Proceedings of the Nutrition Society (2001), **60**, 265–274 DOI: 10.1079/PNS200085

The Summer Meeting of the Nutrition Society was held at University College, Cork, Republic of Ireland on 27–30 June 2000

Clinical Metabolism and Nutrition Group Symposium on 'Nutritional aspects of bone metabolism from molecules to organisms'

Exercise, bone and nutrition

Susan A. New
Centre for Nutrition and Food Safety, School of Biomedical and Life Sciences, University of Surrey, Guildford, Surrey GU2 7XH, UK

Predisposition to poor skeletal health resulting in osteoporotic fracture is a major public health problem, the future economical impact of which is likely to be phenomenal. Two mechanisms principally determine adult bone health: (1) maximum attainment of peak bone mass (PBM); (2) the rate of bone loss with advancing age. Both aspects are regulated by a combination of endogenous and exogenous factors, and although genetic influences are believed to account for up to 75 % of the variation in bone mass, there is still room for modifiable factors to play a vital role. Weight-bearing physical activity is beneficial to the skeleton, but clarification of the exact type, intensity and duration required for optimum bone mass is needed. Excessive levels of exercise, which result in amenorrhoea, are detrimental to skeletal health. The importance of Ca to bone remains controversial. There is evidence that Ca is effective in reducing late post-menopausal bone loss, but more research is required on the long-term benefit of increased Ca intake on PBM attainment. Vitamin D 'insufficiency' appears to be widespread amongst population groups and is an area of considerable public health concern. The role of other micronutrients on bone metabolism remains to be fully quantified, but data from a combination of experimental, clinical and observational studies suggest a positive link between alkaline-forming foods and indices of bone health. The influence of nutrient–gene interactions on the skeleton requires further elucidation, but it may be useful in the future to target nutrition advice at those individuals who are genetically susceptible to osteoporosis.

Osteoporosis: Physical activity: Nutrition: Bone minerals: Vitamin D: Acid–base balance

Bone is a living tissue which undergoes a continuous cycle of bone formation (involving osteocytes and osteoblasts) and bone resorption (involving osteoclasts; Mundy, 1999). Maintenance of bone health throughout the life cycle is essential, since the result of poor skeletal integrity is an increased risk of osteoporotic fracture. Osteoporosis is defined as a metabolic bone disease 'characterised by low bone mass and microarchitectural deterioration of bone tissue, leading to enhanced bone fragility and a consequent increase in fracture risk' (Consensus Development Conference, 1991, 1993). There is a normal mineral: collagen value, unlike that of other metabolic bone diseases such as osteomalacia (which is characterised by relative deficiencies of mineral in relation to collagen). The current definition of osteoporosis (which has remained unchanged since 1991) clearly reflects the recognition that bone weakness is related to poor structural quality as well as decreased bone mass. An example of 'normal' and 'osteoporotic' bone is shown in Fig. 1.

Diagnostic criteria for osteoporosis: current discrepancies

Currently, the clinical diagnosis of osteoporosis can only be undertaken using dual X-ray absorptiometry. Bone mineral density (BMD) data are expressed as absolute BMD (g/cm^2), and defined either as the number of standard deviations from the mean of age-matched controls (known as z-score) or the number of standard deviations from the young normal mean (known as t-score). The World Health Organization (1994) diagnostic criterion for osteoporosis is

Abbreviations: BMD, bone mineral density; PBM, peak bone mass.

Corresponding author: Dr Susan New, fax +44 1483 576978, email s.new@surrey.ac.uk

