Osteoporosis and its management

Nathaniel W Liggett, David M Reid

Osteoporosis is a common systemic disease leading to premature fractures. This article reviews the state of the art of assessing the risk of future osteoporotic fracture and summarizes the prevention and treatment of the condition.

Osteoporosis has become increasingly recognized as a major health-care problem which will affect the lives of a considerable number of individuals. Asymptomatic at onset, insidious bone loss leads to the clinical consequences of painful fractures causing increased mortality, increasing debility and a reduced quality of life. Economically the consequences are dire, with costs of fracture treatment only recently estimated to cost the exchequer nearly £1 000 million annually (Dolan and Torgerson, 1998). The aim of this article is to try and raise the profile of this common disorder and to consider the alternatives to hormone replacement therapy (HRT) which are available for its treatment, and prevention. First we should define what we mean by osteoporosis.

Dr Nathaniel W Liggett is Specialist Registrar in Rheumatology, Aberdeen Royal Hospitals NHS Trust and **Dr David M Reid** is Reader in Rheumatology, University of Aberdeen, Aberdeen AB25 2ZD

Correspondence to: Dr DM Reid

DEFINITION

Osteoporosis has been consistently defined by consensus conferences as:

> **'A systemic skeletal disease characterised by low bone mass and microarchitectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture' (Consensus Development Conference, 1993).**

Clearly this definition relies on a pathological specimen and clinically the condition is not generally recognized until a fracture has occurred. This therefore led the World Health Organization in 1994 to redefine osteoporosis according to bone mass (*Table 1*).

Defining osteoporosis in terms of bone mass allows the condition to be diagnosed before it presents with clinical consequences of fracture (Cooper, 1996). However, the definition is essentially statistical and therefore, with a knowledge of the natural history of bone loss in women with age, it is possible to give the prevalence of the disease at various ages: 15% at the age of 50 years will have osteoporosis; 30% at the age of 70 years and 40% at the age of 80 years (Kanis et al, 1994). Although the use of this statistically-based definition may be useful epidemiologically, it does raise two main difficulties:

- How do we decide who should have their bone mass assessed to examine for osteoporosis?

TABLE 1.
Definition of osteoporosis based on bone mass

Bone mass	Definition
BMC or BMD > 1SD below the young normal mean	Normal
BMC or BMD < 1SD but > 2.5SD below the young normal mean	Osteopenia
BMC or BMD <2.5SD below the young normal mean	Osteoporosis
BMC or BMD <2.5SD below the young normal mean and a fragility fracture	Established osteoporosis

BMC = bone mineral content; BMD = bone mineral density (infra vide); SD = standard deviation. From World Health Organization (1994)

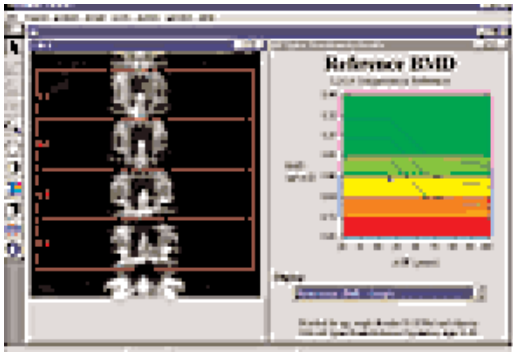

Figure 1. Dual energy X-ray absorptiometry (DXA) scan report showing a fan beam DXA spine image of an osteoporotic patient.

- Should all women defined as having osteoporosis by bone density have treatment?

ASSESSMENT OF BONE MASS

There is no evidence that radiological osteopenia is associated with symptoms and the first sign of the disease clinically is usually the occurrence of a low trauma fracture (a low trauma fracture being defined as a fracture sustained as the result of a force equivalent to the force of a fall from a height equal to, or less than, that of an ordinary chair).

At present the strongest predictor of the risk of future osteoporotic fracture is the finding of low bone mineral density (BMD) and this may account for approximately 75% of the fracture risk in an individual. The best validated technique available currently is dual energy X-ray absorptiometry (DXA). This uses low doses of ionizing radiation and enables accurate and reproducible measurements of BMD to be made at the clinically relevant sites of hip and vertebral bodies (*Figure 1*).

The results are reported in a variety of forms (*Table 1*), giving both the raw bone mineral content or expressing this value statistically in terms of standard deviations (SD) in relation to the patient's age (Z score) or in relation to a young adult mean (T score). It is upon these results that osteoporosis is diagnosed and treatment recommended (if appropriate). Generally speaking a measurement of bone mineral content or BMD at the site of potential future fracture produces the best predictive capacity, with each SD reduction in age-related bone mass being associated with a 1.7–2.6 times increased risk of fracture at that site (Marshall et al, 1996). Clinical indicators for bone densitometry are shown in *Table 2*.

