# HISTOLOGY OF BONE

• Histology of bone tissue
  Cells are surrounded by matrix.
  - 25% water
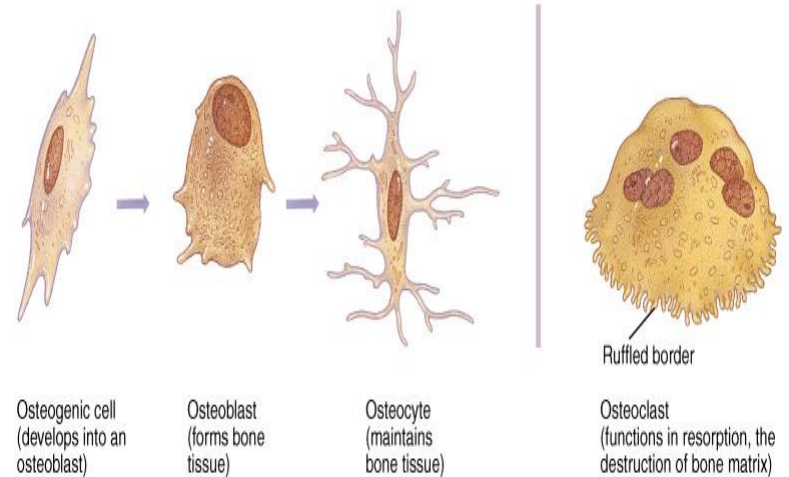  - 25% protein
  - 50% mineral salts

4 cell types make up osseous tissue
Osteoprogenitor cells
Osteoblasts, Osteocytes
Osteoclasts



Cells of Bone Tissue

Ruffled border

Osteogenic cell
(develops into an
osteoblast)

Osteoblast
(forms bone
tissue)

Osteocyte
(maintains
bone tissue)

Osteoclast
(functions in resorption, the
destruction of bone matrix)

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# ❖**Osteoprogenitor cells:**

❏derived from mesenchyme

❏all connective tissue is derived

❏unspecialized stem cells

❏undergo mitosis and develop

❏into osteoblasts

❏found on inner surface of

❏periosteum and endosteum.

**Cells of Bone Tissue**



Osteogenic cell (develops into an osteoblast)

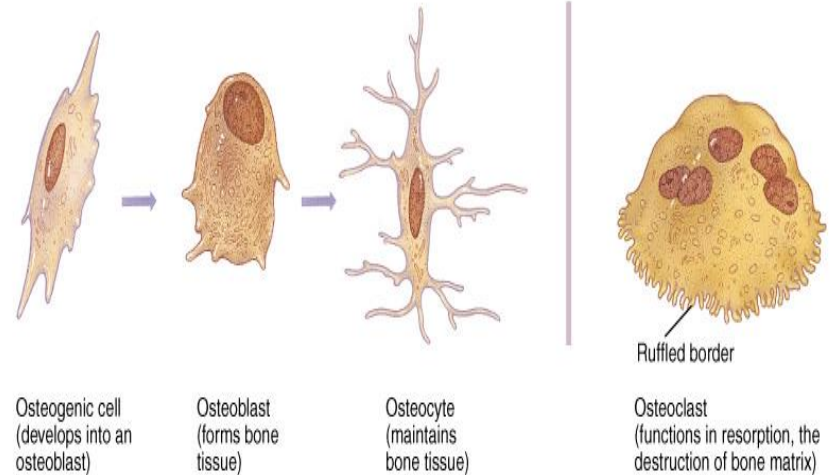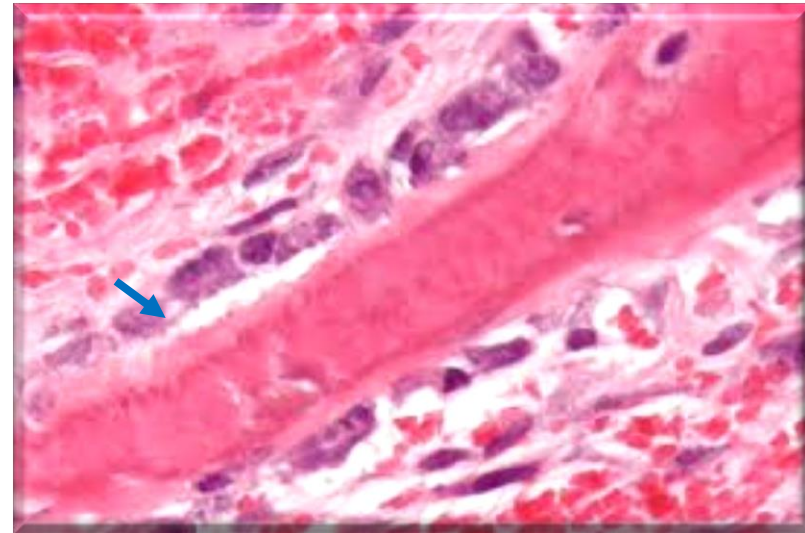Osteoblast (forms bone tissue)

Osteocyte (maintains bone tissue)

Ruffled border

Osteoclast (functions in resorption, the destruction of bone matrix)
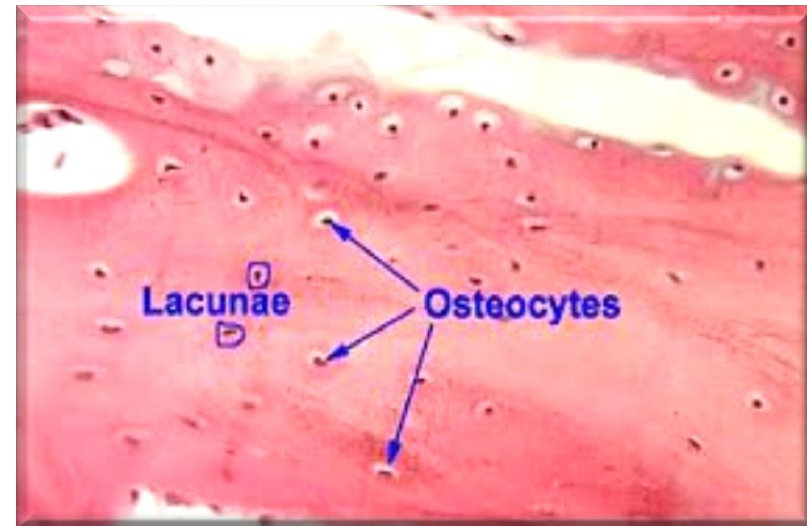
© John Wiley & Sons, Inc.