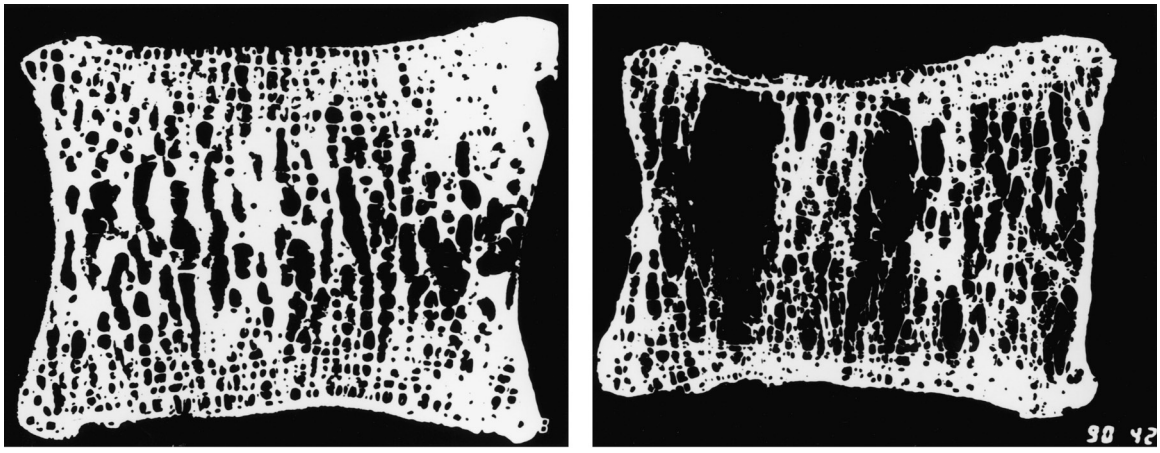

Fig. 1. Comparison of the enlargement of normal healthy bone, as in a woman aged 35 years, with severely-osteoporotic bone in a woman aged over 60 years. (Reproduced with permission from the National Osteoporosis Society, UK.)

based on t-scores, with a t-score value $< -1{\cdot}0$ being defined as osteopenic and a t-score $< -2{\cdot}5$ being referred to as osteoporotic. Although there is a growing appreciation of the value of measurement of (1) markers of bone turnover (particularly with respect to patient responsiveness to anti-resorptive treatment such as bisphosphonates) and (2) quantitative ultrasound as a screening tool for fracture risk, the World Health Organization (1994) definition of osteoporosis is only applicable (at present) to BMD measurements using dual X-ray absorptiometry.

There is concern, however, over the use of the World Health Organization (1994) t-score criterion, particularly with respect to the non-comparability of t-score-based diagnosis with the clinical diagnosis of patients with osteoporosis across bone sites, and with different dual X-ray absorptiometry techniques (Faulkner *et al*. 2000; Hennig, 2000; McClung *et al*. 2000). An important paper was presented and discussed at the 2nd World Congress on Osteoporosis held in Chicago, IL, USA (15–18 June 2000) by the Joint National Osteoporosis Foundation/American Society of Bone and Mineral Research Committee on the simplification of BMD reporting. Black *et al*. (2000) proposed a 'site-specific threshold value' for hip fracture risk and suggested two systems: (1) the definition of a hip fracture risk index level (with the suggestion of a 5-year age-specific hip fracture risk among women with femoral neck BMD score $< -2{\cdot}5$); (2) the creation of 'analogous' ('risk equivalent') thresholds for the non-femoral neck technique, enabling patients who were diagnosed below the device-specific threshold to have a hip fracture risk equal to the risk index.

Whilst further discussions are required, the proposed system, based on risk, would enable (1) the inclusion of other 'risk factors' such as bone turnover markers and/or evidence of previous fracture; (2) would allow a framework for the system to be used with men and different ethnic groups.

Current and future public health implications of osteoporosis

Osteoporotic fracture is a major public health problem, with one in three women and one in twelve men over the age of 55 years affected by the disease, and approximately 90 000 hip fractures occurring in the UK alone last year (National Osteoporosis Society, 2000). It has recently been estimated that overall costs to the Exchequer are in excess of $£1{\cdot}8 \times 10^9$/year, with each hip fracture costing about £20 000 (Torgerson *et al*. 2000). Suprisingly, only 25 % of this amount (about £5000) is for the acute surgical cost, while the predominant cost is the residential care and support services in the first and second year after fracture treatment. Given the projected rise in osteoporotic fracture worldwide to $6{\cdot}26 \times 10^6$ in the year 2050 (compared with $1{\cdot}66 \times 10^6$ in 1990; World Health Organization, 1994), there is an urgent need for the implementation of public health strategies to target prevention of poor bone health on a population-wide basis. There can be no doubt that the future economic impact of osteoporosis will be astronomical.

