TWO DECADES OF OSTEOPOROSIS
John Halsey FRCP, Richard Neary FRCPPath, Lindsey Wilcox MCSP

John Halsey took up a post as Consultant Rheumatologist in Lancaster in 1982. At the time the orthodox view of the management of osteoporosis was summarised by Price’s ‘Textbook of Medicine’, which he had read as a medical student; namely that ‘he who sets out to treat osteoporosis should be modest in his ambitions’. Within ten years Lancaster had become one of the first hospitals in the country to offer open access bone density scanning In 2002 Dr Halsey and his team were awarded the Hospital Doctor ‘Doctor of the Year Award’. This article reviews the epidemiology and diagnosis of osteoporosis, the role of biochemical markers and therapeutic options, and considers the role of multi-disciplinary team working and the need for a coordinated diagnosis of osteoporosis, the role of biochemical markers his team were awarded the Hospital Doctor ‘Doctor of the Year Award’. Richard Neary is a consultant in Clinical Biochemistry with a special interest in metabolic conditions. He has recently moved to Morecambe Bay from the University Hospital of North Staffordshire.

Lindsey Wilcox is Superintendent Physiotherapist (Medicine) at the Royal Lancaster Infirmary, with a clinical lead in rheumatology, and a specific interest in the management of osteoporosis, inflammatory joint disease and ankylosing spondylitis. She was involved in the development of the Physiotherapy Guidelines for the management of osteoporosis, published by the Chartered Society of Physiotherapy in 1999.

Osteoporosis is defined as a progressive, systemic skeletal disorder characterised by low bone mass and micro-architectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture.

EPIDEMIOLOGY AND DIAGNOSIS

The economic and personal consequences of osteoporosis are due to the resultant fractures which principally affect the hip, vertebral and forearm. The lifetime risk of a hip fracture in a woman is greater than the lifetime risks of breast, endometrial and cervical cancer combined. Table 1 shows the variation between men and women in the risk of fracture at different sites at 50 years of age. In women the lifetime risk of fracture is 46% compared with 23% in men. In women the risk of hip fracture is highest followed by forearm, vertebral and proximal humeral fractures. In men the pattern is similar but there are more vertebral than forearm fractures.

- Hip fractures are a major cause of mortality and morbidity in the elderly. Within one year they result in a 20% mortality, and permanent disability occurs in over 30% of patients
- Epidemiological studies have confirmed that only a third of vertebral fractures are symptomatic and diagnosed in clinical practice, and these are also associated with increased mortality
- Unless preventative measures are taken to reduce the burden of these osteoporotic fractures it is estimated that in the next 50 years there will have been a doubling of fractures with the aging population
- The annual cost to the NHS in England and Wales is estimated at £1.7 billion, notwithstanding the personal costs of pain and disability following fractures
- The annual cost of osteoporotic fractures to the local Morecambe Bay health community is estimated at £8.5 million, according to the Primary Care Strategy for Osteoporosis and Falls, published by the National Osteoporosis Society (NOS).

Table 1 Remaining lifetime risk of fracture(%) at 50 years of age

<table>
<thead>
<tr>
<th>Fracture site</th>
<th>Women</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>Forearm</td>
<td>20.8</td>
<td>4.6</td>
</tr>
<tr>
<td>Hip</td>
<td>22.9</td>
<td>10.7</td>
</tr>
<tr>
<td>Proximal humerus</td>
<td>12.9</td>
<td>4.1</td>
</tr>
<tr>
<td>Vertebral</td>
<td>15.1</td>
<td>8.3</td>
</tr>
<tr>
<td>Any of these</td>
<td>46.4</td>
<td>22.4</td>
</tr>
</tbody>
</table>

