Osteoporosis
(هشاشةالعظام)

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Sources :

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Objectives :

1- to knew the definition of the disease

2- etiology of osteoporosis

3-types of osteoporosis

4-Risk factors for osteoporosis and fragility fracture

5 -Clinical features

4-Investigations and Indications for dual-energy X-ray absorptiometry scanning

5-male osteoporosis

6- Assessment of fracture risk

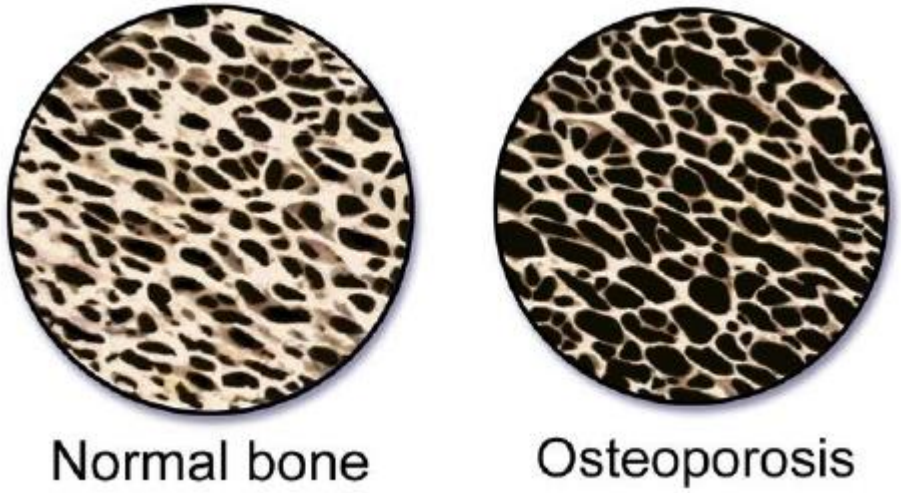
8-Management (Prevention and treatment + Pharmacological intervention)

9-Glucocorticoid-induced osteoporosis

Introduction

Osteoporosis is the most common bone disease.

Osteoporotic fractures affect up to 30% of women and 12% of men at some time during their life.



Defnition :

This reduction in bone mass and micro-architectural deterioration of bone tissue leads to bone fragility and an increased risk of fracture.

Osteoporotic fractures (fragility fractures, low-trauma fractures) occur without major trauma.

**Osteoporosis is defined as a BMD more than

2.5 standard deviations (SDs) below

the young adult mean value(T-score <= 2.5).

**Values between 1 and 2.5 SDs below the young adult mean are termed 'osteopenia'.

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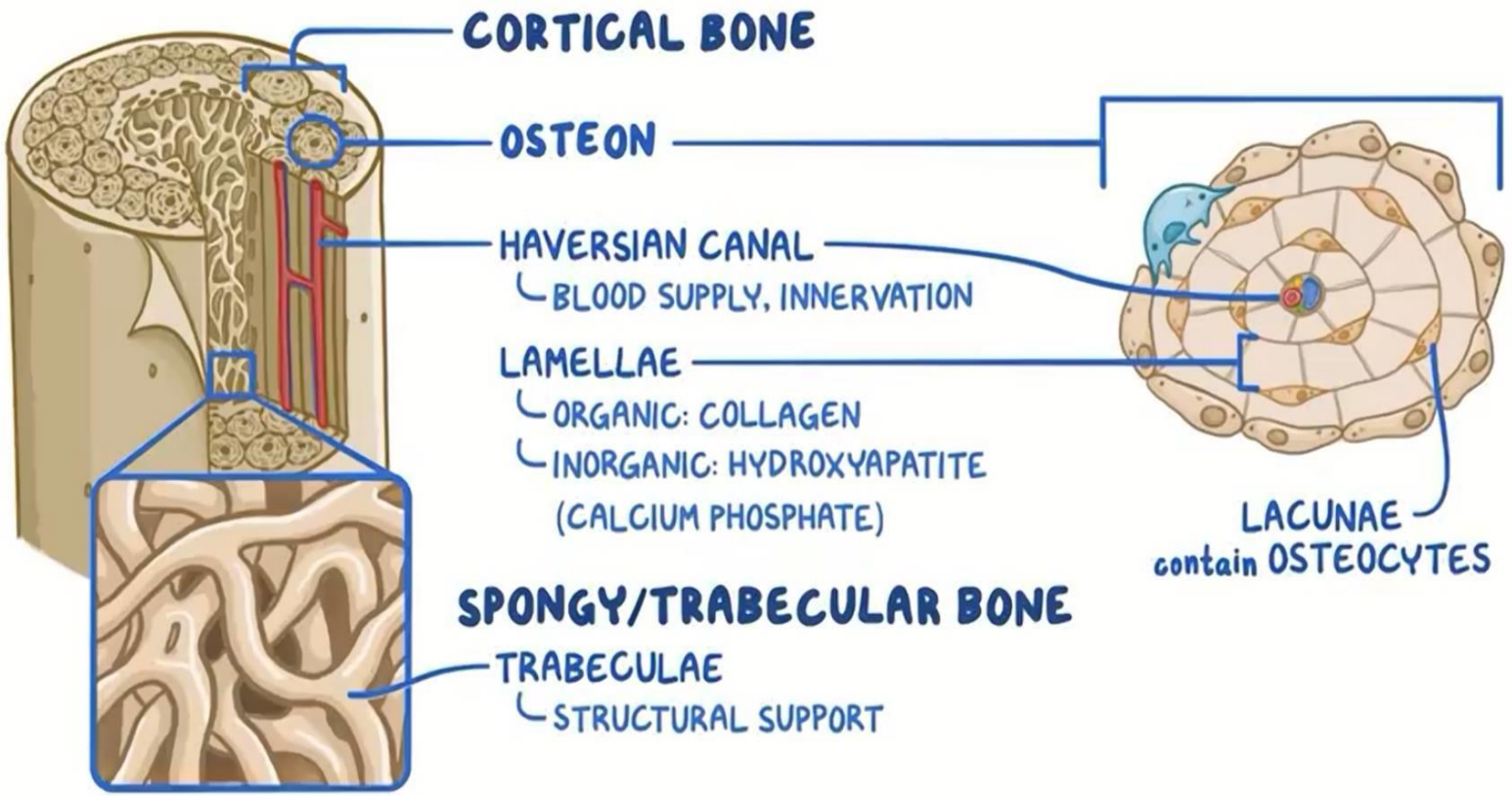
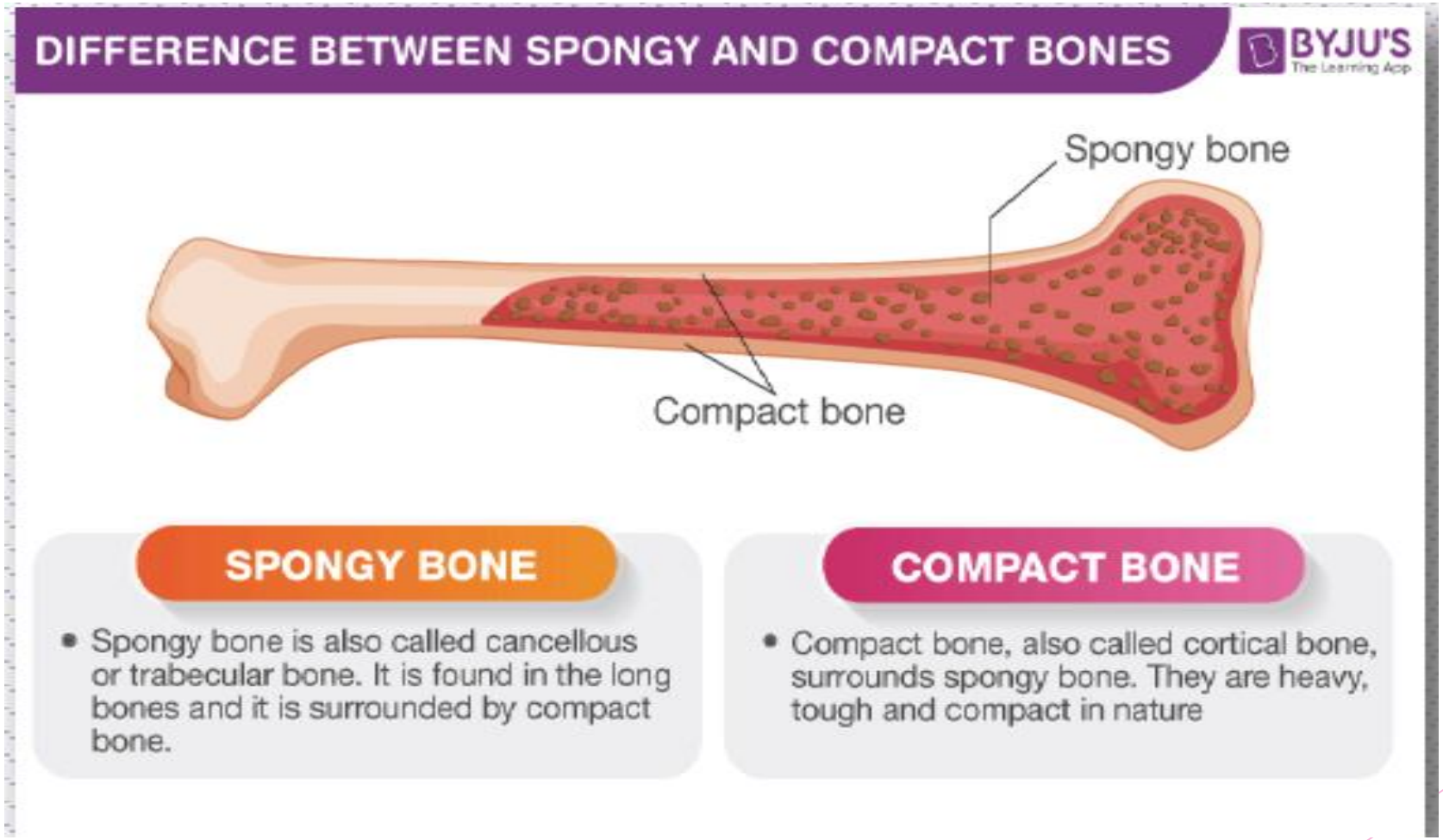
Pathogenesis

