Prevention and treatment of osteoporosis: common sense and science coincide

Osteoporosis is a major cause of fracture and orthopaedic surgeons should know how to prevent and treat it. The facts are simple but the practice difficult. The amount of bone in an adult depends on the peak bone mass and the rate of its subsequent loss, and both of these reflect the balance between resorption by osteoclasts and formation by osteoblasts (Dempster and Lindsay 1993).

Peak bone mass is determined by the interaction of genetic endowment and mechanical stress, modified by nutritional and endocrine influences; bone loss is affected by increasing age, declining activity and – in women – oestrogen deficiency. Common sense therefore dictates that to prevent osteoporosis the skeleton should be vigorously used and properly nourished, and that missing hormones should be replaced. Specific disorders such as thyrotoxicosis and corticosteroid excess should be recognised, and life-style ‘risk factors’ such as smoking, excessive alcohol, excessive thinness and immobility should also be considered.

So far so good. Why have these simple recommendations on exercise, nutrition (specifically calcium) and hormone replacement been so difficult to prove? The main reasons are the relative slowness of skeletal events, the lack of sensitive indicators of bone-cell activity, and the confusing flood of conflicting trials. Recent reviews suggest that common sense and science at last coincide (Riggs and Melton 1992; Lindsay 1993).

Exercise during growth increases bone size and density; prolonged immobility diminishes them. At any age, stress-induced changes in bone mineral density (BMD) are site-specific (Marcus et al 1992; Heinonen et al 1993). Exercise also improves muscle strength, mobility and stability, thus reducing the incidence of falls. It may also reduce cardiovascular mortality (Curfman 1993; Forwood and Burr 1993).

The statement that calcium is good for growing bones was, until recently, an unproved although sensible cliché. A three-year study of 70 identical twin pairs has now shown a significantly greater increase in radial and vertebral BMD in those prepubertal twins given more than the recommended daily allowance of calcium (Johnston et al 1992); similar results have been obtained in adolescent non-twin girls (Lloyd et al 1993).

In women, after the menopause, the daily addition of 1000 mg of oral calcium can also slow axial and appendicular bone loss (Reid et al 1993); and calcium supplements have been shown to reduce bone loss in late menopausal women on a low (< 400 mg daily) calcium intake (Dawson-Hughes et al 1990). Bone loss can be prevented in postmenopausal women with low bone density when additional calcium is combined with exercise (Prince et al 1991). None of these results should be accepted uncritically (Matkovic 1992; Heaney 1993), but they do provide new support for the beneficial skeletal effect of calcium at any age.

Hormone replacement therapy (HRT) produces consistent skeletal benefits, but controversies persist. Oestrogen reverses both the rapid bone loss induced by oophorectomy in young women and the increased rate of bone loss and incidence of fracture after a natural menopause, but this is not the whole story. Epidemiological studies suggest that it has other important benefits: cardiovascular mortality is significantly reduced, and life expectancy is increased (Grady et al 1992).

Unfortunately, oestrogen alone increases the risk of endometrial carcinoma, although this effect can be abolished by progestogen. Women who have not had a hysterectomy should therefore have progestogen as well as oestrogen; it is not known whether the addition of progestogen abolishes the cardiovascular benefit of oestrogen (Nabulsi et al 1993). Two further points about oestrogen remain unsettled. One is the increased risk of breast carcinoma, said to be significant only after ten years of treatment; the other is the possibility of bias in the populations studied. One possible bias is that those who have HRT (and continue with it) often adopt other life-style measures, such as exercise, oral calcium and cessation of smoking which themselves provide skeletal and cardiovascular benefits (Barrett-Connor 1991). These uncertainties mean that a properly controlled prospective trial of HRT is still necessary (Jacobs and Loefller 1992).

How else can we influence bone mass? Sodium fluoride stimulates osteoblasts and increases vertebral bone density, but does not reduce the rate of fracture. All other agents, including calcium and HRT, aim to reduce bone resorption. The time scale of bone remodelling by
bone-cell teams, however, means that reduced osteoclastic activity is not immediately followed by similar osteoblastic behaviour. As a result osteoblasts continue to fill resorption lacunae in the first year of treatment, producing what may be a temporary increase in measured bone density. Many such studies last only a year, measuring changes in bone density rather than fracture incidence, and their significance therefore must be in doubt.

Two other antiresorptive agents have received considerable attention. Disodium etidronate, a bisphosphonate first used in Paget’s disease of bone, has found a role in osteoporosis. In early trials, a smaller, cyclical dose, given for two weeks out of 13 with additional calcium, has been shown to reduce vertebral fracture rate and prevent bone loss (Storm et al 1990; Watts et al 1990; Drugs and Therapeutics Bulletin 1992); longer-term results are less impressive (Marcus 1993). This drug is licensed for the treatment of postmenopausal osteoporosis with vertebral fracture, especially when HRT is contraindicated or unacceptable.

