CALCIUM AND VITAMIN D:
ROLE IN TREATMENT & PREVENTION OF OSTEOPOROSIS

Osteoporosis: Excessive Bone Resorption with Inadequate Bone Formation

Osteoporosis is a common disorder that results from lowered bone mineral density and bony tissue deterioration (Christodoulou & Cooper 2003, p.133), due to excessive bone resorption with inadequate bone formation (Raisz 2005, p.3318). This manifests as skeletal fragility, commonly of the femur and wrist (Raisz 2005, p.3318). Lifestyle may also affect bone strength increasing the risk of osteoporosis (Christodoulou & Cooper 2003, p.135). However, bone metabolism is a complex mechanism involving various factors such as adipocytes (Nishimura et al 2007) and hormones such as estrogens (Urano 2005), so that treatment of bone density imbalances such as osteoporosis is therefore also quite complex.

Despite this however, the notion that osteoporosis is due primarily to calcium deficiency, especially in the elderly, was initially put forward to replace the estrogen deficiency theory (Raisz 2005, p.3318). Calcium has therefore long been associated with the prevention of osteoporosis with many clinical trials focusing on calcium supplementation to demonstrate its effect on minimising bone loss and reducing the risk of bone fractures (Feskanich et al 2003, p.504).

Treatment incorporating vitamin D, however, shows once again that the complex nature of bone loss or fracture risk involves more than mere supplementation with calcium alone (Feskanich et al 2003, p.504). Studies are demonstrating that, at the very least, vitamin D is an important factor in calcium homeostasis, and thus useful in the treatment, and particularly the prevention, of osteoporosis (Feskanich et al 2003, p.504). Both calcium and vitamin D are therefore discussed here in relation to their use in the treatment and prevention of osteoporosis, which includes their dietary sources, recommended daily intake (**RDI**), therapeutic doses and issues around sunlight exposure.

Calcium: Needs Vary Throughout Life

The amount of calcium needed in order to maintain healthy teeth and bones fluctuates throughout our life (Department of Health and Ageing 2006, p.155-6). For example, babies from 7-12 months of age require about 270mg per day if breastfed, and 350mg per day if bottle-fed (Department of Health and Ageing 2006, p.157). The RDI for children aged 1-3 years then rises to 500mg per day (Department of Health and Ageing 2006, p.157). Since magnesium improves the rate of retention of calcium, dairy food with their low magnesium content, should not be the sole source of calcium (Trickey 2003, p.192). Table 1 summarises the main sources of calcium suitable for maintaining healthy bone density with RDI and therapeutic doses.

Vitamin D: Limited Dietary Sources

Vitamin D is found in two forms: one is produced in the skin as cholecalciferol, or vitamin D3, and the other obtained through the diet as ergocalciferol, or vitamin D2 (Department of Health and Ageing 2006, p.129). Vitamin D2 is fat-soluble and used by the body in its biologically active form, namely 1,25-dihydroxy-vitamin D3 (**1,25-OH2-D**), also known as calcitriol (Department of Health and Ageing 2006, p.129). There are limited sources of dietary vitamin D that enable the human body to produce active 1,25-OH2-D, reflecting the importance of supplementation and/or exposure to sunlight (Department of Health and Ageing 2006, p.129). Table 2 summarises dietary sources, RDI, and therapeutic doses.

Source: Calcium	***Amount contained***	***RDI***	***Therapeutic dose/day (from 1 year of age +)***
Milk and milk products *eg cheese, yoghurt, milk*	1 cup milk/200g tub of yoghurt contains approx 300mg calcium	270mg (7-12 months, breastfed) 350mg (7-12 months, bottle-fed) 500mg (1-3 years) 1,000mg (19-70 years) 1,300mg (70 years+)	up to 2,500mg
Leafy green vegetables *eg broccoli, collards, bok choy, chinese cabbage, spinach*	1 cup of cooked broccoli contains approx. 45mg calcium		
Soy and tofu *eg tofu (depending on type), tempeh, calcium-fortified soy drinks*	200ml of calcium fortified soymilk contains approx 300mg calcium		
Fish *eg sardines and salmon (with bones)*	1/2 cup canned salmon contains approx. 402mg calcium		
Nuts and seeds *eg brazil nuts, almonds, tahini*	15 almonds contains approx 40mg calcium		
Calcium-fortified foods *eg breakfast cereals, fruit juices, bread*	-1 cup/40g calcium-fortified breakfast cereal contains up to 200mg calcium -1/2 cup/100ml calcium-fortified orange juice contains up to 80mg calcium -2 slices/30g bread contains 200mg calcium		

