UNIT 1 OSTEOPOROSIS

Structure

1.0 OBJECTIVES

After reading this unit, you should be able to:

- define osteoporosis;
- outline the extent and importance of the problem;
- describe various risk factors for osteoporosis;
- elucidate screening techniques for osteoporosis; and
- discuss different preventative and therapeutic strategies for osteoporosis.

1.1 INTRODUCTION

You have by now learnt about the various joint diseases and musculoskeletal ailments afflicting the elderly. In this unit we propose to tell you about osteoporosis, the 'brittle bone disease', as it is commonly called. Osteoporosis is a disease with great public health importance in the elderly because it is common, often under diagnosed and responsible for substantial morbidity and even mortality. However, osteoporosis has long been neglected in India. Research has now shown that osteoporosis is as amenable to treatment as any other illness and several effective treatment options are available to combat this illness.

In this unit we propose to go over the extent of the problem and its clinical significance. We shall also review the various investigative modalities that help in diagnosis of osteoporosis. You will also get to know about risk factors for this disease and different modalities available for prevention and treatment.

1.2 DEFINITION

"Osteoporosis is a systemic skeletal disease characterized by low bone mass and microarchitectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture." The greatest clinical importance lies in predisposition to fracture, common sites for which are the spine, hip and the wrist. The fractures are not only disabling for the elderly but in case of hip fracture, also an important cause of death.

You must always keep in mind that the key component of osteoporosis is low bone mass. Bone mass is defined in terms of BMD (bone mineral density). BMD results are obtained by bone densitometry done either by DEXA (dual energy x-ray absorptiometry) scan or an ultrasound scan. The BMD is expressed as T score or Z score. **When the BMD is compared with the peak bone mass in a young adult of the same race and sex it is referred to as T-score. When you compare the BMD of a patient with healthy age matched controls of same race and sex it is termed as Z-score. T-scores are more commonly employed than Z-scores.** In the very elderly Z-scores may be preferable to T-scores. Fig. 1.1 and 1.2 show DEXA scan images from the hip and lumbar spine. Fig. 1.3 shows how the results of a DEXA scan are expressed.

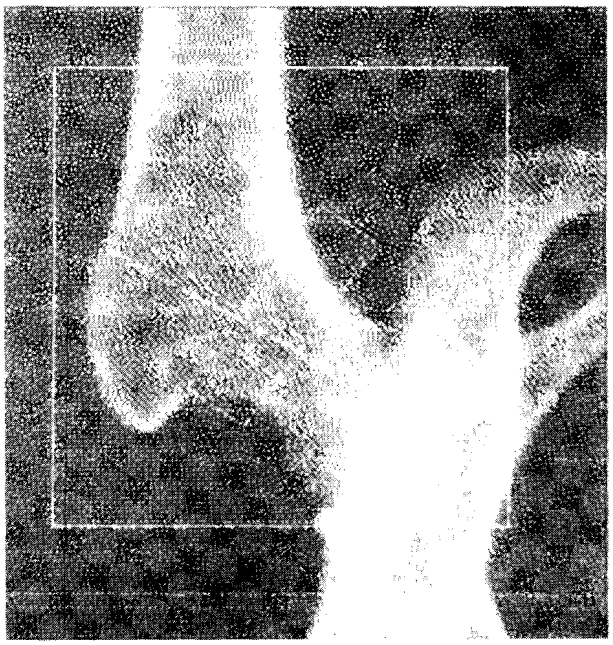


Fig. 1.1: Dexa image from left hip joint (*Courtesy*: Dr. R. Handa)

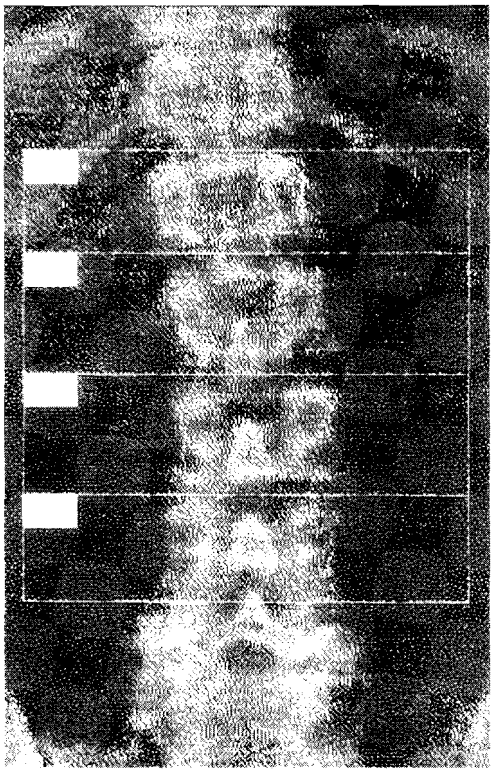
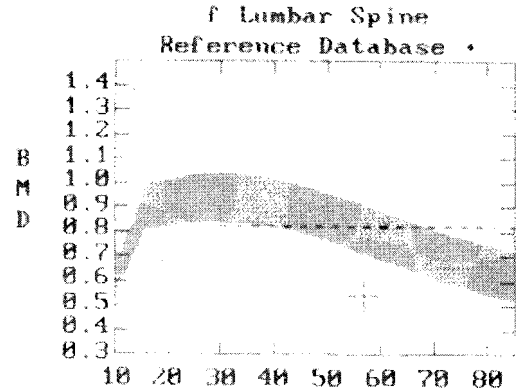


