Medicine 439

MED439
KING SAUD UNIVERSITY

Revised & Approved
Bassam Alasmari
Rania Almutiri

Introduction to Osteoporosis

Editing file

Lecture Objectives:

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

- **Important**
- **Original content**
- **Boys Slides**
- **Girls Slides**
- **Doctor's notes**
- **Extra**

Introduction

Bone has three major functions:

01 Provide rigid support to extremities and body cavities containing vital organs, as in rib cage to protect the heart, lungs, and liver.

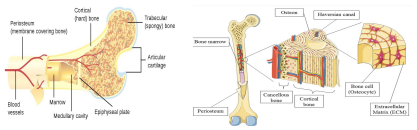
02 Provide efficient levers and sites of attachment of muscles which are all crucial to locomotion.

03 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.

Types of Bone:

Cortical Bone	Trabecular Bone
The compact bone of Haversian systems such as in the shaft of long bones.	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.



Disorders in which cortical bone is scanty or defective lead to:*

fractures of long bones.

Disorders in which trabecular bone is defective or scanty lead to:*

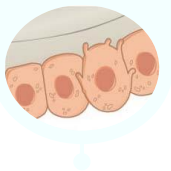
vertebral fractures and also may help in fractures of long bones because of the loss of reinforcement.

The important of understanding the difference between the two types of bones is because when we talk about osteoporosis will talk about fractures and when we understand where is the cortical and trabecular bones we understand what kind of fractures will be affected what type of bones related to osteoporosis.

Introduction

Bone cells:

Bone is resorbed and formed continuously throughout life (not static) is a very active tissue and we actually form a new skeleton every nine years to get totally new skeleton because of this bone formation and resorption going in continuously all the time and these important processes are dependent upon three major types of bone cells.*



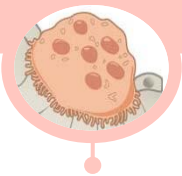
Osteoblasts

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.
(forms bone matrix)

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.
(maintains bone tissue)

It is important cell called master cell, this is the one that actually signaling between osteoblasts and osteoclasts.



Osteoclasts

The bone resorption cells
we never have a dead or abnormal tissue because we have this osteoclast which resorbe them.

Bone marrow remodeling:
Mesenchymal cells >>> osteoblast
Hematopoietic cells >>> osteoclasts

Osteoblasts and osteoclasts they have interaction when one start working it tell the other when it should start working, so there is always a balance between the two which called a coupling mechanism, so normal coupling mechanism means —> osteoblasts and osteoclasts are talking between them in a normal healthy way we will talk about the abnormal unhealthy way later on.

Osteomalacia "لين العظام"

Only in Boys' Slides

Definition:

Failure of organic matrix (osteoid) of bone to mineralize normally.
Osteomalacia is a problem with mineralization not bone mass reduction.

- 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.

Osteoporosis "هشاشة العظام"

"THE SILENT THIEF"

Definition

Skeletal disorder characterized by compromised bone strength predisposing to increased risk of fracture.
Bone strength reflects the integration of bone density and bone quality*
Decrease in bone mass (Density) and strength (Quality) associated with an increased tendency to fractures*.
(1 in 3 women and 1 in 5 men over 50 will experience osteoporosis fracture)*.

Clinical Features:

- It is usually an asymptomatic even with very low bone density , until fractures occur. patient usually come with fracture. (لا يسبب آلام ولكن يسبب كسور)
- 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* (Atraumatic or low impact fractures).
- Subsequent vertebral fractures may contribute to Acute or chronic back pain.
- In well established osteoporosis dorsal Kyphosis and loss of height occurs*.
- Hip fractures with its fatal complications also occur commonly as osteoporosis become more severe, so we have to deal with osteoporosis before it leads to fracture.
- **Common site of fractures**: Spine, Forearm and Hip.

Primary Osteoporosis

Types:

Type 1 Osteoporosis (Post Menopausal)

Fractures of bones composed mainly of **trabecular bone.** (it is the classic/common form). It's typically seen after 55y in women and usually they present with Colles fracture.