Changes in skeletal mass throughout the life cycle

As shown in Fig. 2, there are considerable changes in skeletal mass throughout the life cycle. Two mechanisms principally determine adult bone health: (1) the maximum attainment of peak bone mass (PBM) which is achieved during growth and early adulthood; (2) the rate of bone loss with advancing age, with the menopausal years being a time of considerable concern for women.

Throughout early childhood bone mass increases linearly with skeletal growth and this time point is clearly critical for bone health (Fig. 2; Specker *et al*. 1987; Glastree *et al*. 1990). There is a rapid increase in bone density during the pubertal years (by as much as 40–70 %; Bonjour *et al*. 1991; Gertner, 1999), although this increase is known to vary

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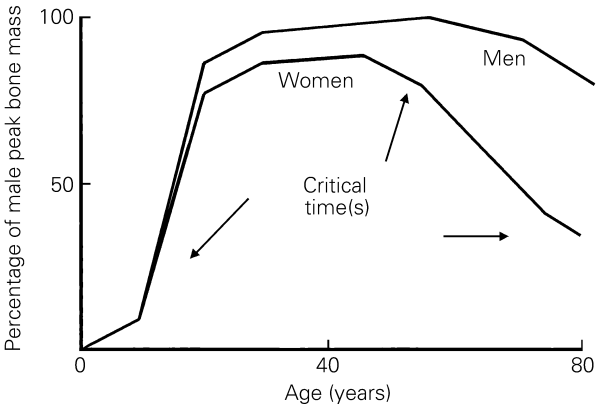

Fig. 2. Changes in skeletal mass throughout the life cycle.

according to skeletal site (Francis *et al*. 1998). The pubertal stage is an all-important time for skeletal development, and careful consideration should be given to the design of studies examining the influences of the 'modifiable' factors (such as nutrition and exercise interventions) on bone health during this period. The optimum time (i.e. pre-, peri- or post-pubertally) for intervention with such exogenous factors remains unclarified.

Bone density continues to increase for several years after the cessation of growth until maximum bone mass is achieved, known as PBM (Johnson & Slemenda, 1998). The exact age at which PBM is attained remains controversial, but is generally believed to be about the late 2nd–early 3rd decade, although it is known to vary between the sexes and according to skeletal site (Recker *et al*. 1992; Theintz *et al*. 1992).

Following attainment of PBM and with the onset of the menopause, rapid bone loss occurs which is believed to average approximately 2–3 % over the next 5–10 years (Cooper, 1999), being greatest in the early post-menopausal years. This time period is a further 'critical time' for bone health, as indicated on Fig. 2. It is important to note that although bone mass continues to decline with ageing (but at a slower rate than during the early menopause), there is some evidence that in those elderly individuals most at risk of 'undernutrition' in the later years this period is a very crucial time with respect to individuals entering the 'danger zone', and hence increasing their risk of fracture (Department of Health, 1992).

Endogenous factors influencing the skeleton

The maximum attainment of PBM and the rate of post-menopausal bone loss are determined by a combination of genetic, endocrine, mechanical and nutritional factors, and there is evidence of extensive interactions between them. Research since 1994 has suggested a link between specific gene polymorphisms and bone mass in different population groups, including the vitamin D receptor gene (Morrison *et al*. 1994), the oestrogen receptor gene (Kobayashi *et al*. 1996) and the collagen type I α 1 gene (Grant *et al*. 1996). More recently, research work has highlighted an association between other gene polymorphisms and indices of bone health such as the interleukin 6-promoter gene (Ferrari *et al*. 2000; Zumda *et al*. 2000) and parathyroid hormone-related peptide receptor gene (Ralston, 1999).

