Current Aspects of the Significance of Vitamin D

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Although vitamin D has up to now played an important role in skeletal development, Rickets prophylaxis and calcium homoeostasis, recent molecular pharmacological findings and human pharmacological discoveries have resulted in consideration of its use for other forms of prophylaxis and therapy, e.g. in cardiovascular diseases, Diabetes mellitus and cancer prevention.

In chemical terms, vitamin D consists of a steroid structure with an open ring. It occurs as the provitamin ergosterol in plants and as 7-Dehydrocholesterol in animal fats, fish and cod liver oil. Only small quantities of vitamin D are taken in in the food, but mostly through the skin in the form of UV-B radiation (280-310 nm), with the previtamin D_3 being formed from 7-Dehydrocholesterol. This is converted by isomerisation into vitamin D_3, from which after hydroxylation by liver microsomes, 25-hydroxyvitamin D is produced, which is bound to a degree of > 99% to vitamin D-binding proteins (DMP), to a lower level to albumin and lipoic proteins, then undergoes glomerular filtration, is reabsorbed in the proximal tubule by endocytosis and converted through 1(?- im Ausgangstext nicht lesbar, d. Ü.)-hydroxylase into biologically active 1.25-OH_2 D_3 with high receptor affinity. Renal 1(?- im Ausgangstext nicht lesbar, d.Ü.)-hydroxylase is important for maintaining calcium homoeostasis, whereby 1.25 $(OH)_2$ D_3 plasma concentrations reflect the calcium balance and kidney function, and less the vitamin D status of the organism. Vitamin D deficiency is considered to be 25 (OH) D_3 plasma concentrations < 20 ng/ml, with levels of between 21-29 ng/ml, > 30 ng/ml and > 150 ng/ml being considered insufficient, sufficient and toxic respectively.

Risk factors and risk groups for vitamin D deficiency include, among others, the filtering of atmospheric UV-B radiation by smog and air pollution, north-south gradients, ethnic groups with dark pigmented skin, and clothing such as veils, headscarves or burkas, low UV-B exposure (staying indoors, residents of homes, autumn and winter), a high sun protection factor (factor 15 reduces 99% of cutaneous formation), obesity as a result of storage in fat depots, immobility, age (due to the reduction in cutaneous vitamin D production, the lower expression of vitamin D receptors, malnourishment and undernourishment, malabsorption), vegetarians, inflammatory bowel diseases, low socio economic status, liver and kidney diseases, medications such as anticonvulsants, glucocorticoids and anti-HIV substances.

The risks associated with low 25-(OH) D_3 concentrations include angina pectoris, fatal, non-fatal myocardial infarction, sudden death, heart failure, hypertrophy of the left ventricle, vascular smooth muscle cells, atherosclerosis, vascular and valvular calcification due to an increase in parathyroid hormone, stroke, peripheral artery oc-

clusive disease, hypertension due to increased RAAS, hypertriglyceridaemia, type II diabetes mellitus, metabolic syndrome, insulin resistance, secondary hyperparathyroidism with a 2-fold cardiovascular risk (PTH > 250 pg/ml).
With respect to the vitamin D effect, physiological, hormone-type effects for the regulation of the calcium metabolism are to be distinguished from pharmacological effects on receptors in the cytoplasm of various cells and tissues, e.g. renal tubules, intestinal epithelium, fibroblasts, keratinocytes, monocytes, macrophages, B-, T-lymphocytes, NK cells, cardiomyocytes, endothelial and smooth muscle cells, pancreas (?- im Ausgangstext nicht lesbar, d.Ü.) cells, osteoblasts, mammary gland, uterus, ovaries, testes, carcinoma such as mammary, colon, pancreas carcinoma, melanoma, osteosarcoma, fibrosarcomas, leukaemia with anti-proliferative activity, influences on cell differentiation and angiogenesis.

In molecular pharmacological terms, $1.25(OH)_2$ D_3 is a nuclear transcription factor which controls more than 200 gene functions and protein synthesis, and is also involved in the production of insulin, renin, the release of cytokines from lymphocytes and in the proliferation of smooth vascular muscle cells and cardiomyocytes. A 25-(OH) D_3 deficiency (< 20 ng/ml) is associated, inter alia, with reduced insulin secretion, insulin resistance, metabolic syndrome, cardiovascular diseases and stroke. 25-(OH) D_3 expresses insulin receptors, protects against diabetes mellitus, metabolic syndrome, improves endothelial function with vasodilation and lowers blood pressure.
Indication-related clinical intervention studies are required on the meaningful supplementation of vitamin D for the purposes of maintaining health.