

# Metabolic bone disease

Andrzej Borowski MD, PhD

# Metabolic Bone Diseases

- RICKETS & OSTEOMALACIA

- Hypercalcaemia

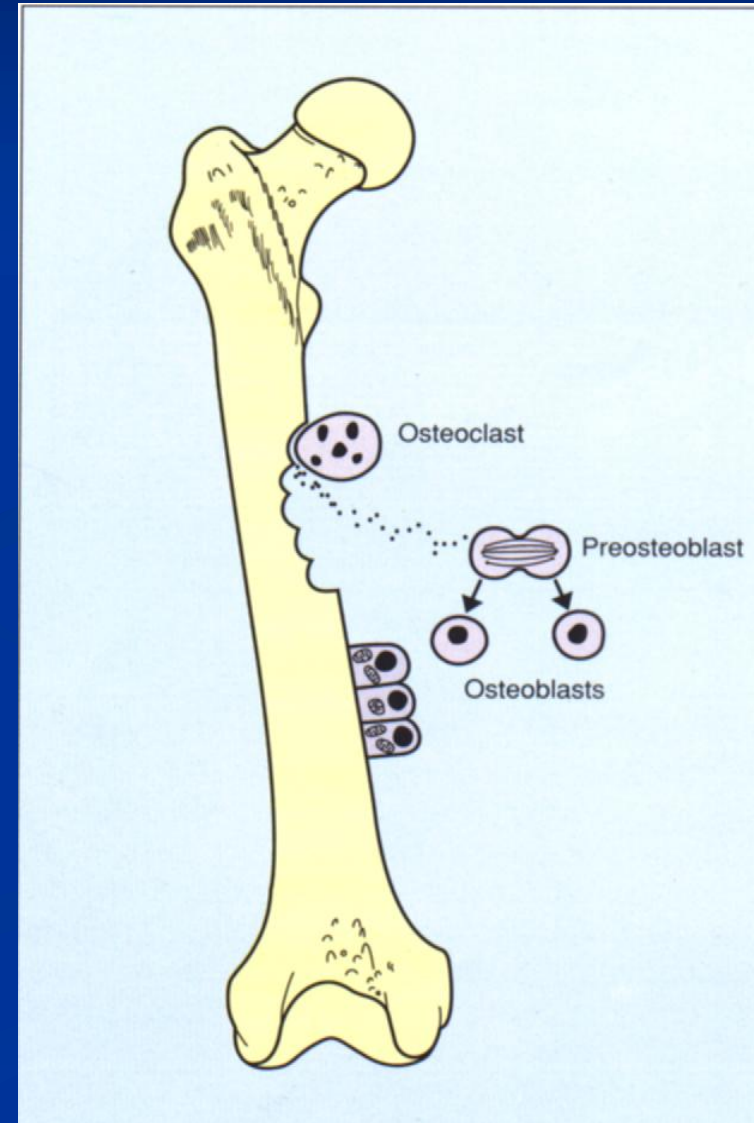


- Osteoporosis is the most common metabolic bone disease

# Bone Turnover

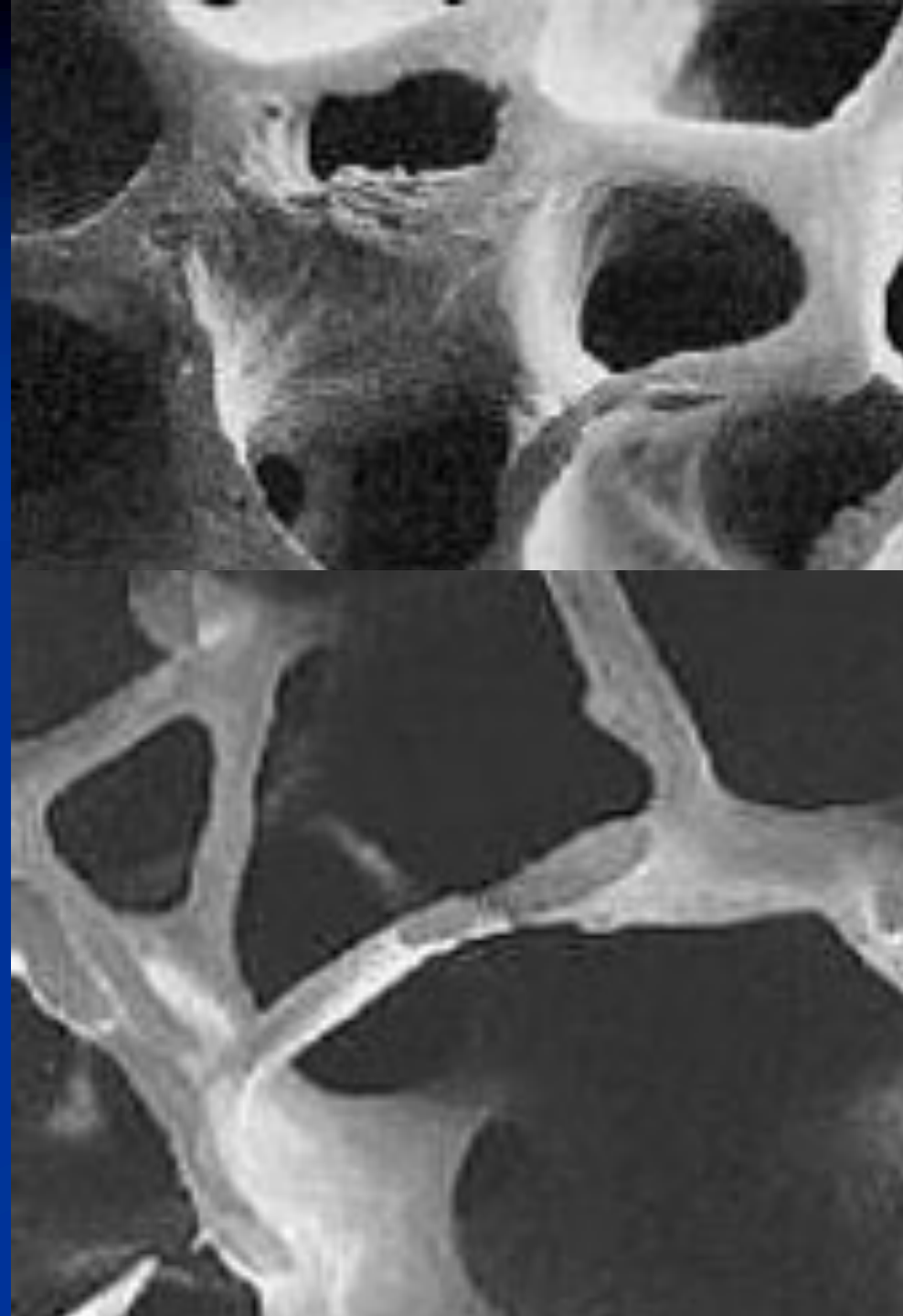
- Osteoclasts - Bone resorption
- Osteoblasts - Bone formation
- Osteocytes

**Formation=Resorption**



## *WHO Definition 1994:*

- A systemic skeletal disease
- characterized by low bone mass
- microarchitectural deterioration of bone tissue
- with increase in bone fragility and susceptibility to fracture

