Proceedings of the Nutrition Society (2002), **61**, 173–180 DOI:10.1079/PNS2002160

The Diamond Jubilee Summer Meeting of the Nutrition Society was held at the University of Sheffield on 10–12 July 2001

Plenary Lecture

Strategies for skeletal health in the elderly

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Osteoporosis is a common disease in the elderly, and the fractures that result from this disorder affect 40 % of women and 14 % of men over the age of 50 years. The risk of fracture relates to bone mineral density and the risk of falling, among other factors. Low bone mineral density in the elderly can result from either low peak bone mass or accelerated bone loss, or a combination of the two. Nutritional factors play a role in both the attainment of peak bone mass and in the rate of age-related bone loss. The main determinants of peak bone mass are genetic factors, early-life nutrition, diet and exercise. Of the nutritional factors Ca, and particularly milk, are the most important contributors to peak bone mass. Some of these factors may interact; for example, a low dietary Ca in addition to an unfavourable vitamin D receptor gene polymorphism may result in low peak bone mass. The age-related changes in bone mass may also have a genetic basis, but deficiency of oestrogen is a major contributor. In addition, undernutrition is common in the elderly, and lack of dietary protein contributes both to impaired bone mineral conservation and increased propensity to fall. There is a decreased ability of the intestine to adapt to a low-Ca diet with increasing age. Other dietary factors include vitamin K, Zn and fruit and vegetables. Adequate nutritional status, particularly of Ca and vitamin D, is essential for the successful pharmaceutical treatment of osteoporosis. Thus, strategies for enhancing skeletal health in the elderly must begin in early childhood, and continue throughout life.

Osteoporosis: Elderly: Bone mineral density: Fracture: Diet

Osteoporosis is a systemic skeletal disease characterised by low bone mass and microarchitectural deterioration, with a consequent increase in bone fragility and susceptibility to fracture. There is an increase in the incidence of fractures with age. After the age of 50 years, the risk of sustaining an osteoporotic fracture is 40 % for a woman and 14 % for a man, and this factor is known as the 'lifetime fracture risk'. Osteoporotic fractures are associated with considerable morbidity as well as increased mortality. Fractures result in pain (which may be prolonged), deformity (including kyphosis), loss of height and abdominal protrusion, and loss of independence. The most severe fracture in terms of morbidity, mortality and cost is that of the hip. The incidence of hip fracture increases exponentially after the age of 45 years in both men and women (see p. 173), and nearly always necessitates hospital admission. The average length of the hospital stay is 30 d, and only about one-third of patients with hip fracture regain their former mobility. Deaths within the first 6 months following hip fracture may be as high as 20 %. In 1999 the total annual cost in the UK was estimated at £942 million (Royal College of Physicians, 1999). The burden on the Health Service is thus high and increasing, and the cost to those affected in terms of quality of life is considerable.

The incidence of these fractures is increasing worldwide, due in part to an ageing population, and in part to an apparent secular trend, possibly related to an increasingly sedentary lifestyle. The pattern of the rise in incidence of fractures with age differs between the various sites, and between men and women. Thus, whilst the fracture rate is higher in women than in men at all sites, this difference is more marked for Colles and pelvic fractures than for those of the hip, where there is a very sharp rise in fracture rate in both men and women above the age of 60–70 years (Melton, 1995). It is therefore likely that factors other than bone density alone contribute considerably to fracture risk.

Abbreviations: BMD, bone mineral density; IGF-I, insulin-like growth factor-I; PBM, peak bone mass; PTH, parathyroid hormone.

