



A Vitamin at the Core of WOMEN'S HEALTH

Vitamin D and New World primates from the Los Angeles Zoo may hold the key to understanding the molecular basis of some women's cancers and osteoporosis.

BY IDELLE DAVIDSON

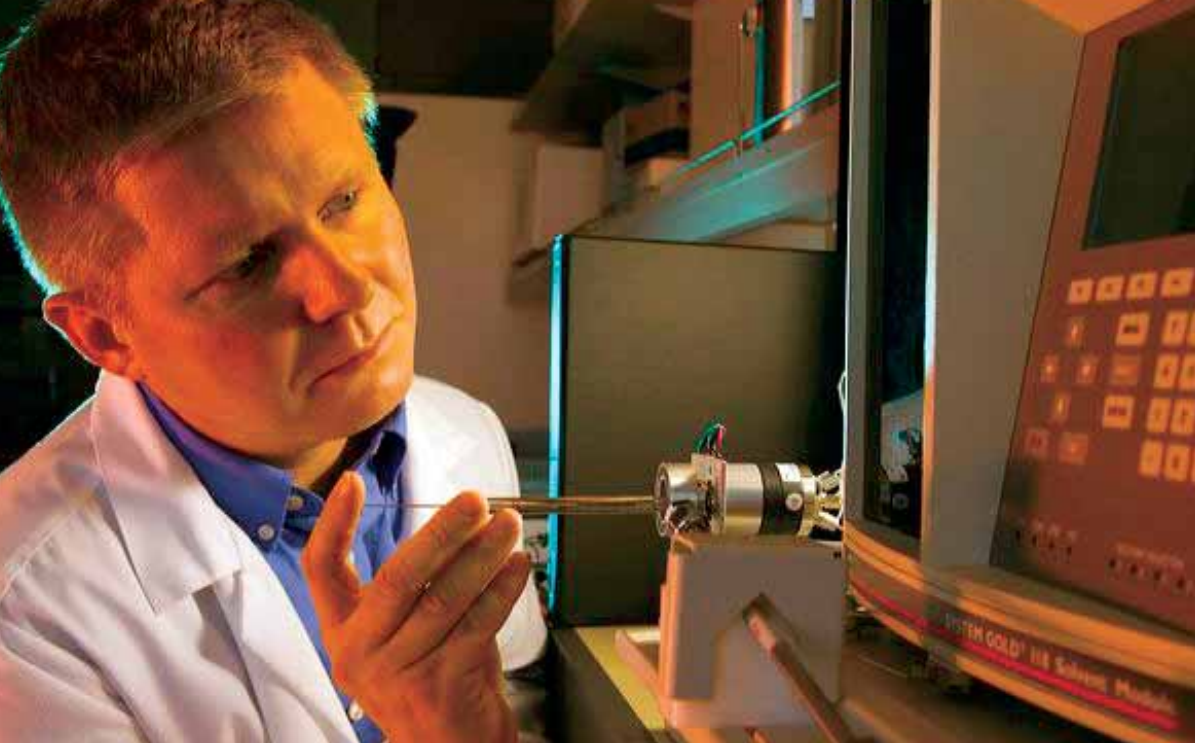
John S. Adams, M.D., still remembers the year. It was 1985, and the chief veterinarian at the Los Angeles Zoo needed his help. The zoo's colony of New World primates had developed rickets. They were dying prematurely, before they could mate and produce offspring. The endocrinologist and his team found that these fierce little monkeys from the Amazon rain forest were resistant to vitamin D as well as other steroid hormones, including estrogen. The question was, why.

Adams studied blood and urine samples and biopsied skin cells from both New and Old World monkeys. He discovered that the New World monkeys were overproducing a family of proteins in their cells. Those proteins were blocking the animals' ability to stimulate the genes that respond to vitamin D and estrogen.

For Dr. Adams, this was a watershed moment. Because these genes are key to good hormonal balance and normal skeletal growth, this was an unexpected opportunity to advance research in women's cancers and bone disease.

"The idea was to figure out how to manipulate the expression of these proteins in normal cells. We knew that if we could do that, we might be able to

John Adams, M.D., with the Los Angeles Zoo's cotton-top tamarins



Martin Hewison, Ph.D. analyzes vitamin D metabolism in different human tissues and diseases using high-performance liquid chromatography equipment.

do two things: either counteract the actions of estrogen, a hormone that's harmful in the case of breast cancer, or amplify the actions of estrogen and vitamin D, which in the case of osteoporosis is beneficial to the prevention of bone loss," he says.

The potential, if Dr. Adams and his team succeed in regulating the protein inside human cells, is considerable: It will be a major step toward new treatments for estrogen-responsive cancers like those of the breast and lining of the uterus. Adams, the director of the Division of Endocrinology, Diabetes and Metabolism at Cedars-Sinai, as well as director of the Bone Center and holder of the Alfred Jay Firestein Chair in Endocrinology, Diabetes, and Metabolism, says that results are about six to seven years off. "We're getting closer," he says.

Today, sitting in his office, Adams speaks of the need to involve more young people in clinical research. Five years back, he co-founded an ongoing semester-long

program at Long Beach Polytechnic High School to involve minorities and women in clinical research. Each student partners with a scientist at Cedars-Sinai or Harbor-UCLA Medical Center. He convinced the National Institutes of Health to fund it. "Every single one of them has gone on to a university," says Adams, beaming. "Most have continued to do some kind of research."