Fig. 1.2: Dexa image from lumbar spine (*Courtesy*: Dr. R. Handa)



BMD(L1-L4) = 0.532 g/cm^2

Region	BMD	T(30.0)		Z	
L1	0.411	-4.68	44%	-3.61	51%
L2	0.450	-5.26	44%	-4.07	58%
L3	0.548	-4.88	51%	-3.63	58%
L4	0.681	-3.96	61%	-2.68	70%
L1-L4	0.532	-4.68	51%	-3.47	58%

• Age and sex matched
T = peak BMD matched
Z = age matched TK 04 Nov 91

Fig. 1.3: Graphic recording of BMD (*Courtesy*: Dr. R. Handa)

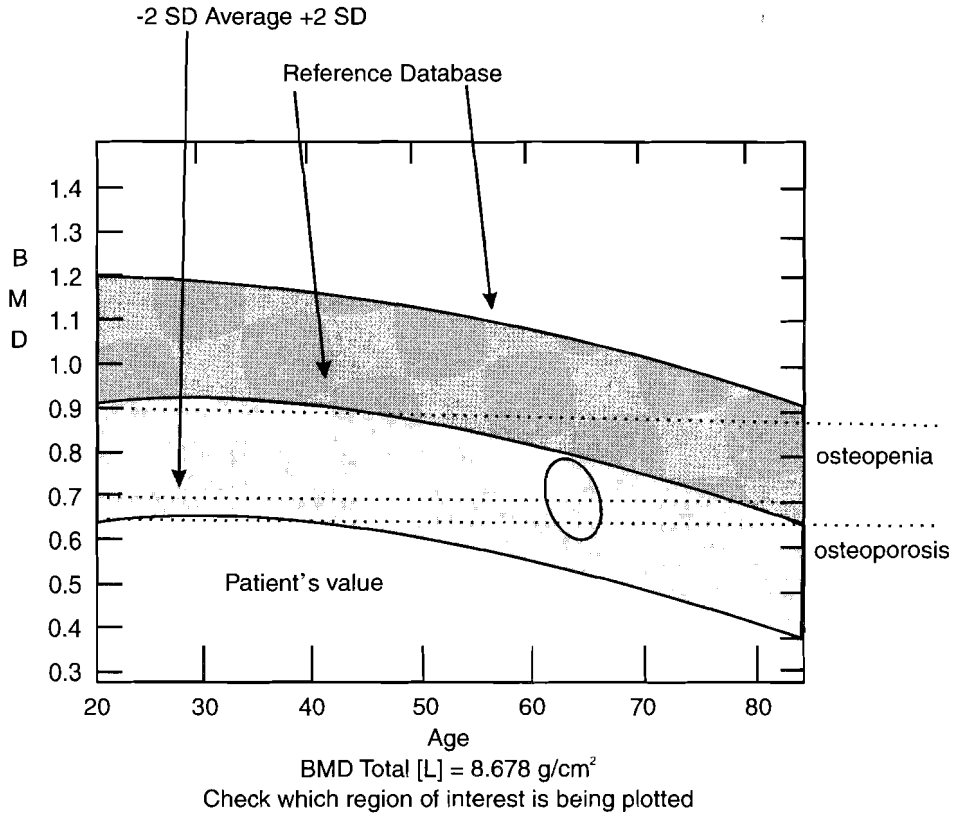
The WHO definitions for osteopenia and osteoporosis are given below:

T- Score

Normal bone density	:	0 to -1 SD below the average value of young adults.
Osteopenia	:	BMD more than 1SD below the young adult average but not more than 2.5 SD below
Osteoporosis	:	BMD value more than 2.5 SD below the young adult average
Established or severe osteoporosis	:	BMD value more than 2.5 SD below the young adult average along with the presence of one or more fragility fractures

Z- score

Z-score < -1 means BMD is lower by more than 1SD as compared to an age matched healthy adult of same sex. This indicates a value in lowest 25% of reference range. Z-score <-2 indicates lowest 2.5% of reference range. A Z-score below -1 reflects a value at which the risk of fracture is approximately doubled while the risk is quadrupled with Z-score below -2.



The entire gray region is the 95% confidence interval for the reference range. The darker grey region is values above average, the lighter grey below average.