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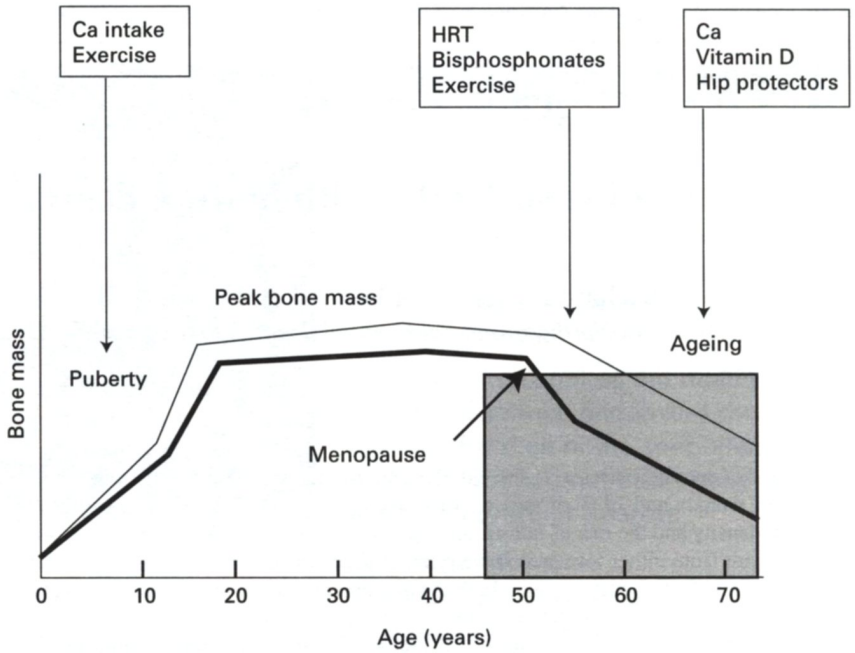

Fig. 1. Bone mass throughout life. (—), Men; (▬), women; (▩), zone of increased risk for fracture. HRT, hormone-replacement therapy.

The main determinant of fracture risk is bone mineral density (BMD), which accounts for 75 % of the risk (Cummings *et al.* 1993). Other contributory factors include bone strength, which is determined by both the geometry and the quality of the bone, and the propensity to fall. This factor relates to a number of characteristics including muscle strength, balance, coordination and visual acuity. The nature of the trauma will also determine whether a fracture occurs, as will the degree of 'padding' (adiposity) of the individual, low body weight being an independent risk factor for fracture. Low BMD in the elderly can result from either low peak bone mass (PBM) or accelerated bone loss, or a combination of the two (Fig. 1).

Determinants of peak bone mass

PBM is the maximum amount of bone acquired at skeletal maturity and is, to a great extent (70–80 %) genetically determined. The genetic influences on PBM are not only a result of effects on BMD, but also on other factors affecting bone strength, such as body size and composition, and bone geometry (Marcus, 1996; Nguyen *et al.* 1998). A number of genetic polymorphisms have been shown recently to be related to PBM, including those of the vitamin D receptor gene and the oestrogen receptor gene (Morrison *et al.* 1994; Viitanen *et al.* 1996; Albagha *et al.* 2001). Hormonal factors, and in particular the age of onset of puberty, are also important determinants of PBM. The remaining 20–30 % of the variation in PBM can be ascribed to environmental factors, the most important of which are exercise and nutrition, particularly Ca and milk intake.

Determinants of bone loss

The most important cause of bone loss in women is the loss of circulating oestrogen associated with the menopause, resulting in an increased rate of bone turnover. There is also a decrease in bone formation relative to bone resorption, leading to a remodelling imbalance and so net bone loss. This imbalance may be related to the decline in renal function which occurs with age, resulting in reduced synthesis of 1,25-dihydroxycholecalciferol, and decreased re-absorption of Ca (Eastell & Riggs, 1997). Intestinal absorption also becomes less efficient with age, and this factor, combined with low concentrations of vitamin D and reduced dietary Ca intakes leads to low serum Ca concentrations and increased concentrations of parathyroid hormone (PTH). Reduced concentrations of physical activity also contribute to accelerated bone loss and, as with PBM, genetic factors are a strong determinant.

Bone mineral density

Dual-energy X-ray absorptiometry is the technique most commonly used to measure BMD. The method is precise, accurate and safe, and can therefore be used for repeated measurements and in children. Dual-energy X-ray absorptiometry is used to predict fracture risk and diagnose osteoporosis, as well as to monitor response to therapy.

