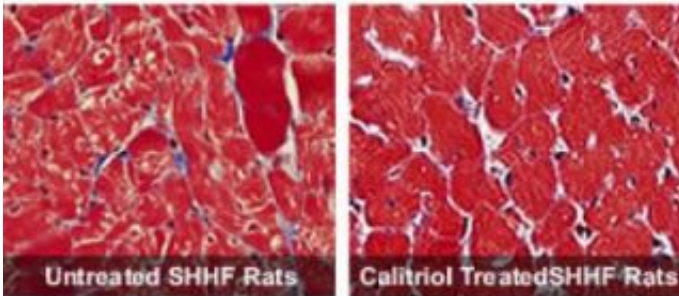


# Vitamin D: New way to treat heart failure?

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Heart muscle cells in untreated rats bred to develop heart failure show signs of disease. Right: Heart muscle cells remain healthy in rats treated with calcitriol, the hormone that Vitamin D becomes in the body. Credit: University of Michigan

Strong bones, a healthy immune system, protection against some types of cancer: Recent studies suggest there's yet another item for the expanding list of vitamin D benefits. Vitamin D, "the sunshine vitamin," keeps the heart, the body's long-distance runner, fit for life's demands.

University of Michigan pharmacologist Robert U. Simpson, Ph.D., thinks it's apt to call vitamin D "the heart tranquilizer."

In studies in rats, Simpson and his team report the first concrete evidence that treatment with activated vitamin D can protect against heart failure. Their results appear online ahead of print in the *Journal of Cardiovascular Pharmacology*.

In the study, treatments with activated vitamin D prevented heart muscle cells from growing bigger – the condition, called hypertrophy, in which the heart becomes enlarged and overworked in people with heart failure. The treatments prevented heart muscle cells from the over-stimulation and increased contractions associated with the progression of heart failure.

About 5.3 million Americans have heart failure, a progressive, disabling condition in which the heart becomes enlarged as it is forced to work harder and harder, making it a challenge even to perform normal daily activities. Many people with heart disease or poorly controlled high blood pressure go on to experience a form of heart failure called congestive heart failure, in which the heart's inability to pump blood around the body causes weakness and fluid build-up in lungs and limbs. Many people with heart failure, who tend to be older, have been found to be deficient in vitamin D.

"Heart failure will progress despite the best medications," says Simpson, a professor of pharmacology at the U-M Medical School. "We think vitamin D retards that progression and protects the heart."

The U-M researchers wanted to show whether a form of vitamin D could have beneficial effects on hearts that have developed or are at risk of developing heart failure. They used a breed of laboratory rats predisposed to develop human-like heart failure.

The researchers measured the effects of activated vitamin D (1,25 dihydroxyvitamin D<sub>3</sub>, a form called calcitriol) in rats given a normal diet or a high-salt diet, compared to control group rats given either of the same two diets, but no vitamin D treatment. The rats on the high-salt diet were likely to develop heart failure within months.

The rats on the high-salt diet, comparable to the fast food that many

humans feast on, quickly revealed the difference vitamin D could make.

"From these animals, we have obtained exciting and very important results," Simpson says.

After 13 weeks, the researchers found that the heart failure-prone rats on the high-salt diet that were given the calcitriol treatment had significantly lower levels of several key indicators of heart failure than the untreated high-salt diet rats in the study. The treated rats had lower heart weight. Also, the left ventricles of the treated rats' hearts were smaller and their hearts worked less for each beat while blood pressure was maintained, indicating that their heart function did not deteriorate as it did in the untreated rats. Decreased heart weight, meaning that enlargement was not occurring, also showed up in the treated rats fed a normal diet, compared to their untreated counterparts.

Simpson and his colleagues have explored vitamin D's effects on heart muscle and the cardiovascular system for more than 20 years. In 1987, when Simpson showed the link between vitamin D and heart health, the idea seemed far-fetched and research funding was scarce. Now, a number of studies worldwide attest to the vitamin D-heart health link (see citations below).

The new heart insights add to the growing awareness that widespread vitamin D deficiency—thought to affect one-third to one-half of U.S. adults middle-aged and older—may be putting people at greater risk of many common diseases. Pharmaceutical companies are developing anti-cancer drugs using vitamin D analogs, which are synthetic compounds that produce vitamin D's effects. There's also increasing interest in using vitamin D or its analogs to treat autoimmune disorders.

In more than a dozen types of tissues and cells in the body, activated vitamin D acts as a powerful hormone, regulating expression of essential

genes and rapidly activating already expressed enzymes and proteins. In the heart, Simpson's team has revealed precisely how activated vitamin D connects with specific vitamin D receptors and produces its calming, protective effects. Those results appeared in the February issue of *Endocrinology*.

Sunlight causes the skin to make activated vitamin D. People also get vitamin D from certain foods and vitamin D supplements. Taking vitamin D supplements and for many people, getting sun exposure in safe ways, are certainly good options for people who want to keep their hearts healthy. But people with heart failure or at risk of heart failure will likely need a drug made of a compound or analog of vitamin D that will more powerfully produce vitamin D's effects in the heart if they are to see improvement in their symptoms, Simpson says.

Vitamin D analogs already are on the market for some conditions. One present drawback of these compounds is that they tend to increase blood calcium to undesirable levels. Simpson's lab is conducting studies of a specific analog which may be less toxic, so efforts to develop a vitamin D-based drug to treat heart failure are moving a step closer to initial trials in people.

Source: University of Michigan

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