Nutrient–gene interactions and indices of bone health

Public health strategies should possibly target dietary advice at those women with a genetic predisposition to low PBM attainment or increased peri- or post-menopausal bone loss, and there is also evidence in the literature that Ca absorption in older women is dependent on vitamin D receptor genotype (Dawson-Hughes *et al*. 1995). More recently, Ca intake has been found to be a determinant of BMD in those peri-menopausal or early post-menopausal women with the 'bb' vitamin D receptor genotype but not those with the 'BB' genotype, a finding that is exclusive to those women not taking exogenous oestrogen (Macdonald *et al*. 2000*a*). Furthermore, modest alcohol intake (1–2 units/d) has been shown to be associated with reduced bone loss in peri-menopausal women carrying the 'p' allele of the oestrogen receptor genotype (Macdonald *et al*. 2000*b*). Nutrient–gene interactions and indices of bone health are an area of considerable interest and require a much greater focus of attention.

Exogenous factors influencing the skeleton

Although there is much evidence to support a strong genetic influence (approximately 75 %) on the skeleton, including the bone health–gene polymorphism studies already detailed, as well as published work on monozygotic and dizygotic twins (Pocock *et al*. 1987) and mother–daughter pairs (Lutz & Tesar, 1990), there is still room for the modifiable factors (such as nutrition and physical activity) to play a vital role in bone health (Prentice, 1997; Fig. 3).

Impact of physical activity on bone health

Principal concepts

More than one century ago, the German scientist Julius Woolf proposed the theory which is now known as 'Woolf's Law'; i.e. 'bone accommodates the forces applied to it by altering its amount and distribution of mass'. More recently, this concept has been refined to a general theory of bone mass regulation, known as the mechanostat model (Frost, 1987, 1992). It is well known that in the absence of weight-bearing exercise bone loss will occur at both axial and appendicular skeletal sites. In a recent study examining bone loss in fifteen Russian cosmonauts, in the weight-bearing tibial site, cancellous BMD loss was already present after the first month in space, and bone mass deteriorated with mission duration (Vico *et al*. 2000). In those cosmonauts who spent 6 months in space losses ranged up to 23 %, and this loss clearly represents a serious problem which may ultimately substantially affect plans for long-distance space travel (Holick, 2000). Whilst the exact mechanism whereby mechanical loading affects bone remains to be clarified, the scientific literature supports a positive relationship between physical activity, physical fitness, muscle strength and bone mass at the lumbar spine and femoral neck sites (Pocock *et al*. 1989).

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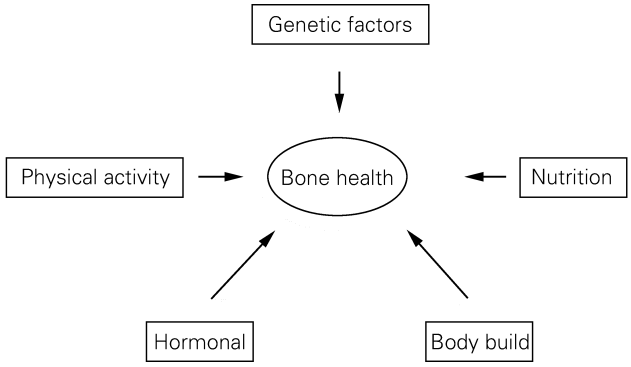

Fig. 3. Endogenous *v.* exogenous factors in bone health.

Role of exercise in peak bone mass development, post-menopausal bone loss reduction and fracture prevention

There is evidence which supports a positive relationship between current weight-bearing exercise and bone mass in children (Slemenda *et al.* 1991), young women (Recker *et al.* 1992), premenopausal women (Jonsson *et al.* 1992) and post-menopausal women (Kohrt *et al.* 1995), as well as for previous physical activity on bone density in young women (Tylavsky *et al.* 1992), premenopausal women (Halioua & Anderson, 1989) and post-menopausal women (Kriska *et al.* 1988).

