

**Decalcit<sup>®</sup>**  
Geistlich

Current knowledge on  
supplementation with vitamin D,  
calcium and phosphate



## Summary

Calcium supplementation has long been recommended for the prevention of falls and associated non-vertebral fractures.

Recent studies suggest, however, that vitamin D could also play a more important role in the prevention of falls and fractures than was previously assumed. On the one hand, vitamin D maintains calcium homeostasis and thus bone mineral density, and thereby contributes to preventing fractures. On the other hand, vitamin D also seems to have a positive effect on the muscular strength in the legs, which in turn can reduce the risk of falls.

Besides calcium and vitamin D supplementation, a sufficient serum phosphate level should also be present to ensure sufficient bone mineral density.

Based on current knowledge, the combined administration of calcium, vitamin D and phosphate therefore appears beneficial in preventing falls and fractures in the elderly.

The term vitamin D as used below is understood to mean the vitamin D<sub>3</sub> form present in the human body.

# Phosphat

Vitamin D-Supplementation

Calcium-Supplementation



## In the leading roles: vitamin D and calcium

Vitamin D and calcium play an important role in the health and function of bone.

Calcium in the form of hydroxyl apatite ( $\text{Ca}_5(\text{PO}_4)_3(\text{OH})$ ) is a major constituent of mineral bone. In calcium deficiency, due for example to insufficient dietary supply, calcium can be released from bone. Demineralisation of this kind can impair bone stability and increase the risk of bone fractures. The consumption of calcium rich food such as milk or cheese or supplementation with calcium is therefore generally recommended for the prevention of bone fractures and osteoporosis.

Recent studies have shown that vitamin D plays a more important role in the health of bone than was previously assumed. Vitamin D together with parathormone regulates the calcium level in the blood. When there is a vitamin D deficiency in the blood, the absorption of calcium from the intestine and thus also the concentration of calcium in serum decreases. This in turn, due to the effect of parathormone, induces the release of calcium from bone, resulting in demineralisation of bone and potentially a higher risk of fractures.

Vitamin D also appears to have an important influence on muscular strength. For example, a correlation was found between high vitamin D levels in serum and improved leg function (Bischoff-Ferrari et al., 2004a, Pfeifer et al., 2004). In this way, vitamin D also contributes indirectly to preventing bone fractures: when there is sufficient muscular strength in the legs, the risk of falls and fractures decreases.

Besides maintaining the calcium balance, vitamin D influences the immune system and the metabolism and also appears to play a role in preventing cardiovascular disease (Cherniack et al., 2008).

## The sources of vitamin D

The body obtains vitamin D from sunlight on the skin and from food.

### 1. Sunlight

On exposure to sunlight, vitamin D is synthesised in the skin (Cherniack et al., 2008): UV light converts the precursor of vitamin D, 7-dehydrocholesterol, to provitamin D<sub>3</sub>, which is itself rapidly isomerised to cholecalciferol (vitamin D<sub>3</sub>). In the liver, cholecalciferol is hydroxylated to 25(OH)D<sub>3</sub> (25-hydroxy-cholecalciferol) and then in the kidney to 1,25(OH)<sub>2</sub>D<sub>3</sub> (calcitriol, 1,25-dihydroxycholecalciferol). Various other peripheral cells can also convert the 25(OH)D<sub>3</sub> to calcitriol. Calcitriol is the active form of vitamin D, which can bind directly to vitamin D receptors. It can therefore also be referred to as a hormone.

### 2. Food

The largest natural source of dietary vitamin D is high-fat fish such as salmon, sardines and mackerel. Smaller amounts of vitamin D are found in eggs, liver and meat (Lowdon 2008). Satisfying vitamin D requirements with the diet therefore tends to be difficult for most people.