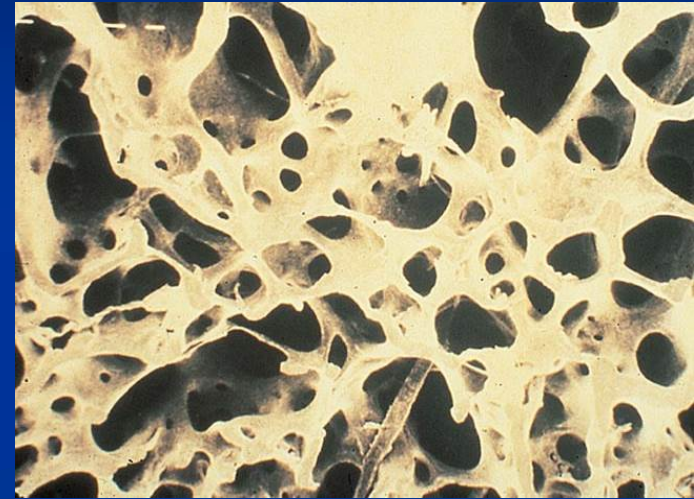


# Osteoporosis

1. Low bone mass and

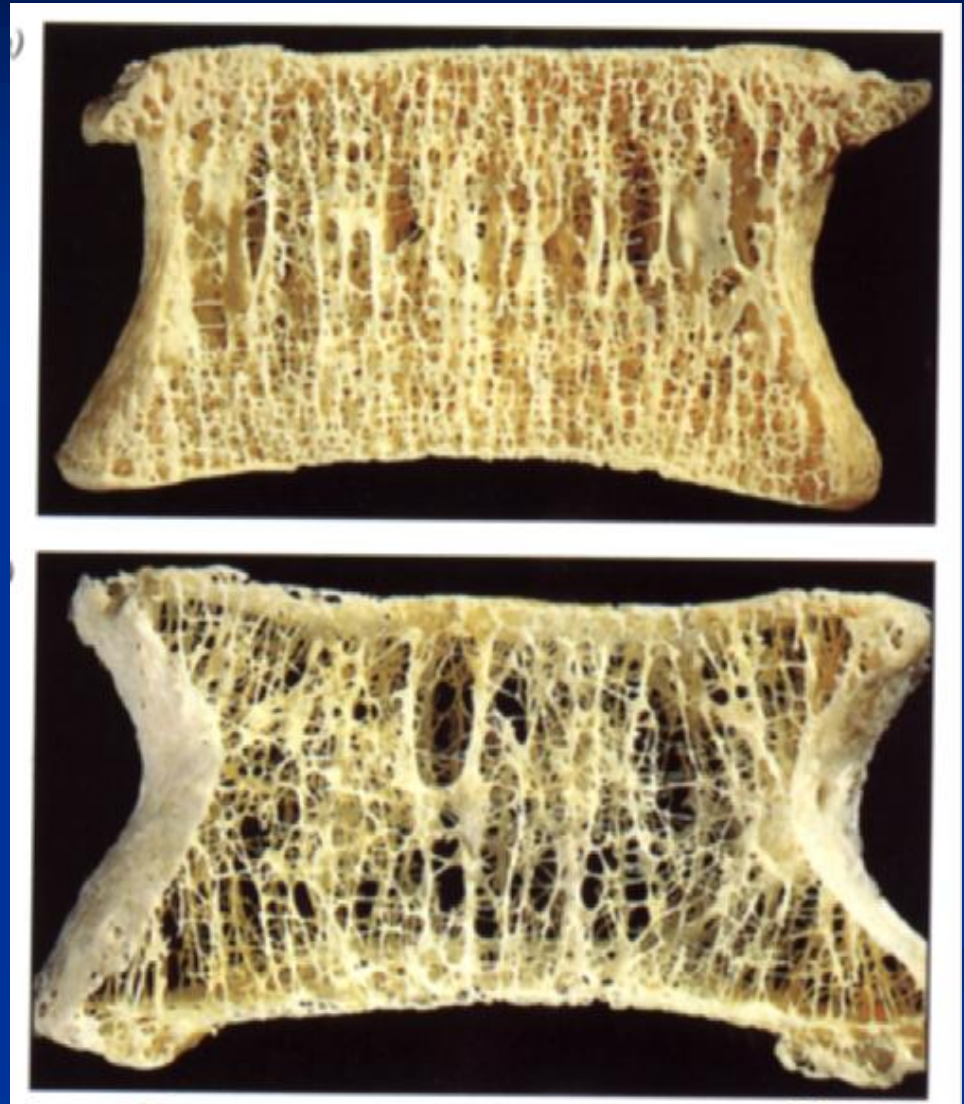
2. Reduced bone quality

Result: Increased risk of fracture



Peak bone mass  
at 16-25  
years.

Bone loss 0.3-  
0.5% per year  
(2-3% per  
year after 6<sup>th</sup>  
decade).



# Peak Bone Mass

Genetic factors 70%

Nutrition



**PBM**



Hormones

Exercises

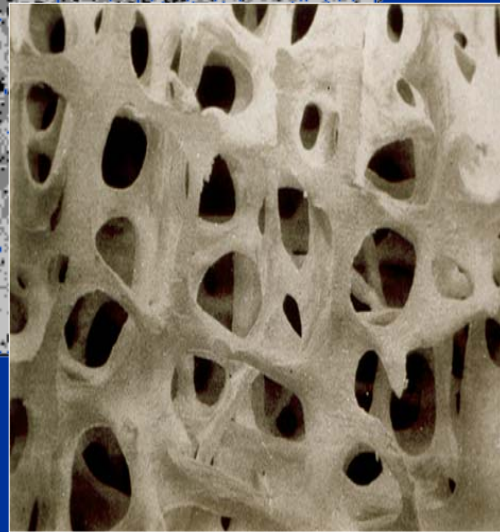
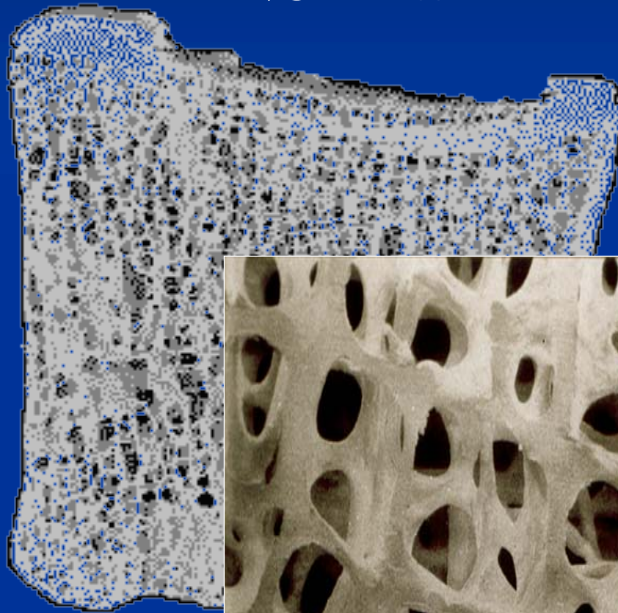