Before we can consider the prevention and treatment of osteoporosis we need first to consider the possible causes and their diagnosis.

CAUSES OF OSTEOPOROSIS

Oestrogen deficiency accounts for the vast majority of cases of osteoporosis, whether postmenopausal or postsurgical (oophorectomy). The next commonest cause is that of the increasingly important (both clinically and medicolegally) situation of corticosteroid-induced osteoporosis. This will be addressed a little later in this article.

However, a small number of cases are secondary to other medical problems and their treatment would obviously include the treatment of the underlying condition:

- Thyrotoxicosis
- Hyperparathyroidism
- Multiple myeloma
- Malabsorption syndrome
- Alcohol abuse
- Anorexia nervosa.

Along with those medical conditions above known to cause osteoporosis, a number of other risk factors have also been associated with osteoporosis and hip fracture (Law et al, 1991). The important primary clinical risk factors are summarized in *Table 3*. These factors also need to be addressed when considering treatment of an individual as some may be modifiable and their alteration beneficial to the patient.

TREATMENT OF OSTEOPOROSIS

Once a diagnosis of osteoporosis has been established (confirmed where possible by BMD estimation) a treatment regimen is then determined for each individual patient, using the knowledge of each patient's own history, lifestyle and problems along with the knowledge of the benefits and side-effect profiles of each of the therapies available. However, all

TABLE 2.
Clinical indications for bone densitometry

Clinical finding	Objective
Oestrogen deficiency (particularly after early natural or surgical menopause, prolonged amenorrhoea, or where critical in decisions over hormone replacement therapy)	Selective case finding
Vertebral deformity, multiple low trauma fractures or osteopenia noted on X-rays	Confirm diagnosis
Monitoring therapy	Quantify response
Long-term corticosteroid use (more than 5 mg/day is thought to be deleterious to bone)	Identify fast bone losers
Other forms of secondary osteoporosis (anorexia nervosa, alcohol abuse, hyperparathyroidism, thyrotoxicosis, hypogonadism, malabsorption syndrome, post-gastrectomy and myeloma)	Quantify bone loss

Adapted from Department of Health (1994)

TABLE 3.
Clinical risk factors for osteoporosis

Previous fragility fracture	
Women with	An early natural or surgical menopause
	Premenopausal amenorrhoea
	Hysterectomy (with at least one ovary conserved) before 45 years of age
Current or planned long-term oral corticosteroid use (>7.5 mg prednisolone per day for 6 months or more)	
Family history of osteoporosis (especially maternal hip fracture)	
Smoking	
High alcohol intake	
Hypogonadism in men	
Physical inactivity	
Low body mass index	

women with reduced BMD, especially those within the osteopenia range (*Table 1*), should receive advice on calcium intake, lifestyle and exercise.

Calcium supplementation

A low calcium intake in the young and elderly may be a 'risk' factor for osteoporosis. It has been shown that calcium supplementation can slow the rate of bone loss in postmenopausal women (Reid et al, 1995) and should therefore be considered for all women who have a low natural intake. Each individual therefore should have an estimate of their calcium intake made and supplementation advised to bring their daily intake to over 800 mg per day.

Advice on lifestyle

From *Table 3* it can be seen that both cigarette smoking and heavy alcohol intake are associated with osteoporosis or low bone mass and therefore patients should be advised to stop smoking and to reduce their alcohol intake.

Exercise

Inactivity leads to an increased rate of bone loss while there is evidence that regular exercise can reduce the rate of further bone loss (Chow et al, 1987), providing that the exercise is weight bearing and undertaken regularly. Brisk walking, aerobics and rhythmic dancing have all been found to be beneficial in this respect. A soon to be published Consensus Working Group Report from the Chartered Society of Physiotherapists has examined the value of exercise on BMD and fall prevention, and have concluded that impact exercise is required for BMD improvement and muscle strengthening exercises for fall prevention, and that these exercises should be undertaken for at least three 20-minute sessions per week for 9 months or more to show benefit.

Prescription of specific drug therapy

The currently available licensed therapies for the prevention and treatment of osteoporosis in the UK are shown in *Table 4*.