UVB

25(OH)<sub>2</sub>-Vitamin D

1,25(OH)<sub>2</sub>-Vitamin D

Vitamin D

Provitamin D<sub>3</sub>

Vitamin D<sub>3</sub>

# Role of vitamin D in the calcium phosphate metabolism

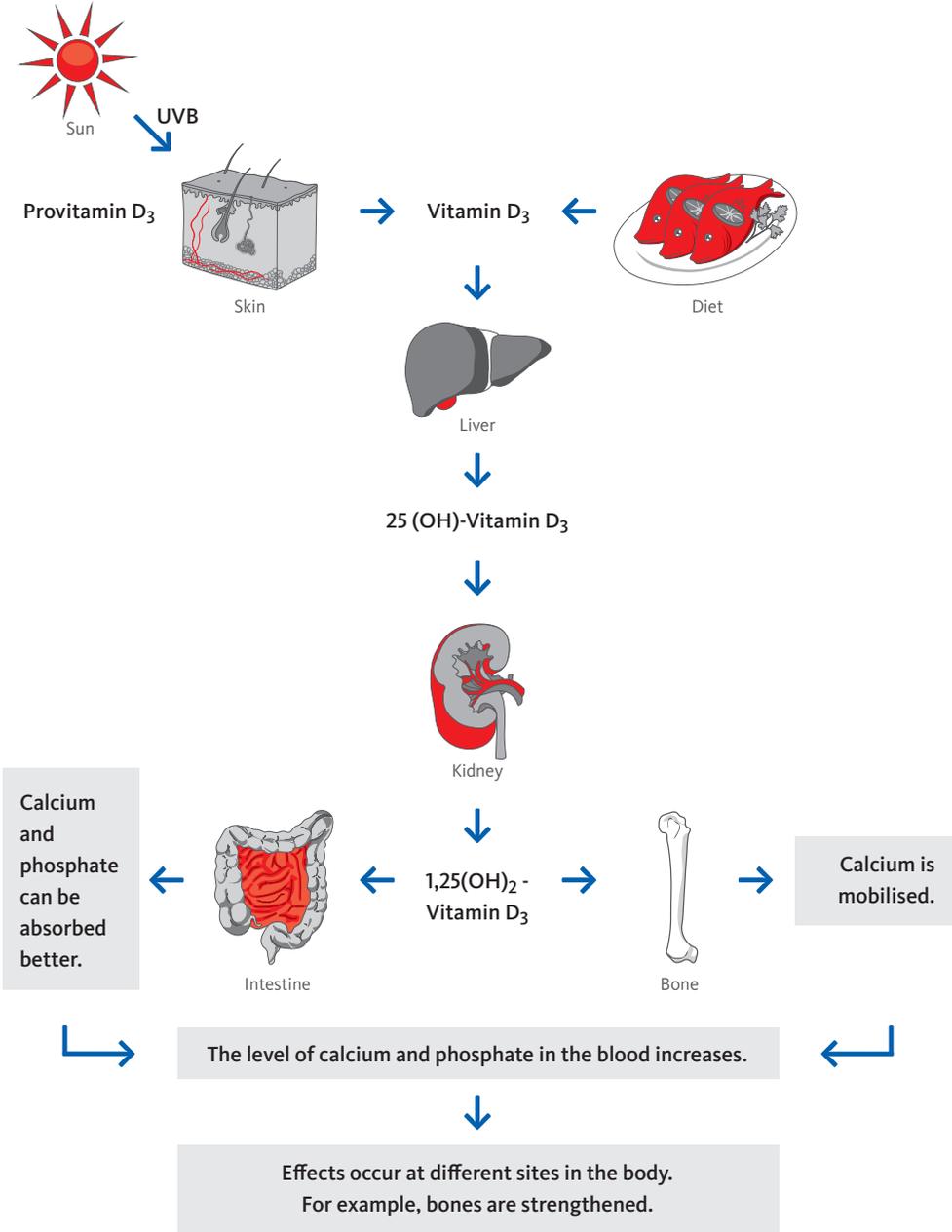


Figure 1: Vitamin D metabolism, from Cherniack et al., Geriatrics, 2008

## Sunshine is often not enough

Although vitamin D synthesis is stimulated by sunlight, vitamin D deficiency is widespread especially among the elderly, regardless of geographical location (Cherniack et al., 2008).