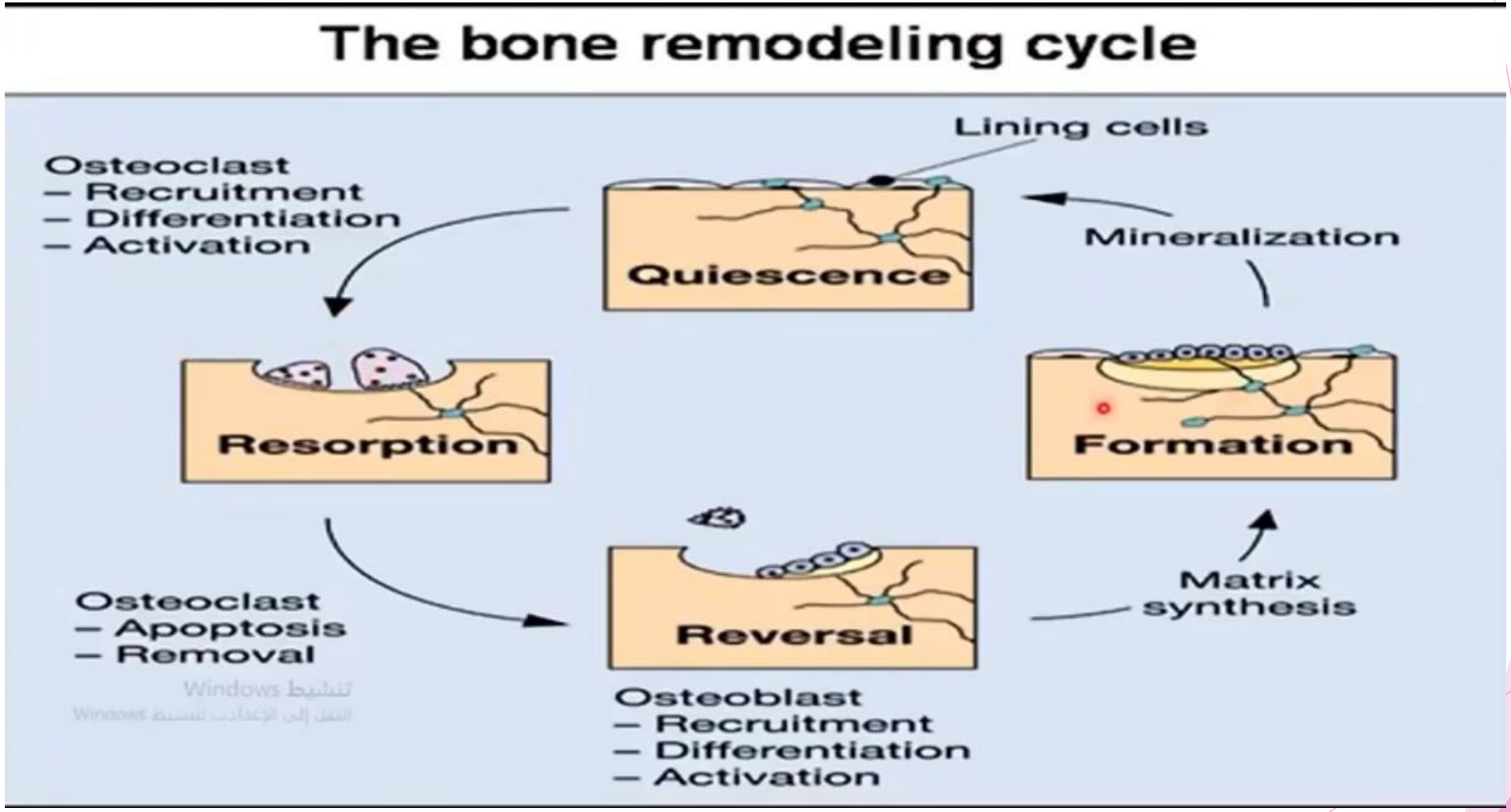
Bone component



Types of bones



Bone remodeling



Throughout life, bone undergoes continuous remodeling, with about 10% of

the skeleton replaced each year.

Bone remodeling serves to remove and replace damaged bone and to maintain calcium homeostasis.

***Osteoclasts** are cells that break down bone, a process known as **bone resorption**.

*Following bone resorption, **osteoblasts** or bone-building cells synthesize new bone.

*Crystals of **calcium phosphate** known **as hydroxyapatite** are deposited in the new bone matrix during the process of **bone mineralization**. Bone mineralization is essential for bone strength.

*Lastly, bone enters a **resting phase** until remodeling begins again.

***Bone loss occurs when bone resorption exceeds bone formation during the remodeling process**.

MECHANISMS OF OSTEOPOROSIS DEVELOPMENT

The three main mechanisms by which osteoporosis develops are :

- An inadequate peak bone mass (the skeleton develops insufficient mass and strength during growth).
- Excesive bone resorption
- Inadequate formation of new bone during remodeling.

Bone Mass

- Peak bone mass occurs in young adulthood
- Many influences: sex, genetics, diet
- Decreases slowly thereafter Each resorption/formation cycle →some bone loss
- Males achieve higher peak bone mass
- Menopause accelerates bone loss Caused by decreased estrogen levels

>>>>>>Female osteoporosis >> male osteoporosis

- Weight-bearing activity →↑ bone mass

OpenStax College/Wikipedia

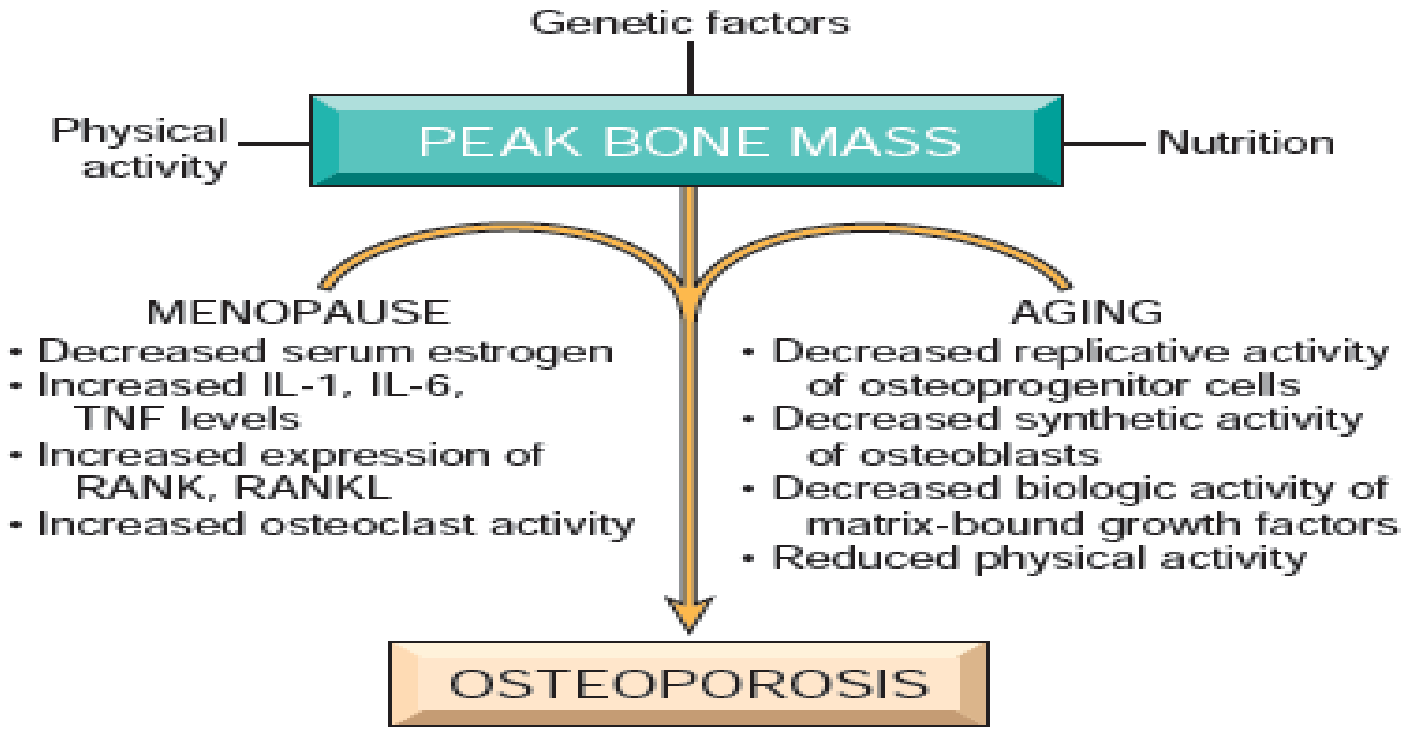


Figure 26-9 Pathophysiology of postmenopausal and senile osteoporosis (see text).

Osteoporosis, Paget disease, and osteomalacia are disorders of the bone.