Data also support a specific role for high-impact exercise in increasing bone density in premenopausal women (Snow-Harter *et al.* 1992; Bassey & Ramsdale, 1994; Lohman *et al.* 1995), post-menopausal women (Kohrt *et al.* 1997) and in both middle-aged and older men (Menke *et al.* 1993). Interestingly, in one study pre- and post-menopausal women were found to respond differently to the same high-impact activity (Bassey *et al.* 1998).

Very little information is available on the relationship between exercise and fracture. Lau *et al.* (1988) reported a significantly decreased relative risk of hip fracture in those subjects who undertook regular walking activities, and in a parallel study Cooper *et al.* (1988) noted that increased daily activity was a protective factor against hip fracture in both males and females.

Whilst exercise is clearly of benefit to the skeleton, what remains undefined is exactly the type, intensity and duration of weight-bearing physical activity required for optimum bone health (Marcus, 1999). Furthermore, exercise may be of benefit in the prevention of osteoporosis, not necessarily via the mechanism of increasing bone mass but instead by increasing muscle strength, coordination, flexibility and balance, and thus reducing the tendency to fall (Eastell, 1999).

'Fit but fragile' phenomena: evidence for detrimental effects of exercise on bone

Whilst bone mass has been shown to be higher in athletes involved in different sports, including tennis players (Jones *et al.* 1977), skaters (Slemenda & Johnson, 1993), rowers (Wolman *et al.* 1991) and volleyball players (Alfredson *et al.* 1997), there is increasing concern for the bone health of women engaged in high-intensity physical training, for whom amenorrhoea is a common characteristic (Keay, 2000). Often, these type of sports also demand extremely low body weights and there is high reported incidence of anorexia nervosa amongst participants. Amenorrhoea (and/or anorexia) is detrimental to bone mass, and there is now good evidence to show that participants 'underachieve' their PBM potential, and thus are at a considerably increased risk of osteoporosis (National Osteoporosis Society, 1996); indeed by World Health Organization (1994) criteria they are often diagnosed as having the disorder (New, 1998). This picture of undernutrition, amenorrhoea and osteoporosis is defined as the 'female athletic triad' (Fig. 4), and the American College of Sports Medicine (1997) published a position stand to 'encourage the prevention, recognition and management of this syndrome'.

The exact mechanisms involved in PBM reduction remain unclarified. There are data to suggest that there is a suppression of the osteoblasts rather than an increase in osteoclastic activity (Zanker & Swaine, 1998), a finding which is further supported by the finding that hormone-replacement therapy is not as effective in reducing bone loss in elite sportswomen as it is in young women with primary ovarian failure (Klibanski *et al.* 1995). Of further interest is the finding that in gymnasts, despite a high prevalence of oligo- and amenorrhoea, bone mass shows a higher than predicted value (Robinson *et al.* 1995; New *et al.* 2000*a*). Clearly this group is an important group to study, since it may provide insight into the type of mechanical loads that are most osteogenic.

Influence of nutrition on bone health

Introductory remarks

As an exogenous factor that is both amenable to change and has significant public health implications, nutrition deserves special attention. Whilst there can be no doubt that diet is important to the development and maintenance of bone health throughout the life cycle, the exact role that it plays remains to be fully quantified (New, 1999).

Role of calcium in peak bone mass development

A topic of debate (and disagreement) is the amount of Ca required for maximal attainment of PBM. Opinions differ not only between countries (Food and Nutrition Board of the Institute of Medicine, 1997; Department of Health, 1998) but also within them (Heaney, 2000; Specker, 2000). In

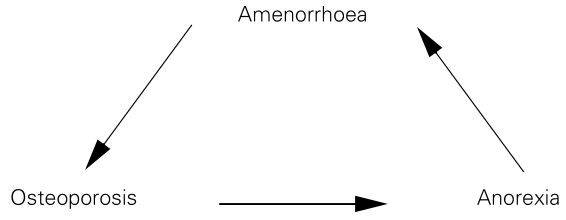

Fig. 4. Detrimental effects of exercise on the skeleton; the female athletic triad. (From American College of Sports Medicine, 1997.)