The quantity of vitamin D present in the body is determined by measuring the serum content of 25(OH) vitamin D<sub>3</sub>. A content of less than 30 - 32 ng/ml (75 - 80 nmol/l) is considered insufficient (Heaney, 2005). Studies have shown, however, that 40 - 90 % of elderly adults have a serum level of less than 30 ng/ml - even in sunny regions like South Florida (Chapuy et al., 1997, Levis et al., 2005).

### There are many reasons for the high prevalence of vitamin D hypovitaminoses:

#### > Insufficient sun exposure

In middle and northern Europe, the sun's radiation during the winter half-year is insufficient for vitamin D production in the skin (Bouillon 2001). In summer, the use of high sun protection factors can greatly reduce vitamin D synthesis (Matsuoka et al. 1987). In addition, many elderly people tend to avoid direct exposure to the sun completely.

#### > Dark skin pigmentation

Dark-skinned persons may require up to 6 times stronger UV insolation to stimulate vitamin D production (Clemens et al., 1982, Matsuoka et al. 1991).

#### > Age

Cutaneous vitamin D synthesis decreases with age (Holick, 1995). The skin then also contains a reduced amount of 7-dehydrocholesterol, the substrate for photoconversion to provitamin D (Holick et al. 1989, MacLaughlin and Holick, 1985).

#### > Overweight

Vitamin D is fat soluble. In persons with a high body fat content, vitamin D is withdrawn from the serum and stored in the fatty tissue. It is then no longer available to the body in sufficient amounts (Parikh et al., 2004).

#### > Atmospheric pollution

Heavy atmospheric pollution can absorb UV-B radiation to a significant extent (Bouillon, 2001, Scharla, 1998).

The sun's radiation may then no longer be sufficient for vitamin D synthesis.

## Vitamin D for bone density and muscular strength

Fractures resulting from falls among over-sixty-year-olds are unfortunately common. The risk of suffering a fracture in the remaining years of life, for example, is 44 - 65 % for women and 24 - 42% for men (Nguyen et al., 2007). The fracture risk is influenced firstly by the bone mineral density and secondly by the probability of suffering a fall. Muscular weakness is a significant risk factor for falls among the elderly (Moreland et al., 2004).

Vitamin D can be used in the prevention of falls and fractures. It has a direct influence on bone mineral density by maintaining calcium homeostasis, and also influences muscular strength in the lower extremities, as has been demonstrated by various studies:

- > Muscular weakness is a symptom of the clinical syndrome of vitamin D deficiency (Boland 1986, Glerup et al., 2000).
- > Human muscle tissue possesses specific receptors for 1,25-dihydroxyvitamin D3 (Boland et al., 1986), which decrease in number with age (Bischoff-Ferrari, 2004c).
- > In the elderly there is a positive association between the 25(OH) vitamin D3 serum level and the function of the lower extremities (Bischoff-Ferrari, 2004a).

### Fewer falls with vitamin D

Meta-analyses show that vitamin A can reduce the risk of falls by 22 % compared to calcium or placebo (Bischoff-Ferrari et al., 2004b). In a three-year study, the risk of falls was reduced by 46 % in over-65-year-old women when the study subjects received a combined dose of 700 IU

vitamin D and 500 mg calcium daily (Bischoff-Ferrari et al., 2006). In women with limited physical activity, the reduction in the risk of falls was even 65 %. In men, however, no effect was observed in this study.

### Fewer fractures with vitamin D

The daily intake of 700 - 800 IU vitamin D can reduce the relative risk of non-vertebral fractures by 23 % and the risk of hip fractures by 26 %, as shown by a meta-analysis (Bischoff-Ferrari et al., 2005). Significant efficacy in preventing fractures was observed in studies at a serum concentration of 74 - 75 nmol/l and above (see Figure 2) - a threshold which was only reached at a daily intake level of 600 - 800 IU vitamin D (Bischoff-Ferrari, 2007a, Bischoff-Ferrari, 2007b, Dawson-Hughes, 2005). The administration of only 400 IU vitamin D, however, is insufficient for fracture prevention.

Based on the research data, international experts therefore recommend a minimum daily dose of 800 - 1000 IU vitamin D (Dawson-Hughes et al., 2005).