Example:

- Distal radius → Colle's fracture
- Vertebra → Crush and wedge fractures.
  - Usually affects woman within 15 years of menopause because of lack of Estrogen.

Type 2 Osteoporosis (Senile)

Fractures of bones composed of both cortical & trabecular bone (affect cortical more).
can affect both men and women equally.

Example:

- Hip → Femur neck fracture that's why we mentioned above it affects cortical more than trabecular.
  - Usually affects individual over age of 70 years, so it's very rare to see 40y old with hip fracture because it only happen in old patients

Primary Osteoporosis

Difference in the two type of involutional Osteoporosis :

	Type 1	Type 2
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
Parathyroid Hormone	Decreased	Increased
Calcium absorption both affected	Decreased	Decreased
Metabolism of 25(OH)2D to 1,25(OH)2d	Secondary Decreased	Primary Decreased
Main cause	**Factors related to menopause**	**Factors related to aging**

★Secondary Factors associated with decreased bone density: دايم يجي عليها اسئلة

Can happen at any age (young and old age), more common in men than women.
Remember: always when you have a young person with osteoporosis you have to look for secondary causes.

Medical Conditions

- Premature menopause
- Hypogonadism (in men)
- Liver disease(hepatic insufficiency)
- Hyperthyroidism الجسم شغال بزيادة عشان كذا يزيد التدمير
- Hyperparathyroidism
- Hemiplegia
- Chronic obstructive lung dis.
- Hypercalciuria
- Malignancy
- Rheumatoid arthritis
- Malabsorption state (eg. Celiac disease, inflammatory bowel disease, short gut syndrome)

Drug Therapy*

- Glucocorticoids
- Anticonvulsants (Phenytoin, Phenobarbitone)

*That's why you should always check the drug history of the patients, because sometimes they would have normal sun exposure and intake of calcium but still present with fractures

Nutrition

- Low calcium & Vitamin D intake
- High phosphorus (carbonated drinks), protein, sodium, caffeine intake

Behavioral factors

- Smoking & Alcohol abuse.

Primary Osteoporosis

Risk Factors : Only in Boys' Slides Dr: دائماً هذي اللسته يجي عليها اسئلة

Non-Modifiable

- Age (increasing)
- Low BMI (small, low weight;< 58 kg)
- Ethnicity:

-Caucasian > Asian

-Latino > African American

- Family History of Fracture

Modifiable اللي يمكن تحسينها

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

Laboratory and 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. So we don't use it to diagnose osteoporosis.

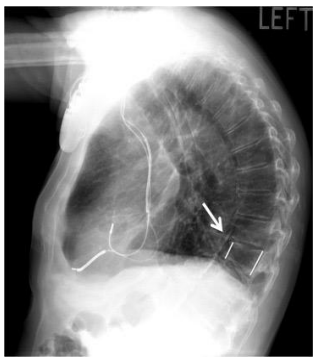
Normal | Midcrush vertebral fractures | Last stage

Skipped by girls doctor :)

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

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.



Primary Osteoporosis

Methods of bone mass assessment:

1 Single-Photon Absorptiometry - SPA

2 Double-Photon Absorptiometry - DPA

3 Computed Tomography - CT

★Very important always come in the exam

Definition based on BMD (bone mineral density (BMD) assessment)

Classification	T score
Normal	-1 or greater
Osteopenia	Between -1 and -2.5
Osteoporosis	-2.5 or less
Severe Osteoporosis	Plus 1 or more > -2.5 or less and fragility fracture

T score: is used for women in postmenopausal age and men above age 50.