Osteoporosis is characterized by progressive loss of bone mass and skeletal fragility. Patients with osteoporosis have an increased risk of fractures, which can cause significant morbidity. Osteoporosis occurs most frequently in postmenopausal women and older adults of both sexes. Decreased BMD + NORMAL minirilization

Paget disease is a disorder of bone remodeling that results in disorganized bone formation and enlarged or misshapen bones. Unlike osteoporosis, Paget disease is usually limited to one or a few bones. Patients may experience bone pain, bone deformities, or fractures.

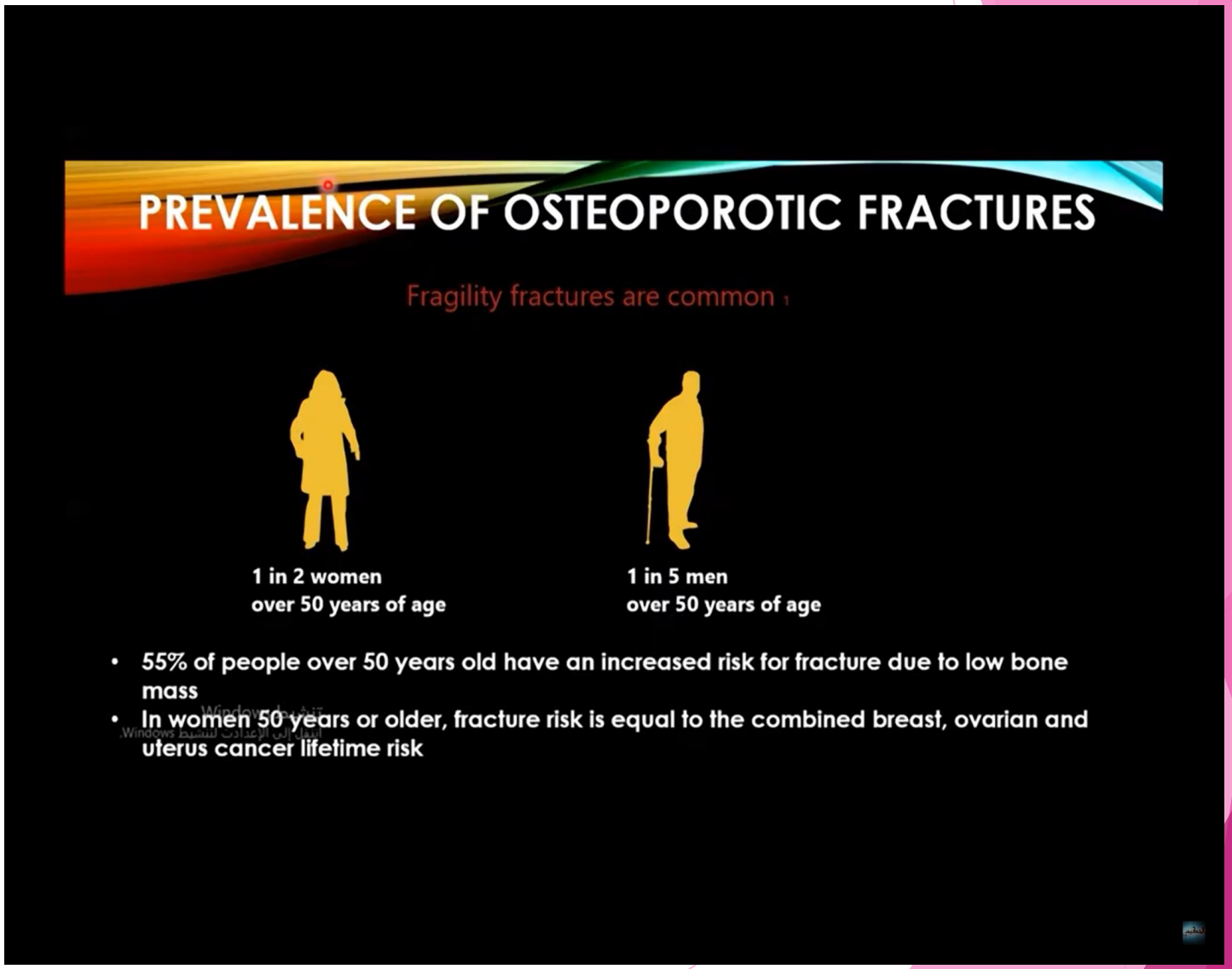
Osteomalacia is softening of the bones that is most often attributed to vitamin D deficiency. [Note: Osteomalacia in children is referred to as rickets]. Normal BMD+ decreased minirilization

Epidemiology

*Worldwide, osteoporosis causes more than 8.9

million fractures annually, resulting in an osteoporotic fracture every 3 seconds

* The combined lifetime risk for hip, forearm and vertebral fractures coming to clinical attention is around 40%, equivalent to the risk of cardiovascular disease
*Osteoporosis is estimated to affect 200 million women worldwide



All of the following are risk factors for Osteoporosis except ?

A . DM .

B . Smoking .

C . Obesity .

D . Steroids .

E . Sedentary life .

Selected Risk Factors

- **Alcohol**
- Heavy use associated with osteoporosis
- Moderate use effects not clear
- **Smoking**
- Accelerates bone loss
- **Low body weight (< 127 lbs)**
- **Sex hormones:** o **Low calcium intake:** a
- **Gastrointestinal surgery:**

Unmodifiable risk factors

o **Your sex:** women are much more likely to develop osteoporosis than are men.

o **Age:** the older you get, the greater your risk of osteoporosis.

o **Race:** you're at greatest risk of osteoporosis if you're white or of Asian descent.

o **Family history:**.

Types of osteoporosis:

Primary	Secondary
•Most common form •Postmenopausal osteoporosis (type I) –estrogen deficiency •Senile osteoporosis (type II) – age-related bone loss (men and women)	•Not related to menopause or aging •Suspected in pre-menopausal women •Caused by drugs or another medical disorder

15.15 Risk factors for osteoporosis

Endocrine disease	Early menopause, hypogonadism, hyperthyroidism, hyperparathyroidism, Cushing's syndrome
Inflammatory disease	Inflammatory bowel disease, RA, ankylosing spondylitis
Drugs	Corticosteroids, anticonvulsants, heparin, alcohol excess
GI disease	Malabsorption, chronic liver disease
Respiratory disease	Chronic obstructive pulmonary disease (COPD), cystic fibrosis
Miscellaneous	Myeloma, anorexia nervosa, lack of exercise, immobilisation, poor diet/low body weight, smoking, HIV

Table 26–4 Categories of Generalized Osteoporosis

Primary
Idiopathic
Postmenopausal
Senile
Secondary
Endocrine Disorders
Addison disease
Diabetes, type 1
Hyperparathyroidism
Hyperthyroidism
Hypothyroidism
Pituitary tumors
Neoplasia
Carcinomatosis
Multiple myeloma
Gastrointestinal
Hepatic insufficiency
Malabsorption
Malnutrition
Vitamin C, D deficiencies
Drugs
Alcohol
Anticoagulants
Anticonvulsants
Chemotherapy
Corticosteroids
Miscellaneous
Anemia
Homocystinuria
Immobilization
Osteogenesis imperfecta
Pulmonary disease

Secondary causes :

Drugs

Aluminum antacids
Anticonvulsants (e.g., *phenytoin*)
Aromatase inhibitors
Furosemide
Glucocorticoids
Heparin
Medroxyprogesterone acetate
Proton pump inhibitors
Selective serotonin reuptake inhibitors
Thiazolidinediones
Thyroid (excessive replacement)

Figure 27.3
Drugs that can contribute to bone loss or increased fracture risk.

1- Glucocorticoid-induced osteoporosis

1- Affect osteoblasts and osteoclasts

•Increase bone resorption + •Reduce bone formation

2- inhibit intestinal calcium absorption and cause renal calcium leak, reducing serum calcium and leading to secondary hyperparathyroidism with increased osteoclastic bone resorption.

3- Hypogonadism may also occur with high-dose steroids

*Individuals requiring continuous oral glucocorticoid therapy for 3 months or more (at any dose) should be assessed for osteoporotic risk factors.

*Postmenopausal women, men aged over 50 years and anyone with a previous fragility fracture should receive bisphosphonate treatment without waiting for DXA scanning.

*Fracture risk assessment and DXA results guide treatment for other patients.

Where possible, glucocorticoid doses should be minimized and consideration given to use of steroid-sparing immunosuppressants and alternative routes of steroid administration (e.g. rectal steroids for distal ulcerative colitis

2- Antiepileptic Drugs

- Phenobarbital,Phenytoin, Carbamazepine
- Risk of osteoporosis with long term therapy
- Increase activity of P450 enzymes
- Increases breakdown of vitamin D
- Less calcium →increased PTH →bone loss

3- Unfractionated Heparin

- Only with long term use
- Decreases bone formation
- Increases resorption
- Low molecular weight heparin: unclear bone effects

Endocrine

Cushing's syndrome or disease (↑ cortisol)

- Hyperthyroidism
- Hyperparathyroidism
- Hypogonadism (↓ estrogen)

Nutritional Associations

- Vitamin D deficiency
- Calcium deficiency
- Malabsorption (celiac disease)

Male osteoporosis

o Osteoporosis is **less common** in men.

o Secondary causes can be identified in about **50%** of cases.

o The most common are hypogonadism, corticosteroid use and alcoholism.

o In hypogonadism, the pathogenesis is as described for post-menopausal osteoporosis; testosterone deficiency

results in an increase in bone turnover and uncoupling of bone resorption from bone formation.

o Genetic factors are important in the **50%** of cases with no identifiable cause.