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trying to make sense of the great disparity in Ca intake recommendations between countries, it is important to understand that some of the differences may be explained by the dissimilar ways in which countries have approached the problem; i.e. the UK Department of Health Committee on Medical Aspects of Health identified Ca intakes deemed adequate for considered populations whereas the US National Academy of Sciences panel targeted intakes optimal for health (Weaver, 1999).

Ca supplementation studies in children and adolescents tend to suggest a difference in BMD at the end of the intervention period of the order of 1–5 % (depending on skeletal site; Table 1). However, the argument in favour of the importance of increasing dietary Ca for PBM maximisation is weakened by the fact that the earlier studies failed to show a difference in bone mass longitudinally once the supplement was withdrawn (Fig. 5(A)), evidence of the 'bone remodelling transient' effect (Heaney, 1994; Kanis, 1994). The two most recent papers presented at key osteoporosis conferences in 2000 do show differences in bone mass at 18 months of follow-up (Dodiuk *et al*. 2001; Stear *et al*. 2000*a*,*b*; Fig. 5(B)). There is now an urgent need for more research on the effect of increased Ca on PBM attainment, with a shorter supplementation period but longer-term follow-up (New, 2001*a*).

Of considerable interest, not least in terms of the public health implications of using 'foods' rather than 'supplements', is the comparison between Ca alone compared with other Ca- 'fortified' supplementation vehicles. Milk and dairy products are an excellent source of Ca, and raised insulin-like growth factor-1 levels have been reported in children supplemented with milk, which may in turn point to a stimulation of periosteal bone apposition resulting in a slightly larger skeletal envelope (Cadogan *et al*. 1997). There is evidence in the literature that milk basic protein directly suppresses osteoclastic-mediated bone resorption, resulting in the prevention of bone loss in the animal model (Toba *et al*. 2000).

Differences in bone mass have also been reported in children consuming Ca-'enriched' foods (Bonjour *et al*.

Table 1. A review of calcium supplementation studies in children and adolescents

Reference	Country	Study details	Short-term effect	Long-term effect
Johnson *et al*. (1992)	USA	Prepubertal	✓	nr
Johnson *et al*. (1992)	USA	Peri- and post-pubertal	X	nr
Slemenda *et al*. (1993)	USA	Pre-, peri- and post-pubertal	—	X
Lloyd *et al*. (1993)	USA	Peri- and post-pubertal	✓	nr
Andon *et al*. (1994)	USA	Peri- and post-pubertal	✓	nr
Lee *et al*. (1994)	China	Prepubertal	✓	nr
Lee *et al*. (1997)	China	Prepubertal	—	X
Lee *et al*. (1995)	Hong Kong	Prepubertal	✓	X
Lee *et al*. (1996)	Hong Kong	Prepubertal	—	X
Nowson *et al*. (1997)	Australia	Pre-, peri- and post-pubertal	✓*	nr
Dibba *et al*. (2000)	Gambia	Pre-, peri- and post-pubertal	✓	nr
Dodiuk *et al*. (2001)	Israel	Peri- and post-pubertal	✓	✓
Stear *et al*. (2000*a*)	UK	Post-pubertal	✓	nr
Stear *et al*. (2000*b*)	UK	Post-pubertal	—	✓

nr, Not recorded; —, follow-up study; ✓, positive effect of Ca supplement on bone mass; X, no difference in bone mass between Ca-supplemented group and placebo group.
* Effect confined to 6 month measurement; no difference at 18 months.