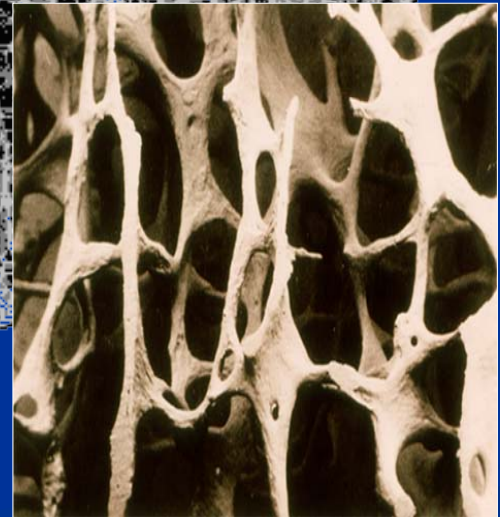
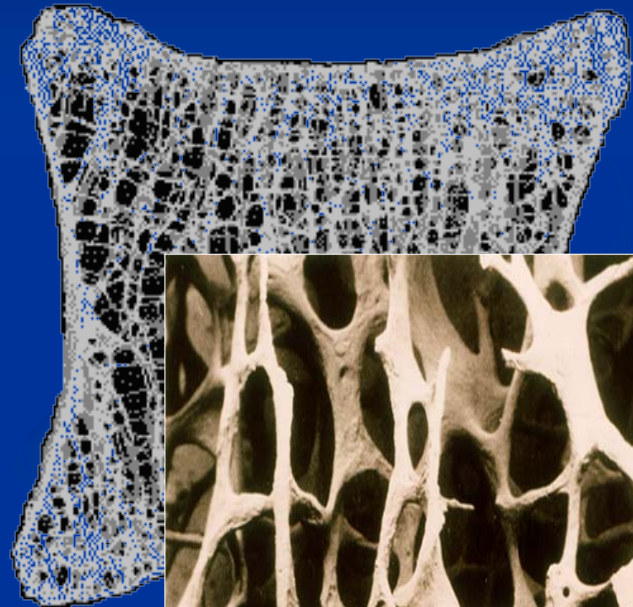


# Vertebral Body

Normal



Osteoporotic



# Background

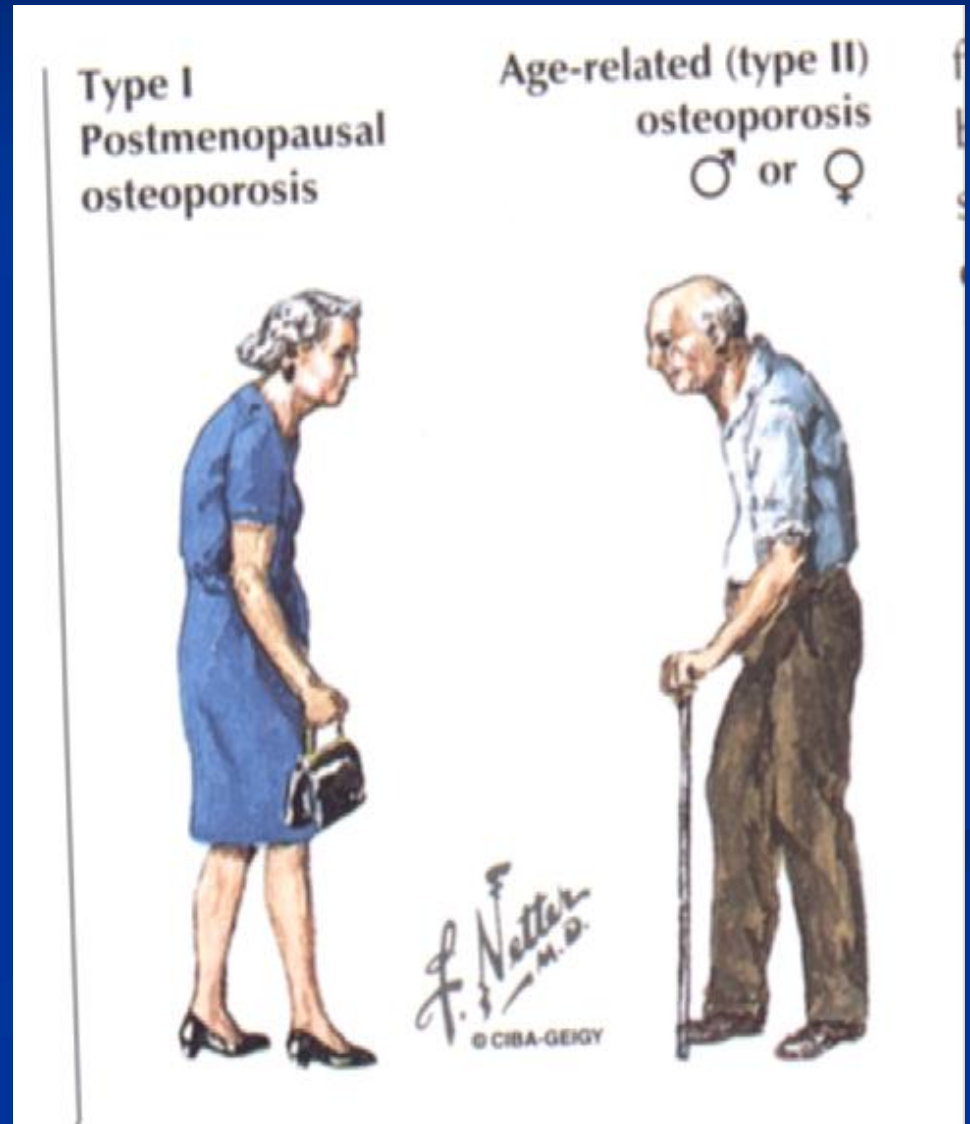
- Osteoporosis is common
- Over 50% of women and 30-45% of men over age 50 have osteopenia/osteoporosis
- White woman over age 50: 50 % lifetime risk of osteoporotic fracture, 25% risk vertebral fracture, 15% risk of hip fracture
- Man over age 60 has 25% risk osteoporotic fracture
- 70% over age 80 have osteoporosis

# Classification

## I. Primary OP

- 1- Postmenopausal
- 2- Senile

## II. Secondary OP



# OSTEOPOROSIS

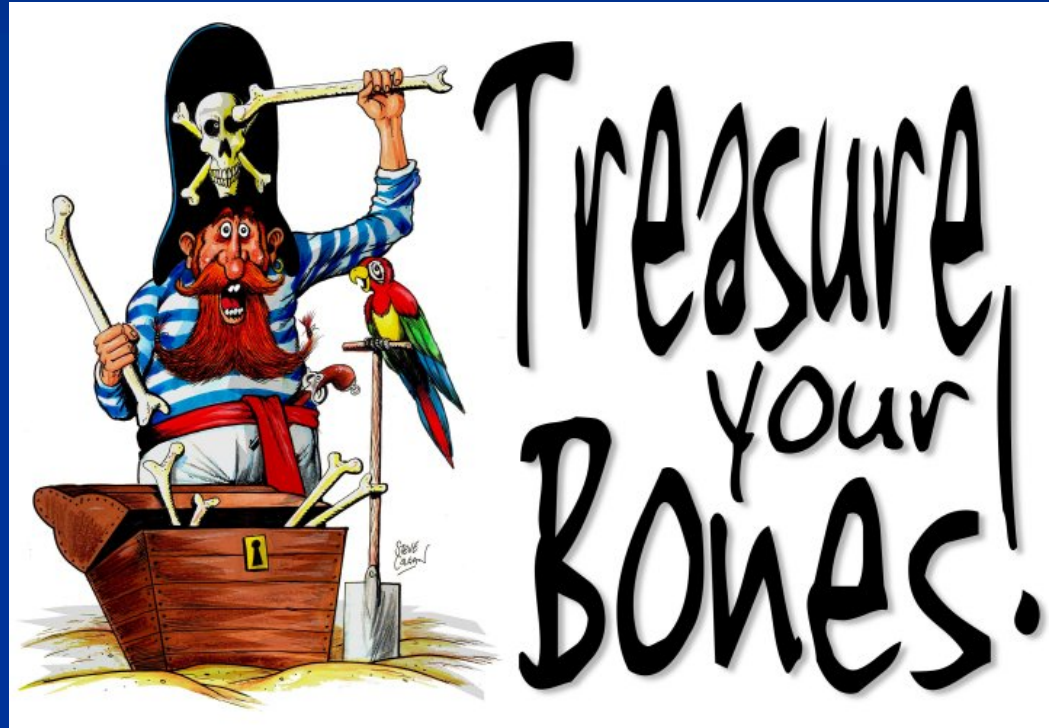
## TYPES :