However, a difficulty with dual-energy X-ray absorptiometry is that an areal bone density (g/cm^2) is derived, based on measurements in two dimensions, rather than a true volumetric (g/cm^3) measurement which would take into

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Table 1. WHO diagnostic criteria for osteoporosis (Kanis *et al.* 1994)

BMD score*	Diagnosis
>−1	Normal
<−1>−2·5	Osteopenia
<−2·5	Osteoporosis
<−2·5 plus fragility fracture	Severe osteoporosis

BMD, bone mineral density.
*Standard deviations from the young adult reference mean for women.

account bone size in three dimensions. There are times when an estimation of the three-dimensional measure becomes important, e.g. during growth, when not only the size but also the shape of the bone is changing, affecting the total bone volume. A number of methods have been developed to correct for the effect of bone size, although each method involves making assumptions about the three-dimensional shape of the bone (Carter *et al.* 1992; Kroger *et al.* 1992; Peel & Eastell, 1994; Prentice *et al.* 1994; Molgaard *et al.* 1997). Nutritional factors may influence bone size to a greater extent than bone density.

Although not the only determinant of fracture rate, low BMD is a major risk factor for fracture. Indeed, the association between fracture rate and BMD is stronger than that for serum cholesterol and CHD (Neaton & Wentworth, 1992; Cummings *et al.* 1993). For each decrease in BMD of 1 SD from mean values for young adults, there is an estimated 2-fold increase in fracture risk. The association is so strong that in 1994 the WHO adopted a definition of osteoporosis based on classification by bone density (Kanis *et al.* 1994; Table 1).

Osteoporosis in women is defined as a condition in which BMD is >2·5 SD below the mean for young adults. If one or more fractures are also present, the condition is defined as severe osteoporosis. BMD between 1 and 2·5 SD below the mean value for young adults is classified as osteopenia.

In addition to reduction in the quantity of bone, skeletal fragility is also a result of a deterioration in the quality of the bone, with thinning and eventual perforation of the trabeculae. As a result, the bone becomes susceptible to fracture following minimal impact.

The most common fracture sites are those of the vertebrae, proximal femur and distal radius (Colles fracture). However, fractures at other sites may also be osteoporotic in origin. Diagnosis is made from radiographs, usually following minor trauma. The presence of vertebral fractures can be difficult to determine, and establishing the most reliable way of diagnosing vertebral deformity from spine radiographs is a subject of current research.

Measuring bone turnover

Bone undergoes a continual process of formation and resorption, and a number of the by-products of these processes can be detected in serum or urine. Analysis of these biochemical markers of bone turnover provides information about the metabolic processes occurring in either healthy or unhealthy (such as osteoporotic) bone. Products of collagen degradation produced by osteoclasts are excreted in the urine, and include the C-terminal and N-terminal cross-linking telopeptides of type I collagen, and deoxypyridinoline. Matrix proteins produced by the osteoblasts during bone formation include osteocalcin and procollagen type I N-terminal and C-terminal propeptides. These by-products of bone turnover, and the enzyme bone alkaline phosphatase are detected in serum. These markers are reasonably bone-specific, and many of them can now be routinely analysed in hospital laboratories using automated analysers, which increase reliability and precision.

Bone turnover markers are increasingly being used in the clinical setting (Delmas *et al.* 2000), both to predict fracture risk and to monitor therapy, as bone turnover markers show a large and rapid response to successful anti-resorptive therapy. It remains to be seen whether the process of monitoring treatment improves compliance, and the extent to which changes in marker levels reflect a true reduction in an individual's risk of fracture.