Table 2 Estimated annual expenditure on fracture management in Morecambe Bay

<table>
<thead>
<tr>
<th>Type of fracture</th>
<th>Predicted number of fractures</th>
<th>Hospital costs per fracture (£)</th>
<th>Per PCO (£)</th>
<th>Total cost per fracture (£)</th>
<th>Total cost per PCO (£)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hip</td>
<td>363</td>
<td>5,300</td>
<td>1,923,900</td>
<td>21,500</td>
<td>7,804,500</td>
</tr>
<tr>
<td>Wrist</td>
<td>363</td>
<td>500</td>
<td>181,500</td>
<td>500</td>
<td>181,500</td>
</tr>
<tr>
<td>Vertebral *</td>
<td>132 (660)</td>
<td>500</td>
<td>66,000</td>
<td>500</td>
<td>66,000</td>
</tr>
<tr>
<td>Other</td>
<td>330</td>
<td>1,400</td>
<td>462,000</td>
<td>1,400</td>
<td>462,000</td>
</tr>
<tr>
<td>Total cost</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>8,514,000</td>
</tr>
</tbody>
</table>

PCO = Primary Care Organisation
* of the 660 patients with vertebral fracture, 132 come to clinical attention. These costs are based on the National Osteoporosis Society Primary Care Strategy for Osteoporosis and Falls, 2002.
Despite the major implications of this silent epidemic the national profile of osteoporosis was very low until the publication in 2002 of the National Service Framework for older people, which acknowledged that strategies needed to be developed to identify those at highest risk of osteoporosis and fracture and ensure that appropriate prevention and treatment is provided to reduce fracture risk if falls occur\(^1\). The recent publication of the NICE Technology Appraisal 87 has confirmed that bone densitometry is the preferred means of establishing a diagnosis of osteoporosis and identifying those at increased risk of fracture who require treatment to reduce fracture risk\(^2\).

**DIAGNOSIS**

**a) Radiological methods**

There are four radiological methods of assessing bone density available to the clinician:

1. Plain radiographs. These are an inadequate means of diagnosing osteoporosis as bone mineral density (BMD) must be decreased by at least 50% for this to be evident. There is also a significant variation between reporting radiologists.

2. Dual Energy X-ray Absorptiometry (DEXA). The World Health Organisation (WHO) has produced classification and diagnostic criteria for osteoporosis based on BMD measurements using DEXA, which is the gold standard for diagnosing osteoporosis.

A patient’s BMD is expressed either as its relationship to the expected BMD for ‘young normal’ adults of the same sex (T-score) or to the expected BMD for the patient’s age and sex (Z-score). The difference between the patient’s score and the norm is expressed in terms of standard deviations (SD) above or below the mean.

Osteoporosis is defined as a BMD T-score of less than or equal to -2.5 and osteopenia as a T-score between -1 and -2.5.

The Lancaster Prodigy DEXA scanner measures the BMD of the lumbar spine (L1-L4) and the total hip. The BMD at a specific site is the best predictor of future fracture at that site. With increasing age caution needs to be exercised in the interpretation of spinal BMD as measurements are increased by the presence of lumbar spondylisis, osteophytes and aortic calcification.

3. Peripheral Instantaneous X-ray Imager (PIXI). This provides a mobile and cost-effective service for assessing the calcaneal BMD in primary care. Studies have confirmed that the calcaneal BMD measurements can predict fractures in postmenopausal women as effectively as a DEXA scanner\(^3\). The absence of a nationally agreed male reference range means that the PIXI scan cannot be used for men and currently it is not possible to provide a follow-up BMD measurement using the PIXI scanner.

4. Quantitative Computed Tomography (QCT). Although this is the best means of measuring trabecula volume density this is now mainly a research tool and compared to DEXA, QCT is less precise, uses high doses of radiation and is more expensive.

It is essential to be aware that the WHO definition of osteoporosis uses a T-score cut-off of -2.5 and this only applies to BMD measurements using DEXA. The T-score cut-off for diagnosing osteoporosis is lower (-1.6) using the PIXI scanner and higher (-3.5) using QCT. If a T-score of -2.5 is applied to QCT then osteoporosis will be over-diagnosed and patients potentially over-treated.