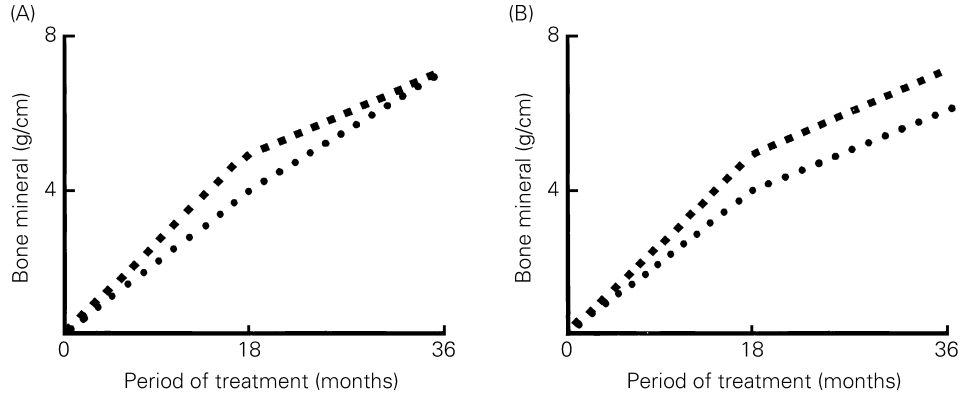

Fig. 5. Calcium supplementation and bone health; short-term and long-term benefits? (A) Earlier studies failed to show a difference in bone mass longitudinally once the supplement was withdrawn (Heaney, 1994; Kanis, 1994); (B) two of the most recent papers show differences in bone mass at 18 months follow-up (Dodiuk *et al*. 2001; Stear *et al*. 2000*a*,*b*). (■ ■ ■), With calcium supplementation; (● ● ●), controls.

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1997), and more recently in Ca-fortified orange juice (Lambert *et al*. 2000). In this latter study neither bone mineral content nor BMD changes were significant at 18 months, but differences were observed in bone turnover markers, suggesting that the additional Ca suppressed bone remodelling which was followed by a contraction of the bone remodelling space (Heaney, 1994). Interestingly, no studies have yet compared directly, within the same study design, Ca supplements alone *v*. other Ca supplementary vehicles.

Role of calcium in post-menopausal bone loss

The last two decades have been a time of marked controversy as to the effectiveness of Ca supplements in reducing peri- and post-menopausal bone loss (Kanis & Passmore, 1989*a*, *b*; Nordin & Heaney, 1990). The distinction between women in early (< 5 years) and late (> 5 years) post-menopause has significantly contributed to our understanding of the role of Ca in bone loss during the menopause (Dawson-Hughes *et al*. 1990). There is now a general consensus of agreement that Ca is effective in reducing bone loss in late post-menopausal women (O'Shea *et al*. 2000), particularly in those women with low habitual Ca intake (< 400 mg/d), but results of trials in the early post-menopausal stage remain inconclusive (Department of Health, 1998).

Role of calcium and vitamin D in prevention of fracture

Vitamin D and Ca supplementation have been shown to significantly reduce fracture rates in both institutionalised ($P < 0{\cdot}02$; Chapuy *et al*. 1992) and free-living elderly populations ($P < 0{\cdot}03$; Dawson-Hughes *et al*. 1997). Of interest is the finding that vitamin D supplementation alone is not effective (Lips *et al*. 1996). In a paper presented at the recent World Congress, a supplementation trial using cod liver oil containing 10 µg (400 IU) vitamin D did not prevent fracture in 1144 nursing home residents compared with controls (Meyer *et al*. 2000). A noteworthy point is the difference between vitamin D supplementation levels. In the studies by Chapuy *et al*. (1992) and Dawson-Hughes *et al*. (1997) the levels of supplementation were 20 and 17·5 µg/d respectively, whereas in the studies by Lips *et al*. (1996) and Meyer *et al*. (2000) only 10 µ g/d were used, without additional Ca.

Evidence of widespread vitamin D 'insufficiency' amongst population groups

Whilst it is well documented that vitamin D synthesis from sunlight is affected by the ageing process, there is a remarkable lack of awareness of this public health nutrition message. Findings of the recent National Diet and Nutrition Survey of older subjects aged 65 years and over (Finch *et al*. 1998) showed that 97 % of free-living elderly women and 99 % of those living in nursing homes had intakes of vitamin D below the reference nutrient intake, and over one-third of the institutionalised elderly were vitamin D deficient, with the likelihood of a much higher prevalence of vitamin D 'insufficiency' amongst this group (Chapuy *et al*. 1997). Furthermore, results of the recent National Diet and Nutrition Survey of young subjects aged 4–18 years (Gregory *et al*. 2000) found that significant proportions of those in the older age-groups had poor vitamin D status, a finding that has been mirrored in studies of other adolescent groups (El-Hajj-Fuleihan *et al*. 2000; Guillemant *et al*. 2000; Puliyel *et al*. 2000). These data (on both the younger and older populations) clearly have important implications for skeletal health.

