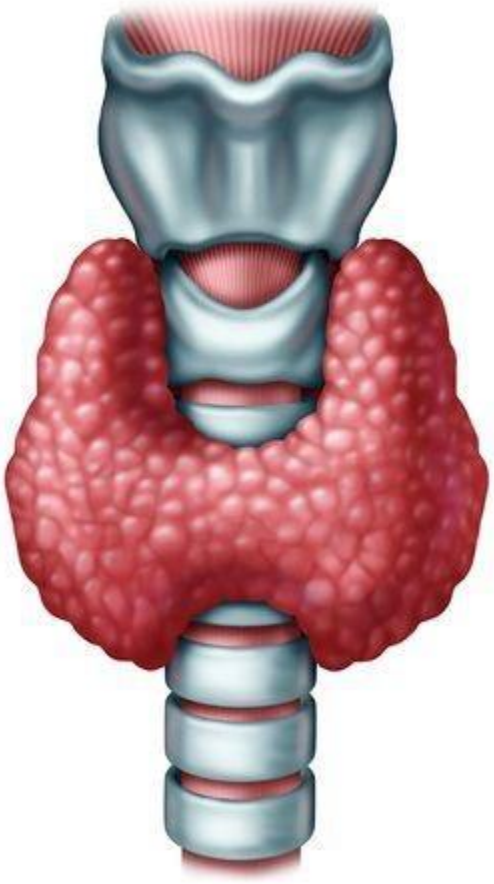

Introduction to osteoporosis

Objectives

Understanding the definition of osteoporosis
Causes of osteoporosis
Impact of osteoporosis
Diagnosis of osteoporosis
Treatment of osteoporosis

Revised By
Hadeel Awartani
Abdullah AlOmar

Color index:

- Important
- Notes
- Extra

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Reference: Girls' & Boys' Slides

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Waiting for your Feedback

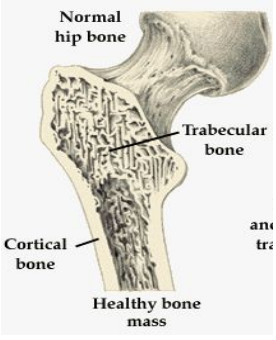
Types of Bone

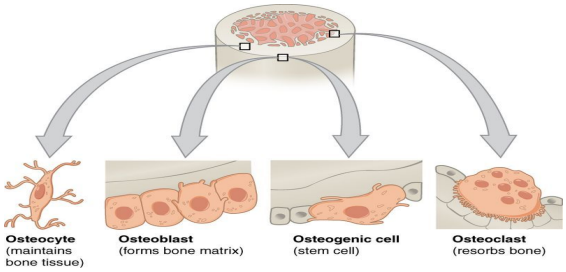
Cortical Bone

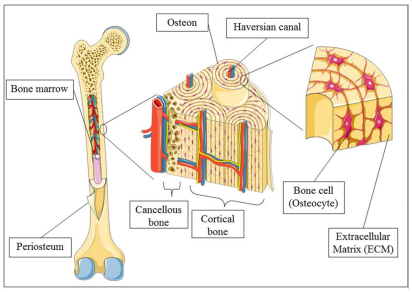
The compact bone of Haversian systems such as in the shaft of long bones. The femur is the classic example.

Trabecular Bone

The lattice-like network of bone found in the **vertebrae** and the ends of long bones.
The difference pattern of bone loss affecting trabecular and cortical bone results in two different fracture syndrome.







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Types of Bone cells

Lay down bones
Osteoblasts

The bone forming cells which are actively involved in the synthesis of the matrix component of bone (primarily collagen) and probably facilitate the movement of minerals ions between extracellular fluids and bone surfaces.

Osteocytes

They are believed to act as a cellular syncytium that permits translocation of mineral in and out of regions of bone removed from surfaces. it is thought that they control the action of both osteoclasts and osteoblasts.

Osteoclasts

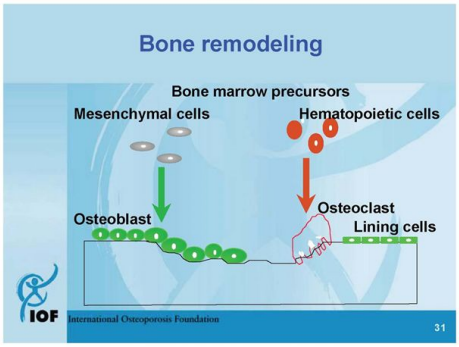
The bone resorption cells.