**Patient:**
- **ID:**
- **Weight:**
- **Ethnicity:**

<table>
<thead>
<tr>
<th>Region</th>
<th>BMD (g/cm²)</th>
<th>Young-Adult</th>
<th>Age-Matched</th>
</tr>
</thead>
<tbody>
<tr>
<td>L1</td>
<td>0.670</td>
<td>59</td>
<td>-3.8</td>
</tr>
<tr>
<td>L2</td>
<td>0.702</td>
<td>58</td>
<td>-4.2</td>
</tr>
<tr>
<td>L3</td>
<td>0.703</td>
<td>59</td>
<td>-4.1</td>
</tr>
<tr>
<td>L4</td>
<td>0.697</td>
<td>58</td>
<td>-4.2</td>
</tr>
<tr>
<td>L1-L4</td>
<td>0.694</td>
<td>59</td>
<td>-4.0</td>
</tr>
</tbody>
</table>

**Reference:**
- **AP Spine L1-L4**
- **Right Femur Total**

**Image not for diagnosis**

**Data from DEXA scan**

302
b) Biochemical methods

Biochemical measurements provide an insight into the state of the bone matrix and collagen backbone as well as clues to the pathological processes affecting their integrity. In addition to assisting our understanding of bone metabolism, biochemical measures in clinical practice have three potential roles:

1. Investigation of the underlying cause of osteoporosis
2. Assessing fracture risk
3. Monitoring the effect of treatment on bone, and the potential reduction in fracture risk

The diagnosis of osteoporosis may be apparent from the clinical picture, but secondary causes need to be excluded by an ‘initial screen’ before treatment is commenced (Table 3). Further investigations (Table 3) may prove beneficial if the initial screen shows an abnormality, if osteoporosis is diagnosed in a young patient, or there is a family history of either osteoporosis or fractures at a young age.

Parathyroid hormone (PTH) determination is essential for differential diagnosis of hypercalcaemia, but has several less immediately obvious roles. Osteoporosis associated with hypercalciuria is not uncommon, particularly in men, and PTH can help determine the cause. Relatively raised levels suggest a renal tubular leak of calcium whereas lower levels are consistent with hyperabsorption, but it is only the former that is associated with osteoporosis. Vitamin D deficiency is suggested by a PTH above or towards the upper end of the range associated with a low, but not necessarily abnormal, serum calcium or phosphate and low urine calcium. This arises as the serum calcium concentration is maintained by release of calcium from bone by PTH to compensate for reduced absorption. Although primary hyperparathyroidism is a well-recognised cause of osteoporosis, an elevated PTH and normocalcaemia can be a harbinger of this and is often associated with reduced BMD well before hypercalcaemia develops.

Vitamin D Assays are not widely available, but can be useful in specific situations. Most vitamin D is derived from the action of sunlight on sterols in the skin and is present in the circulation following 25-hydroxylation in the liver prior to activation by 1-hydroxylation in the kidney. Hypovitaminosis D is relatively common, particularly during the winter and early spring, in the elderly and dark-skinned races.

The importance of sex hormones in maintaining the skeleton is clearly established, but the mechanism remains speculative. Recent studies show that free (unbound) oestadiol and the adrenal androgen DHAS levels are positively correlated to bone density in men as well as women whereas there is an inverse relationship with sex hormone binding globulin, perhaps mediated by a reduction in free oestradiol.

The measurements described so far relate primarily to the bone mineral content, but recent interest has focused on markers of the collagen matrix or osteoblast products. These bone markers can be classified into those reflecting the rate of bone formation and resorption. Formation markers include bone-specific alkaline phosphatase, osteocalcin and procollagen type-1 N-terminal propeptide (PINP), and the resorption markers are deoxypyridinolene (DPD) and the C and N telopeptides (CXT and NTX). The latter are breakdown products of the collagen molecule which are subsequently excreted in the urine.

These markers have three possible roles.

Firstly, as an index of the rate of bone loss predicting so-called ‘fast losers’. The OFELY study shows that mid-range

<table>
<thead>
<tr>
<th>Initial screen (for most patients)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperparathyroidism/malnutrition</td>
<td>calcium, albumin</td>
</tr>
<tr>
<td>Hypophosphataemia</td>
<td>phosphate</td>
</tr>
<tr>
<td>Osteomalacia, hypophosphatasia</td>
<td>alkaline phosphatase</td>
</tr>
<tr>
<td>Hyperthyroidism</td>
<td>thyroid function tests</td>
</tr>
<tr>
<td>Liver/kidney disease</td>
<td>biochemical profile</td>
</tr>
<tr>
<td>Myeloma</td>
<td>electrophoresis (serum and urine)</td>
</tr>
<tr>
<td>‘idiopathic hypercalciuria’</td>
<td>urine calcium – 24-hour excretion</td>
</tr>
<tr>
<td>Previous renal stones</td>
<td></td>
</tr>
<tr>
<td>Malnutrition</td>
<td></td>
</tr>
<tr>
<td>Malabsorption</td>
<td></td>
</tr>
<tr>
<td>Vitamin D deficiency</td>
<td></td>
</tr>
</tbody>
</table>