Diet and the elderly

Protein

Undernutrition is common in the elderly. Protein malnutrition in particular is not only detrimental to bone mass accrual and conservation, but also contributes to the risk of hip fracture by increasing the propensity to fall as a result of muscle weakness and impaired coordination (Geinoz *et al.* 1993). Chronic undernutrition also results in the loss of soft tissue padding around the hip (Grisso *et al.* 1997), so that there is little protection against the impact of a fall. The use of external hip protectors can effectively lower fracture risk in ambulatory frail adults by >50 % (Kannus *et al.* 2000). In a cohort of elderly men and women from the Framingham Osteoporosis Study bone loss was significantly related to protein intake ($P = 0{\cdot}05$) (Hannan *et al.* 2000). In rats fed low-protein diets, loss of BMD was accompanied by a decrease in plasma insulin-like growth factor-I (IGF-I) and an apparent uncoupling of bone remodelling (Ammann *et al.* 2000). In a study of elderly patients with hip fracture (Schurch *et al.* 1998) a protein supplement of 20 g/d for 6 months resulted in reduced bone loss from the proximal femur, increased serum concentrations of IGF-I and a shorter hospital stay. Dietary protein is known to increase Ca excretion, and has therefore been considered to be detrimental to bone health. However, this factor is unlikely to be an important cause of bone fragility in the elderly. Whilst there is some evidence to suggest that protein from animal sources may have a more detrimental effect than that from vegetable sources (Sellmeyer *et al.* 2001), this finding is not supported by the results of the Framingham Study (Hannan *et al.* 2000). Indeed, the negative effects of protein deprivation are likely to be much more important than those of protein excess in this age-group.

Whilst minimising bone loss in the elderly is clearly vital, maximising PBM at the end of the growth period is also a key strategy in preventing osteoporosis. Protein intake is positively associated with an increase in BMD during the pubertal growth spurt (Bonjour *et al.* 1997*a,b*), and increasing protein intake results in raised IGF-I in teenage girls (Cadogan *et al.* 1997).

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Vitamin D

Vitamin D, in its active form, plays an important role in maintaining Ca homeostasis. It acts on intestinal cells to increase the absorption of dietary Ca, and on bone cells to mobilise Ca stores when serum concentrations are low. The major source of vitamin D is not dietary, but is produced from 7-dehydrocholesterol in the skin during exposure to sunlight. Cholecalciferol so-formed is then hydroxylated in the liver to produce 25-hydroxycholecalciferol. This product is the major circulating form of vitamin D, having a half-life of about 2 months, and is used as a measure of long-term vitamin D status. Further hydroxylation in the kidney, catalysed by the 1α-hydroxylase enzyme, results in the formation of the active form of vitamin D, 1,25-dihydroxycholecalciferol. This conversion is stimulated by high serum PTH concentrations, as well as low serum Ca and P concentrations, and low concentrations of 1,25-dihydroxycholecalciferol itself. With ageing there is marked decrease in the concentration of 7-dehydrocholesterol in the skin, resulting in much reduced cholecalciferol production. An elderly individual (>70 years) produces <30 % of the amount of cholecalciferol produced by a young adult when exposed to the same amount of sunlight (Holick *et al.* 1989). This low production rate may be compounded by limited exposure to sunlight due to lack of mobility or institutionalisation. Poor diets, a consequence of anorexia and impaired activities of daily living, can also lead to low dietary intake of vitamin D. In addition, synthesis of 1,25-dihydroxycholecalciferol is reduced in the elderly, possibly due to the loss of the ability of PTH to up regulate 1α-hydroxylase activity (Eastell & Riggs, 1997). Intestinal cells may also exhibit some resistance to vitamin D with ageing. The overall result is decreased Ca absorption, leading to low serum concentrations of Ca and hence increased PTH secretion, increased bone turnover and bone loss. If vitamin D deficiency becomes more severe the result is inadequate mineralisation of the bone matrix (osteoid) and osteomalacia.