Fig. 1.4: Graph showing risk of fracture

1.3 EPIDEMIOLOGY

With increasing numbers of the elderly in India, osteoporosis is fast emerging as a public health problem of massive proportions. It is difficult to get an accurate estimate of the problem since most patients with osteoporotic fractures, with the exception of hip fracture, are not hospitalized. Also an attempt to find out the exact etiology is seldom, if ever, made. All the available studies are hospital based and may grossly under estimate the true extent of the problem in the community. The conclusions that can be drawn from the available data are that:

i) osteoporosis occurs in both males and females in India'

ii) osteoporotic fractures occur more commonly in Indian males than females

iii) osteoporotic fractures usually occur 10-20 years earlier in Indian men and women, compared to Caucasians.

1.4 PATHOPHYSIOLOGY

Bone mineral density in any patient is related to peak bone mass at maturity (usually attained by the age of 30 years). Bone is a living tissue that is in a state of continuous turnover and renewal, which enables it to respond to physiologic loads and to repair microstructural defects. A focus of coupled osteoclastic/osteoblastic activity constitutes a "bone remodeling unit". Bone remodeling occurs at discrete sites within the skeleton and proceeds in an orderly fashion, with bone resorption always being followed by bone formation. This is known as "coupling" and is seen both in cortical and cancellous bone. At any point of time, bone which has been resorbed is yet to be replaced giving rise to what is termed remodeling space. This is increased in post menopausal osteoporosis. In older individuals the rate of resorption exceeds the rate of formation resulting in "too little bone" or osteoporosis. In the first 5 years after menopause, bone density declines by about 2% annually and then declines to 1% loss every year Hormone replacement therapy started soon after menopause slows postmenopausal bone loss to 0.5% annually. Antiresorptive drugs like estrogens, bisphosphonates and calcitonin decrease bone resorption. The term is misleading becauses bone resorption and bone formation are coupled — these drugs decrease the rate of both processes. The rate of bone resorption decreases within weeks and the rate of bone formation within months — due to the time sequence of the bone remodeling cycle. The remodeling space decreases and this filling in of the remodeling space accounts for the 5-10% increase in BMD that occurs after antiresorptive therapy. After an initial increase over 2-3 years the bone density plateaus off. Some drugs like intermittent parathyroid hormone and fluoride increase bone formation. Although, in this case, the BMD may continue to increase beyond the first 2-3 years, this increase does not always translate into increased bone strength.

1.5 CLINICAL FEATURES

There are no pathognomonic signs or symptoms of osteoporosis. In fact, the first manifestation of the illness may be a fracture. This is the reason that osteoporosis is also known as "the silent thief".

Fracture

Osteoporotic fractures commonly occur at three sites:

1) Spine

2) Wrist

3) Hip

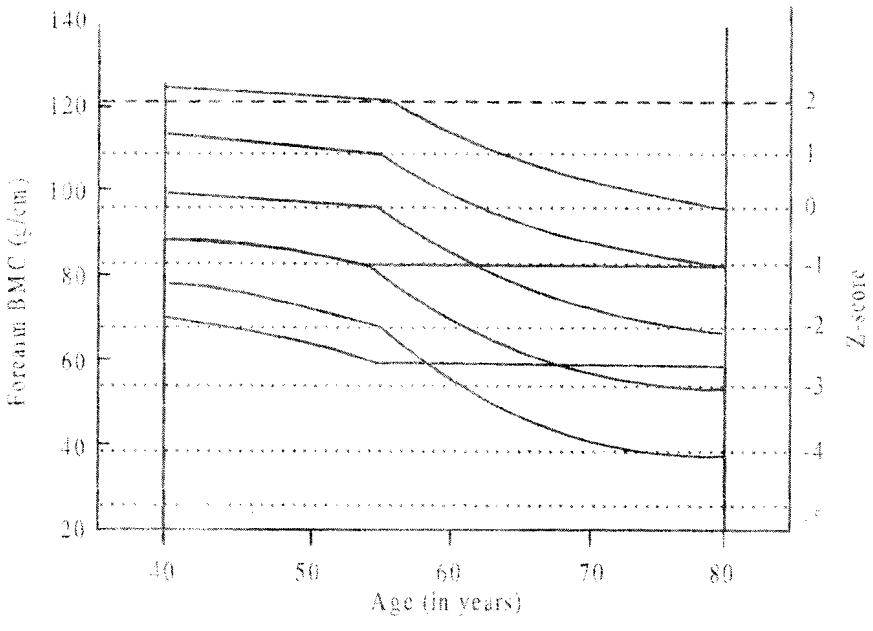


Fig. 1.5: Osteoporotic fracture at the forearm

Osteoporotic fractures occurring at the spine and forearm are associated with significant morbidity, but the hip fractures in elderly are the ones which are associated with an increased mortality as well. Spine fractures lead to back pain, kyphosis and loss of height. The mid thoracic and upper lumber spine are typically affected.