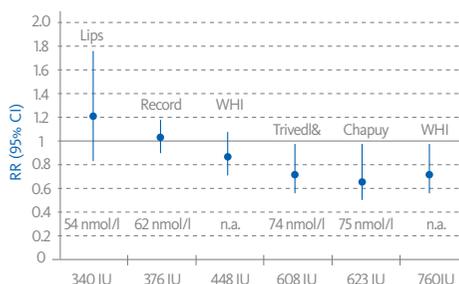


Figure 2: The threshold for prevention of fractures lies at a serum concentration of 74-75 nmol/l (Bischoff-Ferrari 2007b).

## Vitamin D plus calcium

Calcium supplementation is generally recommended to maintain bone mineral density in the elderly. Studies suggest, however, that calcium alone is less effective in preventing fall-related fractures than was previously assumed.

For example, in a meta-analysis calcium provided no reduction in the risk of hip fractures (Bischoff-Ferrari et al., 2007c). Surprisingly, the administration of calcium alone even appeared rather to increase the risk, for which calcium-induced phosphate deficiency may be responsible (see below).

Based on existing knowledge, the combined administration of calcium and vitamin D is beneficial in preventing falls and fractures (Bischoff-Ferrari et al., 2007c, Wolff et al., 2008).

## Ensure phosphate level in blood serum

The mineral portion of bone contains calcium and phosphate in a molar ratio of about 1.6 : 1. A sufficient phosphate level is therefore essential for the synthesis and mineralisation of bone.

Calcium is now usually administered in the form of carbonate or gluconate. Non-absorbed calcium, however, can interfere with phosphate absorption by forming complexes in the intestine (Heaney et al., 2002). Increasing calcium intake alone can therefore result in reduced phosphate uptake, which in turn negatively influences the bone mineral density. Additional phosphate supplementation can counteract this effect (see Figure 3).

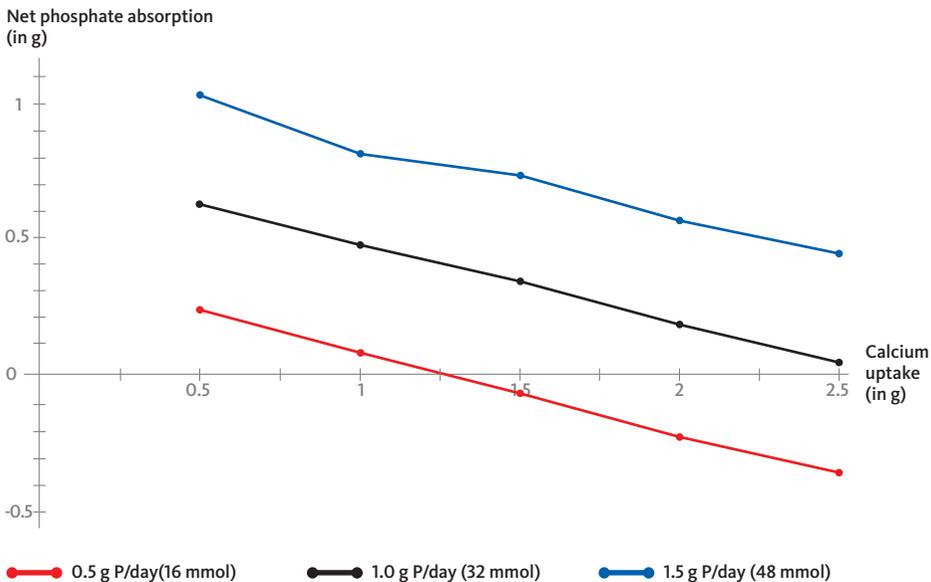


Figure 3: With increased calcium intake, phosphate uptake is inhibited. If only 0.5 g P is ingested daily with the diet, for example, the phosphate level even decreases when calcium intake exceeds 1.25 g. This effect can be counteracted by higher phosphate supplementation (from Heaney et al. 2002)

## Calcium + phosphate + vitamin D Decalcit®

A balanced diet and a healthy lifestyle can usually ensure a sufficient supply of all the necessary nutrients in healthy persons. Milk and cheese are natural sources of calcium and the sun stimulates vitamin D production in the skin. Nevertheless, calcium and vitamin D deficiency are widespread especially among the elderly.