Diagnosis

- **Fragility fracture**
- **T score of -2.5 or lower**

Clinical features

General

*Osteoporosis is asymptomatic until a fracture occurs.

*There typically are no symptoms in the early stages ,but some signs can point toward bone loss:

1. Receding gum.
2. Weaker grip strength.
3. Weak and brittle fingernails.

o Later in disease, bones deteriorate significantly more, symptoms become more obvious:

1. Fragility/ pathological fractures.
2. Back or neck pain.
3. Loss of height.
4. Stooped posture

.

•Fragility fracture

Type of fracture that occurs as a result of an injury that would be insufficient to cause fracture in a normal bone, could result from very mild stress, a fall from standing height or less ,cough ,etc.

*The most common sites are

1- the forearm (Colles fracture)

2- spine (vertebral fractures causing back pain, height loss and kyphosis)

3- femur (hip fracture)

4- Thoracic vertebral fractures may lead to kyphosis and loss of height (‘widow’s stoop’)

Complications of fractures of the femoral neck, pelvis, or spine, such as pulmonary embolism and pneumonia, are frequent and result in

40,000 to 50,000 deaths per years

Vertebral compression fracture

o The most common fracture.

o Frequently occur in the thoracic and lumbar regions.

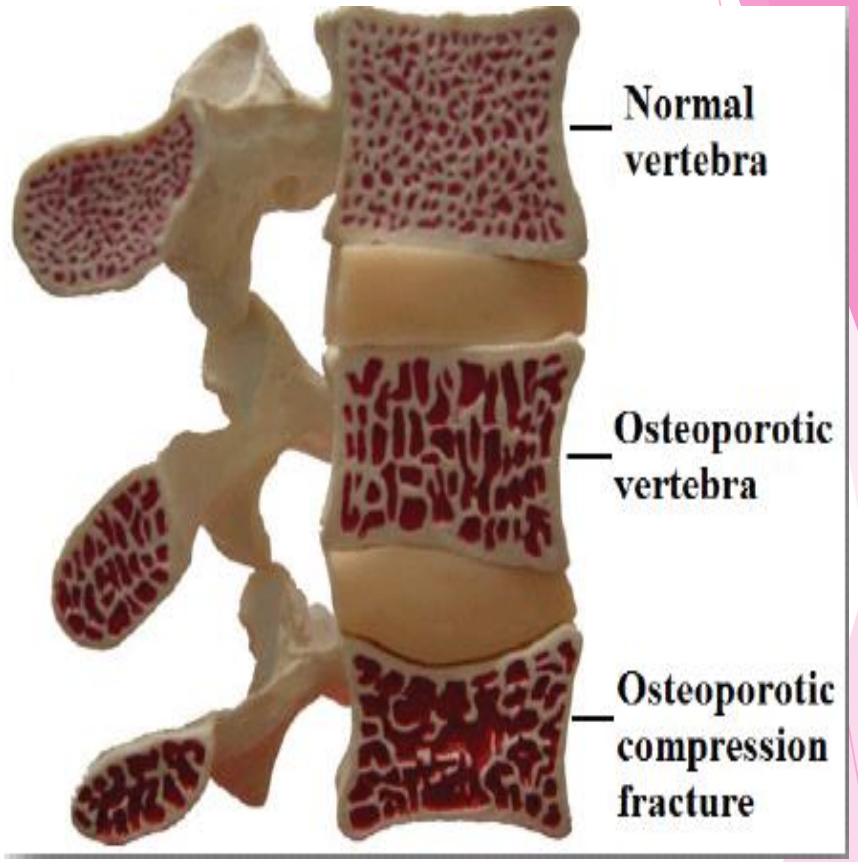
o Vertebral fractures present with:

1. Sudden onset of back pain.

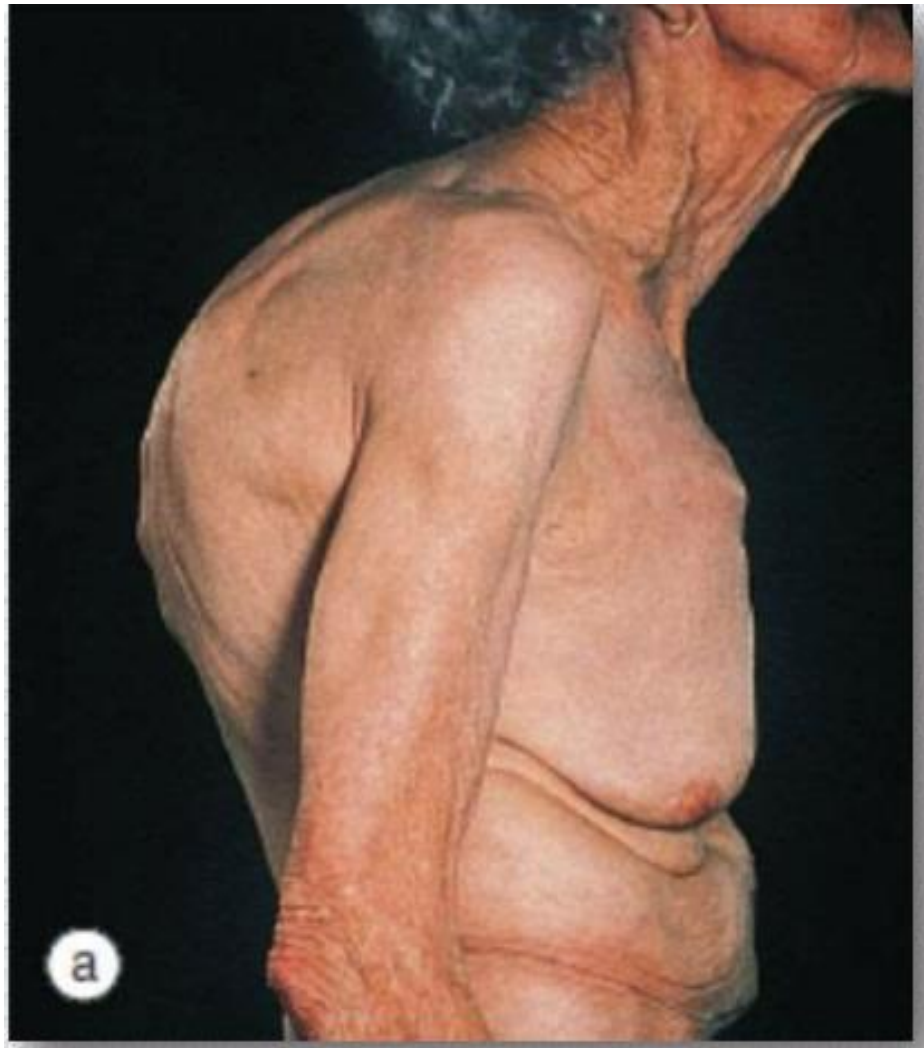
2.Gradual onset of height loss.

3.Kyphosis with chronic pain. “Dowager’s hump”

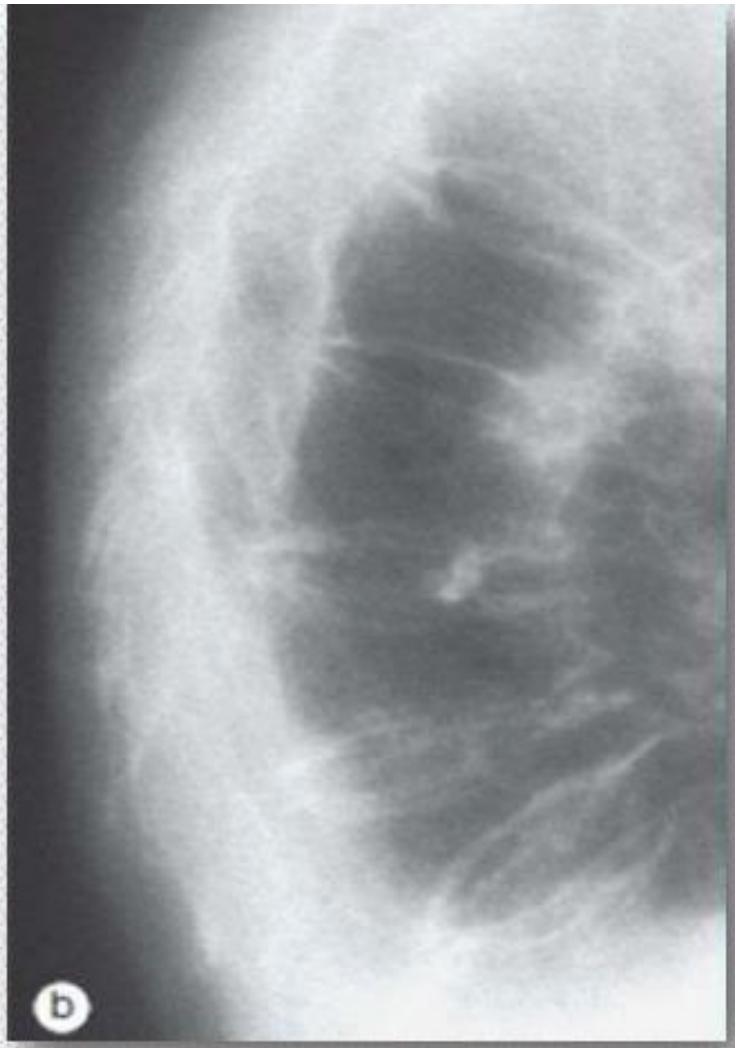
o The pain of acute vertebral fracture can occasionally radiate to the anterior chest or abdominal wall and be mistaken for a myocardial infarction or intra-abdominal pathology, but worsening of pain by movement and local tenderness both suggest vertebral fracture.