Whilst there is evidence for a beneficial effect of both Ca (Storm *et al.* 1998; Ruml *et al.* 1999; Peacock *et al.* 2000) and vitamin D (Heikinheimo *et al.* 1992) on bone health in the elderly, not all studies concur (Lips *et al.* 1996), and treatment is not effective in younger post-menopausal women (Hunter *et al.* 2000). When given in combination, however, vitamin D and Ca have been clearly demonstrated to reduce the incidence of hip and non-vertebral fractures in the elderly (Chapuy *et al.* 1992; Dawson-Hughes *et al.* 1997; Krieg *et al.* 1999). In the Decalyos I study (Chapuy *et al.* 1992), 3270 elderly institutionalised women, mean age 84 years, were given either 1200 mg Ca/d with 20 μg cholecalciferol or a double placebo for 3 years. Fracture rates were decreased by 29 % for hip fracture and 17 % for other non-vertebral fractures, and this decrease was associated with an increase in 25-hydroxycholecalciferol and decrease in serum PTH, both to normal levels. In addition, there was a 7·3 % increase in hip BMD compared with the placebo group.

Ca combined with vitamin D is therefore effective in reducing fracture rates in the elderly, reversing hypovitaminosis D and secondary hyperparathyroidism. It is well tolerated and requires no monitoring, and is relatively cheap. It may also be used as an adjunct to other anti-resorptive therapies.

Other nutrients

A large number of other nutrients are likely to be essential in the maintenance of skeletal health in the elderly, and indeed throughout life. There is some evidence for a negative effect of high-Na diets on bone mass in young girls (Matkovic *et al.* 1994) and post-menopausal women (Devine *et al.* 1995). Increasing dietary Na intake results in increased urinary excretion of Na and Ca, leading to low serum Ca and hence raised PTH and increased bone turnover and bone loss. Evans *et al.* (1997) investigated the effect on Ca homeostasis and bone turnover of administering a high- (300 mmol/d) or low- (50 mmol/d) Na diet to eleven premenopausal and eleven post-menopausal women for 1 week. All those on the low-Na diet had significantly lower concentrations of urinary Na and Ca ($P < 0{\cdot}05$) at the end of the study compared with those on the high-Na diet. In addition, concentrations of bone turnover markers were lower in the post-menopausal women on the low-Na diet. High intakes of dietary Na may therefore have a detrimental effect on bone metabolism, but the long-term effects on BMD and fracture risk remain unknown.

Despite concerns that high intakes of P might be detrimental to the skeleton (Calvo, 1994), it has been difficult to demonstrate that this is the case. Metz *et al.* (1993) found a negative association of dietary P and BMD in premenopausal women; however, Whybro *et al.* (1998) found no effect of high phosphate intakes on bone turnover. Low P intakes are relatively common among the elderly, and P could therefore be a limiting factor for bone mineralisation, but the extent to which this factor might contribute to the problem of osteoporosis is not known.

Interest has recently focused on the importance of acid–base metabolism in bone health, and particularly the role of fruit and vegetables (for reviews, see Tucker *et al.* 1999; Curtis Morris *et al.* 2001). There is evidence that intakes of nutrients found in fruit and vegetables (notably K, Mg, fibre, vitamin C and β-carotene), as well as fruit and vegetables themselves, are positively associated with BMD in elderly men and women (Tucker *et al.* 1999; Curtis Morris *et al.* 2001). In addition, dietary Mg intake has been shown to negatively predict urinary excretion of bone resorption markers in post-menopausal women (New *et al.* 2000). It is likely that there is an interaction between a number of the nutrients important to bone, and indeed other therapeutic agents. For example, post-menopausal women who used vitamin C supplements and also used oestrogen therapy and took Ca supplements had higher femoral neck BMD than those who took vitamin C alone or vitamin C and oestrogen therapy without additional Ca (Morton *et al.* 2001).

Vitamin K is essential for the γ-carboxylation of bone-matrix proteins, such as osteocalcin. In patients with osteoporosis, especially hip fractures, osteocalcin is often undercarboxylated, and this deficit can be corrected by administering vitamin K (Vermeer *et al.* 1995). Low dietary intakes of vitamin K are associated with an increased risk of hip fracture, but not with BMD (Booth *et al.* 2000). The

protective role of vitamin K against age-related bone loss needs to be confirmed with long-term supplementation trials, and the mechanism further elucidated.