- I. Postmenoposal: thin trabecular bone  
55-75y  
f:m 6:1
- II. Senile : thin both trabecular & cortical bone  
70-85 y  
f:m 2:1

# Risk Factors for Osteoporosis

## *Modifiable*

- Inadequate exercise
- Inadequate nutrition
  - calcium
  - vitamin D
  - balanced diet
- Medications
  - glucocorticoids
  - excess thyroid - etc.
- Smoking
- Excessive alcohol intake



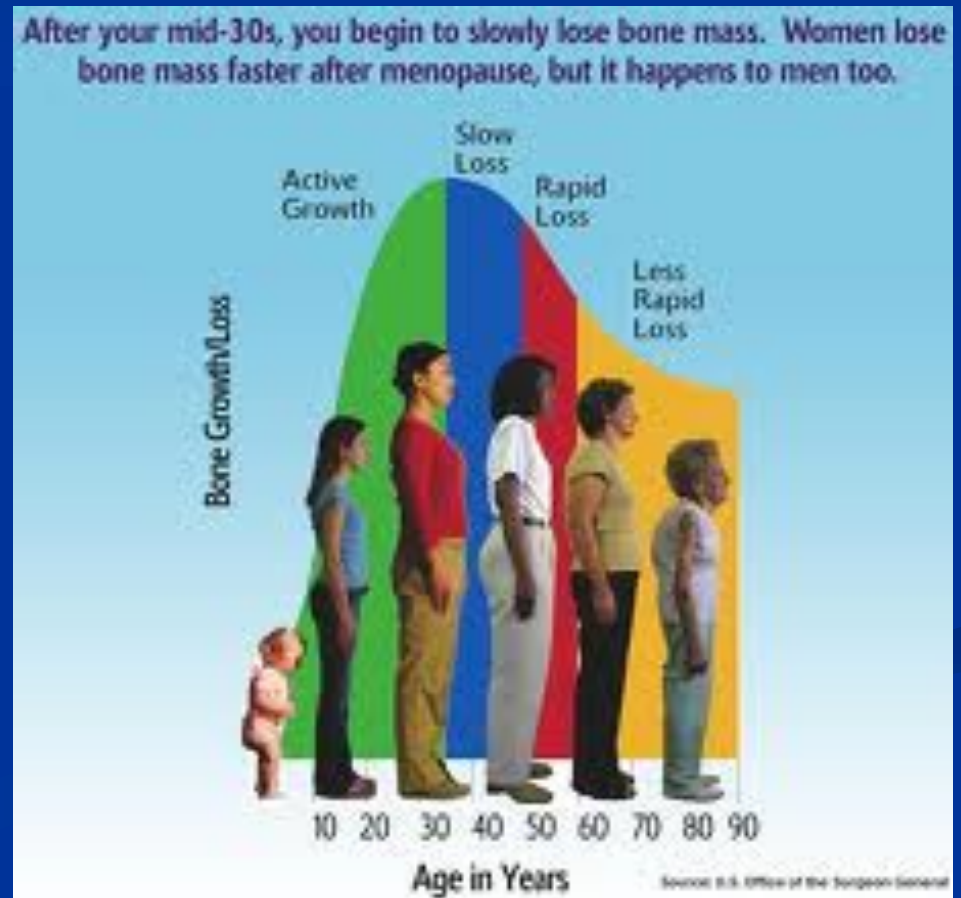


"I think we can rule out osteoporosis."