Dr's note: The activity of both the osteoblasts and the osteoclasts is balanced.
In osteoporosis, the activity will be unbalanced.
Osteoporosis can occur due to 3 mechanisms:
1- The peak bones mass is not that sufficient to last for living.
2- Rapid bone resorbing due to overactive osteoclasts.
3- The bones anabolism is not that efficient due to suppressed osteoblast.

1:29

Bone has three major functions

1. Provide rigid support to extremities and body cavities containing vital organs.
2. Provide efficient levers and sites of attachment of muscles which are all crucial to locomotion.
3. Provide a large reservoir of ions such as calcium, phosphorus, magnesium and sodium which are critical for life and can be mobilized when the external environment fails to provide them. Recall hyper and hypoparathyroidism.



Osteomalacia

"Rickets in children's/تلين العظام"

Failure of organic matrix (osteoid) of bone to mineralize normally. Abnormal remodeling of the bones

A number of factors are critical for normal bone mineralization. An absence or a defect in any one of them may lead to osteomalacia, the most common biochemical causes are a decrease in the product of concentrations of calcium and phosphate in the extracellular fluid so that the **supply of minerals to bone forming surfaces is inadequate.**

A mineralization problem due to inadequate conc. of Ca , P or vit D, Fracture will happen by very minor trauma.

Extra: Introduction to Osteoporosis—Decreased Bone Matrix

Osteoporosis is the most common of all bone diseases in adults, especially in old age. It is different from osteomalacia and rickets because it results from diminished organic bone matrix rather than from poor bone calcification.

In persons with osteoporosis the osteoblastic activity in the bone is usually less than normal, and consequently the rate of bone osteoid deposition is depressed. Occasionally, however, as in hyperparathyroidism, the cause of the diminished bone is excess osteoclastic activity.

5:30

Primary Osteoporosis

Type I Osteoporosis (Post Menopausal)

Primary osteoporosis is due to normal aging processes

Fractures of bones composed mainly of Trabecular bone + flat bone

e.g., Distal Radius – Colle's fracture

Vertebra – Crush & Wedge fractures

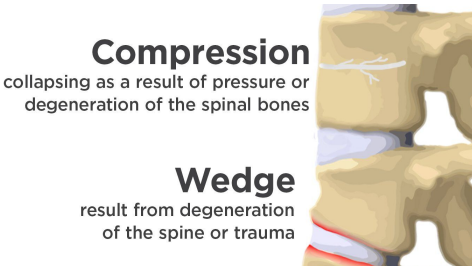
Usually affects woman within 15 years of menopause.

Type II Osteoporosis (Senile)

Fractures of bones composed of both cortical & Trabecular bone.

e.g., Hip– Femur neck fracture

Usually affects individual over age of **70 years**. The doctor stressed at this point.



هنا الدكتورة قالت مو مهم تحفظونه بس الدكتور قال مهم اللي محدد!

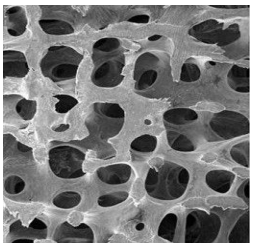
Important	Type I	Type II
Age (Yr.) *	51 : 75 Both are more common in female.	>70
Sex Ratio (F:M)*	**6** : 1	2 : 1
Type of bone loss*	Mainly trabecular	Trabecular & Cortical
Rate of bone loss*	Accelerated	Not accelerated
Fracture sites*	Vertebrae (Crush) & **distal radius**	Vertebrae (Multiple wedge), **hip, pelvis, proximal humerus**
Parathyroid Hormone	Decreased	**Increased**
Calcium absorption	Decreased	Decreased
Metabolism of 25(OH)2D to 1,25(OH)2d	**Secondary** Decreased	**Primary** Decreased
Main causes*	Factors related to **menopause**	Factors related to **aging**

Definition of osteoporosis

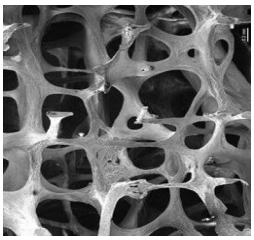
Skeletal disorder characterized by **compromised bone strength predisposing a person to an increased risk of fracture**. Bone strength reflects the integration of bone density and **bone quality.** The most characteristic feature of osteoporosis is the easily fractured due to fragile bones.