In younger individuals:*

- Use Z SCORE
- If ≤ 2 (below expected range of age)

4 Dual-Energy X-Ray Absorptiometry DEXA/DXA it is used to diagnose osteoporosis

- Current golden standard for diagnosis of osteoporosis.
- Diagnosis based on comparing patients BMD to that of young, healthy individuals of same sex

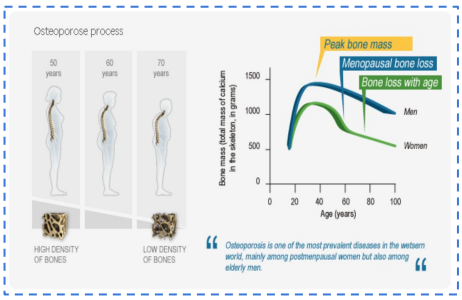
We can also use it to follow up the patient after treatment, normally we ask them to come after 1 year (the longer the better we see the results).

WHEN TO SCREEN WITH DXA SCAN

- VERY CONTROVERSIAL
- 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

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

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



Peak bone mass is best at 20-30 age

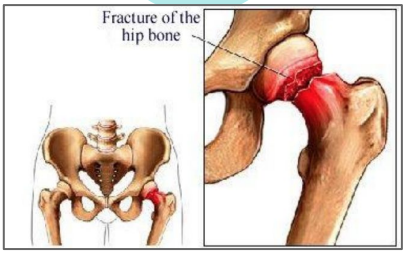
- It is appropriate to begin to look for risk factors that predispose a person to osteoporosis and develop a rational prevention program tailored to the person's risk before the menopause*
- **High risk groups** (in the presence of one or more of such risk factors measurement of BMD provides further information to the risk of fractures):*

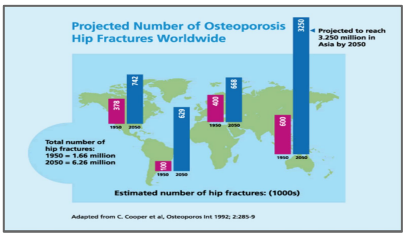
- Women with thin light frame
- History of low calcium intake
- Decreased physical activity
- Smoking
- High alcohol or caffeine consumption
- Family history of osteoporosis, don't forget peak bone mass is an 80% genetically determined but you can do a lot to improve it.
- History of prior menstrual disturbances
- History of drugs like antiepileptics or steroids

Hip Fractures

This slide was found in boys' slides only

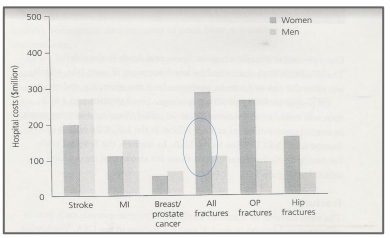
- They are bad
- 20% patients with hip fractures die within the year
- 25-35% need replacement in skilled nursing facility
- Cause serious disability and excess mortality
- Highest incidence in Scandinavian and N American countries.
- Women who have sustained fracture have a 10-20 % higher mortality 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

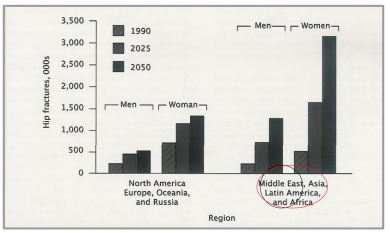




Economic Impact

- Huge, Osteoporotic fractures costs:
- US : 17.9 billion/ annum
- UK : 1.7 billion/ annum
- Cost is largely attributed to hip fractures





Identification of fracture risk

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

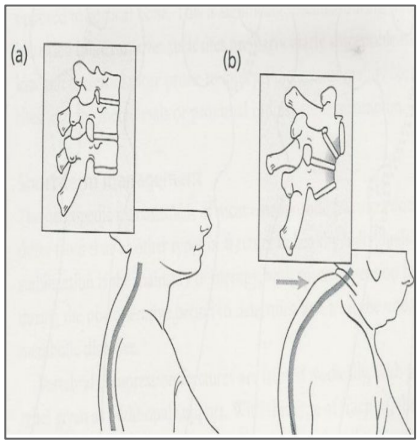
• **Variables :** (it is important to remember all these)

Ethnicity/Race is also important

- Age
- RA
- Alcohol
- BMI
- Secondary causes
- Steroids
- Current Smoking
- Femoral neck BMD
- Previous fracture

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.