# Risk Factors for Osteoporosis 2

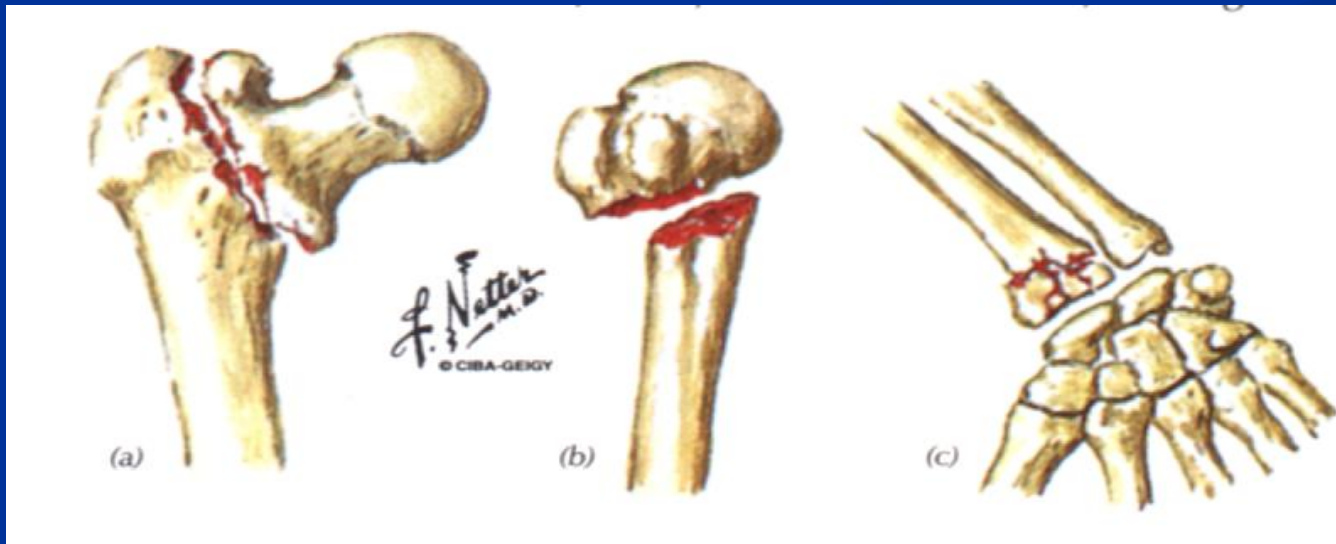
## *Nonmodifiable*

- Genetics
- Gender
- Race
- Age



# Major Osteoporotic Fractures

	Colles	Vertebral	Hip
Typical age	55	65	75
Female:male ratio	4:1	3:1	2:1



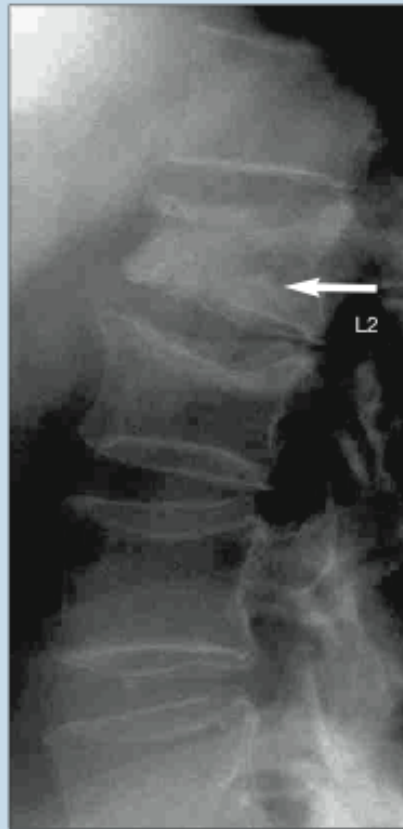


# OP fractures

## Compression fractures of lumbar vertebrae



First fracture



10 years after first fracture

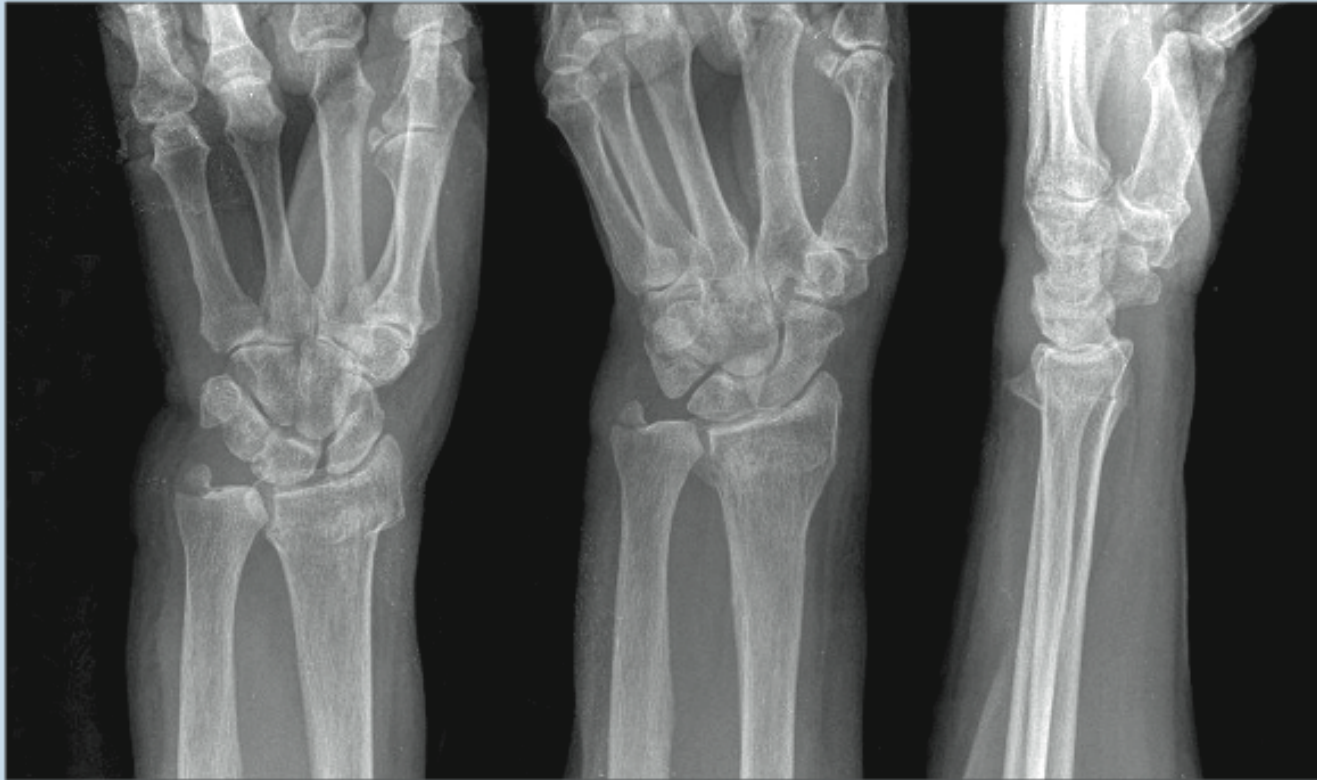


20 years after first fracture

## Femoral neck fracture



## Colles' fracture of the wrist

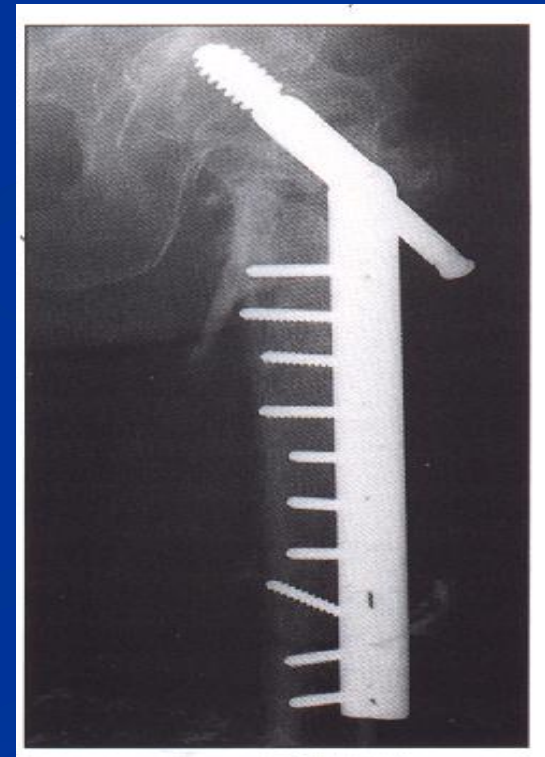