Hormone replacement therapy: HRT is still considered to be the therapy of choice in the prevention and treatment of osteoporosis. Although evidence for its efficacy in preventing fractures is mainly derived from case-control and cohort studies rather than randomized controlled trials, it would be the most effective long-term therapy, especially in view of its potential cardiovascular benefit, were it not for the excess breast cancer risk which accompanies its long-term use (Torgerson and Reid, 1999).

It is likely to reduce fracture rates by about 50%, although its efficacy may only last as long as the therapy continues and may be rapidly lost thereafter. Its impact on hip fracture rates in the very elderly is therefore likely to be minimal.

Bisphosphonates: The bisphosphonates have made an impact in recent years, and will continue to make a major contribution to the management of osteoporosis. Working as specific anti-resorptive drugs they have been used extensively in the management of Paget's disease of bone and tumour-related hypercalcaemia. Although a number of bisphosphonates have been studied only two are licensed in the UK for use in the management of osteoporosis (Francis, 1995).

Disodium etidronate: Disodium etidronate (Didronel PMO™, Procter & Gamble, Staines), for the prevention and treatment of osteoporosis, is taken as a 14-day pulse of oral etidronate followed by 76 days of calcium supplementation. The cycle is then repeated. Although originally only licensed for 3 years continuous use, it now holds an open-ended license unlimited by time, with data from 7 years use being available (Miller et al, 1997). Although it is considered to have primarily anti-vertebral fracture efficacy, a recent cohort study using a clinical practice database has suggested efficacy in the prevention of hip fractures (van Staa et al, 1998). It is also the only drug currently licensed for the prevention and treatment of corticosteroid-induced osteoporosis (see below).

Alendronate: Alendronate (Fosamax™, Merck, Sharp & Dohme, Herts) is licensed for the treatment of osteoporosis in postmenopausal women and is taken as a single tablet, once daily, continuously. If additional calcium supplementation is required it must be taken at a different time of the day to the bisphosphonate.

The major difficulty with these drugs is their poor absorption from the gastrointestinal tract and, especially with alendronate, oesophagitis. Both need to be taken on an empty stomach,

TABLE 4.
Licensed therapies for osteoporosis prevention and treatment in the UK

Hormone replacement therapy	
Bisphosphonates	Etidronate
	Alendronate
Activated vitamin D	Calcitriol
Calcium and vitamin D	
Parental calcitonin	

with water, with the additional need for alendronate to be taken in an upright position. However, both preparations appear to reduce further vertebral fractures by 50%, with now additional good evidence that non-vertebral fractures, and perhaps even hip fractures, are similarly reduced especially in those patients taking alendronate (Liberman et al, 1995; Black et al, 1996). The non-response rate to bisphosphonates is around 10% and therefore assessment of efficacy, with repeat BMD assessment, is usually recommended.

Activated vitamin D: Calcitriol (1,25 dihydroxyvitamin D3, Roche Products, Welwyn Garden City) has been promoted as a treatment for established postmenopausal osteoporosis (Tilyard et al, 1992). As well as working by regulating intestinal calcium absorption it also has direct effects on osteoblasts to stimulate new bone synthesis as well as acting on osteoclasts. Although studies suggest a reduction in all fracture risk this may not be seen until after 2–3 years of treatment. The fear of additional 1,25 dihydroxyvitamin D3 causing increased calcium absorption leading to hypercalcaemia appears to occur in only a very small percentage of patients (0.4%), but would suggest that patients receiving Calcitriol should have their serum calcium levels monitored.

Calcium and vitamin D supplementation has been shown to reduce the rate of bone loss in postmenopausal women and in those over 65 years (Dawson-Hughes et al, 1997). Calcium and vitamin D supplementation is particularly important in the elderly, where a randomized controlled trial has shown effectiveness in preventing hip fractures (Chapuy et al, 1992). Use of 800 IU of vitamin D per day + 1 g of calcium can therefore be considered potentially useful in the frail or institutionalized elderly. Whether calcium, vitamin D or the combination has antifracture efficacy is unclear and a large Medical Research Council-funded study has just commenced in the UK to give an answer.

Calcitonin has been in and out of favour as a treatment for osteoporosis over the years. Its main drawback was that it has to be given parentally (by subcutaneous injection) in the UK, although a nasal preparation is available in main European countries and even the USA. A high incidence of systemic reactions and expense may limit its use, although in the USA nasal calcitonin is priced at the same level as alendronate. The intranasal preparation appears to reduce subsequent bone loss in patients with established osteoporosis (Overgaard et al, 1992) and has anti-vertebral fracture efficacy.