Zn is necessary for optimal growth, and stimulates production of IGF-I (Ninh *et al.* 1996; Blostein-Fujii *et al.* 1997). However, short-term Zn supplementation in healthy 12-year-old girls had no effect on IGF-I or biochemical markers of bone turnover (Clark *et al.* 1999). Low intakes of Zn were associated with increased risk of fracture in 46–68-year-old men (Elmstahl *et al.* 1998). The importance of Zn deficiency among the elderly is not known, but the role of Zn in regulating appetite (possibly via leptin production; Mantzoros *et al.* 1998) might be important for nutritional status in general in the elderly.

Other minerals such as Mn and Cu are cofactors of enzymes necessary for the synthesis or post-translational modification of bone-matrix proteins.

The place of nutrition alongside standard therapy for osteoporosis

The aim of current treatment of osteoporosis is to maintain or increase bone strength by inhibiting bone resorption or stimulating formation. Currently-available treatments can halt bone loss, and may even result in a small increase in bone mass, and may reduce fracture risk by up to 50 %. However, no treatment is able to restore the damaged architecture of osteoporotic bone.

Drug treatments include hormone-replacement therapy, raloxifene, the bisphosphonates (including cyclical etidronate, alendronate and risedronate), as well as 1,25-dihydroxycholecalciferol, calcitonin and fluoride. The use of these treatments is often supported with supplementary Ca and vitamin D, as an adequate supply of these nutrients is essential for these agents to achieve their full therapeutic potential (Pereda & Eastell, 2001).

A number of clinical trials have compared the use of therapeutic agents alone with those combined with Ca. In a review of such studies investigating the effect of oestrogen on bone mass in post-menopausal women, the mean increase in BMD at the lumbar spine, femoral neck or forearm was shown to be up to 2 % higher when given in conjunction with Ca supplements than when given alone (Nieves *et al.* 1998). The effect of calcitonin was similarly enhanced when combined with Ca. In the case of bisphosphonate treatment, these relatively new anti-resorptive agents are frequently administered with Ca supplements. Clinical trials investigating their effectiveness have tended to compare the effects of the drug combined with Ca with those of Ca alone. As a result, the extent to which Ca enhances the effect of these agents is not clear. However, it is likely that their efficiency is compromised in the absence of adequate Ca nutrition.

Thus, while the action of Ca on bone is not as strong as that of anti-resorptive drugs such as oestrogen, bisphosphonates and calcitonin, it appears that there is a synergistic effect when Ca is administered in combination with these agents. The mechanism for this enhanced effect is not clear. Ca alone causes an increase in bone density by reducing the remodelling space. However, this effect on the remodelling space would be expected to be weak in comparison with that of anti-resorptive agents. Also, if the effect were only one of filling in of the remodelling space, it might be expected to be transient, when this is clearly not the case. Nieves *et al.* (1998) have proposed that the effect of Ca, superimposed on that of oestrogen, might be to allow secondary mineralisation of newly-formed bone to occur, such that each packet of bone would be hypermineralised. This process would result in an increase in BMD and reduced fracture risk (Pereda & Eastell, 2001).

Skeletal health across life

Whilst nutritional strategies have an important part to play in minimising age-related bone loss, it is clear that they cannot halt the progress of established osteoporosis. Indeed, even the role of drug treatment is limited. It is therefore important to consider ways of optimising skeletal health earlier in life as a preventive strategy.

Epidemiological studies first provided an indication that Ca nutrition might be important in the development of PBM. Milk consumption during childhood and adolescence was shown to predict adult bone mass (Matkovic *et al.* 1979; Halioua & Anderson, 1989; Murphy *et al.* 1994; Nieves *et al.* 1995).

Numerous intervention trials have subsequently confirmed the key role of Ca in bone development, showing that Ca supplementation during childhood and adolescence increases BMD in children (Johnston *et al.* 1992; Lee *et al.* 1995; Bonjour *et al.* 1997*a*) and adolescents (Lloyd *et al.* 1993; Cadogan *et al.* 1997; Nowson *et al.* 1997; Lambert *et al.* 2000).