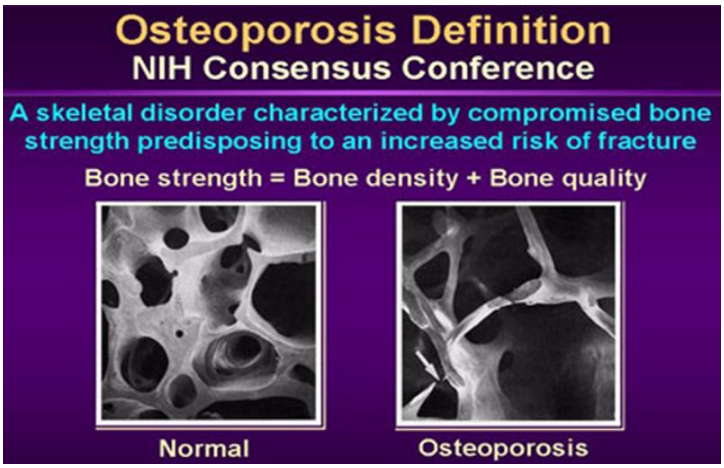
Decrease in bone mass and strength associated with an increased tendency to fractures

Normal bone



Osteoporotic bone "Huge pores"





Osteo = bones Prosis = holes

Risk Factors non-modifiable

- Age (increasing)
- Low BMI (small, low weight;< 58 kg)
- Ethnicity: Caucasian > Asian/Latino > African American
- Family History of Fracture

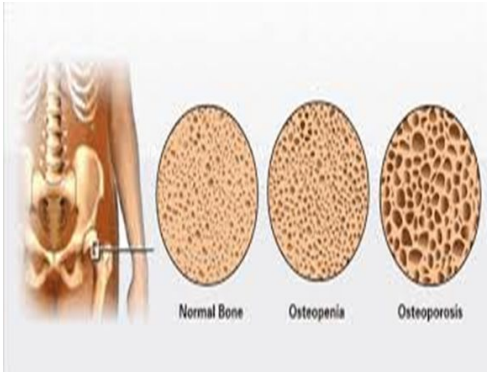
Very important. MCQ AND SAQ.

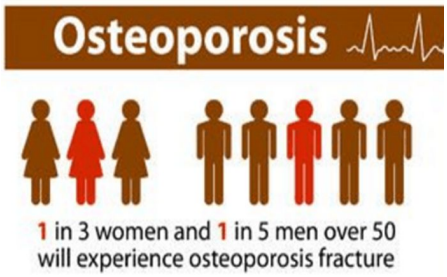
Risk Factors Modifiable

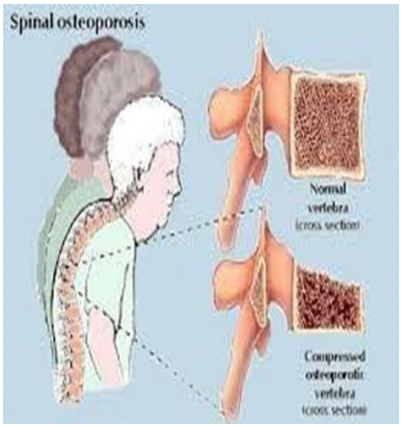
- Sex Hormones (low estrogen/testosterone)
- Inactive lifestyle
- Cigarette smoking
- **Hyperparathyroidism** (primary or secondary)
- GI conditions which impair adequate nutrition
- **Proton pump inhibitors**
- Low calcium and vitamin D
- **Hyperthyroidism**
- Steroids or Cushing's
- Excessive alcohol
- Rheumatoid arthritis

Clinical presentation of osteoporosis

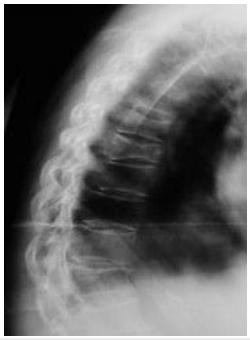
- Generally patients are **Asymptomatic** even with very low bone densities Hip Fractures. It is impossible that osteoporosis can cause pain, the pain is secondary to bone fractures , osteoarthritis or others.(asymptomatic until a fracture occurs)
- **The first manifestation of reduced bone mass is usually a wrist fracture or a vertebral crush fracture caused by a small amount of force which produces severe localized pain.**
- Hip fractures with its fatal complications also occur commonly as osteoporosis become more severe.
- Acute or chronic **Back pain** secondary to vertebral fractures
- In well established osteoporosis dorsal Kyphosis and loss of height occurs.
- Atraumatic or low impact fractures يصحو المريض من النوم ويتفاجئ بكسر في الرسغ او الساق







