor of pathology, provided the final clue. In 1991, he showed that DHEA causes T cells, one arm of the immune system, to produce more of a particular signaling molecule called IL-2. This and other results suggest that DHEA could bias the immune system toward the destruction of infected and defective cells and away from the antibody production

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that is overactive in lupus.

Does this mean that books making claims about the broad healing powers of DHEA, such as "The Hormone from Heaven" and "Bountiful Health, Boundless Energy, Brilliant Youth: The Facts about DHEA," were right all along? Van Vollenhoven is skeptical. The lupus trials are the first large-scale controlled trials of DHEA, he says. The few trials for DHEA-treatment of other conditions (diabetes, AIDS, cancer, obesity and aging) have been either small, poorly designed, uncontrolled, unencouraging, or all four, he adds. Still, some claims, such as those for depression and osteoporosis, may prove correct.

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feres with most physical fitness and exercise programs — just one more reason to QUIT.

When the above preventive measures fail, modern urogynecologists can cure or help more than 90 percent of stress urinary incontinence patients with surgery or a

In the meantime, DHEA is available on U.S. supermarket shelves as a result of legislation decreasing the power of the Food and Drug Administration (FDA) to regulate anything deemed a dietary supplement. "You can make something in your backyard and call it vitamin X," says van Vollenhoven. "You are not allowed to make specific health claims, but a lot of the advertising is stepping over the line."

The Web site for a DHEA preparation called "Invigorate", for example, states that "This is the youth hormone!" One of the studies used to support the proposed anti-aging properties, says van Vollenhoven, showed only that mice with lupus survive longer when treated with DHEA. "The anti-aging claim is one that people have heard so many times that they start believing it," he says. "It's really far out in left field."

medical regimen.

After stress urinary incontinence, the next most common cause of incontinence is "bladder spasms," or nervous imbalance of the bladder control mechanism. Avoidance of the intake of agents that produce bladder irritation — such as coffee, tea, cola soft drinks and hard liquor — helps people with this condition. Bladder-training exercises and biofeedback may also help. For more

Van Vollenhoven recommends lupus patients who seek DHEA obtain the drug by participating in a clinical trial. Failing that, since some of the commercial brands are unreliable, the next best solution is to get DHEA from a pharmacy that compounds the drug itself.

Kathleen Whitehurst is feeling much better these days, and she is back at work in her gift shop in time for Christmas. Lupus is a notoriously unpredictable disease, a roller coaster of flares and calm periods. So she is unsure about DHEA's benefits, especially given that she still doesn't know if she was taking sugar pills throughout the trial. The test of her resolve came recently, when her participation in the trial concluded. When given the chance to go on taking what was now guaranteed to be DHEA, she said yes. *sm*

severe cases, the many antispasmodic agents available are often effective.

In summary, this disabling, humiliating condition can almost always be improved or cured with good health practices or, when necessary, medical intervention.

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