One crucial point is that bone mass is not the only determinant of fracture risk. It has received the maximum attention because it can be easily measured and manipulated. Fracture risk is affected by several other important factors such as neuromuscular in-coordination in the elderly, environmental hazards, falls etc. Attention to these factors, like improvement of lighting, removal of loose rugs, avoidance of slippery surfaces can help prevent falls and eventually osteoporotic fractures.

Some people classify osteoporosis into Type I and Type II osteoporosis.

Type I osteoporosis mainly affects postmenopausal females and accounts for cancellous bone fractures e.g. vertebral fracture.

Type II osteoporosis (also known as "senile osteoporosis") typically affects elderly men and gives rise to mainly cortical fractures e.g. at the hip.

The investigative and treatment modalities for both types of osteoporosis are similar.

Biochemical investigations like serum calcium, phosphorus, alkaline phosphatase etc. are normal in osteoporosis. Bone biopsy is seldom required in routine clinical practice, perhaps the only indication being to definitively exclude osteomalacia. Osteomalacia may co-exist with osteoporosis.

1.6 DIFFERENTIATING OSTEOPOROSIS FROM OSTEOMALACIA

Osteoporosis has to be differentiated from osteomalacia. Osteoporosis is 'too little of normal bone' while osteomalacia is 'bone with poor mineralization'. These differences are given in following Table 1.1.

Table 1.1: Differentiating Osteoporosis from Osteomalacia

	Osteoporosis	Osteomalacia
History		
Diffuse aches and pains	–	+
Localized back pain	+	–
Examination		
Pain by pressing bones	–	+
Loss of height	+	–
Serum chemistry		
Serum calcium	normal	normal or ↓
Serum phosphorus	normal	normal or ↓
Serum alkaline phosphatase	normal	increased
Vitamin D	normal	decreased
Radiology		
Looser's zones	–	+
Osteopenia and/or fractures	+	–

1.7 SCREENING

For screening it is important to be clear about the target group and the risk factors for determining whom it screen. For screening, various techniques for measuring bone mass are used. Biochemical markers of bone turnover are also useful.

1.7.1 Target Group

You will agree that due to resource constraints, universal screening of all post menopausal women, while ideal, is not practical or feasible in any country. The emphasis, therefore, has to be on "case finding". It is only women or men who are perceived to be at risk for osteoporosis who need screening. Let us take a look at these at risk groups:

1) Post menopausal women with risk factors (see Table 1.2)

2) Patients with history of osteoporosis related fractures

3) Patients with osteopenia or spinal deformities on spine x-rays

4) Patients on long term corticosteroids (>6 months)

5) Men with hypogonadism/other risk factors.

In the next section we propose to tell you more about these risk factors.

1.7.2 Risk Factors

You have just learnt that screening for osteoporosis should be ordered only in individuals with risk factors. Risk factors are situations, which predispose an individual to increased risk for that condition. These could include familial or personal factors, life style factors, drugs, or medical disorders as given below in Table 1.2.

Table 1.2: Risk Factors for Osteoporosis

Familiar factors/personal factors	Low BMI (<19)
	Familial prevalence
	Early menopause (< 45 years)
	White/Asian > Blacks
	Oophorectomy/hysterectomy
Life style factors	Smoking
	Alcoholism
	Physical inactivity
	Low calcium intake
	Lack of exposure to sunlight
Drugs	Long term steroids
	Dilantin sodium
	Replacement therapy (thyroxine, hydrocortisone)
	Heparin, warfarin
Medical disorders	Primary hyperparathyroidism
	Thyrotoxicosis
	Addison's disease
	Cushing's syndrome
	Rheumatoid arthritis
	Malabsorption syndromes
	Chronic liver disease
	Organ transplantation
	Chronic renal failure
	Prolonged immobilization
Men at risk for osteoporosis	Hypogonadism

Once you have made up your mind that you need to screen a given patient for osteoporosis you have a wide range of options available to you for measuring the bone mass. These range from conventional radiographs to bone densitometry.

Conventional radiographs are an insensitive way to assess osteoporosis since bone loss becomes apparent only when mass has decreased by about 30-50%. The single best technique to measure bone mineral density is DEXA (dual energy x-ray absorptiometry). DEXA scans are fast becoming available at Mumbai, Chennai, Hyderabad, Lucknow, Delhi and a few other cities in the country. Single energy x-ray absorptiometry can be used only for forearm and heel. In contrast, DEXA can be used for lumbar spine, proximal femur, forearm and even for assessment of total body composition. Ideally DEXA measurements should be made at 2 sites at least: lumbar spine (which may be a better site for assessing response to therapy) and femoral neck (which is a better site for fracture prediction). If resource constraints permit only one site, it is recommended that lumbar spine measurements be obtained in patients <60 years and femoral neck in patients >60 years. This is because osteophyte formation at the vertebral bodies and facet joints may interfere with BMD measurement. Ultrasound based BMD measurements at heel are inexpensive, do not have risk of radiation exposure and are portable. However, they are yet to be validated in large trials. For your convenience we have listed the various techniques for assessing bone mass and listed them in Table 1.3 given below.