Mechanism for supplements and milk may differ

Milk, a 'food', may act on the skeleton in a different way from Ca, a single nutrient. An 18-month trial of milk supplementation in teenage girls (Cadogan *et al.* 1997) resulted in greater gains in total body bone mineral content and total body BMD in the supplemented girls compared with the controls. This observation was coupled with a significantly greater increase ($P = 0{\cdot}02$) in serum IGF-I concentrations in those girls. The effect on bone mass appeared to be maintained 18 months after withdrawal of the supplement (Barker *et al.* 1998). In a trial of similar design, but using a Ca-fortified fruit drink as the supplement, an even greater effect on BMD was observed during the 18-month intervention (Lambert *et al.* 2000). Unlike the milk intervention, there was no effect on IGF-I. There was, however, a significant reduction in PTH and bone turnover markers ($P < 0{\cdot}05$), which had not been seen with milk. The mechanism for the effect of Ca is likely, therefore, to be due to a suppression of bone remodelling mediated by PTH. In contrast, milk is likely to act by stimulating bone growth via IGF-I, concentrations of which rise in response to the increased dietary protein provided by the milk. The majority of follow-up studies of Ca intervention trials have to date not shown a persisting effect beyond the supplementation period. The only exception to this trend was a trial using a milk-derived Ca salt as the supplement (Bonjour *et al.* 1997*a*). The issue of whether the effect of a supplement is maintained is clearly critical in terms of maximising PBM

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and preventing fractures in later life. It is estimated that an increase in BMD as small as 2–3 % (i.e. of the magnitude observed in most supplementation trials) could, if maintained, result in a 10–20 % decrease in fracture risk.

Nutrition and genetics

Whilst many factors contribute to the development of osteoporosis, there is a strong genetic component. The first gene to be implicated in the development of bone phenotype was the vitamin D receptor gene (Morrison *et al.* 1994). Common allelic variations of this gene include the Bsm1 (B/b), Fok1 (F/f), Apa1 (A/a) and Taq1 (T/t) polymorphisms. These variations have now been shown to be important in both the determination of PBM (Viitanen *et al.* 1996; Sainz *et al.* 1997; Ferrari *et al.* 1998) and postmenopausal bone loss (Gennari *et al.* 1999; Gomez *et al.* 1999). It is likely that their role is at the level of intestinal Ca absorption (Dawson-Hughes *et al.* 1995; Ames *et al.* 1999), and that their effect interacts with Ca intake. In peripubertal girls consuming a low-Ca diet, the number of favourable alleles (F or b) was shown to be associated with greater total body bone mineral content and total body BMD, using an allele scoring system (Rogers *et al.* 2000). In a Swiss study of 101 pubertal girls (Ferrari *et al.* 1998), baseline BMD and increment in BMD was related to the Bsm1 genotype, and the effect of the Ca was only seen in those with the less-favourable genotypes (Bb or BB). There was also a possible interaction between Ca intake and the Fok1 genotype. Other candidate genes have been identified as likely to be important in the development of low bone mass. Amongst others, polymorphisms of the oestrogen receptor α gene (Albagha *et al.* 2001) and the collagen type 1 α 1 gene have been shown to be associated with increased bone loss and fracture risk (Uitterlinden *et al.* 1998; Keen *et al.* 1999; Sainz *et al.* 1999; McGuigan *et al.* 2001), and may be useful in identifying those at increased risk of osteoporosis. However, not all results concur (Heegaard *et al.* 2000), and the extent to which these genes interact with dietary and other environmental factors has not yet been explored.

In conclusion, skeletal health in the elderly is dependent on foundations laid in early childhood, developed and maintained throughout life (Fig. 1). Appropriate and successful strategies encompass good nutrition in combination with an active lifestyle at all ages, with particular emphasis on an adequate Ca intake and exposure to sunshine. Drug therapy, when required, should be supported by such lifestyle factors in order to maximise their effect. Thus, it is possible to minimise the impact of the less-modifiable influences on bone loss and reduce the risk of fractures into old age.

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