COMMON SITES OF FRACTURE



SPINE

FOREARM

HIP

2:46

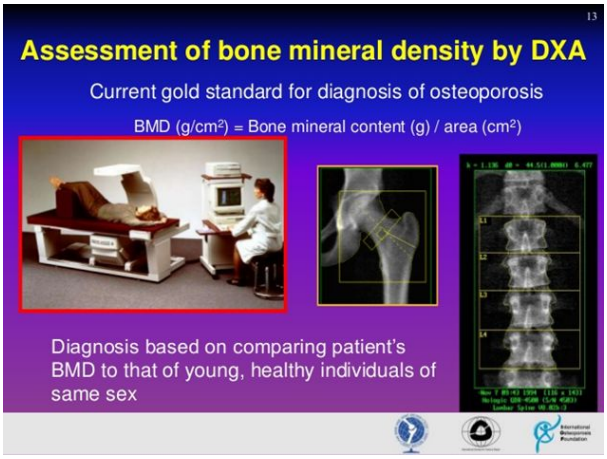
DIAGNOSIS OF OSTEOPOROSIS

Assessment of bone mass available methods

Single-Photon absorptiometry	SPA
Dual-Photon absorptiometry	DPA
Computed Tomography	CT
Dual-Energy X-ray Absorptiometry	**DEXA/DXA**

They **measure** **bone mass** by the ability of the tissue to absorb the photons emitted from the radionuclide source or the X-ray tube.

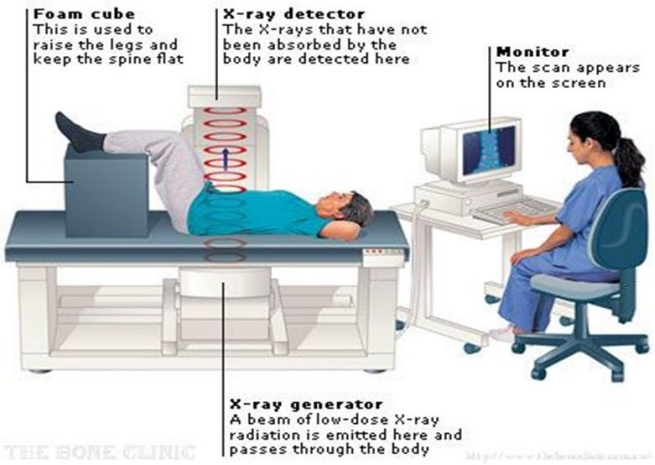
Age related bone loss particularly trabecular bone in the spine begins in women before menopause.



The most common sites to measure bone density are:

1- Hip

2- Lumbar vertebrae (1-4)



DEXA is what is used to diagnose osteoporosis

Other methods are not used anymore for osteoporosis diagnosing

Female Slides

- It is appropriate to begin to look for risk factors that predispose a person to osteoporosis and develop a rational prevention program tailored to person's risk before the menopause.
- Women with thin light frame, history of low calcium intake, decreased physical activity, high alcohol or caffeine consumption, smoking, family history of osteoporosis, history of prior menstrual disturbances or history of drug like antiepileptic's or steroids are all high risk groups and in the presence of one or more of such risk factors measurement of BMD provides further information to the risk of fractures.

Important WHO 1994 Definition based on BMD **"T score"**

T-score: Difference expressed as standard deviation compared to young (20's) reference population

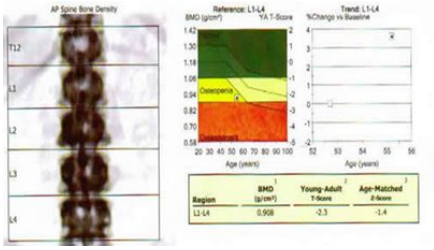
Normal: greater than or equal to −1 SD

Osteopenia: BMD which lies **between** − 1 and −2.5 SD

Osteoporosis: less than or equal to − 2.5 SD

Severe (established) osteoporosis : osteoporosis with 1 or more fragility fractures, −2.5 and below, plus one or more osteoporotic fracture(s)

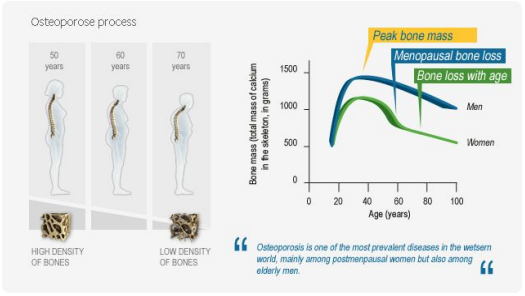
Bones density cannot be measured by an absolute number. To diagnose osteoporosis, you have to compare a patient's bone density with the bone density of her or his age group.