(widow’s stoop’) =Dowager’s hump

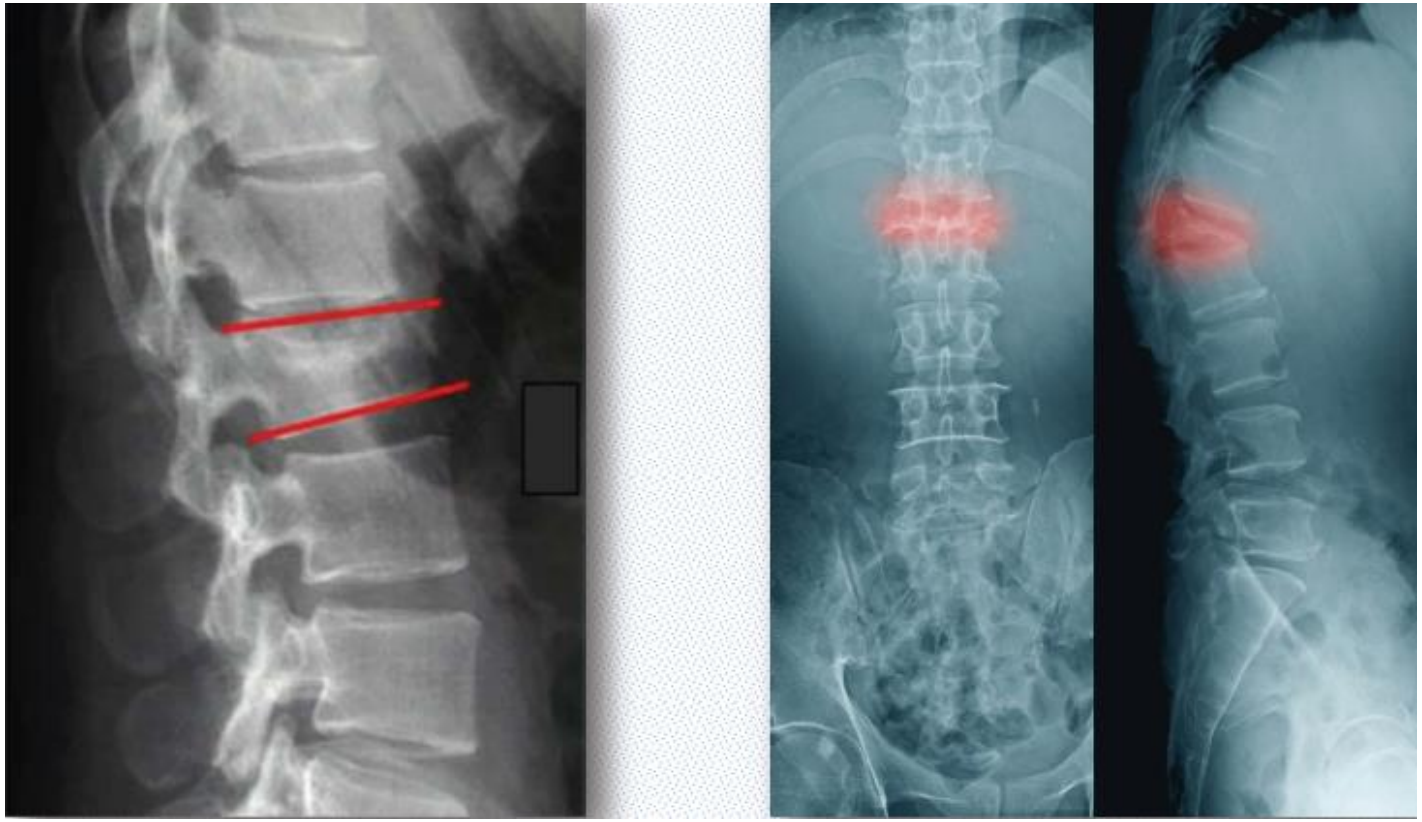


Dowager's hump



Corresponding radiography

Vertebral compression fracture



Colles fracture

o A complete fracture of the distal radius resulting in an

upward (posterior) displacement of the radius and obvious deformity.

o Symptoms include sudden pain, swelling, deformity and bruising.

o Complications may include damage to the median nerve

Hip fracture

- In patients with hip fracture, the affected leg is shortened and externally rotated .
- Most hip fractures occur in one of two locations; femoral neck or intertrochanteric region.
- Of all fragility fractures, hip fractures have highest morbidity and mortality.

Minor fractures

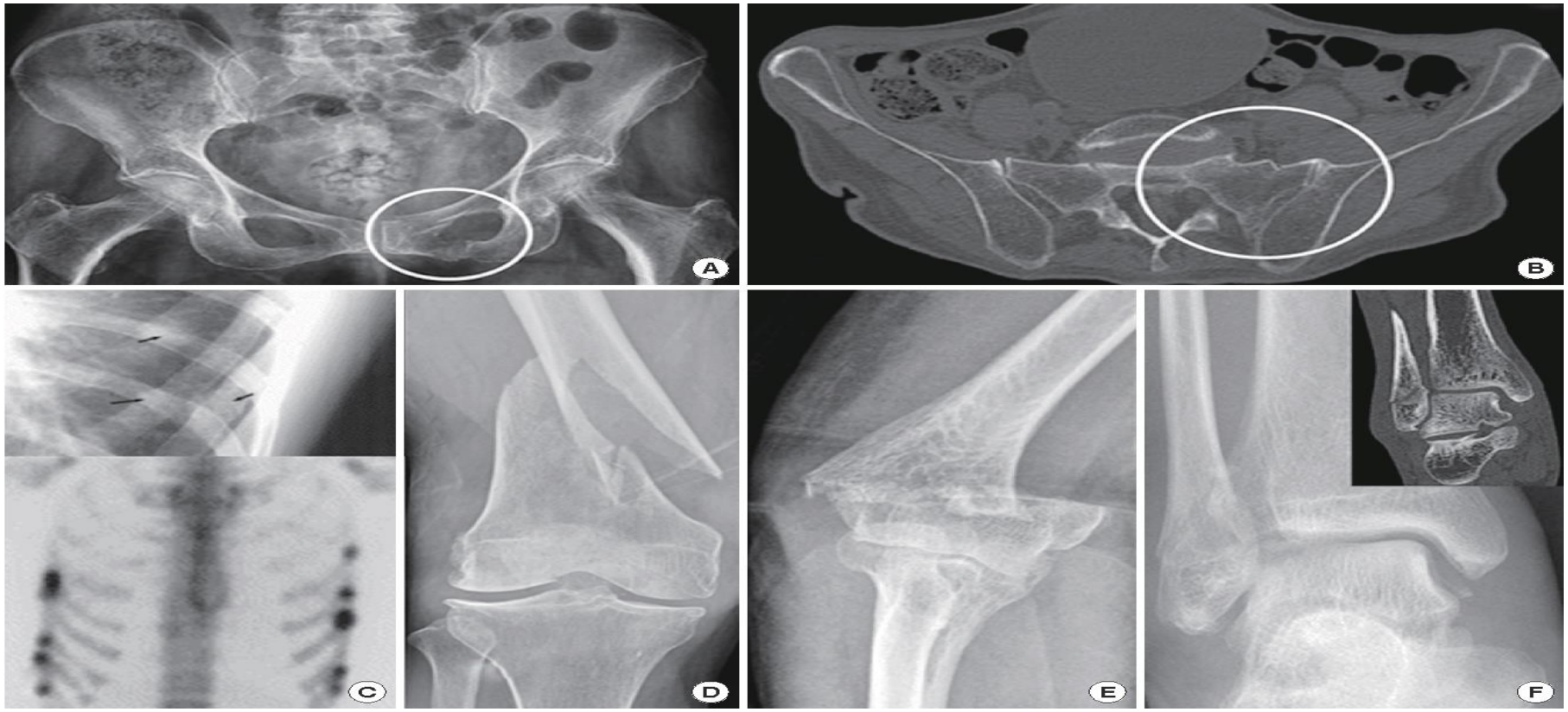


Fig. 3. Typical osteoporotic fractures at minor sites. (A) Pelvis, (B) Sacrum, (C) Ribs, (D) Distal femur, (E) Distal humerus, (F) Ankle.

Other clinical picture

- Immobility.
- Depression.
- Fear & low self-esteem from physical limitations and deformities.
- Many patients present with **incidental** osteopenia on an X-ray performed for other reasons, which requires further evaluation

Screening

Laboratory findings are ALL NORMAL in primary osteoporosis (i.e. ALP, Calcium, Phosphate, PTH).

o Osteoporosis cannot be reliably detected in plain radiographs until 30% to 40% of the bone mass is lost

**Screening in women

- Every 3 to 5 years
- All women >65 years old
- Women < 65 with risk factors
- Screening not recommended in men

INVESTIGATIONS

Bone mineral density (BMD) test

o A bone mineral density test is an easy, reliable test that measures the density or thickness of bones.

o It measures the amount of mineral (calcium) in a specific area of the bone.

1- Detect osteoporosis before a fracture occurs.

2- Monitor the effectiveness of treatments for osteoporosis and osteopenia.

BMD test is done in:

Bone mineral density (BMD) measurement is recommended in the following patients :

1-Women age 65 years and older and men age 70 years and older, regardless of clinical risk factors

2-Postmenopausal women and men above age 50–69, younger postmenopausal women and women in menopausal transition based on risk factor profile

3-Postmenopausal women and men age 50 and older who have had an adult-age fracture, to diagnose and determine the degree of osteoporosis

4-Adults with a condition (eg, rheumatoid arthritis) or taking medication (eg, glucocorticoids in a daily dose ≥5 mg prednisone or equivalent for ≥3 months) associated with low bone mass or bone loss

Thalassemia pt + chemotherapy treated pt +hypogonadism

.

