

Here comes the sun: How vitamin D relaxes blood vessels

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The sun in the mountains allows the body to produce vitamin D in winter. Credit: Heike Hochhauser/Vetmeduni Vienna

It's not just your mood that the dark months of winter can influence. Low levels of sunlight also mean lower levels of vitamin D in the body. Vitamin D deficiency can trigger a range of diseases but until recently little was known about the exact biological mechanisms behind this. A research team at the University of Veterinary Medicine, Vienna has now decrypted one of these unknown molecular mechanisms. Vitamin D regulates the elasticity of blood vessels and thus also affects blood



pressure amplitude. The results were published earlier this year in the journal *Molecular Endocrinology*.

UV-B radiation in sunlight is the most important factor for the production of vitamin D, and that is why many people suffer from low levels of vitamin D during the winter months. Although certain foods do contain vitamin D, it is not usually possible to get an adequate supply of the vitamin from food. Many clinical studies have indicated that low vitamin D levels are related to cardiovascular disease such as <u>high blood</u> pressure, but also other diseases such as diabetes mellitus, autoimmune diseases and even cancer. However, the underlying <u>molecular</u> <u>mechanisms</u> were unclear.

Vitamin D deficiency leads to stiffening of the blood vessels

The two primary authors, molecular biologist Olena Andrukhova and medical doctor Svetlana Slavic, of the Institute of Physiology, Pathophysiology and Biophysics at the Vetmeduni Vienna, found that prolonged vitamin D deficiency can stiffen <u>blood vessels</u>. Examining the aorta, an elastic blood vessel that expands with each pulse of blood and then constricts again, the researchers showed that vitamin D deficiency makes the vessel less flexible. Andrukhova explains in detail: "Vitamin D enhances the production of the enzyme eNOS (endothelial nitric oxide synthase) in the inner layer of blood vessels, the endothelium. This is critical for the regulation of blood pressure. The enzyme produces a molecule called nitric oxide (NO), an important factor for the relaxation of smooth muscles in the blood vessels. When too little NO is formed, the vessels become less flexible. This ultimately leads to higher blood pressure which can give rise to other circulatory diseases. So indirectly, vitamin D controls blood pressure."



Co-author Slavic continues: "Stiffness of the blood vessels generally increases with age. Blood pressure amplitude thus tends to increase with age and leads to structural changes in the aorta. Elasticity deteriorates, and prolonged vitamin D deficiency can accelerate this process."

Simulation of vitamin D deficiency in mice

The scientists worked with genetically modified mice to explore the details of the mechanism. The vitamin D receptors in the animals were changed so that no vitamin D signalling was possible. Vitamin D also regulates the body's calcium and phosphate balance, so the rodents were given a special diet to ensure that they had enough calcium and phosphorus. The lack of vitamin D was therefore the only deficiency that could have affected the physiology of the animals.

After about a year without vitamin D signalling, the mice had increased blood pressure amplitude. The researchers conducted a series of studies on various tissues from the animals. To understand what lies behind the increased blood pressure amplitude, they focused particularly on the aorta and found decreased expression of eNOS, increased deposition of collagen and fewer elastic fibres. Over time, the blood vessels had become more rigid and less able to adapt flexibly to the volume of blood streaming through them. The consequence was increased blood pressure amplitude and changes in cardiac structure and function. In future studies, the researchers want to examine whether vitamin D affects different cell types in blood vessels in different ways.

Refuelling light for the heart and the circulation

In Europe, it has often been considered to enrich certain foods with vitamin D, as is customary in the United States, for example. However, an external source of vitamin D also carries risks since any excess



vitamin D cannot be excreted by the body. When used at very high doses it can lead to calcium deposits in blood vessels, kidneys, lungs and the heart. However, a lack of vitamin D can also have dramatic consequences. Institute board Professor Reinhold Erben states: "It is not that vitamin D deficiency will lead immediately to an increase in blood pressure amplitude or <u>blood pressure</u>, but over the long term it can lead to cardiovascular damage. Vitamin D is the chemical translation of the sun in our bodies and we should stock up on a regular basis, especially in winter. We have to remember that in Central Europe, vitamin D synthesis in the skin is physically impossible from November to February at sea level. Levels of UV-B radiation are just too low. The alternatives are vitamin D supplements or a stay in the mountains."

More information: "Vitamin D Is a Regulator of Endothelial Nitric Oxide Synthase and Arterial Stiffness in Mice." Olena Andrukhova, Svetlana Slavic, Ute Zeitz, Sabine C. Riesen, Monika S. Heppelmann, Tamas D. Ambrisko, Mato Markovic, Wolfgang M. Kuebler, and Reinhold G. Erben. *Molecular Endocrinology* 2014 28:1, 53-64. DOI: dx.doi.org/10.1210/me.2013-1252

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