Table 1.3: Techniques for Measuring Bone Mass

	Technique	Comments
1)	Conventional skeletal radiography	Insensitive method. Detects greater than 30-50% loss of bone mass only
2)	Photon absorptiometry (single and dual)	Requires radionuclide source of I photons. Largely replaced by x-ray absorptiometry
3)	Single energy x-ray absorptiometry	Useful only for peripheral sites, like forearm or heel. Cannot be used for axial skeleton
4)	Dual energy x-ray absorptiometry (DEXA)	Preferred method. Useful both for axial and appendicular skeleton. Can measure total body mineral content.
5)	Quantitative computed tomography	Can be used for forearm and spine. Drawbacks are high cost and high radiation dose. Can measure cancellous bone only.
6)	Ultrasonography	Used for cancellous bone in heel. Advantages low cost, no radiation and easy portability. Still to be validated but preliminary results are encouraging.

1.7.3 Biochemical Markers of Bone Turnover

Biochemical markers of bone turnover provide an integrated assessment of total disease activity in contrast to DEXA which is regional, and bone biopsy which is focal. Markers of both bone formation and bone resorption given below in Table 1.4, are increased in osteoporosis.

Immunoassays for osteocalcin, bone alkaline phosphatase, and intact type I collagen N-terminal propeptide represent the most effective markers of bone formation in osteoporosis. Pyridinium cross links and some of the type I collagen breakdown products in urine and serum are the most sensitive markers of bone resorption. Commercial kits are available for these tests.

Biochemical assessment has the potential advantage of obviating the need for repeated BMD measurements. It also has the theoretical advantage of being more useful for monitoring treatment efficacy, since changes in BMD may not become apparent for 2 years. The precise role of biochemical markers, however, is in a state of evaluation and we would like you to note that according to the present state of knowledge, biochemical markers of bone turnover should be considered adjunctive not substitutive to BMD measurements.

Table 1.4: Biochemical Markers of Bone Turnover

Bone formation	
a)	***Serum***
1)	Alkaline phosphatase (total & bone-specific)
2)	Osteocalcin
3)	Procollagen peptides
Bone resorption	
a)	***Urine***
1)	Pyridinium cross links of collagen (Pyridinoline, deoxy-pyridinoline)
2)	C&N telopeptide of type I collagen
3)	Hydroxylysine glycosides
4)	Hydroxyproline
b)	***Serum***
	— Tartarate resistant acid phosphatase

1.8 PREVENTION

Like most other public health problems of widespread magnitude, treatment alone cannot help a society or nation to cope with the problem of osteoporosis. This is especially so for populous countries like India. The importance of prevention cannot but be emphasized. It is never too late to start prevention, although earlier the better. Educating the public about measures to improve bone health is very important. It is vital to begin early, right at menarche. Young girls should be told about the various measures to improve bone health. Young girls should be encouraged to optimize peak bone mass through exercise and adequate dietary calcium and vitamin D (best obtained through milk and milk products). Perimenopausal women need to be acquainted with measures to reduce bone loss. These include hormone replacement therapy, regular exercise, life style modification (esp. alcohol, smoking), adequate dietary calcium, alendronate and calcitonin.

1.8.1 Life-style Habits

- Life style factors form the cornerstone of prevention.
- The basic strategy is to invest in bone health during childhood so that a high peak bone mass is reached. The beneficial activities include regular exercise, adequate dietary calcium (1-1.5 gm/day), and cessation of smoking and alcohol intake.
- Both isometric and isotonic exercises help. Isometric or resistance exercises require the body to work against gravity or against a force such as weights or springs. Isotonic exercises include walking, tennis, aerobics etc. Exercise increases muscle mass and strength and stimulates the building of bones. Exercise has a host of other beneficial effects like on the heart.
- Smoking is an important risk factor for hip and vertebral fractures.
- Cessation of smoking and giving up alcohol are general measures to help prevent osteoporosis.
- A calcium rich diet is essential for building bone tissue. Milk and milk products are rich not only in calcium but also in vitamin D.
- Vitamin D is essential for absorption of calcium. As you already know our body produces vitamin D through the action of sun on our skin. However, elderly people who stay indoors may need supplemental vitamin D. A daily intake of 400-800 units is adequate for most people.

1.8.2 Hormone Replacement Therapy

Hormone Replacement Therapy (HRT) is the most important means of reducing rate of bone loss. Women with BMD above the mean for young adults do not require HRT. However, women with BMD >1 SD below the mean for their age benefit the most from HRT.