Further tests (depending on clinical picture and initial biochemistry results)

| Menopausal status uncertain | FSH – women |
| Possible hypogonadism       | testosterone – men |
| Unexplained amenorrhoea     | gonadotrophins, oestradiol, prolactin |
| Investigation of underlying causes for: | parathyroid hormone – see text |
| Hyper/hypocalcaemia         |  |
| Idiopathic hypercalciuria – renal leak |  |
| Low urine calcium excretion |  |
| Osteomalacia due to vitamin D deficiency |  |
| Unexplained myopathy, familial osteoporosis | vitamin D – see text |
| Cushing’s disease           | urine cortisol |

New biochemical markers

| Assessment of rate of bone loss, fracture risk, response to treatment | See text |

Table 3 Initial screening and further tests in the diagnosis of osteoporosis
radius bone mineral density measured over four years decreases by up to 2.6% in “fast losers” compared to less than 0.7% in slow losers\(^9\). However, these measurements do not appear useful in predicting the rate of bone loss in an individual patient.

A second role for biochemical markers, also suggested by the OFELY study, is the prediction of fracture risk. Nevertheless, as a single predictor of fracture risk, BMD appears more reliable. This may be because it is a stable measurement whereas bone markers show greater day-to-day variability.

A third possible role is in prediction of the response to treatment. The studies on alendronate\(^6\), raloxifene\(^7\) and risedronate\(^8\) showed that the greatest reduction in fracture risk occurred in patients showing the greatest change in bone markers. Furthermore, bone markers respond in the first few months in response to treatment whereas improvements in bone mineral density take one to two years to become significant. Consequently, bone markers could provide an opportunity for optimising treatment much sooner and possibly obviate the need for repeat DEXA scanning.

Despite the potential benefits in using these markers their use remains under evaluation by specialist units.

**TREATMENT**

The management of osteoporosis has advanced enormously in the past 20 years with the introduction of new drugs with proven efficacy against fractures. The decision on which drug to select will depend on the age of the patient, the stage of the disease and the respective risk of vertebral and non-vertebral fractures.

The most significant change in the prevention and treatment of osteoporosis has been the demise of hormone replacement therapy (HRT), which was claimed to be the most important advance in preventative medicine. Although HRT results in a significant reduction in all fractures, following the publication of the women’s health initiative trial\(^9\) HRT is no longer the preferred option for the treatment of osteoporosis due to major health risks with prolonged therapy. These health risks relate to the increased risk of breast cancer and cardiovascular disease, which outweigh the beneficial effects on fracture reduction and the reduced incidence of bowel cancer. HRT is still appropriate in women with a premature menopause and may also be considered in young postmenopausal women with osteoporosis, provided the potential risks are appreciated.

Bisphosphonates represent the most major advance in osteoporosis management in the past decade and they work by inhibiting bone resorption. They currently account for 70% of the worldwide market for osteoporotic drugs. The fracture prevention date is more robust for alendronate and risedronate than cyclical etidronate for vertebral, hip and other non-vertebral fractures. There are no head-to-head comparisons for alendronate and risedronate, which appear to have similar efficacy. They are conveniently prescribed as a weekly preparation and apart from occasional oesophageal effects they are relatively free from adverse events. Cyclical etidronate was the first available bisphosphonate, but is now outdated and less well tolerated. As all studies examining the effectiveness of bisphosphonates gave calcium and vitamin D supplements it is recommended that these should be co-prescribed. For those patients who are unable to tolerate oral bisphosphonates there is data to confirm that bolus pamidronate (a non-licensed indication) is also effective when given by three-monthly infusions. Zolendronic acid is still being evaluated by clinical trials and the potential that therapy can be given by an annual infusion is potentially attractive. Until further studies are available it is assumed that treatment should be continued long term.