Adequate calcium and phosphate levels in the blood are essential for a good bone mineral density, which in turn can reduce the risk of fractures. Vitamin D maintains the calcium and phosphate balance. It also appears to positively influence muscular strength in the legs, which can reduce the risk of falls. The daily intake of Decalcit® can additionally safeguard the supply of calcium, vitamin D and phosphate especially in the elderly.

Decalcit® from Geistlich contains vitamin D and calcium hydrogen phosphate. Vitamin D and calcium are suitable for the prevention of falls and fractures. Existing knowledge indicates that together with the sun, a glass of milk and a piece of cheese daily, Decalcit® is suitable for supplementation in the elderly.

### Summary:

1 chewable tablet contains:

Vitamin D<sub>3</sub> 500 IU, calcium hydrogen phosphate 480 mg, aspartame, flavouring agents, excipients

1 measuring spoon of powder (=1g) contains:

Vitamin D<sub>3</sub> 750 IU, calcium hydrogen phosphate 600 mg, sugar, glucose, excipients

### Note for diabetics

1 chewable tablet contains 306 mg Emdex, a maltodextrin with a high glucose content. One chewable tablet is equivalent to about 0.031 bread units.

1 g powder contains 0.193 g Saccharum pulvis and 0.189 g Glucosum anhydricum. 1 measuring spoon (=1g powder) is equivalent to about 0.021 bread units.



## Literature references

- > Bischoff-Ferrari H.A., Dietrich T., Orav E.J. et al. Higher 25-hydroxyvitamin D concentrations are associated with better lower-extremity function in both active and inactive persons aged > or = 60 y. *Am J Clin Nutr* 2004a; 80(3): 752 – 758.
- > Bischoff-Ferrari H.A., Dawson-Hughes B., Willett C.W. et al. Effect of Vitamin D on falls: a meta-analysis. *JAMA* 2004b; 293(18): 2257 – 2264. Review
- > Bischoff-Ferrari H.a., Borchers M., Gudat F., Durmuller U., Stahelin H.B., Dick W. Vitamin D Receptor expression in human muscle tissue decreases with age. *J. Bone Miner Res* 2004c; 19: 265 – 269.
- > Bischoff-Ferrari H.A., Willet W.C., Wong J.B., Giovannucci E., dietrich T., Dawson Huges B. Fracture prevention with vitamin D supplementation. A meta-analysis of randomized controlled trials. *JAMA* 2005; 293: 2257 – 2264.
- > Bischoff-Ferrari HA., Orav E.J., Dawson-Huges B. Effect of Cholecalciferol plus calcium on falling in ambulatory older men and women. A 3-year randomized controlled trial. *Arch Intern. Med* 2006; 166: 424 – 430.
- > Bischoff-Ferrari H.A. How to select the sodes of vitamin D in the management of osteoporosis. *Osteoporos Int* 2007a; 18: 401 – 407.
- > Bischoff-Ferrari H.A. The 25-hydroxyvitamin D threshold for better health. *J Steroid Biochem Mol Biol*.2007b; 103 (3-5): 614 – 619.
- > Bischoff-Ferrari H.A., Dawson Huges B., Baron H.A., Burckhardt P, Li R., et al.Calcium intake and hip fracture risk in men and women: a meta-analysis of prospective cohort studies and randomized controlled trials. *Am J Clin Nutr* 2007c; 86: 1780 – 1790.
- > Boland R. Role of Vitamin D in skeletal muscle function. *Endocrine Rev* 1986; 7: 434 – 447.
- > Bouillon R. Vitamin D: from photosynthesis metabolism, and action to clinical applications. In : DeGroot L.J., Jameson J.L. (eds). *Endocrinology*. Philadelphia: W.B. Saunders, 2001, 1009 – 1028.
- > Chapuy M.C.; Preziosi P., Maamer M. et al. Prevalence of vitamin D insufficiency in an adult normal population. *Osteoporos Int* 1997; 7(5): 439 – 443.
- > Cherniack E.P., Levis S., Troen B.R. Hypovitaminosis D: a stealthy epidemic that requires treatment. *Geriatrics* 2008; 64 (4): 24 – 30.
- > Clemens T.L., Adams J.S., Henderson S.L., Holick M.F. Increased skin pigment reduces the capacity of skin to synthesize vitamin D3. *Lancet* 1982; 1(8263): 74 – 76.
- > Dawson-Hughes B., Heaney R.P., Holick MF., Lips P., Meunier P.J., Vieth R. Estimates of optimal vitamin D status. *Osteoporos Int*. 2005; 16(7): 713 – 716.
- > Glerup H., Mikkelsen K, Poulsen L. et al. Hypovitaminosis D myopathy without biochemical signs of osteomalacic bone involvement. *Calcif Tissue Int* 2000; 66(6): 419 – 424.
- > Heaney R.P., Nordin B.E.C. Calcium effects on phosphorus absorption: Implications for the prevention and co-therapy of osteoporosis. *J Am Coll Nutr* 2002; 21(3): 239 – 244.
- > Heaney R.P. The vitamin D requirement in health and disease. *J Steroid Biochem Mol Biol* 2005; 97 (1-2): 13 – 19.
- > Holick M.F. Environmental factors that influence the cutaneous production of vitamin D. *Am J Clin Nutr* 1995; 61: 638S – 645S. (suppl)