1.8.3 Other Methods

In women who refuse HRT or cannot be considered for HRT, bisphosphonates can be used. Recently alendronate at doses (5 mg/day for 3 years has been shown to be a safe and effective nonhormonal option for prevention of post menopausal bone loss.

Another interesting alternative to conventional HRT in preventing post menopausal blood loss is tibolone. Tibolone is a synthetic steroid with simultaneous weak estrogenic androgenic and progestational activities. The daily dose is 2.5 mg given orally. The progestogenic metabolite of tibolone predominates at the level of endometrium, so that an atrophic endometrium is produced. This "non-bleeding HRT" has great inherent appeal. Other clinical situations where tibolone is particularly useful include: women who have had hormone- dependent tumors in the past, women who have had endometriosis and women taking gonadotrophin-releasing hormone agonists. Although overcoming the problem of withdrawal bleeding may be an important advantage of tibolone over the classic cyclic sequential HRT to improve compliance, other aspects such as cardiovascular protection and cancer risk need to be addressed on a long-term basis.

1.9 TREATMENT

Let us begin by taking a look at the goals of treatment which include:

a) Symptom relief

b) Improvement of bone mass

Symptom relief from the fracture pain is provided by use of analgesics. Calcitonin too has an analgesic action. Both parenteral and intranasal preparations are available. Common side effects of calcitonin include nausea, vomiting, nasal irritation and dizziness.

Bone mass increase is achieved by the use of antiresorptive agents and stimulators of bone formation, which are given below in Table 1.5.

Table 1.5: Drug Therapy of Osteoporosis

Anti resorptive drugs	• HRT • Bisphosphonates — Etidronate — Alendronate (available in India) — Pamidronate — Tiludronate — Risedronate • Calcitonin (parenteral and intranasal) • Tibolone
Other therapies	• Selective estrogen receptor modulators — Raloxifene — Idoxifene • Fluorides • Anabolic steroids • Parathyroid hormone (intermittent)

1.9.1 Calcium and Vitamin D

A large number of studies have shown that calcium is capable of slowing the rate of bone loss in women after menopause. This appears to be due to the ability of calcium to decrease bone turnover. Recommended daily intake is 1-1.5 gm of elemental calcium. Adequate Vitamin D (800 units daily) is essential for optimal calcium absorption.

1.9.2 Hormone Replacement Therapy

The term HRT refers to estrogen replacement with or without progesterone. Since prolonged use of unopposed estrogen can cause endometrial hyperplasia and carcinoma, women with an intact uterus should be given estrogen in combination with progestogens. Apart from prevention of bone loss and reduction of fracture risk, HRT has several other advantages like relief from menopausal symptoms and reduction in risk of coronary artery disease due to favorable influence on lipids. HRT is also said to protect against Alzheimer's disease. The drawbacks are return of menses, risk of endometrial carcinoma and predisposition to deep vein thrombosis and hypercoagulable disease. The return of menses precludes the widespread use of HRT by many Indian women. Estrogens increase the risk of endometrial cancer "during" and "after use" unless it is taken with adequate progestogen. Estrogen induced uterine cancer is usually but not always of a low stage and grade at diagnosis. The issue of risk of breast cancer is controversial. However, in contrast to endometrial cancer, the risk is limited only to current use. Women need a thorough breast and pelvic examination prior to starting HRT. The contraindications to use of HRT are summarised in Table 1.6.

Table 1.6: Contraindications to HRT

Absolute	Relative
Active breast cancer	– Migraine
Active endometrial cancer	– Past history of DVT
Pregnancy	– Uncontrolled HT
Severe liver disease	– Diabetes mellitus
Undiagnosed vaginal bleeding	– Gall stones
	– Fibroid/endometriosis
	– History of endometrial/breast cancer

The beneficial effects of HRT are more marked in women who begin therapy soon after menopause, but it is never too late to start. Bone protection requires continued use although long term studies are limited to 10 years or so. Most authorities now agree that on stopping treatment with HRT bone loss is not accelerated. However, the beneficial effects persist only as long as HRT is given.

Types of Estrogens and Estrogen Delivery Systems

Estrogens may be "natural" or "synthetic". Most HRT preparations contain natural estrogens, so named because they given rise to plasma estrogens identical to those produced by the ovary. However, many of these so called natural estrogens are prepared synthetically from plant sources. The natural estrogens commonly used are:

- Estrone
- Estriol
- Estradiol

Conjugated equine estrogens (CEE) contain about 50-65% estrone and are extracted from urine of pregnant mares.

Synthetic estrogens are more potent, less expensive and less commonly used. These include **ethinyl estradiol** and **mestranol**. Estradiol is available as transdermal patches 25 mcg, 50 mcg and 100 mcg. Estrogens may be given orally, as transdermal patches or as subcutaneous implants. Transdermal patches avoid the first- pass effect in the liver. Therefore, lower doses

can be used and it may be preferable in women with hepatobiliary or gastrointestinal diseases. The skeletal effects depend on the concentrations and not the route of HRT.