Selective oestrogen receptor modulators (SERMs) have an agonist action on the skeleton and antagonistic effect on the breast and endometrium. Raloxifene is the only available SERM and studies have shown it modestly increases BMD in women aged 31 to 80 with osteoporosis and reduces the risk of vertebral fractures, but not non-vertebral fractures\(^9\). It has major non-skeletal benefits with a significant reduction in the incidence of breast cancer, and possible cardiovascular benefits are under investigation. It is most appropriate in the management of younger postmenopausal women who are at high risk of vertebral fractures and it may also be useful for women who cannot tolerate, or who have had an unsatisfactory response to, bisphosphonates.

Strontium was launched in 2004 and works by reducing bone resorption and increasing bone formation. In postmenopausal women it has been shown to be effective in reducing vertebral and non-vertebral fractures in patients with low bone density, with or without prevalent fractures. Caution needs to be exercised in the interpretation of follow-up bone densitometry as approximately 50% of the apparent increase in BMD is spurious and due to the skeletal incorporation of strontium, which has a higher atomic number than calcium. It is likely to be useful in the management of older women, particularly those unable to tolerate bisphosphonates.

Calcitriol is licensed for the treatment of postmenopausal osteoporosis and is the active metabolite of vitamin D. It can cause hypercalcaemia and therefore requires regular monitoring. It is appropriate for elderly patients at high risk of further osteoporotic fracture in whom other treatments cannot be tolerated.

Unless a patient’s calcium intake is satisfactory (>1000mg daily) supplementation with calcium and vitamin D (Adcal D3 1 bd) is indicated, particularly in the elderly in whom there is a high prevalence of vitamin D deficiency. Vitamin D may be given to residential home patients as an annual injection to reduce fractures. Calcium and vitamin D supplements, however, should not be seen as an alternative to bisphosphonate or other therapies in patients who have already sustained a low trauma fracture. Two recently published studies from the UK do not support routine calcium and vitamin D supplementation for either the primary or secondary prevention of osteoporotic fractures\(^10,11\).

Teriparatide is a recombinant human parathyroid hormone licensed in 2004 for postmenopausal women who are at high risk of fracture. It is recommended by NICE as a treatment option for the secondary prevention of osteoporotic fragility fractures in women aged over 65 years who have had an unsatisfactory response to bisphosphonates or intolerance to bisphosphonates and who have an extremely low BMD (T-score >-4) or have a low BMD (T-score >-3) plus multiple fractures, plus additional risk factors. (An unsatisfactory response to bisphosphonates occurs when the patient has had another fragility fracture despite adhering fully to treatment for one year and there is a decline in BMD below pre-treatment baseline. Intolerance is defined as oesophageal ulceration, erosion or stricture or severe lower GI symptoms which warrant discontinuation of the bisphosphonate.) Teriparatide is classified by MBPCT as shared care prescribing only (Amber).

An algorithm based on NICE guidance for patients with >1 clinically apparent fracture is shown in Figure 1.
The treatment of osteoporosis should not solely be considered as the prescription of these effective therapies as all patients should be provided with general lifestyle advice, assessed for falls risk and offered patient education literature available from the National Osteoporosis Society. General lifestyle advice may need to include recommendations about smoking cessation, moderation of alcohol intake, regular weight-bearing exercise and dietary advice, particularly about achieving an adequate calcium intake. There is convincing evidence for the benefits of hip protectors, provided patients...
PHYSIOTHERAPY MANAGEMENT OF OSTEOPOROSIS

The role of physiotherapy in the management of osteoporosis is well established, standardised and evidence based. Improving a patient's balance through exercise and maintaining his or her bone density will reduce the risk of falling and, in turn, the risk of fracture and its related costs. Clinicians need to identify patients who are at risk of falling and should consider a physiotherapy referral, with a view to preventing this. For those with established disease, vertebral collapse and all its sequelae, techniques to improve respiratory function, mobility and pain management are all core elements in physiotherapy practise.