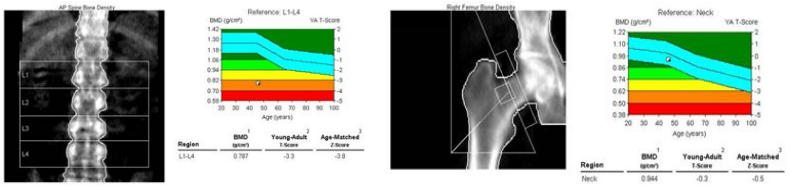
Younger individuals

- USE Z SCORE (comparison to age-matched norms)
- If ≤ 2 (below expected range for age)

BMD= bone mineral content / area



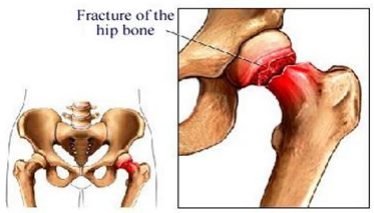
DXA RESULT



Epidemiology of fractures: Hip fractures

- **Hip fractures are bad**
- 20% patients with hip fracture die within the year
- 25-30% need placement in skilled nursing facility

The best(peak) bone mass for human is between 20-30 years



Cause serious disability and excess **mortality**

Highest incidence in Scandinavian and N American countries.

Women who have sustained fracture have a 10-20 % higher mortality than would be expected for their age.

Above 50 years of age , female to male ratio is 2: 1.

Mortality is higher in men , greater with co existent diseases

1-year mortality : 31 % in men and 17% in women

Risk of death is greatest immediately post fracture

Epidemiology of fractures: Vertebral fractures

Affected Vertebral fractures : rarely reported by physicians

10 % of vertebral fractures result in hospitalizations

Prevalence increases with age

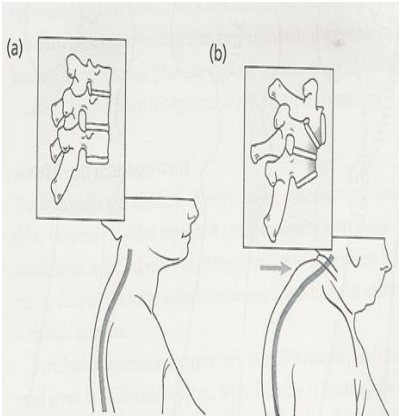
Male to female ratio **1: 1**

Mid thoracolumbar region are most commonly affected.

Cause lower energy,poor sleep,pain,immobility and social isolation especially in men.

Back deformities :loss of height and kyphosis.

Kyphosis happens because of multiple vertebral fractures



Economic Impact

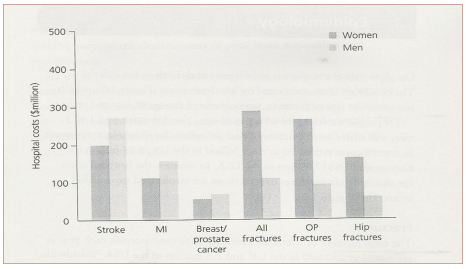
Huge

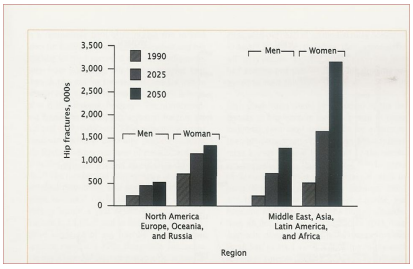
Osteoporotic fractures cost the US 17.9 billion per annum

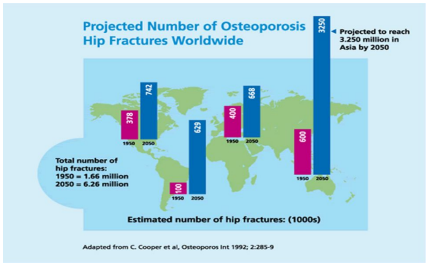
UK : 1.7 billion

Cost is largely attributed to **hip fractures**

Impact of osteoporosis and cost







Identification of fracture risk

FRAX (WHO fracture risk assessment tool) : 10 year probability of clinical fracture: hip & major osteoporotic fracture – hip,spine and forearm–

Variables: age

BMI

previous fracture

current smoking

steroids

RA

secondary causes

alcohol

femoral neck BMD

Dr.mona doesn't mention it in her slides.

WHEN TO SCREEN WITH DXA SCAN

VERY CONTROVERSIAL

Men usually presented with secondary osteoporosis while women usually with primary osteoporosis

IN US AND CANADA : WOMEN≥ 65 YEARS

MEN≥ 70 YEARS

SCREEN IN INDIVIDUALS WITH RISK FACTORS EG. STEROIDS

EUROPE : CASE FINDING IE IN PEOPLE WITH RISK FACTORS

Exclude secondary causes especially in younger individuals and men

Box 2: Common secondary causes of bone loss

- Hyperparathyroidism (primary or secondary)
- Vitamin D inadequacy
- Malabsorption state (e.g., celiac disease, inflammatory bowel disease, short gut syndrome)
- Hypercalciuria
- Hyperthyroidism
- Chronic lung disease
- Malignancy (e.g., myeloma, bony metastasis)
- Rheumatoid arthritis
- Hepatic insufficiency