THE VITAL VITAMIN

Dr. Adams continues to work in endocrinology, the field he loves, focusing on the untapped potential of vitamin D. Vitamin D has the distinction of being both a vitamin and a hormone. We assimilate it from our diet in fortified milk, salmon, sardines, and other foods. It is also manufactured in our skin from exposure to sunlight. Vitamin D plays a crucial role in the body. In its active form, it becomes the steroid hormone known as calcitriol, which helps maintain blood calcium levels. Vitamin D pro-

motes normal cell growth. It is also a potent regulator of the immune system. It may even play a large part in cancer prevention, especially leukemia and breast, colon, and skin cancers.

But what causes vitamin D to shift into its active state and become calcitriol? This is the question that captivates Martin Hewison, Ph.D., a molecular endocrinologist who relocated from the United Kingdom last year to work with Dr. Adams at Cedars-Sinai. His research focuses on understanding the role of an enzyme called 1alpha-hydroxylase, which shifts vitamin D from inactive to active. (Adams was the first scientist to describe the existence of that enzyme in immune cells.)

"This quite important" says Dr. Hewison. "If you have good access to vitamin D, through sunlight for example, or from your diet, then your body can more readily generate active vitamin D. And when certain white blood cells, called macrophages, are exposed to active vitamin D they can destroy bacteria."

"VITAMIN D IS NOT ONLY IMPORTANT TO BONE HEALTH; IT IS ALSO IMPORTANT TO YOUR IMMUNE SYSTEM. IT GETS RID OF CERTAIN INVADERS, SUCH AS BACTERIA OR CANCER CELLS."

INVADERS REPELLED

This new knowledge is profoundly relevant in the Third World. There, some two million people will die next year of tuberculosis, a bacterial disease that affects the lungs.

In a recent article in the prestigious journal *Science*, Drs. Adams, Hewison, and colleagues from other institutions identified a cellular mechanism that helps explain why people of African descent are more susceptible to TB. "The dose of ultraviolet radiation needed for the skin to produce vitamin D is 10 times higher in black subjects than in white subjects," says Hewison. The study of vitamin D has potential for people throughout the world, says Adams. He believes it is possible for the body to fight cancer cells the way it fights the bacteria that cause TB. "If your vitamin D level is insufficient, your body's ability to kill a cancer cell is lessened," says Adams. "Vitamin D is not only important to bone health; it is also important to your immune system. It gets rid of certain invaders, such as bacteria or cancer cells."

GOOD TO THE BONE

Like many of his colleagues at Cedars-Sinai, Dr. Adams is not only a research scientist but also a clinician. Most of his patients have osteoporosis, a disease of low bone mass that can lead to fractures. Osteoporosis affects

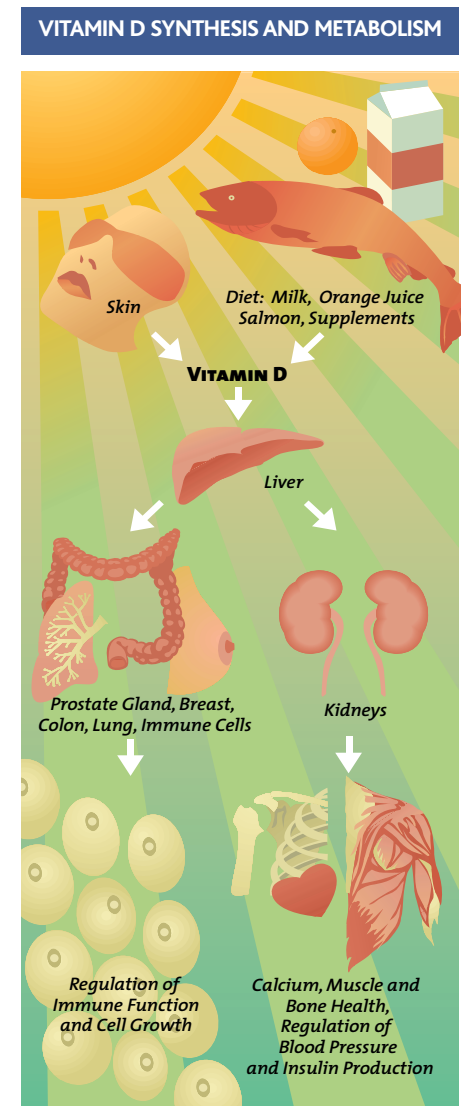
some 10 million Americans, eight million of whom are women. Women are four times more likely

than men to develop the disease. Since estrogen helps protect against bone loss, women are at higher risk once they hit menopause and their ovaries stop producing the hormone. Other risk factors include heredity and body weight.

Adams reduces this to basics: Women who don't get enough vitamin D—and there are probably millions of them worldwide—are unable to absorb adequate amounts of ingested calcium to strengthen their bones.

Certain populations are more susceptible to osteoporosis than others: Men and women of Jewish Ashkenazi descent and those from the Korean Peninsula are genetically predisposed to the disease. Isolating the still-unknown genes that account for this predisposition is another focus of Dr. Adams's research.

When Dr. Adams speaks of his major advances, he remembers that fortuitous call from the Los Angeles Zoo. Today, should he visit any large zoo in elevated northern or southern latitudes in the Americas or Europe, he'll likely see a direct result of his work: sunlamps installed in New World primate exhibits. "We treated these animals with artificial sunlight and cured their disease," says Adams. "When you can take experiments in nature and relate them to normal or abnormal human physiology, that is a pretty good feeling."



25-hydroxyvitamin D is produced in the liver from other forms of vitamin D found either in the diet or made in the skin after exposure to sunlight. 25-hydroxyvitamin D is then converted to its active form 1,25-dihydroxyvitamin D which is functionally similar to a hormone. 1,25-dihydroxyvitamin D is produced in many tissues but the most well-characterized is the kidney.