Prevention & Treatment

Prevention: only In Boys' Slides

how to obtain good peak bone mass?

01 Adequate nutrition, particularly calcium and vitamin D
1. Calcium: 1000 – 1200 mg daily (diet plus supplementation)
2. Vitamin D: goal level above 50-75 nmol/l

02 Weight bearing exercise.

03 Discourage smoking.

04 Reduction risk of falling: consider OT evaluation for home hazards, minimize sedating medications.

05 Hip protectors: Can be useful if worn properly but often have low compliance.

Strategy for management of osteoporosis: Only in girls' slides

1 Prevent osteoporosis

2 Detect and treat early to decrease further progression

3 Limit disability and provide rehabilitation

Management: only In Boys' Slides

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

Calcium and vitamin D only In Boys' Slides

- At least 1000 mg daily for men ≤ 65 or younger
- 1500 mg/day for older men.
- Ca Citrate vs. Ca carbonate

- Vitamin D: check 25(OH) vitamin 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.
- Higher doses may need to be used especially in Saudi Arabia.
- Optimum level: at least 50 nmol/L patients with high risk of fracture: 75 nmol/L

Treatment

This slide was found in girls' slides only

"Senile osteoporosis is a pediatric disease" this means if you don't achieve best peak bone mass as possible in your twenties and therties you always start at a lower level than the normal and then you are more likely to have osteoporosis when you get old and more likely lead to fracture so the best way to prevent osteoporosis is starting from a young age! from a pediatric age group by optimizing calcium intake, vitamin D exposure, nutrition and exercise all these stuff are very important!!

<table>
<tr><th>Adolescent
(peak bone mass attainment)</th><th>Premenopausal female
(maintenance of bone mass)</th></tr>
<tr><td>Calcium intake 1200 mg/day</td><td>Calcium intake 1000-1500 mg/day
(too much can lead to nephrocalcinosis)</td></tr>
<tr><td colspan="2">Adequate (direct) sun exposure or vit D supplementation to ensure adequate level.</td></tr>
<tr><td colspan="2">Reasonable exercise program is recommended,
remember being too thin is not good why? because you loose the mechanical loading on the bone, osteoblasts respond to mechanical loading and that's how exercise is good for the bone.
(too thin + not exercising = will not have this mechanical physiological loading that allowed the osteoblasts to build bones)</td></tr>
<tr><td>Genetic influence on peak bone mass attainment</td><td>Avoidance of osteopenia-producing conditions /medications/lifestyle:
1. Smoking & excessive Alcohol intake, excessive caffeine/protein intake.
2. Amenorrhea/oligomenorrhea.
3. Cortisone, excessive thyroid hormone replacement, loop diuretics, prolonged heparin exposure.</td></tr>
</table>

Immediately Postmenopausal Female (prevention of bone mass loss)

- Consideration of Hormone replacement therapy and it has many side effects so they shouldn't use them in long period (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 (Discussed in pharma in details)
  1- Bisphosphonates
  2- SERMS (Selective estrogen receptor modulators e.g., Evista)
  3- Anabolic Hormones e.g. PTH.