## ❖Osteoblasts:

❑Bone forming cells

❑Found on surface of bone (arrow)

❑No ability to mitotically divide

❑Collagen secretors

## ❖Osteocytes:

❑Mature bone cells

❑Derived form osteoblasts

❑Do not secrete matrix material

❑Cellular duties include exchange of nutrients and waste with blood.
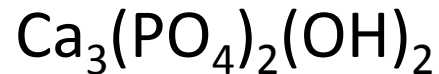


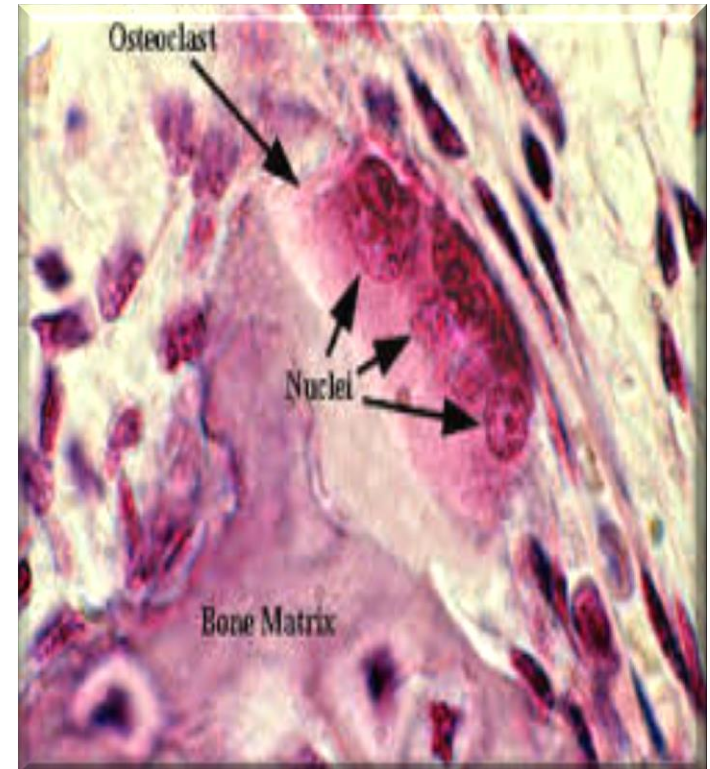

Lacunae  Osteocytes

# ❖Osteoclasts

- ❑ Bone resorbing cells
- ❑ Bone surface
- ❑ Growth, maintenance and bone repair

Abundant inorganic mineral salts:
- Tricalcium phosphate in crystalline form called hydroxyapatite

$$Ca_3(PO_4)_2(OH)_2$$

- Calcium Carbonate: $CaCO_3$
- Magnesium Hydroxide: $Mg(OH)_2$
- Fluoride and Sulfate