Table 7.14 Indications for dual-energy X-ray absorptiometry scanning

Radiographic osteopenia
Previous fragility fracture (in those aged less than 75 years)
Glucocorticoid therapy (in those aged less than 65 years)
Body mass index below 19 kg/m^2
Maternal history of hip fracture
BMD-dependent risk factors in Table 7.13

In patients presenting with height loss and/or kyphosis, lateral thoracic spine X-ray is the initial investigation and shows loss of anterior vertebral body height and wedging due to fracture.

BMD, bone mineral density.

There are several different ways to measure BMD:

1. **Dual-energy X-ray absorptiometry (DEXA).**
2. **Peripheral dual-energy X-ray absorptiometry (P-DEXA).**
3. Dual photon absorptiometry (DPA).
4. Quantitative computed tomography (QCT).
5. Quantitative ultrasound.

PERIPHERAL DEXA

P-DEXA is a type of DEXA test.

o It measures the density of bones in the arms or legs , such as the wrist.

o P-DEXA machines are portable units.

o The results are quicker than standard DEXA measurements.

o P-DEXA has a disadvantage of not being able to monitor the treatment of osteoporosis.

o Four Informative Skeletal Sites:

1. Radius: the distal one-third of the radius (wrist) is efficacious in predicting fracture risk.

2. Phalanx: the proximal phalanx.

3.Metatarsus: the 5th metatarsus.

4. Tibia: the mid-shaft of the tibia

. Peripheral DXA is used to measure BMD at the wrist; it may be most useful in identifying patients at very low fracture risk who require no further workup.

Dual-energy X-ray absorptiometry (DEXA):

Dual-energy x-ray absorptiometry (DXA) is currently the criterion standard for the evaluation of BMD

*It uses two different X-ray beams, with different energy levels, to estimate bone density in the spine and hip.

*It is a quick, easy and painless test where nothing is injected or swallowed.

* A low-dose x-ray is taken which is only 10% of the radiation exposure of a chest x-ray

DXA provides the patient's T-score, which is the BMD value compared with that of control subjects who are at their peak BMD.

World Health Organization (WHO) criteria define a normal **T-score value** as within 1 standard deviation (SD) of the mean BMD value in a healthy young adult. Values lying farther from the mean are stratified as follows :

Table 1. WHO osteoporosis classification

Diagnosis	T-score
Normal	> −1.0
Osteopenia	< −1.0, > −2.5
Osteoporosis	< −2.5
Severe osteoporosis	< −2.5 plus fragility fractures

>>>>The more negative the number, the higher your risk of a bone fracture.

o T-score:

§ The T-score compares your bone density with that of a 30 yrs healthy young adult .

.

DXA also provides the **patient's Z-score**, which reflects a value compared with that of persons matched for age and sex. Z-scores adjusted for ethnicity or race should be used in the following patients:

1- Premenopausal women

2- Men younger than 50 years

3- Children

range for age" and those above –2.0 SD as **"within the expected range for age."
****The diagnosis of osteoporosis in these groups should not be based on densitometric criteria alone.

Z-score values of –2.0 SD or lower are defined as **"below the expected"

o Z-score:

The Z-score compares your bone density with that of other people of same age and gender and ethnicity

o Contraindications for BMD test :

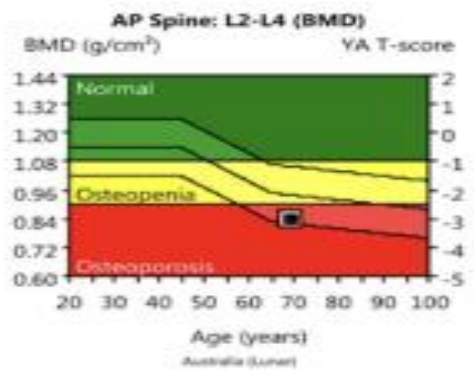
1- Pregnancy.

2- Recent gastrointestinal contrast studies (recommend waiting for at least 72 hours before central DEXA Scan).

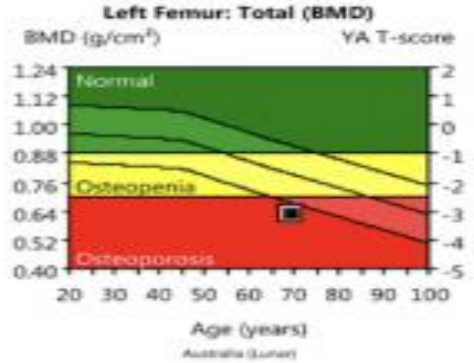
3- Body weight exceeding limit for DEXA scanners (>120-130kgs).

4- Bilateral hip replacements or bilateral hip pins or screws would prevent the hip sites from being scanned.

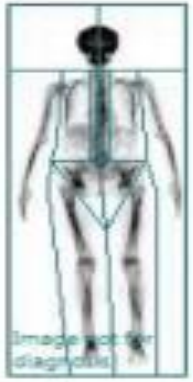
Metallic rods or spinal fusion devices in the lumbar spine prevent scanning at this site

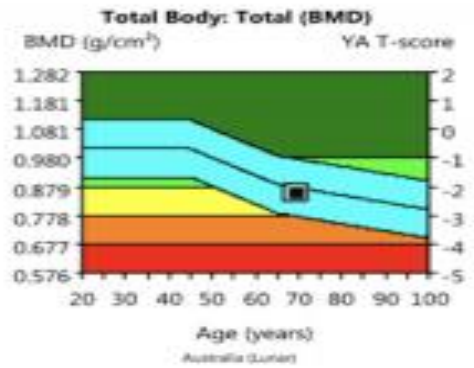


Region	BMD (g/cm²)	YA T-score	AM Z-score
L1	0.693	-3.7	-1.5
L2	0.734	-3.9	-1.7
L3	0.815	-3.2	-1.0
L4	0.950	-2.1	0.1
L1-L2	0.712	-3.8	-1.6
L1-L3	0.749	-3.5	-1.3
L1-L4	0.803	-3.1	-1.0
L2-L3	0.777	-3.5	-1.4
L2-L4	0.838	-3.0	-0.8
L3-L4	0.884	-2.6	-0.5



Region	BMD (g/cm²)	YA T-score	AM Z-score
Neck	0.635	-3.0	-1.1
Total	0.633	-3.1	-1.4





Region	BMD (g/cm²)	YA T-score	AM Z-score
Head	1.872	-	-
Arms	0.679	-	-
Legs	0.815	-	-
Trunk	0.645	-	-
Ribs	0.504	-	-
Spine	0.848	-	-
Pelvis	0.663	-	-
Total	0.857	-2.2	-0.2

Radiology (X-rays) demonstrates fractures but is insensitive for detecting osteopenia.

https://www.youtube.com/watch?v=AsHO-JxTqvA

If osteoporosis is confirmed by bone densitometry, any predisposing factors should be sought (see Box 15.15). Relevant blood tests include:

- U&Es, calcium, phosphate.
- TFTs.
- Immunoglobulins.
- ESR.
- Anti-tissue transglutaminase (for coeliac disease).
- 25(OH) vitaminD
- Parathyroid hormone (PTH).
- Sex hormone and gonadotrophin levels

- **or** Serum biochemistry is normal (Table 7.12).

Table 7.12 Biochemistry results in bone disorders

	Calcium	Phosphate	ALP	PTH
Osteoporosis	N	N	N	N
Osteomalacia	↓ (may be N)	N (may be ↓)		May be raised (secondary hyperparathyroidism)
Paget's disease	N	N	↑	N
Primary hyperparathyroidism	↑	↓	N	↑
Secondary hyperparathyroidism	↓/N	N	N/↑	↑
Hypoparathyroidism	↓	↑	N	↓