- > Holick M.F., Matsuoka L.Y., Wortsman J. Age, vitamin D, and solar ultraviolet. *Lancet* 1989; 2(8671): 1104 – 1105.
- > Levis S., Gomez A., Jimenez C. et al. Vitamin D deficiency and seasonal variation in an adult South Florida population. *J Clin Endocrinol Metab* 200; 90(3): 1557 – 1562.
- > Lowdon J. Low vitamin D status: on the increase. *J Family Health Care* 2008; 18(2): 55 – 57.
- > Matsuoka L.Y., Ide L, Wortsman J, MacLaughlin JA, Holick MF. Sunscreens suppress cutaneous vitamin D3 synthesis. *J Clin Endocrinol Meta* 1987; 64 (6): 1165 – 1168.
- > Matsuoka L.Y., Wortsman J, Haddad .G., Kolm P, Hollis B.W. Racial pigmentation and the cutaneous synthesis of vitamin D. *Arch Dermatol* 1991; 127 (4): 536 – 538.
- > McLaughlin J., Holick M.F. Aging decreases the capacity of human skin to produce vitamin D3. *J Clin Invest* 1985; 76(4): 1536 – 1538.
- > Moreland J.D., Richardson J.A., Goldsmith CH, Clase C.M. Muscle weakness and falls in older adults: a systematic review and meta-analysis. *J Am Geriatr Soc* 2004; 52: 1121 – 1129.
- > Nguyen N.D., Ahlborg H.G., Center J.R., Eisman J.A., Nguyen T.V. Residual lifetime risk of fractures in woman and men. *J. Bone Miner Res* 2007; 22(6): 781 – 788.
- > Parikh S.J., Edelman M., Uwaifo G.I. et al. 2004; The relationship between obesity and serum 1,25-dihydroxy vitamin D concentrations in healthy adults. *J. Clin Endocrinol Metab* 89 (3): 1196 – 1199.
- > Pfeifer M., Dobnig H., Begerow B., Suppan K. Effects of vitamin D and calcium supplementation on falls and parameters of muscle function – a prospective, randomized, double-blind, multi-center study. *J Bone Miner Res* 2004; 19 (suppl 1): S. 58.
- > Scharla S.H. Prevalence of subclinical vitamin D deficiency in different European countries. *Osteoporosis International* 1998; 8(Suppl 2): S. 7 – S. 12.
- > Wolff A.E., Jones A.N., Hansen K.E. Vitamin D and musculoskeletal health. *Nat Clin Pract Rheumatol* 2008, 4(11): 580 – 588.

31367.1/0909/e

**Geistlich**  
Pharma

Geistlich Pharma AG  
Business Unit Medical  
Bahnhofstrasse 40  
CH-6110 Wolhusen

Phone +41 41 492 56 25  
Fax +41 41 492 67 14  
decalcit@geistlich.ch  
www.geistlich.de