Osteoclast

Nuclei

Bone Matrix

# Normal Bone Remodeling
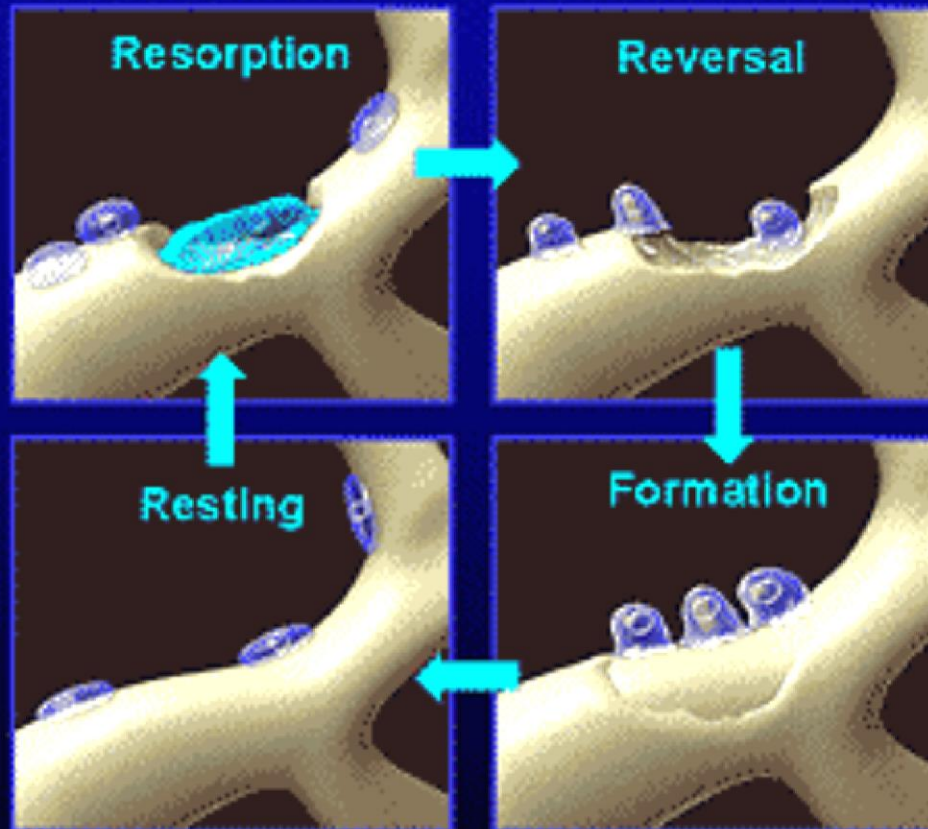


**Resorption**
Osteoclasts remove bone mineral and matrix, creating an erosion cavity (3-4 weeks)

**Reversal**
Mononuclear cells prepare bone surface for new osteoblasts to begin building bone

**Formation**
Osteoblasts synthesize a matrix to replace resorbed bone with new bone (3-4 months)

**Resting**
A prolonged resting period follows until a new remodeling cycle begins
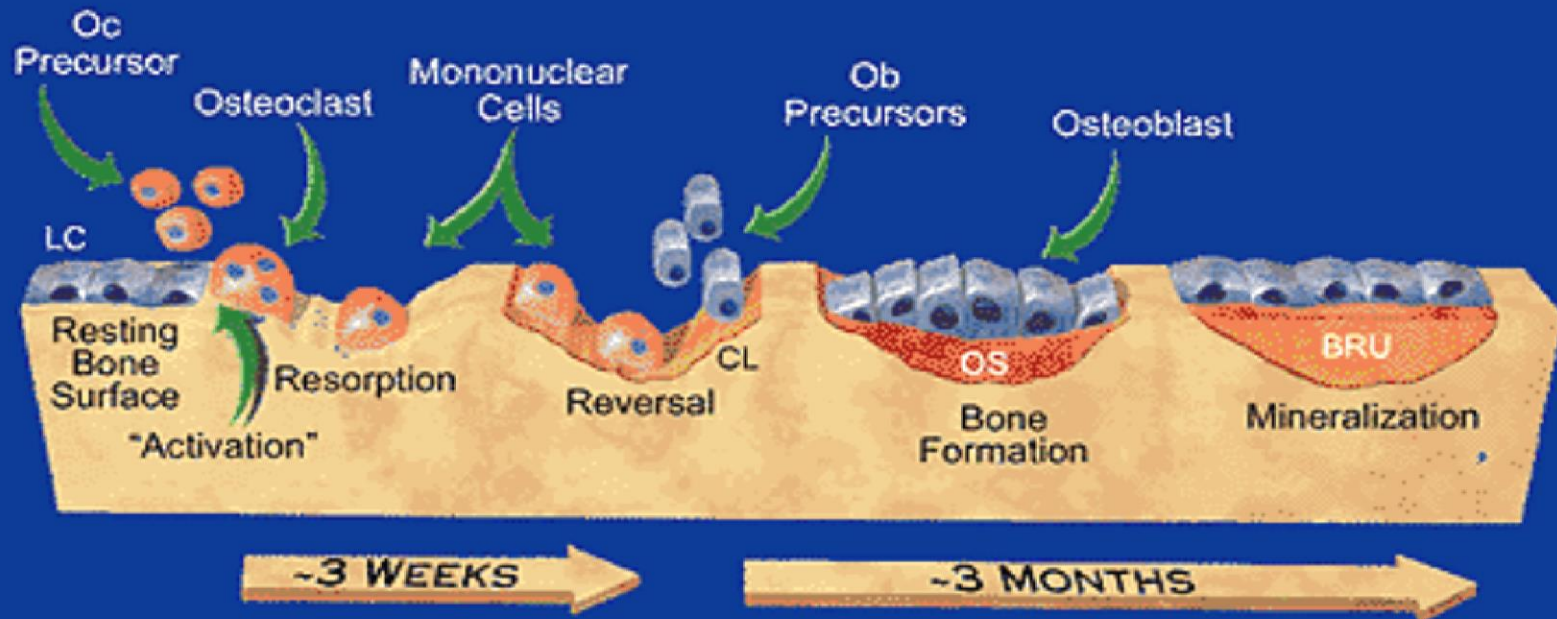
# Background

□ **The problem**

- ❑ Osteoporosis is common

- ❑ Over 50% of women and 30-45% of men over age 50 have osteopenia/osteoporosis

- ❑ White woman over age 50: 50 % lifetime risk of osteoporotic fracture, 25% risk vertebral fracture, 15% risk of hip fracture

- ❑ Man over age 60 has 25% risk osteoporotic fracture

- ❑ 70% over age 80 have osteopo

# Background

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

# What is Osteoporosis?

- Loss in total mineralized bone
- Disruption of normal balance of bone breakdown and build up
- Osteoclasts: bone resorption, stimulated by PTH
- Calcitonin: inhibits osteoclastic bone resorption
- Major mechanisms:
    - Slow down of bone build up: osteoporosis seen in older women and men (men after age 70)
    - Accelerated bone breakdown: postmenopausal
        - Normal loss .5% per year after peak in 20s
        - Up to 5% loss/year during first 5 years after menopause

# Defining Osteoporosis

- "systemic skeletal disease characterized by low bone mass and microarchitectural deterioration of bone tissue, leading to enhanced bone fragility and a consequent increase in fracture risk"

- True Definition: bone with lower density and higher fracture risk

- WHO: utilizes Bone Mineral Density as definition (T score <-2.5); surrogate marker

# Risk factor

- Age
- Estrogen deficiency
- Testosterone deficiency
- Family history/genetics
- Female sex
- Low calcium/vitamin D intake
- Poor exercise
- Smoking
- Alcohol
- Low body weight/anorexia

OSTEOPOROSIS RISK FACTORS

- Alcohol Use
- Corticosteroid Use
- Calcium Low
- Estrogen Low
- Smoking
- Sedentary Lifestyle

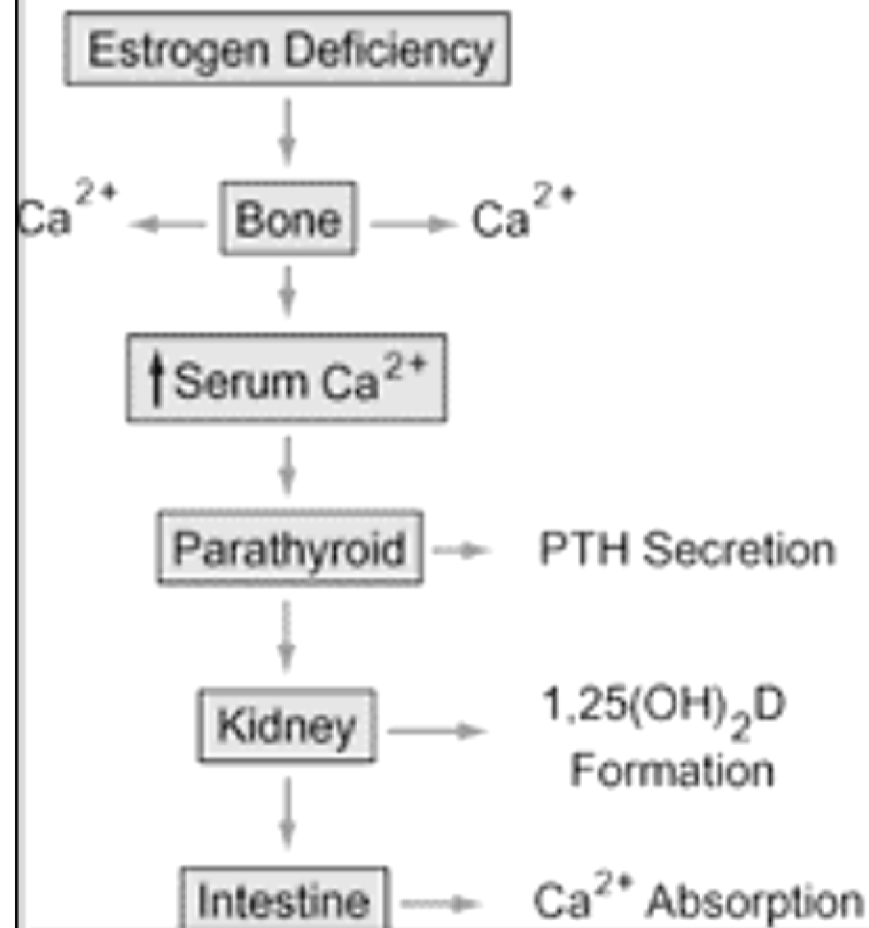©2007 Nursing Education Consultants, Inc.