# Background

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

# Femoral Fractures

- Mortality in 20% of patients over 60 years of age
- Morbidity in 50%

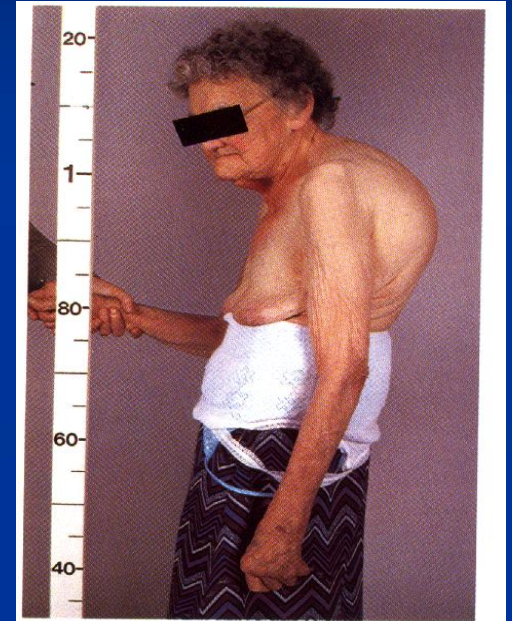


# Risk Factors for Fracture

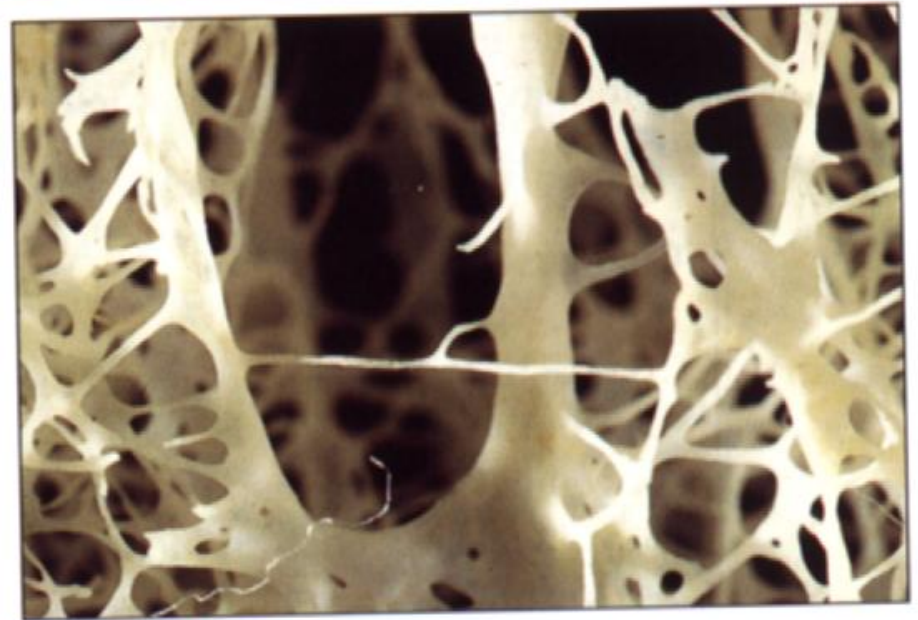
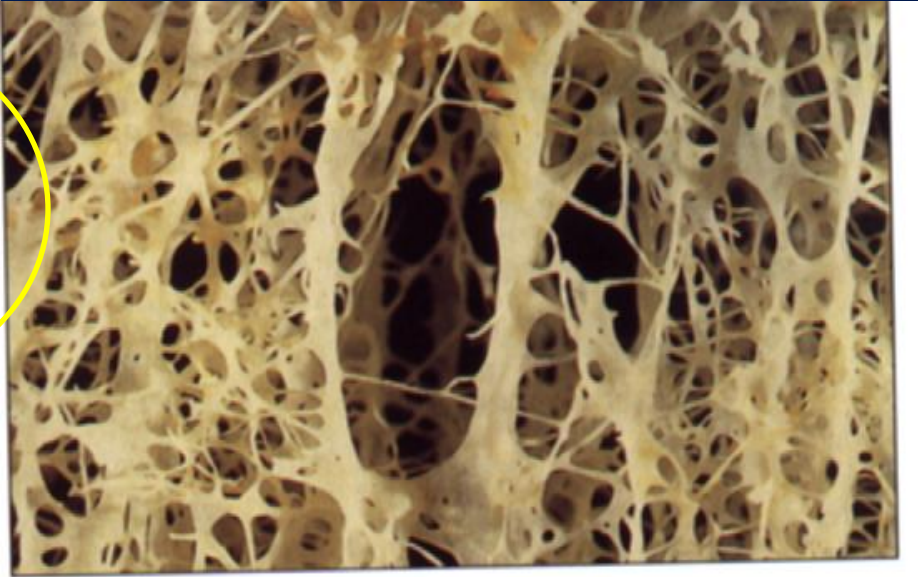
- Age
- Female sex
- Family fx
- Previous fx
- Glucocorticoids

# Clinical Picture

The traditional picture of an individual with osteoporosis:



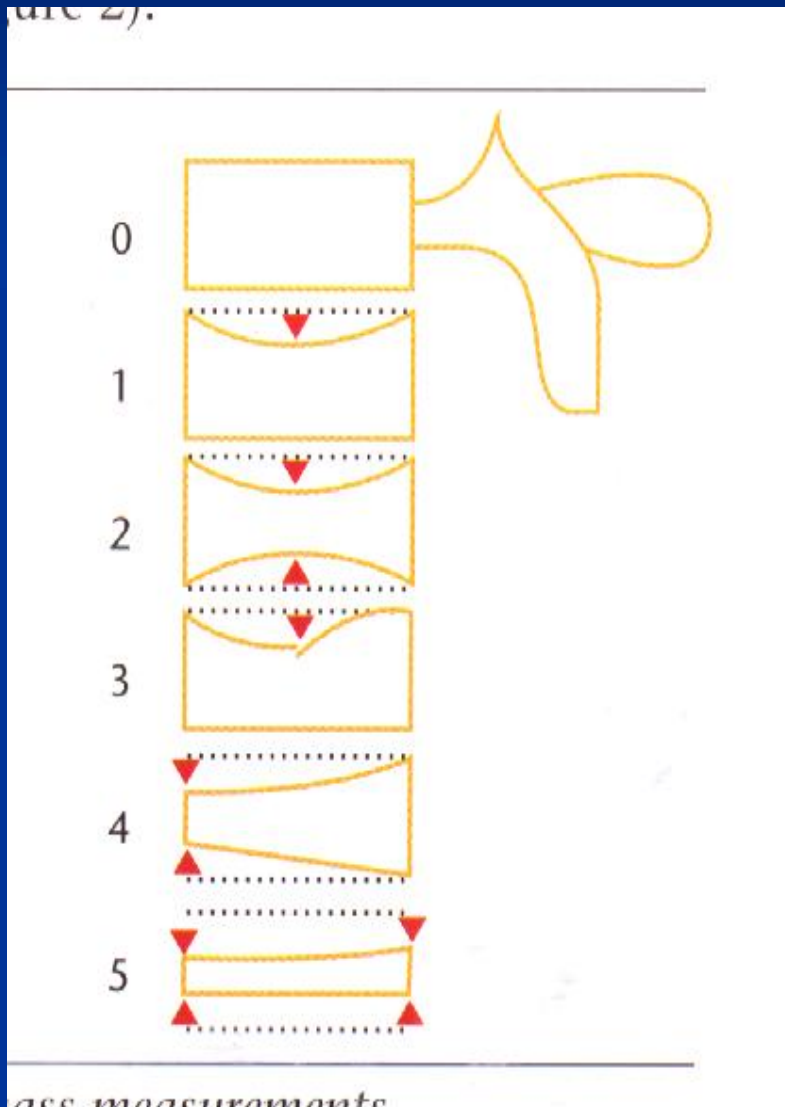
An elderly woman with a curved back and stooped posture, a woman who has lost height and who appears small and frail