Table 1: *Sources of dietary calcium with RDI and therapeutic dose range (Adapted from Department of Health and Ageing 2006, p.155-9).*

Calcium Homeostasis- Vitamin D Metabolites Regulate Calcium Metabolism

1,25-OH2-D regulates calcium metabolism through interactions with its major target tissues, namely bone and the gastrointestinal tract (Holick 2004, p.1680S). Maintaining blood concentrations of 25-hydroxy-vitamin D3 (**25-OH-D**) above the recommended adequate level of 80nmol/L (30ng/mL) not only is important for maximising intestinal calcium absorption but also may be important for providing renal 1-alpha-hydroxylase that is present in most tissues needed to produce 1,25-OH2-D, necessary for calcium absorption in the gut (Holick 2004, pp.1678S–88S).

Source: Vitamin D2 (ergocalciferol)	***Amount contained/100g***	***RDI***	***Therapeutic dose ranges/ day***
Eggs	40-80IU	400IU (infant and children) 200IU (adult) 800IU (pregnancy/lactation)	3,000–5,000 IU for 6–12 weeks to effect serum 25-OH-D changes
Fish eg tuna, salmon, sardines, herring, mackerel	200-480IU		10,000 IU oral dose over 90 days to increase serum 25-OH-D levels to 86 nmol/L in postmenopausal women at latitude 34°S
Vitamin D-fortified foods eg Milk, margarine	200-240IU		50,000–500,000 IU oral dose or 600, 000 IU intramuscularly can effectively treat vitamin D deficiency

Table 2: *Sources of dietary vitamin D with RDI and therapeutic dose range (Adapted from Nowson et al 2004, p.136 and Rodda 2006).*

Vitamin D3 Synthesis and Sufficiency: Importance of Sunlight Exposure

In humans, vitamin D is stored in adipose tissue and muscle and slowly released especially during winter (Reid 2005, p.20). As it is a fat-soluble compound with a half-life about 1 month, adequate exposure to sunlight is necessary to avoid deficiency (Nowson et al 2004, p.136). In a healthy individual, the skin absorbs ultraviolet B radiation and converts 7-dehydrocholesterol, found in the plasma membrane of dermal fibroblasts (Holick 2004, p.1679S) and epidermal keratinocytes, to pre-vitamin D3 (**pre-D**; Vantieghem et al 2006). Pre-D is then thermally induced to create its active form (Vantieghem et al 2006).

In addition, pre-D and vitamin D3 are converted by sunlight to biologically inert forms (Holick 2004, p.1680S). Once formed by the skin, or taken in through the diet, vitamin D3 then enters the circulation and is converted in the liver to 25-OH-D by the enzyme 25-hydroxylase (Holick 2004, p.1680S). The 25-OH-D then enters the circulation and is further converted in the kidneys to the active 1,25-OH2-D by renal 1-alpha-hydroxylase (Holick 2004, p.1680S). The production of renal 1,25-OH2-D is regulated by a variety of factors, including serum phosphorus and parathyroid hormone (PTH; Holick 2004, p.1680S). This complex inter-dependent sequence of events is depicted in the figure below, which demonstrates the conversion of pre-D to the active form and its subsequent effects on bone and tissue. This cascade of events leading to 1,25-OH2-D ensures serum calcium is maintained at supersaturated levels and thereby deposited in bone (Department of Health and Ageing 2006, p.129).

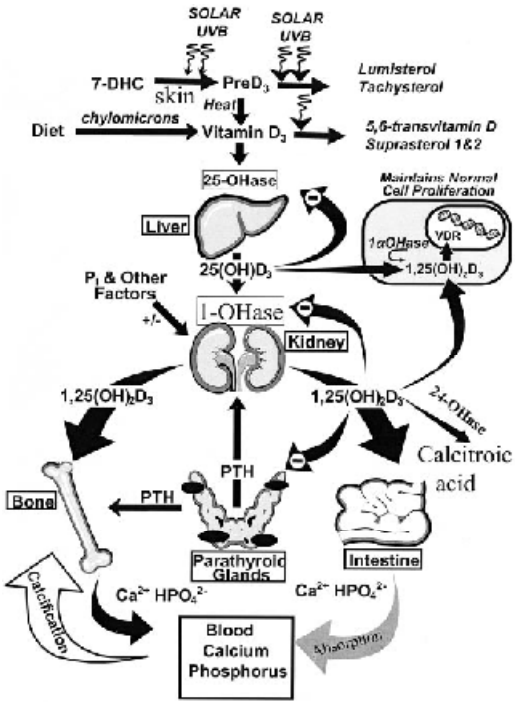

Figure 1: *Cutaneous (skin) production of vitamin D and its metabolism and regulation for calcium homeostasis and cellular growth (Taken from Holick 2004, p.1680S).*