"Access" (leads to) Osteoporosis

# Risk factor

- Hyperthyroidism
- Hyperparathyroidism
- Prednisone use
- Liver and renal disease (think about vit d synthesis)
- Low sun exposure
- Medications (antiepileptics, heparin)
- Malignancies (metastatic disease; multiple myeloma can present as osteopenia!)
- Hemiplegia s/p CVA/ immobility

# TYPE I OSTEOPOROSIS
## " Postmenopausal "

# TYPE II OSTEOPOROSIS
## " Senile "

Estrogen Deficiency

$Ca^{2+}$ ← Bone → $Ca^{2+}$

↑Serum $Ca^{2+}$

Parathyroid → PTH Secretion

Kidney → $1,25(OH)_2D$ Formation

Intestine → $Ca^{2+}$ Absorption

Kidney → $1,25(OH)_2D$ Formation

Intestine → $Ca^{2+}$ Absorption

Parathyroid → PTH Secretion

$Ca^{2+}$ ← Bone → $Ca^{2+}$
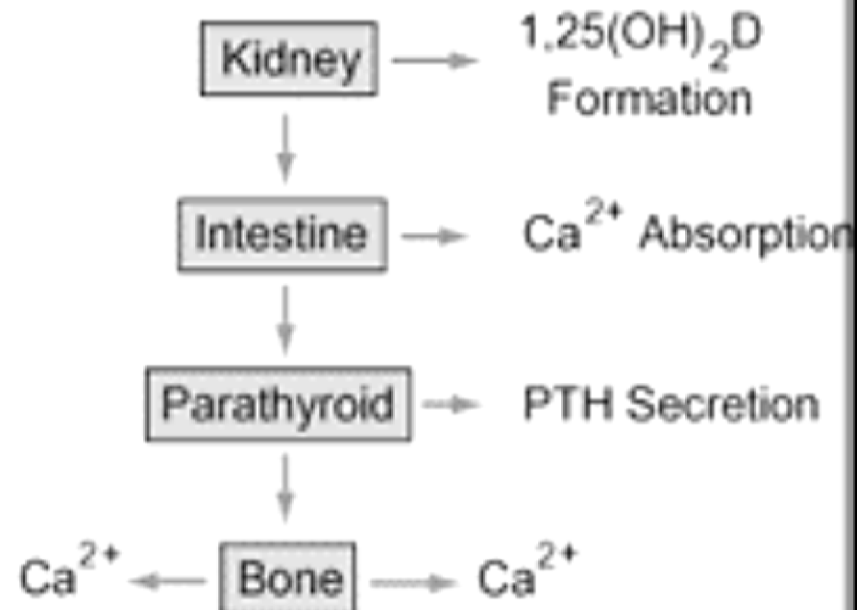
# Pathophysiology of Osteoporosis

Early menopausal bone loss

Calcium/ vitamin D deficiency

Other factors

Inadequate peak bone mass

Decrease in bone mass/bone quality

Low bone mass/ impaired bone quality

Trauma
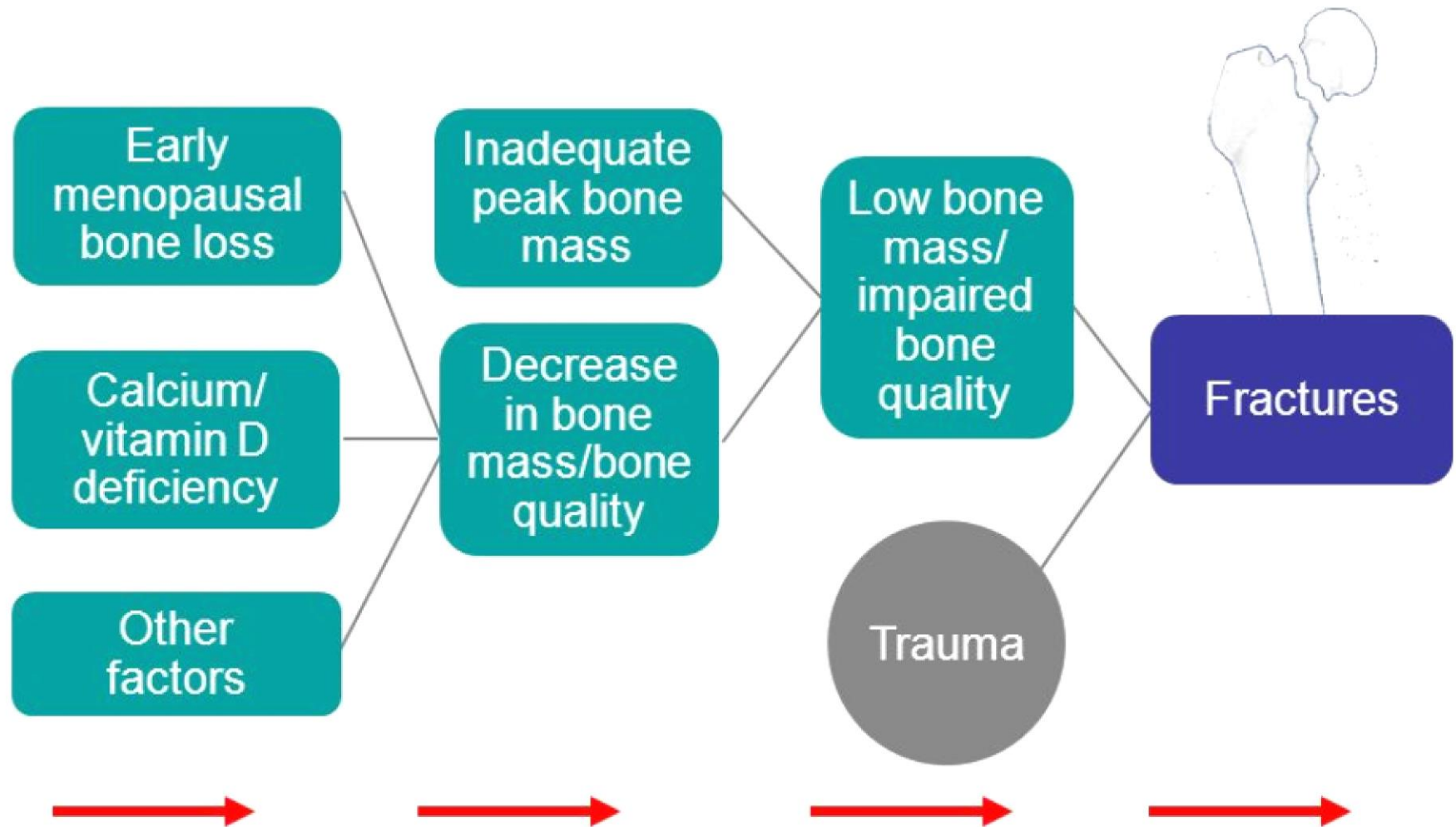
Fractures

# Signs and symptoms

- Pain may affect the lower back or thoracic spinal area.
- A loss of height may occur.
- Joint pain.
- weakness.
- Kyphosis, or dowager's hump, may be present.
- A minor twist or turn can cause a sudden fracture.
- Numbness or tingling in arms or legs may occur.