Link between fruit and vegetables and bone health

The role of the skeleton in acid–base balance has been gaining increasing prominence in the literature from a combination of experimental (at the human, animal and cellular level), clinical and observational studies (New, 2001*b*). As shown in Table 2, there have been a number of population-based studies suggesting a positive association between high intakes of fruit and vegetables and bone health, with remarkable similarities in the findings of two of the largest (and most recent) nutrition and bone health observation studies (New *et al*. 1997, 2001*b*; Tucker *et al*. 1999). These findings are considerably strengthened by the results of the first population-based fruit and vegetable intervention trial (Dietary Approaches to Stopping Hypertension) which showed, as a secondary finding, a positive effect on Ca economy (Appel *et al*. 1997). An increase in fruit and vegetable intake from 3·6 to 9·5 daily servings decreased urinary Ca excretion from 157 mg/24 h to 110 mg/24 h. A noteworthy point is that measurements of markers of bone formation and bone resorption are planned for the forthcoming trial (Dietary Approaches to Stopping Hypertension II; D Barclay, personal communication).

Table 2. Impact of fruit and vegetables on bone: a review of population-based studies showing a positive link (from New, 2000*c*)

Reference	Country	Details	Findings
Eaton-Evans *et al.* (1993)	UK	Seventy-seven females, 46–56 years	✓ Vegetables
Michaelsson *et al.* (1995)	Sweden	175 Females, 28–74 years	✓ K intake
New *et al.* (1997)	UK	994 Females, 45–49 years	✓ K, Mg, fibre, vitamin C ✓ Past intake of fruit and vegetable
New *et al.* (1998)	UK	164 Females, 55–87 years	✓ K, fruit and vegetables
Tucker *et al.* (1999)	USA	229 Males, 349 females, 75 years	✓ K, Mg, fruit and vegetables
New *et al.* (2000*b*)	UK	Sixty-two females, 45–54 years	✓ K, Mg, fibre, vitamin C ✓ Past intake of fruit and vegetable

✓, Positive effect of nutrients with indices of bone health.

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The fruit and vegetable link with bone health is an exciting area for further research, the theoretical considerations of which have been discussed for over three decades (Wachman & Berstein, 1968; Barzel, 1970) but have only recently received much greater attention (Barzel, 1995; Bushinsky, 1998; New, 2001*c*).

Influence of other micronutrients on the skeleton

There is a growing awareness of the importance of vitamin K to bone metabolism, since several vitamin K-dependent proteins (such as osteocalcin and matrix gla protein) are involved in bone mineralisation (Shearer, 1997). The role of other micronutrients (including Mg, P, F and trace elements) and additional dietary components (including alcohol, caffeine and phyto-oestrogens) on skeletal health remains relatively undefined.

Concluding remarks

Exercise is important and beneficial to the skeleton, but more research is required on the exact type, intensity and duration of weight-bearing physical activity required for optimum bone health. Extreme levels of exercise which induce amenorrhoea are likely to result in a considerably lower attainment of PBM, the long-term effects of which remain unquantified. The importance of Ca to PBM attainment is controversial, and whilst Ca supplementation in the short term appear to be beneficial, a question mark remains over any long-term beneficial effects on bone mass. There is evidence that Ca is effective in reducing late post-menopausal bone loss, but further work is required in the peri-menopausal time period. The emergence of widespread vitamin D 'insufficiency' in a number of population groups requires urgent attention, particularly given the positive results from Ca and vitamin D supplementation trials on fracture reduction. On a final note, establishment of the essential 'ingredients' for optimum bone health, with a focus on individuals who are genetically susceptible to osteoporosis, is clearly a sensible way forward.

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