Treatment

This slide was found in girls' slides only

<table>
<tr><th colspan="2">The elderly (>62) postmenopausal female</th><th>Male</th></tr>
<tr><td>With low bone mass but no compression fractures
(Prevention of bone mass loss & restoration of bone mass previously lost)</td><td>With fragility fracture
(prevention of further fractures)s</td><td>with low bone mass and/or fractures
(Prevention of bone mass loss & restoration of bone mass previously lost; prevention of further fractures)</td></tr>
<tr><td colspan="3">Adequate calcium intake; 1000-1500 mgm/day
(too much can lead to nephrocalcinosis)</td></tr>
<tr><td>Reasonable exercise program with physical therapy instructions in paraspinous muscle group strengthening exercise.</td><td>Careful exercise program with physical therapy instructions in paraspinous muscle group strengthening exercises.</td><td>Exercise</td></tr>
<tr><td colspan="3">Avoidance of osteopenia-producing conditions/medications/lifestyle:
1. Smoking and excessive alcohol intake, excessive caffeine/protein intake.
2. Cortisone, excessive thyroid hormone replacement, loop diuretics, prolonged heparin exposure.</td></tr>
<tr><td>-</td><td colspan="2">Consideration of short-term back bracing
(non-rigid brace)</td></tr>
<tr><td colspan="2">Adequate supplementation with vitamin D.</td><td>-</td></tr>
<tr><td colspan="2">Consideration of Hormone replacement therapy.</td><td>consideration of testosterone therapy if total and free testosterone levels are low.
1. Prostate concerns.
2. Cholesterol concerns.</td></tr>
<tr><td colspan="3">Other modalities of therapy:
1. Bisphosphonates.
2. SERMS (Selective estrogen receptor modulators e.g. Evista).*Only for female
3. Anabolic Hormones e.g. PTH.</td></tr>
</table>

Treatment

This slide was found in girls' slides only

The amenorrheic female (Exercise induced amenorrhea, eating disorders,etc) (Prevention of bone loss)

1. General measures; decrease exercise if appropriate,regain body weight, adequate calcium intake 1000- 1500 mg/day
2. avoidance of other osteopenia-producing situations.
3. Regain menses.
4. Other modalities of therapy:
   1. Estrogen replacement.
   2. Bisphosphonates.

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).
  (too much can lead to nephrocalcinosis)
- exercise, & avoidance of other osteopenia-producing situations is indicated.
- Adequate supplementation with vitamin D.
- Other modalities of therapy:
  1- Estrogen (Females)
  2- Testosterone (males)
  3- Bisphosphonates
  4- PTH

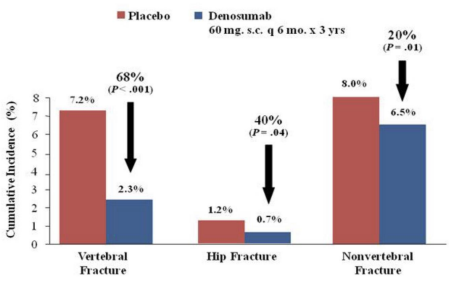
Treatment

This slide was found in boys' slides only

Treatment Options

1.Bisphosphonates (anti resorptive)
2. Denosumab (anti resorptive)
3. Teriperatide (anabolic) not used for more than 2 years, because it may cause osteosarcoma
4. SERMs (Selective estrogen receptor modulators)
5. Hormone replacement therapy
6. Romosozumab(anabolic)

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

Summary*

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).

Quiz

Q1- The lattice like network of bone found in the vertebrae and the ends of long bones , best describes which type of bone?			
A.Cortical	B.Trabecular	C.Compact	D.None
Q2- X-rays of skeleton do not show a decrease in osseous density until at least how much of bone mass is lost?			
A.20%	B.50%	C.30%	D.40%
Q3- Which of the following is the Current golden standard for diagnosis of osteoporosis?			
A. X- ray	B. MRI	C. DEXA	D. CT
Q4- Short-term back bracing is considered for :			
A. postmenopausal female With fragility fracture	B. The amenorrheic female	C. Adolescent	D. premenopausal female
Q5- which of the following is non-modifiable risk factor for primary osteoporosis?			
A. Low calcium	B.Low BMI	C. Excessive alcohol	D.Rheumatoid arthritis

Answers

1.B 2.C 3.C 4.A 5.B

Leaders

Fahad Alajmi

Shahad Alrasheed

Members

Shatha aldossary

Shayma Alghanoum

Sarah Almuqati

Muneerah Alsadhan

Mohammed Alsunaidi

Ahmad Alkhayatt

Abdulrahman Alshabnan

Ibrahim Alabdulkarim

Note Takers

Saud Alrsheed

Albandari Alanazi

Give us your feedback