# dowager's hump

12 lb.  32 lb.  42 lb.
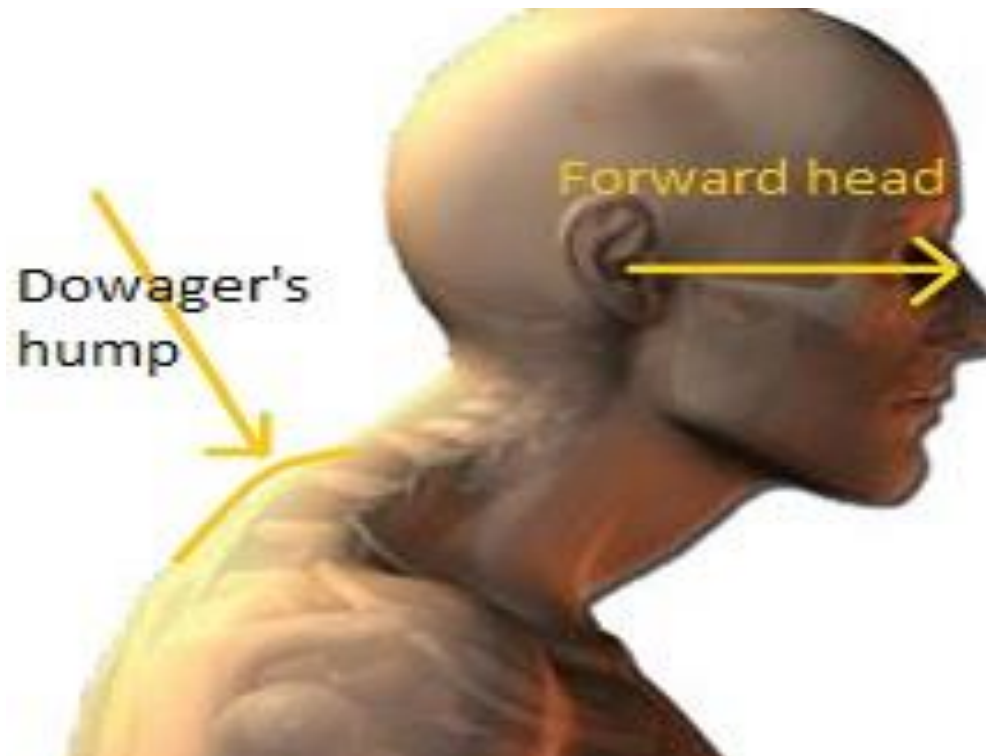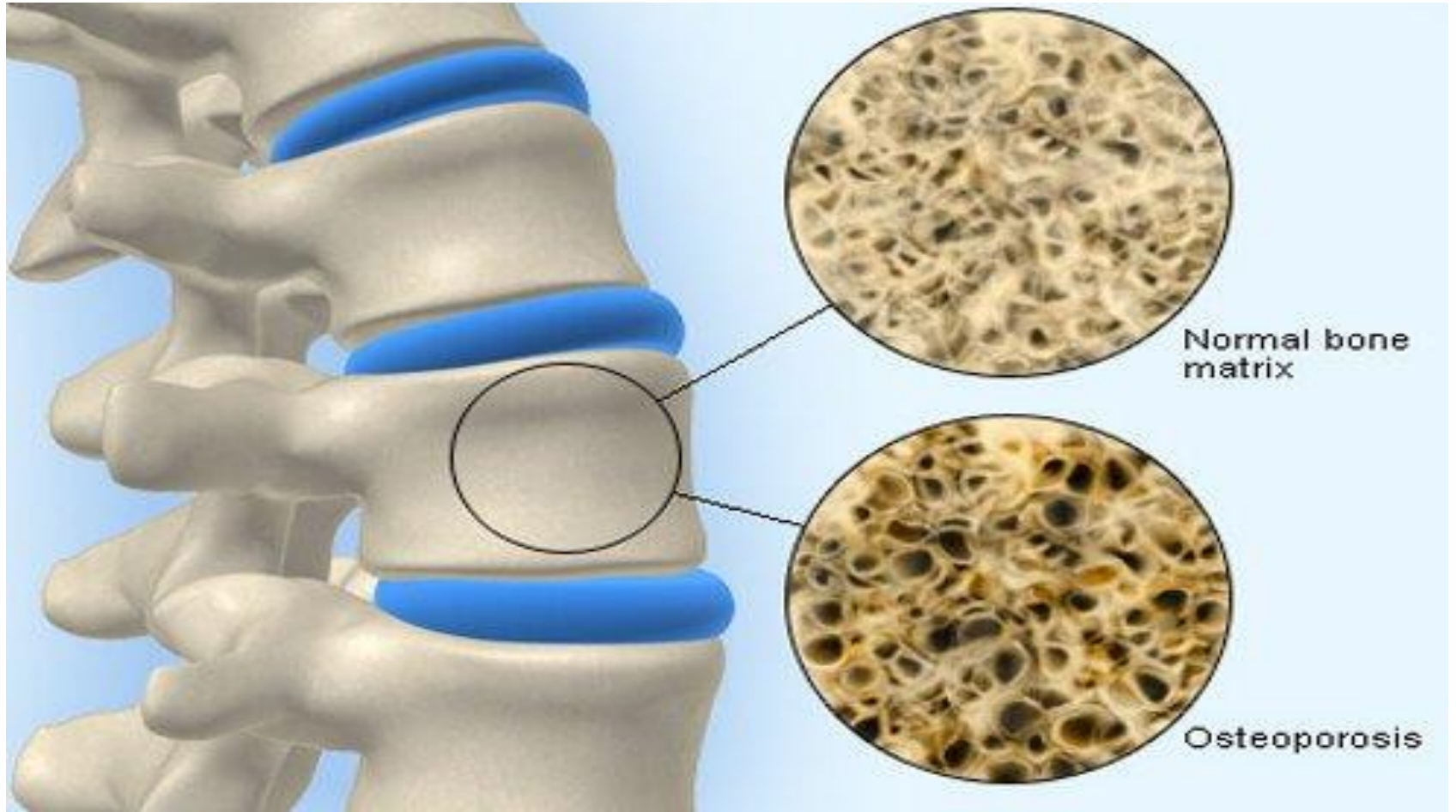
# OSTEOPOROSIS



Normal Bone

Bone with Osteoporosis

Normal bone matrix

Osteoporosis

Osteoporosis: disease of bone that increases risk of fracture; more than BMD goes into causing a fracture; BMD is important, but in reducing fractures must also consider falls risk, age and other factors!!!