# Radiographic Evaluation

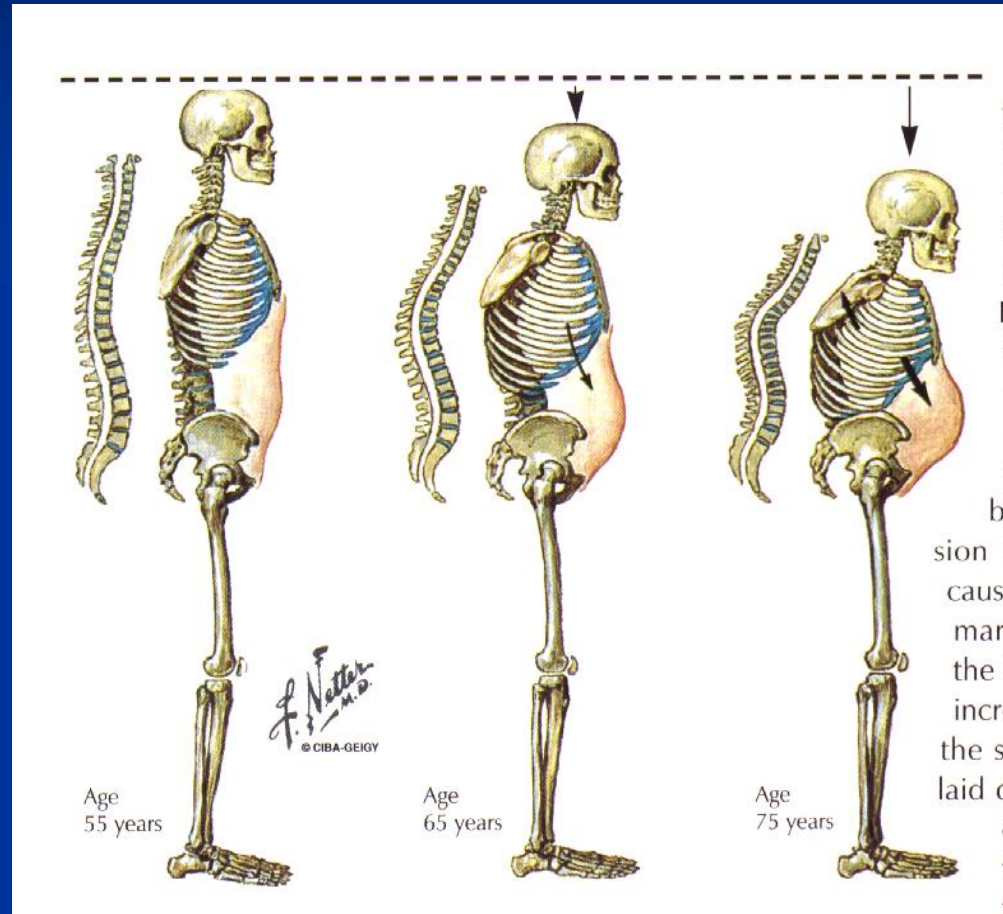
Figure 2).



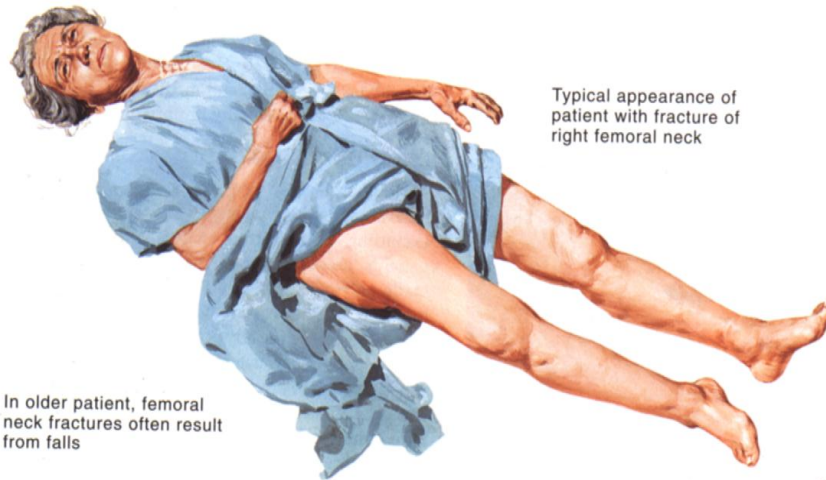
- 0 Normal
- 1 End plate deformity
- 2 Fish vertebrae
- 3 End plate fracture
- 4 Wedge vertebrae
- 5 **Compression fracture**

disc measurements

# Progressive loss of height; Development of kyphosis



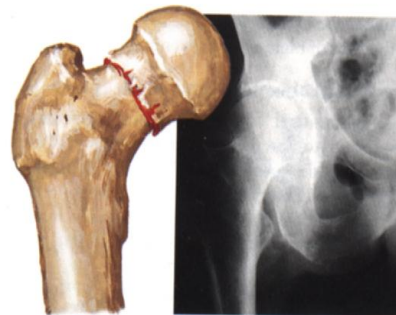
# Hip Fx



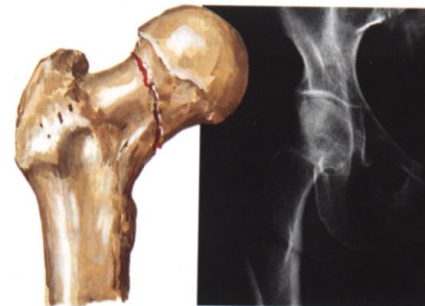
Typical appearance of patient with fracture of right femoral neck

In older patient, femoral neck fractures often result from falls

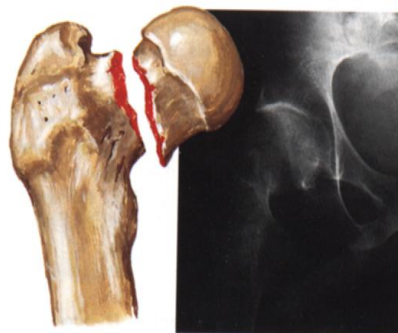
F. Netter  
© Ciba



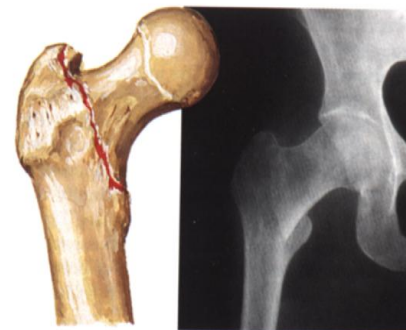
Impacted intracapsular fracture of femoral neck



Nondisplaced intracapsular fracture of femoral neck



Displaced fracture. Vertical fracture line generally suggests poor outcome



Nondisplaced intertrochanteric fracture of femur

# OSTEOPOROSIS

The Gold standard test in clinical practice is measurement of **Bone Mineral Density** (g/cm<sup>3</sup>), of the vertebral spine and the hip.