Progestogens

For women with an intact uterus a progestogen (synthetic progesterone) has to be added for endometrial protection. The addition of progestogen to estrogens does not compromise the bone protective effect. However the beneficial effect of estrogens on lipids may be attenuated depending on the type of progestogen and its influence on hepatic lipase activity.

Oral natural progesterone is seldom used because rapid metabolisation in the liver necessitates divided daily doses which is inconvenient. It may also cause drowsiness. The **progestogens** used include:

- Norethisterone
- Medroxy progesterone acetate
- Norgestrel
- Dydrogesterone

Hormones may be administered in several ways so as to ensure maximum patient compliance. These include **cyclic sequential, continuous sequential, continuous combined,** and **cyclic combined.**

Non-bleeding Therapies

Non-bleeding HRT can improve compliance markedly. The various strategies are:

i) Continuous combined therapy

ii) Estrogen replacement therapy and a progestogen intrauterine system

iii) Tibolone

Side-effects of HRT

Side effects of estrogens include breast tenderness, leg cramps, nausea and mild fluid retention. Side effects are relatively few with low dose HRT employed these days. Progestogens produce side effects similar to the pre-menstrual syndrome and include mood swings, irritability and depression, breast tenderness, fluid retention and abdominal bloating. Changing the types of progestogen and giving the lowest dose possible may help overcome these side effects. Withdrawal of cyclical progestogens induces withdrawal bleeding which is often responsible for poor compliance.

Phytoestrogens

These are plant derived molecules that have estrogenic actions. The best dietary sources are dry soya beans and all soya based products apart from variable amounts in the whole grain products and vegetables. **Ipriflavone** is a phytoestrogen that has been shown in some studies to increase bone mass in patients with established osteoporosis.

Designer Estrogens-Raloxifene

Raloxifene, a selective estrogen receptor modulator has mixed estrogen agonist and antagonist activity. **It has estrogen like beneficial effects on bone and lipids but lacks estrogen like effects on breast and uterine tissue.** The usual dose is 60 mg orally once a day without any relation to food. It has recently been approved by FDA for prevention of osteoporosis. The effects on fracture risk are not known. Another molecule under development is **idoxifene**.

1.9.3 Bisphosphonates

Bisphosphonates are synthetic analogues of pyrophosphate that inhibit bone resorption by decreasing osteoclastic activity. **Cyclical etidronate** and **alendronate** are the most extensively studies bisphosphonates in the management of osteoporosis, but limited data are also available for **pamidronate, clodronate, tiludronate, and risedronate.** Of the various bisphosphonates, **only alendronate is available in India.** Bisphosphonates are primarily used in the treatment of osteoporosis when HRT is contraindicated or refused. The optimal duration of therapy is not known. Combinations of HRT and bisphosphonates are generally believed not to confer added advantage over either agent alone.

Alendronate has been shown to reduce the risk of radiographically defined vertebral fractures in women with low BMD. The Fracture Intervention Trial, a land mark trial, demonstrated that among women with low bone mass and existing vertebral fractures, alendronate substantially reduces the frequency of hip, wrist and clinical vertebral fractures. Recently alendronate has been shown to be useful in the prevention and treatment of glucocorticoid induced osteoporosis. The benefit is not influenced by the age or sex of the patient underlying disease, or the glucocorticoid dose. All these studies have firmly established the role of alendronate in the prevention and treatment of osteoporosis.

You should always instruct the patient to take alendronate on empty stomach with plain water on awakening. Alendronate should not be taken with coffee, tea or juice. The tablet should not be chewed or sucked but should be swallowed as a whole. Remember to ask the patient to stay upright for at least half an hour after alendronate. Also no food/beverages are to be allowed till at least 30 minutes have elapsed. Adherence to these instructions will help you to avoid reflux esophagitis which is a common side effect with this drug. Finally you should remember that esophageal stricture or achalasia are absolute contraindications to alendronate while gastroesophageal reflux disease (GERD) is a relative contraindication.

1.9.4 Other Methods

Fluoride increases bone density, and recent studies have shown that when it is given along with calcium, it may even decrease vertebral fracture rates. However, the precise role of fluoride therapy in the treatment of osteoporosis is yet to be established. Anabolic steroids are no longer recommended. Newer drugs being tried out include intermittent parathyroid hormone therapy.