# Diagnosing Osteoporosis

- Laboratory Data
  - Limited value in diagnosis
  - Markers of bone turnover (telopeptide) more useful in monitoring effects of treatment than in diagnosis
  - Helpful to exclude secondary causes
    - Hyperthyroidism
    - Hyperparathyroidism
    - Estrogen or testosterone deficiency
    - Malignancy
    - Multiple myeloma
    - Calcium/Vitamin D deficiency
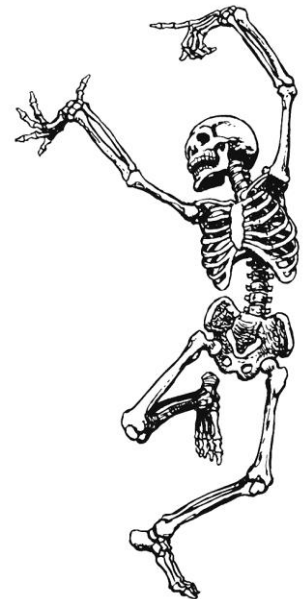
# Methods to evaluate for osteoporosis

- Quantitative Ultrasonography
- Quantitative computed tomography
- Dual Energy X-ray Absorptiometry (DEXA)
  - ?"gold standard"
  - Measurements vary by site
  - Heel and forearm: easy but less reliable (outcome of interest is fracture of vertebra or hip!)
  - Hip site: best correlation with future risk hip fracture
  - Vertebral spine: predict vertebral fractures; risk of falsely HIGH scores if underlying OA/osteophytes

# T-score

+ 1.0

0.0 — normal bone density

- 1.0 —

low bone mass

- 2.0 —

- 2.5 —

- 3.0 — presence of osteoporosis

- 4.0
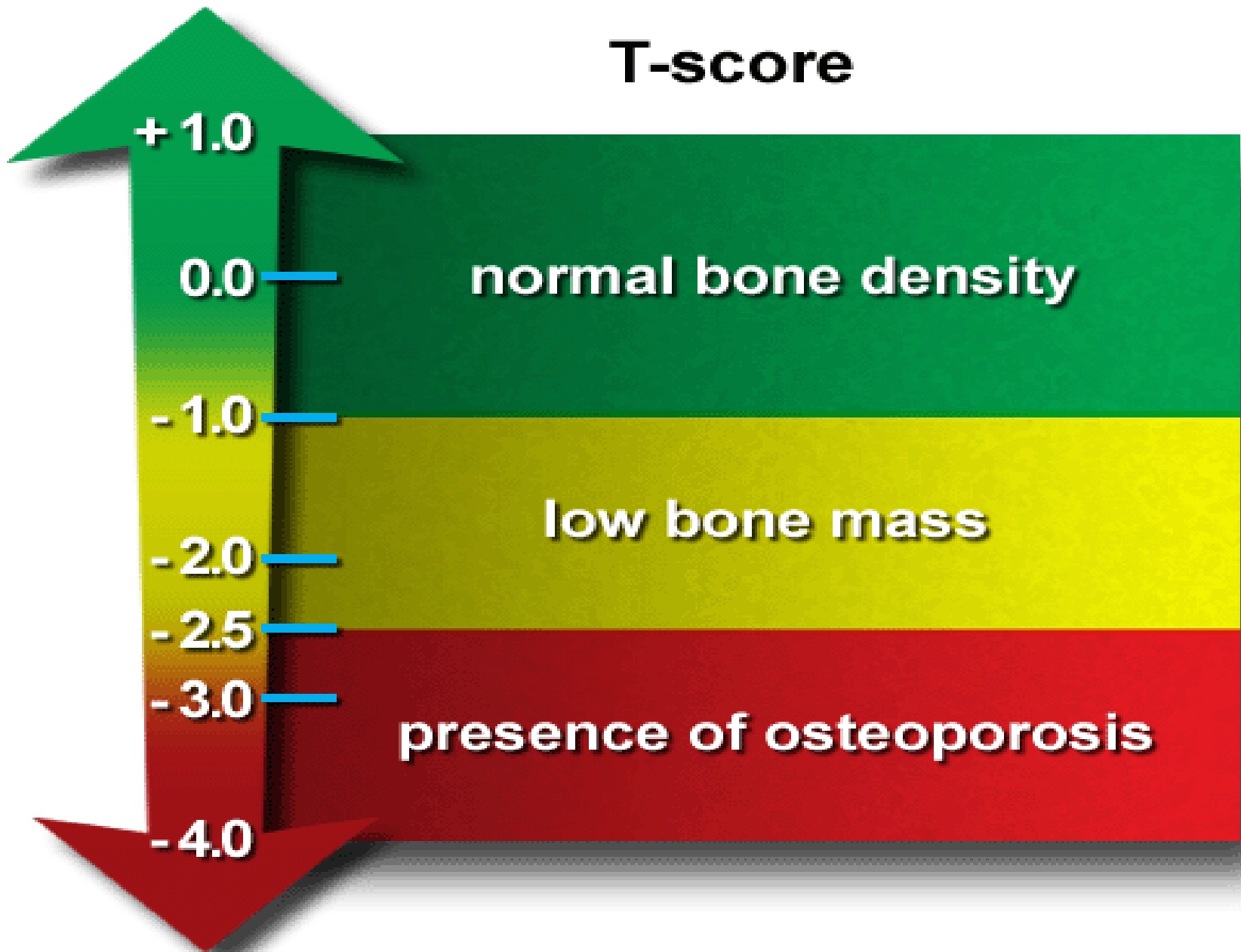
**Columna AP Densidad ósea Tendencia**

T11
T12
L1
L2
L3
L4
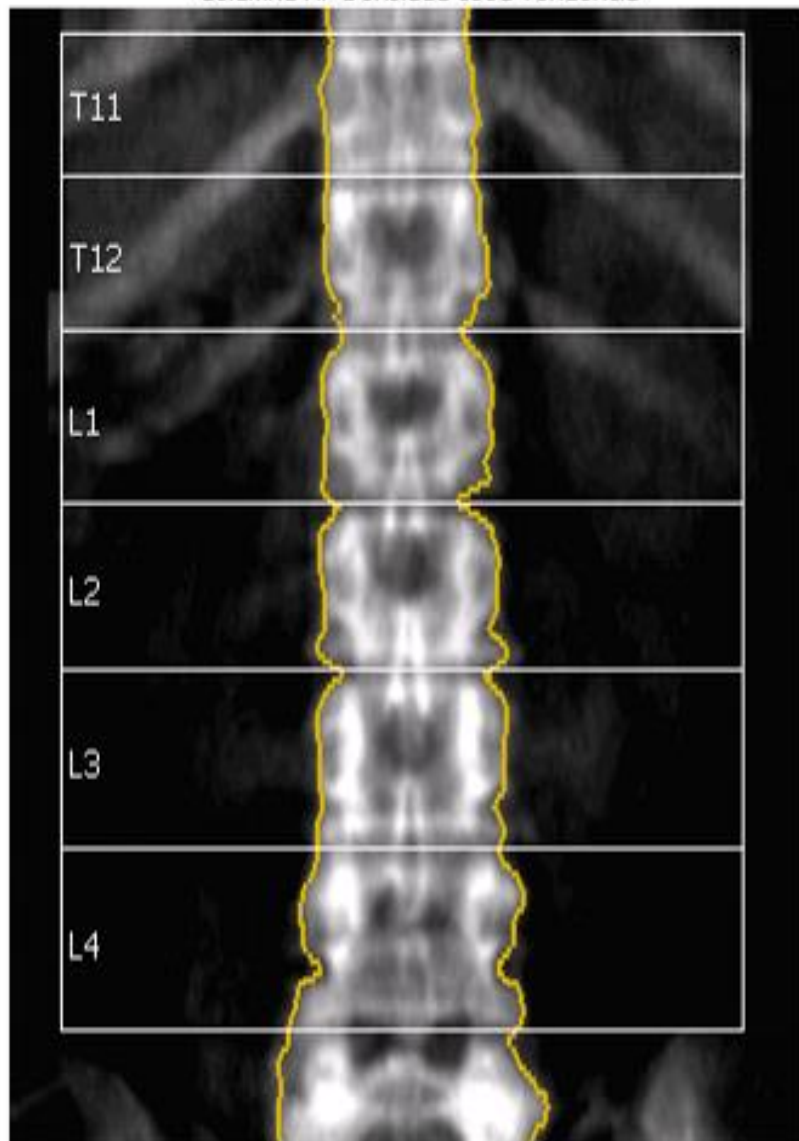
**Ref. de la densitometría: L1-L4 (DMO**