CORTICOSTEROID-INDUCED OSTEOPOROSIS

This has been a contentious issue leading to a number of high profile court cases. A recent systematic review of the literature has concluded that excessive bone loss is likely to occur when synthetic corticosteroids are used in doses of ≥7.5 mg of prednisolone per day or more, when prescribed for 6 months or more (Eastell et al, 1998). This review was used as the basis for drawing up a National Osteoporosis Society guidance algorithm (*Figure 2*; National Osteoporosis Society, 1998) on the management of corticosteroid-induced osteoporosis which has recently been published following a consensus meeting and wide consultation process.

CONCLUSIONS

Clearly osteoporosis is a major scourge of Western society but interest in the condition has risen exponentially in the last 10 years, partly because of advances in our understanding of the disease process, the ability to predict its onset, to reverse the process of bone loss and to measure the consequences of treatment, but also in part because of increased public awareness. Further advances are likely, especially in our understand-

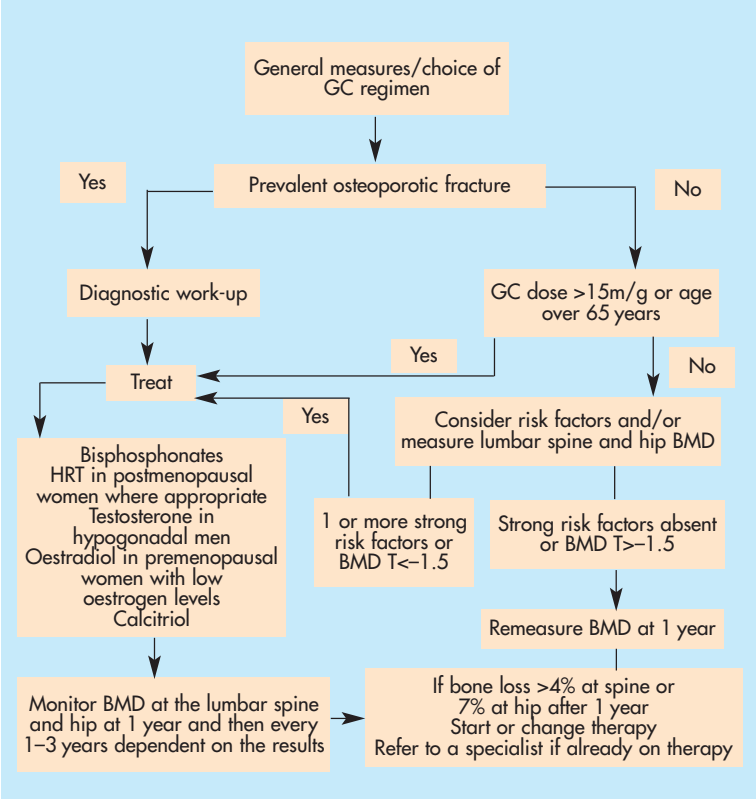

Figure 2. A national consensus algorithm on the management of corticosteroid-induced osteoporosis. BMD = bone mineral density; GC = glucocorticoid; HRT = hormone replacement therapy. From National Osteoporosis Society (1998).

ing of the genetic background of the disorder, and our ability not only to reduce bone resorption but also to enhance bone formation. The challenge will be how to target our improved therapies at the expanding elderly population to reduce the impact and costs of fracture. HM

DMR is grateful to the Arthritis Research Campaign and the National Osteoporosis Society for continued financial support. Figure 1 *is reproduced from Lunar Corporation Web site (www.lunarcorp.com) with permission.*

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Further information

The Royal College of Physicians of London has published national guidelines on the management of osteoporosis recently. Further information on the publication 'Clinical Guidelines for Strategies to Prevent and Treat Osteoporosis. London: Royal College of Physicians 1999' from the Royal College of Physicians, 11 St Andrews Place, London NW1 4LE.

The Department of Health have recently (June 1998) published a GP guidance document on the management of osteoporosis. Copies of the 'Quick Reference Primary Care Guide on the Prevention and Treatment of Osteoporosis' are obtainable from the Department of Health, Wellington House, 133–135 Waterloo Road, London SE1 8UG or via the World Wide Web (www.open.gov.uk/doh/osteop.htm)

KEY POINTS

- In women, oestrogen deficiency, in those genetically susceptible is the main risk factor for osteoporosis.
- Postmenopausal osteoporosis can be effectively prevented and treated with hormone replacement therapy, bisphosphonates, vitamin D + calcium.
- Bone densitometry assessment is cost effective in targeting preventative treatment for osteoporosis.
- A guidance document has recently been released outlining a strategy for the prevention and management of corticosteroid-induced osteoporosis.