

## Invited commentary

# Can osteoporosis be prevented with dietary strategies during adolescence?

Osteoporosis is characterised by low bone mass and deterioration of skeletal architecture, resulting in increased bone fragility and risk of fracture at the wrist, vertebrae and hip. It is a major public health problem worldwide; in the UK alone, more than 3 million people have osteoporosis with one in three women and one in twelve men aged >50 years experiencing a fragility fracture. Similar fracture rates have been reported in white populations of northern Europe, the USA and Australasia. However, in other populations, such as those of Africa and China, the incidence is much lower. For example in Shenyang, China, the incidence of hip fracture is low (81 per 100 000 men and 67 per 100 000 women) compared with that in European countries (approximately 200–900 per 100 000), and similar to that in Beijing (Yan *et al.* 1999). With increasing life expectancy, the incidence of hip fracture is expected to increase 4-fold by the year 2050 across all ethnic groups (Cooper *et al.* 1992). There is currently no effective means of preventing osteoporosis and patients are often not identified until they have had their first fracture.

Optimisation of peak bone mass during adolescence and early adulthood may be an effective means of offsetting age-related bone loss and thus reducing the risk of osteoporosis later in life. Although genotype is believed to be one of the most important determinants of skeletal development and bone mineral accretion, diet and lifestyle may modify the genetic potential for achievement of optimum peak bone mass. Approximately 30% of adult mineral is deposited in the skeleton during adolescence and consolidation continues during early adulthood (Parsons *et al.* 1996). Ca- supplementation studies in children and adolescents have shown that bone mineral content can be increased beyond that achieved with usual intakes; however, the optimum duration of supplementation remains uncertain and the effects on future fracture risk are unknown (Prentice, 2004). It is also unclear as to whether the provision of Ca as salts or as milk offers different benefits for bone.

In the present issue of the *British Journal of Nutrition*, Du *et al.* (2004) have shown that supplementation of 757 Chinese girls aged 10 years, with Ca-fortified milk with or without vitamin D, over a 24-month period resulted in significant increases in the percentage changes in height, sitting height, body weight, and size-adjusted whole-body bone mineral content and bone mineral density, compared with unsupplemented controls. Those receiving additional

vitamin D had a significantly greater gain of 1.3% in size-adjusted bone mineral content compared with subjects who had received the milk supplement without vitamin D. The authors attribute these differences to their higher plasma vitamin D, which was more than double that of girls in the milk-supplemented group and the control group. There was a non-significant trend towards earlier onset of menstruation among the supplemented girls, suggesting that accelerated pubertal development may have contributed to greater bone mineral content in subjects in the milk-supplemented groups.

Based largely on studies in adults, the currently accepted mechanism of action of supplementary Ca on bone is thought to be mediated by reduced secretion of parathyroid hormone. This decreases osteoclast (bone resorbing cells) activation and skeletal turnover rate is in turn reduced. This phenomenon has been described as a bone-remodelling transient and the gains in bone mineral are usually reversed once bone turnover rate is restored to its basal rate (Heaney, 2001). However, it is unknown whether this mechanism of action applies during adolescence, as bone turnover may be regulated differently compared with adulthood. It is also uncertain whether a reduction in bone turnover rate, while the skeleton is still in an anabolic state, benefits long-term skeletal health.

Bone size and geometry at maturity may also be important determinants of future fracture risk. Duan *et al.* (2003) found that men with hip fractures may enter adulthood with a narrow femoral neck diameter, resulting in a reduced bending strength, and they suggest that structural abnormalities in women and men with hip fractures may have their origins during growth. Growth of the appendicular skeleton (or the long bones) is stimulated by the growth hormone (GH)–insulin-like growth factor (IGF)-1 axis and begins before the onset of puberty. IGF-1 also has an important role in regulation of Ca and P metabolism, as it stimulates renal transport of inorganic phosphate and kidney production of calcitriol. It has been proposed that any alteration of the GH–IGF-1 axis may affect growth and mineralisation of the appendicular skeleton, resulting in greater susceptibility to fragility fractures later in life (Bradney *et al.* 2000). Hepatic IGF-1 production, plasma IGF-1 concentration and the proportion of free or active IGF-1 (i.e. the portion not bound to its principal binding proteins) is regulated by dietary protein intake (Clemmons & Underwood, 1991). Although an adequate intake of dietary protein is essential for growth, it is not known whether

variations in protein intake and quality contribute to variations in bone size, mineral content and ultimately the achievement of optimal peak bone mass. Two studies have shown that increased milk and dairy product consumption were associated with higher plasma IGF-1 concentration in 12-year-old girls (Cadogan *et al.* 1997) and older men and women (Heaney *et al.* 1999). The mechanism has been attributed to increased protein intake from milk. In the study of Du *et al.* (2004) protein intake was increased by approximately 8%, but it is not known whether IGF-1 was increased and whether this might have led to the observed gains in body and sitting height.

Vitamin D (25-hydroxycholecalciferol, 25OHD) status is recognised to be an important determinant of bone health in all age groups. Overt 25OHD deficiency results in under-mineralisation of the bone collagen matrix, resulting in rickets in children and osteomalacia in older adults. Controversy exists over the definitions of 25OHD insufficiency across the lifecycle and the relative importance of ensuring adequate 25OHD for the achievement of optimum peak bone mass. Parathyroid hormone has been used as a functional indicator of vitamin D insufficiency and it has been proposed that 50–80 nmol 25OHD/l would be optimal for suppression of parathyroid hormone in the elderly (Meunier, 2001). Whether the same approach should be applied for defining insufficiency in adolescents (and other age groups) is uncertain. To date there has been some evidence to suggest that 25OHD insufficiency during adolescence may result in lower bone mineral status at maturity. The study of Du *et al.* (2004) showed that fortification of milk with vitamin D resulted in higher plasma 25OHD concentration compared with the other two groups, and that bone mineral gains were also greater compared with those consuming just the Ca-fortified milk. These findings suggest that achievement of optimum peak bone mass may be compromised by poorer 25OHD. Follow-up measurements of the subjects would determine whether the effects seen are maintained and whether factors other than bone mineral content, such as bone size and geometry, have been affected. It is also apparent that further work is needed to elucidate the role of Ca in bone development and whether the form of Ca is of importance.

Although Asian countries have a lower incidence of hip fracture, the incidence is increasing in some parts, such as Hong Kong (Lau *et al.* 2001). In addition to its growing elderly population, increased urbanisation and changing lifestyle may be explanatory factors. With adolescents in China accounting for approximately 19% of the nation's population (Wang *et al.* 1998), it is extremely important to identify the dietary and lifestyle determinants of optimum peak bone mass and to increase understanding of the relative importance of bone size and geometry and their determinants; thus, the potential

public burden of osteoporotic fracture could be reduced in the future.

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