Vitamin D: Issues Around Sunlight Exposure

Most humans depend on sunlight to meet their vitamin D requirements (Holick 2004, p.1678S). However, optimal skin production of pre-D relies on season, latitude, the time of day, degree of skin pigmentation, age, use of sunscreens, use of full-body veils, presence of glass (Holick 2004, p.1678S), angle of the sun, amount of cloud cover, and amount of particulate matter in the atmosphere (Department of Health and Ageing 2006, p.130).

In addition, as melanin efficiently absorbs ultraviolet B radiation, those with increased skin pigmentation need longer sunlight exposure times to make the same amount of vitamin D3, compared with light-skinned people (Holick 2004, pp.S1680-81). For example, a young adult with skin type III[1] exposed to 1 minimal erythemal dose (**MED**) exhibited a 50-fold increase in blood concentrations of vitamin D3 within 8 hours, whereas an adult of the same age with skin type V[2], also exposed to 1 MED, did not demonstrate a significant increase in vitamin D3 blood concentrations (Holick 2004, p.S1681). The adult with skin type V therefore seems to require 5-10 times the exposure while exhibiting only a 30-fold increase in vitamin D3 blood concentration (Holick 2004, p.S1681).

Therefore, although chronic excessive exposure to sunlight increases the risk of non-melanoma skin cancer, the avoidance of all direct sun exposure increases the risk of vitamin D deficiency. Annual monitoring of serum 25-OH-D concentrations may thus assist in revealing potential vitamin D deficiencies (Holick 2004, pp.1678S-88S). Sensible sun exposure (usually 5-10 minutes of exposure of the arms and legs or the hands, arms and face, 2 or 3 times per week), and increased dietary and supplemental vitamin D intakes are reasonable approaches to guarantee vitamin D sufficiency (Holick 2004, p.1678S-88S).

[1] *Based on the Fitzpatrick skin type scale, which describes how individuals react to the sun, skin type 3 individuals sometimes burn, often tan (Warthan et al 2005, p.964).*

[2] *Skin type 5 never burns, always tan (Warthan et al 2005, p.964).*

Osteoporosis- Calcium and Vitamin D Role in Treatment and Prevention

As both calcium and vitamin D are necessary for normal development and maintenance of bone (Department of Health and Ageing 2006, p.129, 155), they do play a role in the treatment and prevention of osteoporosis, particularly for institutionalised or housebound elderly, or where significant calcium and vitamin D deficiency is present (Raisz 2005, p.3320). For example, vitamin D deficiency may be contributing not only to accelerated bone loss and increasing fragility, but also to the impairment in the neuromuscular system that may then increase the risk of falls. Therefore, studies involving older individuals at high risk for calcium and vitamin D deficiency indicate that supplementation of both can decrease bone resorption, increase bone mass, decrease fracture rates, and even decrease the frequency of falling (Raisz 2005, p.3320). They enable an increase in peak bone mass but also slow bone loss and reduce fracture risk throughout life (Raisz 2005, p.3323). Consequently, RDI for calcium as well as adequate vitamin D status, which includes adequate sunlight exposure, across all age groups and lifestyles has been set for the Australian population in order to prevent and treat skeletal deficiencies such as osteoporosis, as well as numerous other conditions related to the immune and cardiovascular systems (Department of Health and Ageing 2006, p.129-135).

Conclusion

While failure to achieve optimal peak bone mass is predominantly determined largely by genetics, other factors such as nutrition, physical activity, and lifestyle may all have an impact during human growth and development. In addition, adequate calcium and vitamin D intake may not only increase peak bone mass but also slow bone loss and reduce fracture risk throughout life. Therefore, while supplementation and sunlight later in life assist in the treatment of such conditions, it seems essential to ensure adequate levels of calcium and vitamin D early in life in order to <u>prevent</u> bone density disorders such as osteoporosis.

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