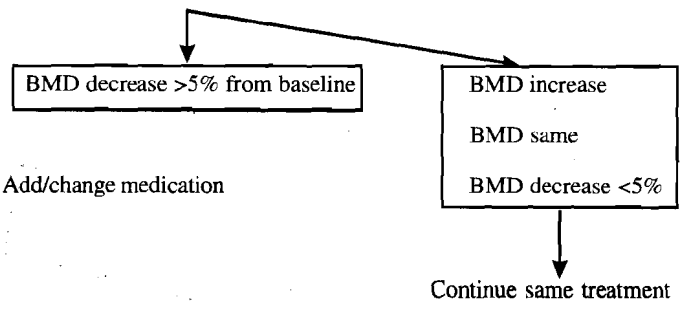
1.10 SPECIAL SITUATIONS

1.10.1 Corticosteroid Induced Osteoporosis

Since corticosteroids are widely used in medicine this topic warrants special mention. Corticosteroids by any route (parenteral, oral, topical or inhalation) increase bone loss. Daily prednisolone in doses ^{3} 7.5 mg result in significant loss. However, there is no dose or route which can be considered absolutely safe. Primary prevention should begin as soon as steroids are prescribed. The key points are tabulated and given below in Table 1.7.

Table 1.7: Corticosteroid Induced Osteoporosis

- Baseline BMD indicated before long term (6 months) of steroid therapy is started.
- Calcium (1.5 cm/day) and vitamin D (800 iu/day) given to all patients
- If 24 hour urine calcium > 300 mg/day, add thiazides
- If BMD T score -1 consider HRT
- If HRT refused /contraindicated consider alendronate or calcitonin
- Repeat BMD after 1 year



The lowest effective dose of steroids should be used. Calcium and vitamin D supplements, HRT, and a weight bearing exercise programme that maintains muscle mass are suitable first line therapies. Thiazide diuretics and sodium restriction are useful in reducing hypercalciuria due to steroids. Calcitonin and bisphosphonates are useful in patients unable to take HRT or who continue to worsen despite HRT.

1.10.2 Male Osteoporosis

Osteoporosis in women has relegated male osteoporosis to the background although 30% of the hip fractures and 20% vertebral fractures occur in men. Treatment options in men include bisphoshonates, testosterone and calcitonin. Bisphosphonates are agents of choice in idiopathic osteoporosis. Testosterone treatment is most effective in hypogonadal men where epiphyses have not closed completely. It may even help eugonadal men although there are concerns about risk of prostate cancer and HDL lowering in these patients. Whether testosterone induced increase in BMD translates into reduced fracture risk is not yet known.

Check Your Progress

1) Define the term osteoporosis.

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2) What are the common sites of osteoporotic fracture?

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3) How is bone mineral density measured?

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4) Tabulate the important risk factors for osteoporosis.

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5) Indicate True (T) or False (F) :

a) Ultrasound is the best method for BMD measurement. T/F

b) Patients with intact uterus need to add progestrone to estrogens during HRT. T/F

c) Reflux esophagitis is an important side effect of alendronate. T/F

d) HRT can safely be given to women with undiagnosed vaginal bleeding. T/F

e) T-scores on DEXA compare the BMD with age matched healthy subjects of same sex. T/F

1.11 LET US SUM UP

The past few decades have seen a sea change in the approach to management of osteoporosis—from passively accepting osteoporosis as an inevitable consequence of aging to active, aggressive management with rewarding results. With the introduction of safer, newer agents like alendronate, tiludronate, raloxifene and idoxifene, the whole field is one of cautious optimism. Increased public and physician awareness, and wider availability of bone densitometry are the need of the day in our country.

1.12 KEY WORDS

BMD (Bone Mineral Density) : It reflects the mineral content of bone and is measured by bone densitometer.

Bisphosphonate : Synthetic analogues of pyrophosphate that inhibit bone resorption.

HRT (Human Replacement Therapy) : Term refers to estrogen replacement with or without progesterone.

Osteomalacia : Group of disorder in which defect is laying down of calcium defect in laying down of calcium in already preformed osteoid tissue due to lack of Vitamin D.

Osteoporosis : The term describes a group of bone disorders in which the absolute bone mass is less than normal.

1.13 ANSWERS TO CHECK YOUR PROGRESS

1) Osteoporosis is a systemic skeletal disease characterized by low bone mass and microarchitectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture.

2) Osteoporotic fractures commonly occur at three sites:

   1) Spine
   2) Wrist
   3) Hip

3) Bone mineral density is measured by Bonedensitometry done either by DEXA or ultrasound scan.

4) Risk Factors for Osteoporosis

Familiar factors/personal factors	Low BMI (<19) Familial prevalence Early menopause (< 45 years) White/Asian > Blacks Oophorectomy/hysterectomy
Life style factors	Smoking Alcoholism Physical inactivity Low calcium intake Lack of exposure to sunlight

Drugs	Long term steroids Dilantin sodium Replacement therapy (thyroxine, hydrocortisone) Heparin, warfarin
Medical disorders	Primary hyperparathyroidism Thyrotoxicosis Addision's disease Cushing's syndrome Rheumatoid arthritis Malabsorption syndromes Chromic liver disease Organ transplantation Chromic renal failure Prolonged immobilization
Men at risk for osteoporosis	Hypogonadism

5) a) F

b) T

c) T

d) F

e) F

1.14 FURTHER READINGS

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