Secondary Factors causing Bone Loss

Factors Associated with Decreased Bone density

Medical Conditions	Premature menopause Hypogonadism (in men) Liver disease Hyperthyroidism Hyperparathyroidism Hemiplegia Chronic obstructive lung dis.
Drug Therapy	Glucocorticoids Anticonvulsants (Phenytoin, Phenobarbitone)
Nutrition	? Low calcium & Vit. D intake ? High phosphorus, protein, sodium, caffeine intake
Behavioral factors	Smoking & Alcohol abuse

Laboratory & Radiological Findings

Bone profile ,ALP and PTH are within normal in patients with osteoporosis due to sex hormones deficiency and aging.

X-rays of skeleton do not show a decrease in osseous density until at least **30%** of bone mass has been lost.

X-ray of spine show prominent trabeculae and prominent end plates of the vertebral bodies.

-Plane x-ray cannot diagnose osteoporosis but it can give a clue in case of severe osteoporosis that can show cod fish appearance.

-This x-ray shows compressed vertebrae with wedge shaped fractures.

Cod fish appearance indicates protrusion of the disk into the body of the vertebrae secondary to mechanical failure.

X-ray of the upper part of the femur may also be helpful in assessing reduced bone mass and calculating the risk for hip fracture.

PREVENTION

- Adequate nutrition, particularly calcium and vitamin D
  - -Calcium: 1000 – 1200 mg daily (diet plus supplementation)
  - -Vitamin D: goal level above 50-75 nmol/l
- Weight bearing exercise
- Discourage smoking
- Reduction of risks for falling: consider OT evaluation for home hazards, minimize sedating medications.
- Hip protectors: can be useful if worn properly but often have low compliance

Nonpharmacologic Management

Adequate calcium and vitamin D intake	Prevention of falls
Modification of lifestyle measures	Stopping smoking
Exercise	More sun exposure

Calcium and Vitamin D

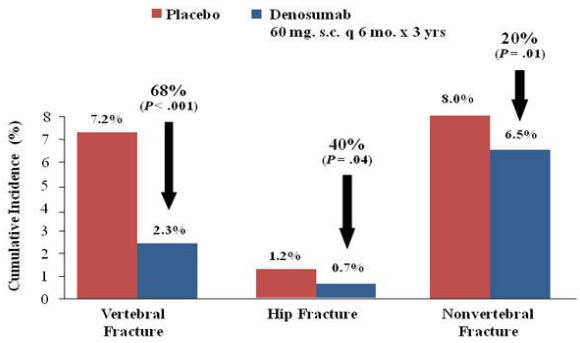
- At least 1000 mg /day for men ≤ 65 or younger
- 1500 mg /day for older men. Ca citrate vs. Ca carbonate.
- Vitamin D : check 25 (OH) vit. D level . If very low you need to "replete" the stores first . Maintenance dose is 800 IU for men younger than 50 and 800-1000 IU for men older than 50
- 1000 IU for all patients with osteoporosis or reduced bone mass regardless of their age.

Treatment Options

- Bisphosphonates
- Denosumab
- Teriperatide
- SERMs (Selective estrogen receptor modulators)
- Hormone replacement therapy
- Calcitonin : no longer used

Screening
All women > 65 years
Men > 70
Women 50-64 with risk factors
Patients on steroids or anti-estrogen/anti-testosterone treatment
2. Prevention with adequate calcium/vitamin D, weight bearing exercise should be advised for all.
3. DXA scan is the primary screening tool
4. Aggressive therapy should be offered to patients with atraumatic/low-impact fractures and those with osteoporosis, osteopenia with multiple risk factors, patients on steroids, anti-estrogen, and anti-testosterone therapy with abnormal bone densities (T score <-1).

Denosumab: monoclonal Ab to the receptor activator(RANKL)



Prescription Agents for Osteoporosis

Medication	Prevention Dose	Treatment Dose
Bisphosphonates		
Alendronate sodium (Fosamax)—Merck	5 mg po daily 35 mg po weekly	10 mg po daily 70 mg po weekly
Risedronate sodium (Actonel)—Procter & Gamble/Aventis	5 mg po daily 35 mg po weekly	5 mg po daily 35 mg po weekly
Estrogens (various)	Equivalent to 0.3-0.625 mg conjugated equine estrogen daily	Not indicated
SERMs		
Raloxifene (Evista)—Lilly	60 mg po daily	60 mg po daily
Calcitonin-Salmon		
(Miacalcin)—Novartis	Not indicated	200 IUs intranasally daily
Parathyroid Hormone		
Teriparatide (Forteo)—Lilly	Not indicated	20 mcg sq daily

Po = by mouth; SERMs = selective estrogen receptor modulators; IUs = international units; sq = subcutaneously.