Calcitonin, given by injection or nasally, also reduces bone resorption and, at least temporarily, increases bone mass. Its effect on fracture rate is currently being assessed. Neither etidronate nor calcitonin has the hormonal advantages of HRT.

For many years vitamin D was used either on its own or with calcium. Elderly and institutionalised people may be vitamin-D-deficient, as shown by a low plasma level of 25-hydroxy-vitamin D, and a proportion of them develop osteomalacia. It has been suggested that in old people increased parathyroid-hormone-mediated bone resorption stimulated by hypocalcaemia may contribute to osteoporosis, and that this may be prevented by increasing intestinal calcium absorption with vitamin D. Be that as it may, there is increasing enthusiasm to add physiological amounts of vitamin D (or its metabolites) to the intake of the elderly. This view is encouraged by the finding that vitamin D can reduce the observed loss in bone mass during late winter in the northern hemisphere (Dawson-Hughes et al 1991), and by the demonstration that giving both calcium and vitamin D to elderly women reduces the risk of hip and non-vertebral fractures (Chapuy et al 1992).

What does all this mean in practice? Ideally, bone loss should be prevented before fractures occur; but in real life medical attention is sought only after the first, often vertebral, fracture. The immediate steps are to establish the diagnosis, exclude any precipitating cause, deal with immediate symptoms, and explain the situation to the patient. The aim is then to prevent any further bone loss. This means continuing mobility, avoiding any lifestyle risk factors, taking sufficient oral calcium and making a decision about HRT or an alternative, probably etidronate. For the woman who has had a hysterectomy, the cardiovascular and skeletal advantages of HRT are currently thought to outweigh the possible slight increase in breast cancer (Grady et al 1992). For a woman with an intact uterus who needs progestogen, the advantages are less obvious and the immediate side-effects such as intermittent bleeding, are more troublesome.

HRT is most effective in maintaining bone mass in the early menopause, but the distinction between giving it for prevention of osteoporosis rather than for treatment, such as after an osteoporotic fracture, appears to be largely artificial (Ott 1992). The skeletal advantage of oestrogen is greatest during its administration and declines thereafter, since the rate of bone loss when oestrogen is stopped is similar to that just after the menopause (Felson et al 1993). Thus, women aged 75 to 80 years who had a ten-year course of oestrogen which stopped ten to twenty years earlier showed little difference in bone density from those who had not had oestrogen. Strategies can be devised to overcome this waning effect of oestrogen (Ettinger and Gray 1993).

The mean bone density in a population of hip-fracture patients is not significantly different from that of an age-matched non-fracture group, and there is therefore little enthusiasm for population screening to detect those at risk of fracture (Law, Wald and Meade 1991). For each individual, however, low bone density adds an additional risk of future fracture and this is normally the most important risk factor (Spector, Edwards and Thompson 1992; Slemenda 1993).

The accepted clinical indications for measurement of bone density include the assessment of bone mass as an indication of the likelihood of fracture (Melton et al 1993), the exclusion (or otherwise) of osteopenia suspected on radiography and the investigation of patients with bone disease. Measurement of bone density is probably unnecessary for a postmenopausal woman who has already had a vertebral compression fracture presumed to be due to osteoporosis. Such measurements have introduced science to the skeleton, but their clinical application needs to be selective.

Most osteoporotic fractures occur in postmenopausal women; thus, osteoporosis at this age has received most investigation. Osteoporosis in men (Anderson 1992) or that due to corticosteroid therapy (Meunier 1993), however, should not be neglected; rare forms of osteoporosis such as osteogenesis imperfecta and idiopathic juvenile osteoporosis provide some useful skeletal lessons.

Osteoporosis is only one factor influencing hip fracture; in the elderly, falls become increasingly more important (Evans 1988) as the benefits of previous HRT decline. Two recent papers emphasise the importance of falls and how their effect may be minimised (Hayes et al 1993; Lauritzen, Petersen and Lund 1993). In elderly patients, the propensity to hip fracture may depend more on simple geometry such as hip-axis length (the distance from greater trochanter to inner pelvic brim) than on BMD (Faulkner et al 1993). Despite this the maintenance of bone mass remains a priority for prevention, and ideally should start early in life and not when age and falls have already wreaked havoc. It has been suggested that many
women attending fracture clinics have risk factors for further fractures and would benefit from informed advice on the prevention of further bone loss (Gundle and Simpson 1993). For future advances in the prevention of osteoporosis the bone biologist must look to the further understanding of bone cells (Smith 1993); this needs to explain the recently described close linkage between bone density and vitamin D receptor alleles (Morrison et al 1994).

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REFERENCES

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