DMO (g/cm²)                    AJ T-score

Normal

Osteopenia

Osteoporosis

Edad (años)

**Tendencia:L1-L4 (DMO)**

DMO (g/cm²)                    AJ T-score

Normal

Osteopenia

Osteoporosis

Edad (años)
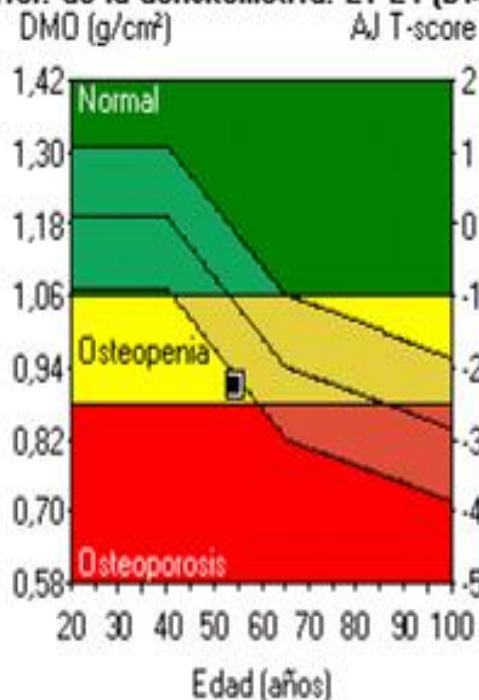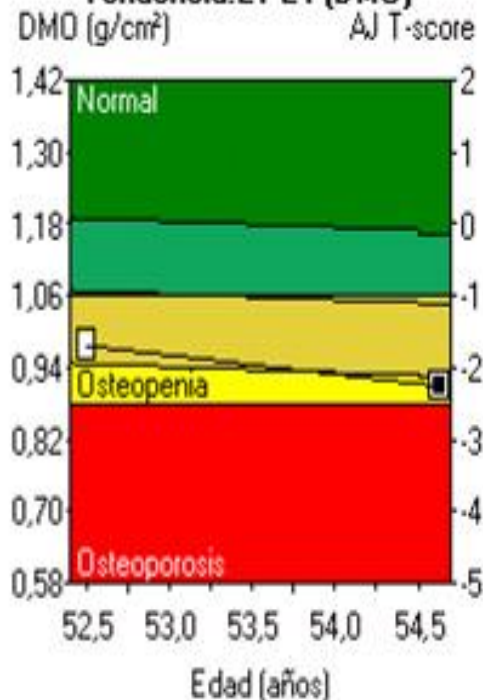
| Región | 1 DMO (g/cm²) | 2 Adulto-Joven (%) | Puntuació | 3 Ajust. a edad (%) | Puntuació |
|--------|-----------|---------|-----------|---------|-----------|
| L1 | 0,845 | 75 | -2,4 | 85 | -1,3 |
| L2 | 0,934 | 78 | -2,2 | 88 | -1,1 |
| L3 | 1,005 | 84 | -1,6 | 94 | -0,5 |
| L4 | 0,862 | 72 | -2,8 | 81 | -1,7 |
| L1-L4 | 0,911 | 77 | -2,2 | 87 | -1,1 |

## Reference: AP Spine L2-L4
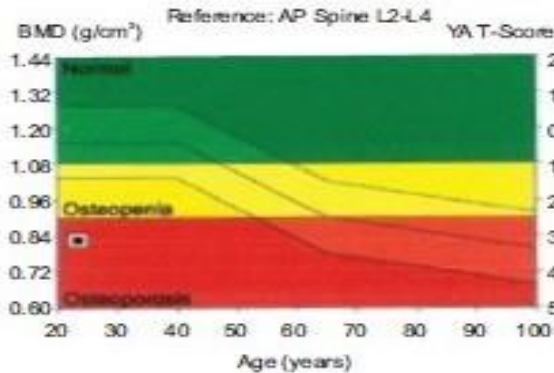


| Region | BMD (g/cm²) | Young-Adult (%) | Young-Adult T-Score | Age-Matched (%) | Age-Matched Z-Score |
|--------|-------------|-----------------|---------------------|-----------------|---------------------|
| L1 | 0.764 | 68 | 3.1- | 71 | 2.7- |
| L2 | 0.863 | 72 | 2.8- | 75 | 2.4- |
| L3 | 0.825 | 69 | 3.1- | 72 | 2.7- |
| L4 | 0.793 | 66 | 3.4- | 69 | 3.0- |
| L1-L2 | 0.811 | 70 | 3.0- | 73 | 2.6- |
| L1-L3 | 0.815 | 70 | 3.0- | 73 | 2.6- |
| L1-L4 | 0.809 | 69 | 3.1- | 71 | 2.7- |
| L2-L3 | 0.843 | 70 | 3.0- | 73 | 2.6- |
| L2-L4 | 0.823 | 69 | 3.1- | 71 | 2.7- |
| L3-L4 | 0.807 | 67 | 3.3- | 70 | 2.9- |