The natural stimulus for bone to maintain its functional strength is the loading, which results from gravitational forces and the tensions exerted by muscular activity. Exercise, therefore, has a role in reducing the long term risk of developing osteoporotic fracture. Exercise needs to be weight-bearing. Each of the three target groups mentioned below has unique exercise and lifestyle requirements for enhancing bone health and functional independence.

### Physiotherapy Assessment

For purposes of physiotherapy assessment patients referred are divided into one of three target groups:

1. **Osteopenia**
2. **Osteoporosis (no fracture history)**
3. **Osteoporosis (with previous fracture)**

**Target group 1.** Those diagnosed with mild bone change who are concerned with reducing the risk of further bone loss need high-impact exercise such as skipping and jogging or strength training (for the more normally, sedentary individual).

**Target group 2.** Those who have been diagnosed with osteoporosis but have not yet sustained any fractures require targeted weight-bearing exercise to load the sites predominantly affected, ie hip, vertebrae and wrist. Strength training is also needed using the principle of high load and low repetition focusing on muscle groups around the hip and wrist, the quadriceps, rhomboids and back extensors.

**Target group 3.** The frailer group of patients with severe osteoporotic change nearly always comprises a more elderly population. A gentle low-impact programme using gravity and body resistance exercise is recommended, along with stretching and balance training activities.

A detailed assessment is then carried out to identify all aspects of impairment, disability and handicap. This will include the following:

- **Height**
- **Weight**
- **Chest expansion**
- **Cervical/thoracic deformity**
- **Shoulder elevation**
- **Lumbar extension**
- **Lumbar endurance**
- **20 metre timed walk**
- **Balance**
- **Function**
- **Pain**

### Physiotherapy Management

Core elements in the physiotherapy management plan include:

- Education with regard to the disease process
- Lifestyle advice – smoking cessation, alcohol reduction, increasing dietary Ca intake
- Lifting and handling
- Postural awareness and re-education
- Exercise – what to do/what not to do

In 2004, 1500 patients were identified by DEXA as having osteoporosis, but in Lancaster only 26 of these patients were referred for physiotherapy. Although referral of patients with osteoporosis to physiotherapy is not standard practice, this is an important resource for patients which should be recognised more and used.

### THE NEXT DECADE

We have been very fortunate to have had a fully-funded high quality DEXA and peripheral scanning service, which means that we are equipped to deal with the increased requirements imposed by the NICE appraisal on the secondary prevention of low fragility fractures. The purchase of a new DEXA scanner has resulted in the potential to double the throughput of scans in excess of 4000 patients per year. However, service development needs to be based on quality rather than quantity, and this can only be achieved by the establishment of a fully-integrated service with involvement of primary and secondary care, physiotherapy, pharmacy and allied health professionals, biochemical services, falls prevention services, health promotion, public health, and patients’ agencies and charities. The trust and PCT need to develop a NICE implementation group to ensure that patients are managed in accordance with national guidance and that the statutory funding to develop this integrated service is provided.

The bone densitometry service is planning on developing an electronic DEXA reporting system and referrals which are currently directed though the Community Patient Contact Centre (CPCC) have the potential to be made electronically. Software is being installed to identify all low fragility fracture patients who attend fracture clinics at all hospital sites and this will enable DEXA scans to be offered to patient groups recommended by NICE guidance.

The enhancement of a fracture liaison service with the establishment of an osteoporosis/fracture reduction nurse specialist, with a key role in patient education and responsibilities between primary and secondary care, is a priority for service development. A one-stop service for osteoporotic patients identified by DEXA, with an education programme, investigations to exclude secondary causes of osteoporosis and treatment recommendations would improve quality and efficiency.

The importance of increasing public awareness has been recognised and to assist in this process and the re-establishment of a local branch of the National Osteoporosis Society the rheumatology department will be holding another patient awareness day with involvement of the key players in an integrated service. The days of ‘being modest with one’s ambitions in treating osteoporosis’ are gone forever: the time is here to prevent and treat the silent epidemic and reduce the burden of fractures to individuals and health and community services.

### FURTHER READING


REFERENCES


ACKNOWLEDGEMENTS

Dr Halsey acknowledges the invaluable contributions made by members of the rheumatology team who contributed to a study half-day on local osteoporosis services in January 2005, and especially to Cathi Greenbank and Bronwen Evans who run the bone densitometry service.