	Indications	Dosage	Notes
Raloxifene	Prevention and treatment of postmenopausal osteoporosis	60 mg/day	• May reduce risk of breast cancer; improves lipids • Associated with increased risk of deep vein thrombosis and pulmonary embolism
Teriparatide*	Treatment of osteoporosis in postmenopausal women at high risk for fracture	20 µg/day (subcutaneous injection)	• Teriparatide given to rats for most of their lifetime caused some rats to develop a form of bone cancer • Use of the drug for > 2 years not recommended
Calcitonin	Treatment of postmenopausal osteoporosis in women who have been menopausal for ≥5 yr	200 IU/day intranasally; alternate nostrils daily	• Generally safe; patients may experience rhinitis or epistaxis
Certain estrogens	Prevention of postmenopausal osteoporosis	Various doses and regimens	• Increased risk of thrombosis and stroke

Strategy for Management of Osteoporosis (Female Slides)

- Prevent Osteoporosis
- Detect and treat early to decrease further progression
- Limit disability and provide rehabilitation

Extra: a mainstay of treatment involves the use of bisphosphonates that are rapidly incorporated into bone and reduce the activity of osteoclasts. l Calcitonin inhibits bone resorption.
Osteoporosis can also be treated with:
l Denosumab: inhibitor of RANKL. RANKL is a TNF family of cytokine that activates osteoclasts; denosumab therefore, inhibits osteoclasts.
l Teriparatide: synthetic PTH. When used intermittently, teriparatide has a stimulatory effect on osteoblastic bone formation.
l Calcitonin l Raloxifene: selective estrogen receptor modifier

Treatment

Females Dr said: i have been told not to concentrate on treatment as it will be covered in pharmacology

The Adolescent Group (Peak bone mass attainment)

"Senile Osteoporosis is a pediatric disease".

- A calcium intake of 1200 mg/day is recommended.
- Adequate sun exposure or vit D supplementation to ensure adequate level.
- A reasonable exercise program is recommended.
- Genetic influence on peak bone mass attainment.

The Premenopausal Female (Maintenance of bone mass)

- Adequate calcium intake; 1000–1500 mgm/day disease.
- Adequate sun exposure or vit D supplementation
- A reasonable exercise program is recommended, but not to the point of amenorrhea.
- Avoidance of osteopenia-producing conditions/medications/lifestyle:
  - Smoking & excessive alcohol intake, excessive caffeine/protein intake.
  - Amenorrhea/oligomenorrhea.
  - Cortisone, excessive thyroid hormone replacement (?), loop diuretics, prolonged heparin exposure.

Treatment (Female Slides)

The Immediately Postmenopausal Female (Prevention of bone mass loss)	• Consideration of Hormone replacement therapy (conjugated equine estrogen (CEE) or its equivalent, 0.625 mg daily or cycled, or transdermal estrogen by patch 0.05–0.1 mg/day daily or cycled). • If intact uterus, consideration of medroxyprogesterone 5–10 mg daily or cycled Other modalities of therapy: • Bisphosphonates • SERMS (Selective estrogen receptor modulators e.g., Evista) • Anabolic hormones e.g.PTH

The elderly (>62) postmenopausal female with low bone mass but no compression fractures (Prevention of bone mass loss & restoration of bone mass previously lost)	• Adequate calcium intake: 1000–1500 mgm/day
	• A reasonable exercise program with physical therapy instruction in paraspinous muscle group strengthening exercise.
	• Avoidance of osteopenia-producing conditions/medications/lifestyle:
	  ○ Smoking & excessive alcohol intake, excessive caffeine/protein intake.
	  ○ Cortisone, excessive thyroid hormone replacement (?), loop diuretics, prolonged heparin exposure.
	• Adequate supplementation with vitamin D
	• Consideration of Hormone replacement therapy
	• Other modalities of therapy
	  ○ Bisphosphonates
	  ○ SERMS (Selective estrogen receptor modulators e.g. Evista)
	  ○ Anabolic Hormones e.g. PTH

Treatment (Female Slides)