## Reference: Left Femur Total
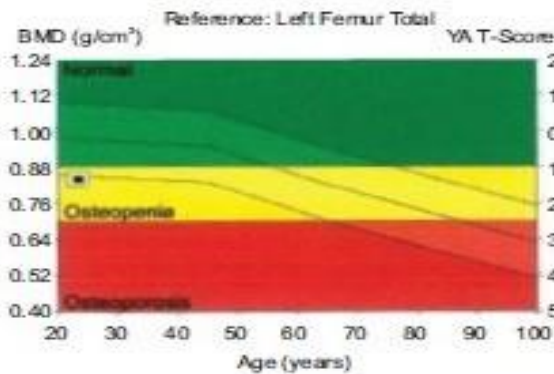


| Region | BMD (g/cm²) | Young-Adult (%) | Young-Adult T-Score | Age-Matched (%) | Age-Matched Z-Score |
|--------|-------------|-----------------|---------------------|-----------------|---------------------|
| Neck | 0.755 | 77 | 1.9- | 79 | 1.7- |
| Upper Neck | 0.646 | - | - | - | - |
| Lower Neck | 0.858 | - | - | - | - |
| Wards | 0.700 | 77 | 1.6- | 79 | 1.4- |
| Troch | 0.720 | 91 | 0.6- | 95 | 0.3- |
| Shaft | 0.991 | - | - | - | - |
| Total | 0.839 | 84 | 1.3- | 86 | 1.1- |

## Reference: Left Forearm Radius 33%
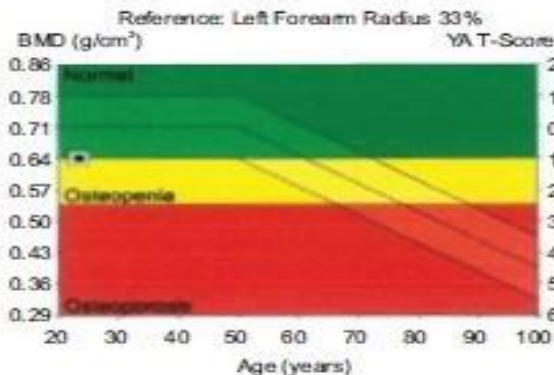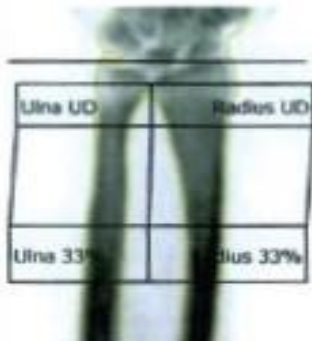


| Region | BMD (g/cm²) | Young-Adult (%) | Young-Adult T-Score | Age-Matched (%) | Age-Matched Z-Score |
|--------|-------------|-----------------|---------------------|-----------------|---------------------|
| Radius UD | 0.374 | 99 | 0.1- | 99 | 0.1- |
| Ulna UD | 0.327 | - | - | - | - |
| Radius 33% | 0.642 | 90 | 1.0- | 90 | 1.0- |
| Ulna 33% | 0.555 | - | - | - | - |
| Both UD | 0.356 | - | - | - | - |
| Both 33% | 0.597 | - | - | - | - |
| Radius Total | 0.504 | 92 | 0.9- | 92 | 0.9- |
| Ulna Total | 0.465 | - | - | - | - |
| Both Total | 0.487 | - | - | - | - |

# Fracture Reduction

- **Goal: prevent fracture, not just treat BMD**
  Osteoporosis treatment options
  - Calcium and vitamin D
  - Calcitonin
  - Bisphosphonates
  - Estrogen replacement
  - Selective Estrogen Receptor Modulators
  - Parathyroid Hormone

# Osteoporosis Treatment: Calcium and Vitamin D

- Fewer than half adults take recommended amounts
- Higher risk: malabsorption, renal disease, liver disease
- Calcium and vit D supplementation shown to decrease risk of hip fracture in older adults
- 1000 mg/day standard; 1500 mg/day in postmenopausal women/osteoporosis
- Vitamin D (25 and 1,25): 400 IU day at least;
  - Frail older patients with limited sun exposure may need up to 800 IU/day

# Osteoporosis Treatment: Calcitonin

- Likely not as effective as bisphosphonates
- 200 IU nasally/day (alternating nares)
- Decrease pain with acute vertebral compression fracture

# Osteoporosis Treatment: Bisphosphonates

- Decrease bone resorption
- Multiple studies demonstrate decrease in hip and vertebral fractures
- Alendronate, risodronate
- IV: pamidronate, zolendronate (usually used for hypercalcemia of malignancy, malignancy related fractures, and multiple myeloma related osteopenia)
- Ibandronate (boniva): once/month
- Those at highest risk of fracture (pre-existing vertebral fractures) had greatest benefit with treatment

# Bisphosphonates: Contraindications

- Renal failure
- Esophageal erosions
  - GERD, benign strictures, most benign GI problems are NOT a contraindication
  - Concern for esophageal irritation/erosions from direct irritation, recommendations to drink water after and not lie down at least 30 minutes
  - Reality: no increased GI side effects compared to placebo group in multiple studies

# Osteoporosis Treatment: Estrogen Replacement

- Reduction in bone resorption

- Proven benefits in treatment

- FDA approval, now limited because of recent concerns from HERS trial and other data suggesting possible increased total risks with HRT (?increased cardiac risk, increased risk VTE, increased risk cancer)

# Osteoporosis Treatment: PTH

- Teriparatide

- Why PTH when well known association with hyperparathyroidism and osteoporosis???

- INTERMITTENT PTH: overall improvement in bone density

  - Optimal bone strength relies upon balance between bone breakdown and bone build up; studies with increased density but increased fracture risk/fragility with flouride show that just building up bone is not enough!!!

# Reducing Fractures

□ 1. Decrease osteoporosis/improve BMD

□ 2. Decrease risk of break: hip protectors

□ 3. Decrease risk of fall

# Falls Reduction

- Falls are a marker of frailty
- Hip fracture is a marker of frailty
  - Mortality after hip fracture:?due to hip fracture or hip fracture as marker for those who are declining?
- Increased risk of falls:
  - Prior fall (fear of falling)
  - Cognitive decline
  - Loss of vision
  - Peripheral neuropathy
  - Weakness
  - Stroke
  - Medications: anticholinergics, tcas, benzos…
  - ETOH

# Nursing interventions

- Assess musculoskeletal status

- Monitor the amount and type of pain to determine its extent

- Give an analgesic as prescribed to relieve pain and promote mobility

- Teach the patient how to use an ambulatory aid to maintain mobility, and apply a neck or back support, if ordered

- Teach the patient about dietary sources of calcium and calcium supplements; increased calcium intake decreases the risk of fractures

- Refer the patient to a practitioner for possible estrogen replacement therapy (controversial)

- Discuss how to ensure a safe home environment to decrease the risk of falls, for example, by removing loose rugs and avoiding long, uncovered electrical cords

- Encourage the patient to participate in active, weight-bearing exercises, such as walking and swimming, to maintain calcium in bones and preserve muscle strength

- Encourage the patient to modify lifestyle choices by avoiding smoking, alcohol, caffeine, and carbonated beverages, and increasing protein intake.