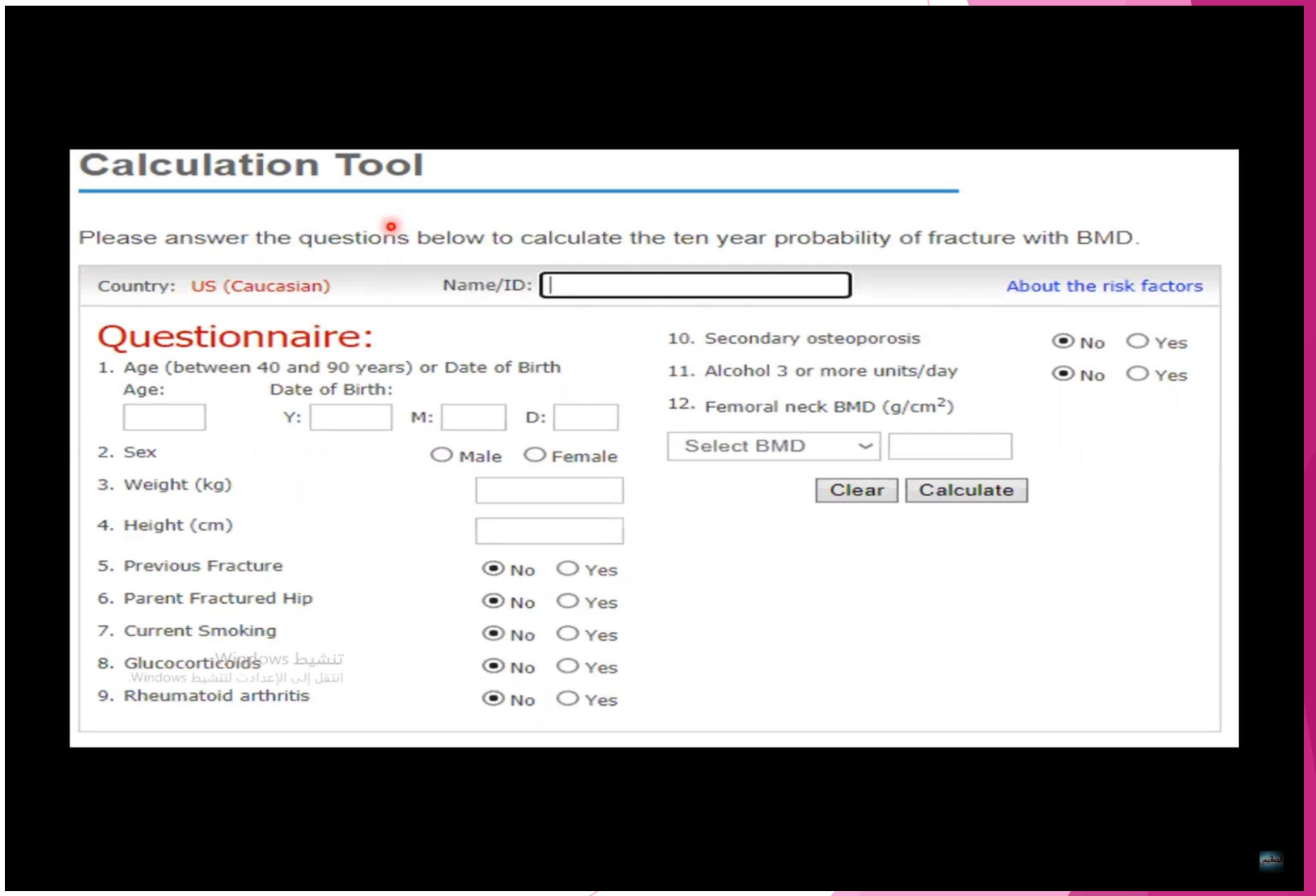
↑, increased; ↓, decreased; ALP, alkaline phosphatase; N, normal; PTH, parathyroid hormone.

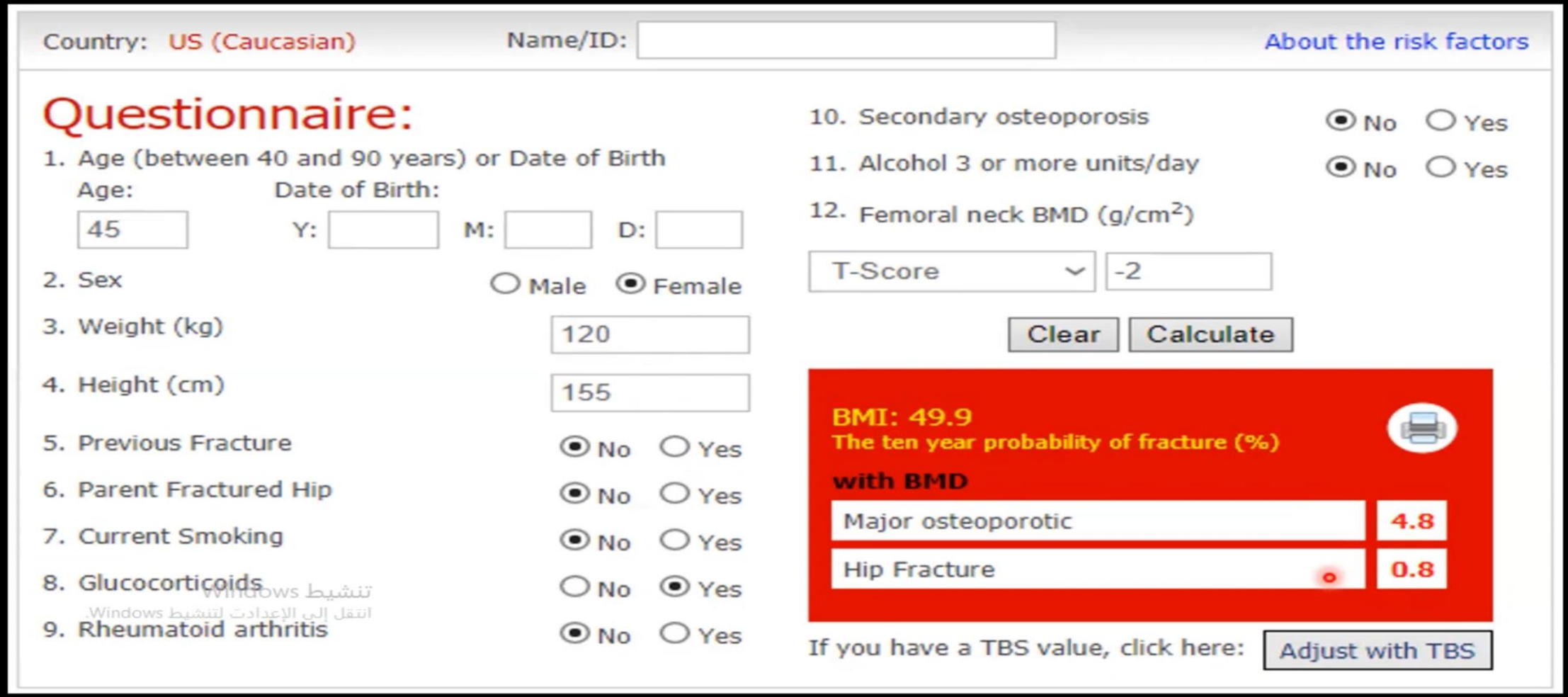
- Secondary causes of osteoporosis (Table 7.13) should be looked for by appropriate blood tests in men and pre-menopausal women

Disorder	Testing
Celiac Disease	CBC (anemia)
Calcium deficiency	Serum calcium
Vitamin D deficiency	25-hydroxyvitamin D
Hyperthyroidism	TSH
Hyperparathyroidism	Calcium, phosphate +/- PTH
Chronic renal/liver disease	Creatinine and LFTs

FRAX score calculator

After you or your doctor fills in all your information on the questionnaire, your FRAX score will be calculated. You'll receive a **10-year risk percentage of a major osteoporotic fracture and a 10-year risk percentage of a hip fracture**.




Country: US (Caucasian)
Name/ID:
About the risk factors
Questionnaire:
1. Age (between 40 and 90 years) or Date of Birth
Age:
Date of Birth:
45
Y:
M:
D:
2. Sex
Male
Female
3. Weight (kg)
120
4. Height (cm)
155
5. Previous Fracture
No
Yes
6. Parent Fractured Hip
No
Yes
7. Current Smoking
No
Yes
8. Glucocorticoids
No
Yes
9. Rheumatoid arthritis
No
Yes
10. Secondary osteoporosis
No
Yes
11. Alcohol 3 or more units/day
No
Yes
12. Femoral neck BMD (g/cm2)
T-Score
-2
Clear
Calculate
BMI: 49.9
The ten year probability of fracture (%)
with BMD
Major osteoporotic
4.8
Hip Fracture
0.8
If you have a TBS value, click here:
Adjust with TBS

Osteoporosis

Treatment

Lifestyle modification

- Weight-bearing exercise
- Exercise while standing and bearing body weight
- Walking, hiking, jogging, playing tennis, etc.
- Not swimming, cycling, rowing
- Avoidance of heavy alcohol use
- Smoking cessation
- Calcium and vitamin D supplementation
- Calcium 1200 (700–1000 mg/day, 1500 mg post-menopausally)
- Vitamin D 800 international unitsdaily

***New vertebral fractures require :**

1- bed rest for 1–2 weeks

2- strong analgesia.

3- Muscle relaxants (e.g. diazepam 2 mg three times daily),

4- subcutaneous calcitonin (50 IU daily) or intravenous pamidronate (single dose 60–90 mg) are also given for pain relief.

***Non-spinal fractures** are treated by conventional orthopaedic means.

*In the elderly, **physiotherapy and assessment of**

home safety are performed to reduce the risk of falls.

***Hip protectors** may reduce the risk of hip fracture in residential care

calcium supplementation

*Calcium carbonate is an inexpensive and commonly used calcium supplement. It contains 40% elemental calcium and should be taken with meals for best absorption

*Calcium citrate (21% elemental calcium) is better tolerated and may be taken with or without food.

*Adverse effects of calcium supplementation include

1- gas and bloating.

2- Calcium may interfere with absorption of iron preparations, thyroid replacement, and fluoroquinolone and tetracycline antibiotics, and administration of these drugs should be separated by several hours.

Vitamin D is essential for absorption of calcium and bone health, and older patients are often at risk for vitamin D deficiency.

Supplementation with vitamin D2 (ergocaciferol) or vitamin 03 (cholecalciferol) is used for treatment.