The elderly (age>62) postmenopausal female with fragility fractures (Prevention of further fractures)	• Adequate calcium intake; 1000–1500 mgm/day disease.
	• A careful exercise program with physical therapy instruction in paraspinous muscle group strengthning exercises
	• Consideration of short-term back bracing (non-rigid brace)
	• Avoidance of osteopenia-producing conditions/medications/lifestyle:
	  ○ Smoking & excessive alcohol intake, excessive caffeine/protein intake.
	  ○ Cortisone, excessive thyroid hormone replacement (?), loop diuretics, prolonged heparin exposure.
	• Adequate supplementation with vitamin D
	• Consideration of Hormone replacement therapy
	• Other modalities of therapy
	  ○ Bisphosphonates
	  ○ SERMS (Selective estrogen receptor modulators e.g. Evista)
	  ○ Anabolic Hormones e.g. PTH

The male with low bone mass and/or fractures (Prevention of bone mass loss & restoration of bone mass previously lost; prevention of further fractures.)	• A program of reasonable calcium intake (1000–1500 mg daily), exercise, short term back bracing and avoidance of osteopenia-producing situation is indicated.
	• Consideration of testosterone therapy if total and free testosterone levels are low.
	  ○ Prostate concerns
	  ○ Cholesterol concerns
	• Other modalities of therapy
	  ○ Bisphosphonates
	  ○ Anabolic Hormones e.g. PTH

Treatment (Female Slides)

The male or female with corticosteroid induced osteopenia (Prevention of bone mass loss & restoration of bone mass previously lost)	• Bone mass measurement if possible to identify bone mass loss • Lowest possible dose of corticosteroids. • A program of reasonable calcium intake (1000–1500 mg), exercise, & avoidance of other osteopenia-producing situations is indicated. • Adequate supplementation with vitamin D • Other modalities of therapy ○ Estrogen (Females), Testosterone (males), Bisphosphonates, PTH

The amenorrheic female (Exercise induced amenorrhea, eating disorders, etc) (Prevention of bone loss)	• General measures; decrease exercise if appropriate, regain body weight, adequate calcium intake (1000–1500 mg/day) and avoidance of other osteopenia-producing situations.
	• Regain menses
	• Other modalities of therapy
	  ○ Estrogen replacement
	  ○ Bisphosphonates

Quick Revision

Osteoporosis

What's Osteoporosis? it is a condition where we have a compromised bone strength predisposing a person to an **increased risk of fracture**

What's the Clinical Presentation of Osteoporosis? it is an **Asymptomatic** disease so patient won't know if he/she has it until a fracture is encountered.

How to Diagnose Osteoporosis? We assess the bone mass using **DEXA** tests.

Difference between Osteoporosis Type 1 and 2

	Type I	Type II
Age (Yr.)	51 : 75	**>70**
Sex Ratio (F:M)	**6** : 1	2 : 1
Type of bone loss	Mainly trabecular	Trabecular & Cortical
Rate of bone loss	Accelerated	Not accelerated
Fracture sites	Vertebrae (Crush) & **distal radius**	Vertebrae (Multiple wedge), **hip, pelvis, proximal humerus**
Main causes	Factors related to **menopause**	Factors related to **aging**

Modifiable Risk Factors for Osteoporosis

Sex Hormones (low estrogen/testosterone)
Inactive lifestyle
Cigarette smoking
Hyperparathyroidism (primary or secondary)
GI conditions which impair adequate nutrition
Proton pump inhibitors
Low calcium and vitamin D
Hyperthyroidism
Steroids or Cushing's
Excessive alcohol
Rheumatoid arthritis

MCQs

Q1/ What are the most common region in vertebral fracture ?

A. Mid thoracolumbar region
B. Low thoracolumbar region
C. Cervical
D. Mid Cervical

Q2/ Which BMD results indicate Osteopenia?

A. greater than or equal to −1 SD
B. BMD which lies between − 1 and −2.5 SD
C. less than or equal to – 2.5 SD
D. 1 or more fragility fractures

Q3/ Which of the following is true about hip fracture ?

A. Mortality is higher in women
B. female to male ratio is 2: 1
C. Risk of Coma is greatest immediately post fracture
D. Harmless

Q4/ X−rays of skeleton do not show a decrease in osseous density until what percentage of bone mass has been lost?

A. 20%
B. 35%
C. 30%
D. 15%

Q5/Which of the following is no longer used in the treatment of osteoporosis ?

A. Calcitonin
B. Denosumab
C. Bisphosphonates
D. SERMs

Q6/What cell is responsible for The bone resorption cells?

A. Osteoblast
B. Osteoclast
C. Osteocyte
D. Osteogen

Q7/Which drug is considered as a Factor Associated with Decreased Bone density?

A. Phenobarbitone
B. Clarithromycin
C. Sremolin
D. Octreotide

Q8/Which of the following is not considered as a Factor Associated with Decreased Bone density?

A. Anemia
B. Hyperthyroidism
C. Hyperparathyroidism
D. Hemiplegia

1- A 2-B 3-B 4-C 5-A 6-B 7-A 8-A