Bisphosphonates

Alendronate, Risedronate, Zoledronate, Ibandronate

- First line medical therapy
- Analogs of pyrophosphate
- Two phosphonate (PO_3) groups attached to carbon

Bisphosphonates decrease osteoclastic bone resorption mainly through an increase in osteoclastic apoptosis (programmed cell death) and inhibition of the cholesterol biosynthetic pathway important for osteoclast function

- Vary by side chains (R1 and R2)
- **Inhibit osteoclasts**
- Oral and IV drugs

- The oral bisphosphonates alendronate, risedronate, and ibandronate are dosed on a daily, weekly, or monthly
- Absorption of oral administration is poor, with less than 1% of the dose absorbed
- Food and other medications significantly interfere with absorption of oral bisphosphonates take 30 m (60 m for ibandronate) before
- Bisphosphonates are rapidly cleared from the plasma, primarily because they bind to hydroxyapatite in the bone
- . Once bound to bone, they are cleared over a period of hours to years.
- Elimination is primarily via the kidney, and bisphosphonates should be avoided in severe renal impairment.
- For patients unable to tolerate oral bisphosphonates, intravenous ibandronate and zoledronic acid are alternatives.
-
- Take with water on empty stomach

Remain upright for 30 minutes

BISPHOSPHONATE	FORMULATION	DOSING FREQUENCY*
Alendronate	Oral tablet Effervescent tablet	Daily or weekly Weekly
Ibandronate	Oral tablet Intravenous	Daily or monthly Every 3 months
Risedronate	Oral tablet Oral delayed-release tablet	Daily, weekly, or monthly Weekly
Zoledronic acid	Intravenous	Yearly

DOSING INSTRUCTIONS FOR ORAL BISPHOSPHONATES

- Take with 6 to 8 ounces of plain water only
  [Note: Take *risedronate* delayed-release tablet with at least 4 ounces of plain water]
- Take at least 30 minutes (60 minutes for *ibandronate*) BEFORE other food, drink, or medications
  [Note: Take *risedronate* delayed-release tablet immediately AFTER breakfast]
- Remain upright and do not lie down or recline for at least 30 minutes (60 minutes for *ibandronate*) after taking

Figure 27.5
Dosage formulations and instructions for administration of bisphosphonates for the treatment of osteoporosis. *Frequency of administration for individual agents varies with dosage, with higher doses administered less frequently.

adverse effects

m include diarrhea, abdominal pain, and musculoskeletal pain.

Alendronate, risedronate, and ibandronate are associated with esophagitis and esophageal ulcers. To minimize esophageal irritation, patients should remain upright after taking oral bisphosphonates

*Osteonecrosis of the jaw has been reported with bisphosphonates but is usually associated with higher intravenous doses used for hypercalcemia of malignancy.

*uncommon, use of bisphosphonates may be associated with atypical fractures. The risk of atypical fractures may increase with long-term use of bisphosphonate therapy

Bisphosphonates

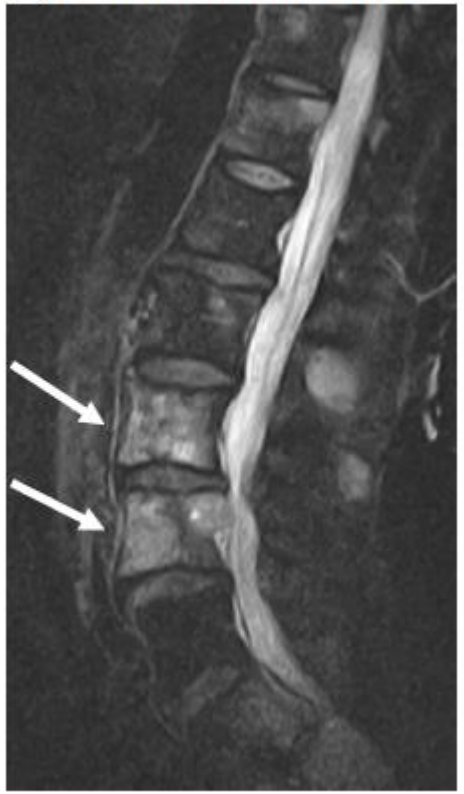
Other Indications

- **Hypercalcemia**

↓ bone resorption →↓ serum calcium

- **Paget's disease of bone**
- **Metastatic bone disease**
- **Improve outcomes**
- ↓ pathologic fractures and spinal cord compression
- ↓ hypercalcemia of malignancy
- ↓ need for radiation or bone surgery

Spinal Bone Mets MRI



Other Treatments

Used in patients who cannot take bisphosphonates

- Or who do not respond to bisphosphonates
- Teriparatide
- Raloxifene
- Calcitonin
- Denosumab

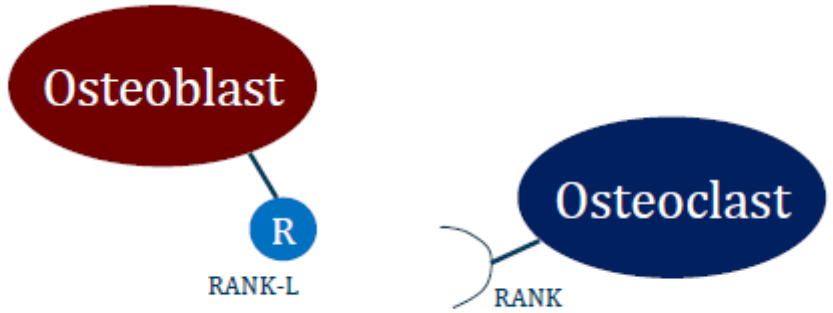
Denosumab

- Monoclonal RANK-L antibody
- Blocks osteoblast activation of osteoclasts
- Given subcutaneously every six months

Denosumab is considered a first-line agent for osteoporosis, particularly in patients at higher risk of fractures

- Usually well-tolerated with few adverse effects

AE :. The drug has been associated with an increased risk of infection dermatological reactions hypocalcemia, and rarely, osteonecrosis of the jaw, and atypical fractures



Raloxifene

SERM (Selective Estrogen Receptor **Modulator**)

Estrogen replacement is an effective therapy for the prevention of po;
menopausal bone loss

estrogen therapy prevents osteoporosis and reduces the
risk of hip fracture. [Note: Estrogen-progestogen therapy is no longe
the therapy of choice for the treatment of osteoporosis in postmen
pausal women because of increased risk of breast cancer, stroke, venous
thromboembolism, and coronary disease

Raloxifene

is a selective estrogen-receptor modulator approved for the prevention and treatment of osteoporosis. It increases bone density without

increasing the risk of endometrial cancer. In addition, raloxifene reduces

the risk of invasive breast cancer in women at high risk. Raloxifene is a

»first-line alternative for postmenopausal osteoporosis in women who

are intolerant to bisphosphonates. Raloxifene reduces serum total and

LDH low-density lipoprotein cholesterol concentrations. The risk of venous

thromboembolism appears to be comparable to that with estrogen.

Other adverse effects include hot flashes and leg cramps.

Teriparatide

Recombinant **human parathyroid hormone (PTH)**

It increases spinal bone density and decrease the risk of vertebral fracture

Teriparatide is the first approved treatment for osteoporosis that stimulate bone formation

It is effective in treatment of glucocorticoid -induced osteoporosis

The safety and efficacy of this agent have not been evaluated beyond 2 years

The cause nausea and dizziness and hypercalcemia•

•Teriparatide : subcutaneous daily injection

Calcitonin

- Hormone produced by thyroid
- Binds to osteoclasts
- Inhibits bone resorption
- Salmon calcitonin used for osteoporosis
- **Second-line therapy**

-is indicated for the treatment of osteoporosis in women who are at least 5 years postmenopausal.

-less effective than other agents, and is no longer routinely -

A unique property of calcitonin is **relief of pain** associated with osteoporotic fracture. - Therefore, calcitonin is sometimes prescribed for the **short-term treatment of patients with a recent painful vertebral fracture**.

- Intranasal administration
- May cause hypocalcemia
- May cause rhinitis

AACE/ACE 2020 POSTMENOPAUSAL OSTEOPOROSIS TREATMENT ALGORITHM

Lumbar spine or femoral neck or total hip T-score of ≤ -2.5, a history of fragility fracture, or high FRAX® fracture probability*

Evaluate for causes of secondary osteoporosis

Correct calcium/vitamin D deficiency and address causes of secondary osteoporosis

- Recommend pharmacologic therapy
- Education on lifestyle measures, fall prevention, benefits and risks of medications

High risk/no prior fractures**

- Alendronate, denosumab, risedronate, zoledronate***
- **Alternate therapy:** Ibandronate, raloxifene

Increasing or stable BMD and no fractures

Consider a drug holiday after 5 years of oral and 3 years of IV bisphosphonate therapy

Resume therapy when a fracture occurs, BMD declines beyond LSC, BTM's rise to pretreatment values or patient meets initial treatment criteria

Progression of bone loss or recurrent fractures

- Assess compliance
- Re-evaluate for causes of secondary osteoporosis and factors leading to suboptimal response to therapy

- Switch to injectable antiresorptive if on oral agent
- Switch to abaloparatide, romosozumab, or teriparatide if on injectable antiresorptive or at very high risk of fracture
- Factors leading to suboptimal response

ABBREVIATIONS GUIDE

BMD – bone mineral density
LSC – least significant change
BTM – bone turnover marker

Very high risk/prior fractures**

- Abaloparatide, denosumab, romosozumab, teriparatide, zoledronate***
- Alternate therapy: Alendronate, risedronate

Reassess yearly for response to therapy and fracture risk

Denosumab	Romosozumab for 1 year	Abaloparatide or teriparatide for up to 2 years	Zoledronate
Continue therapy until the patient is no longer high risk and ensure transition with another antiresorptive agent.	Sequential therapy with oral or injectable antiresorptive agent	Sequential therapy with oral or injectable antiresorptive agent	• If stable, continue therapy for 6 years**** • If progression of bone loss or recurrent fractures, consider switching to abaloparatide, teriparatide or romosozumab

* 10 year major osteoporotic fracture risk ≥ 20% or hip fracture risk ≥ 3%. Non-US countries/regions may have different thresholds.
** Indicators of very high fracture risk in patients with low bone density would include advanced age, frailty, glucocorticoids, very low T scores, or increased fall risk.
*** Medications are listed alphabetically.
**** Consider a drug holiday after 6 years of IV zoledronate. During the holiday, an anabolic agent or a weaker antiresorptive such as raloxifene could be used.

THANK YOU