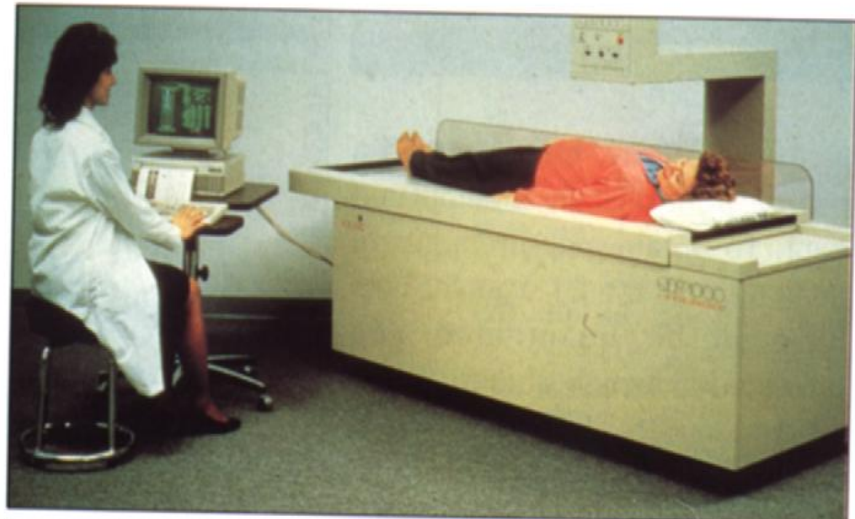
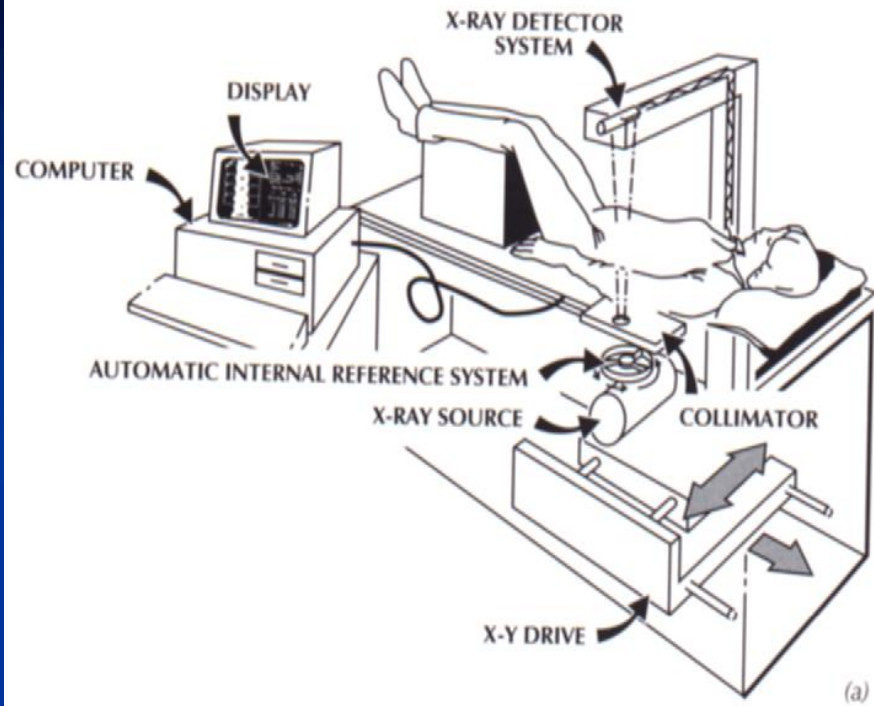
1. **DEXA scans**
2. **Radiographic Absorptiometry**
3. **Single Photon X-ray absorptiometry (SPA)**
4. **Quantitative Computer tomography**
5. **Quantitative Ultrasound**

# Diagnosis of Osteoporosis

- Osteodensitometry **DXA**

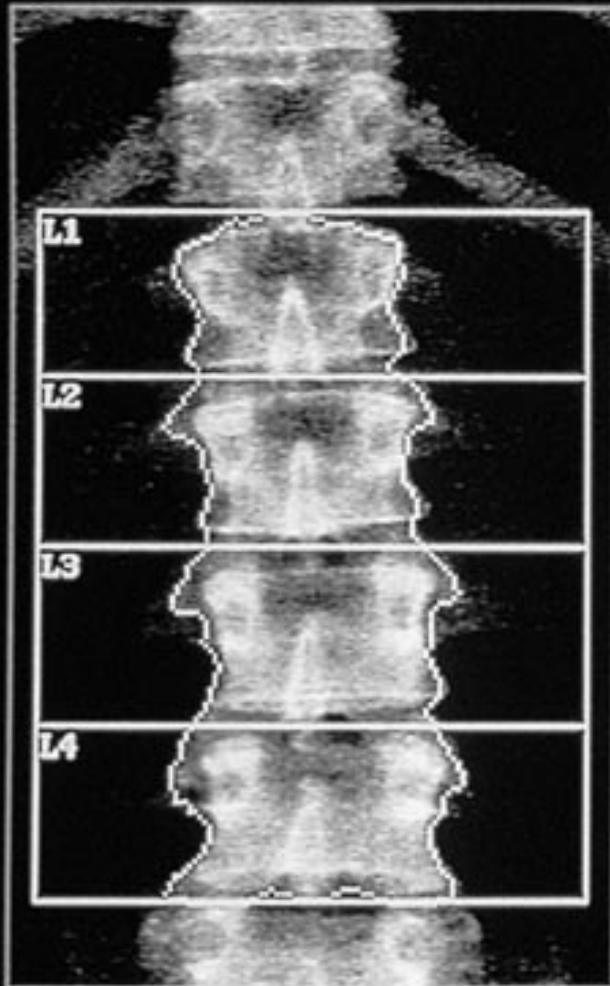
DXA = Dual X- ray Absorptiometry

Bone Mineral Density BMD



# DEXA

k = 1.136 d0 = 44.5(1.000H) 6.477



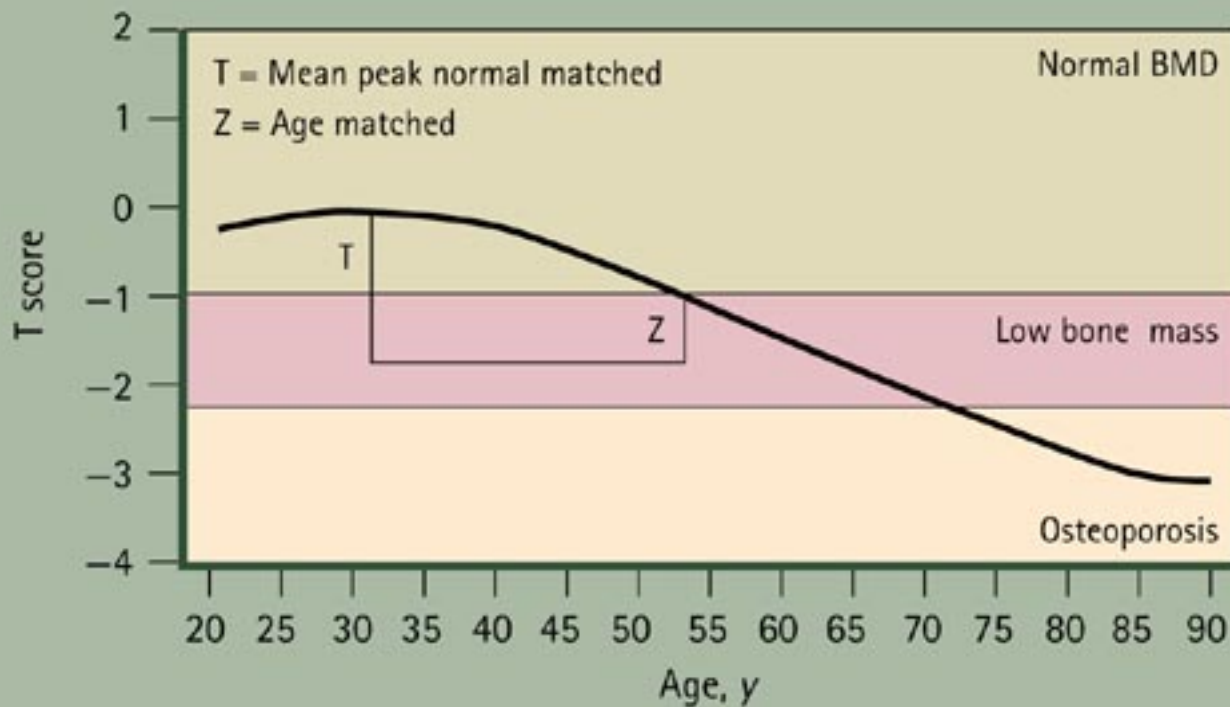
Y11879483 Mon Nov 7 09:41 1994  
 Name: AP/LATERAL DM  
 Comment:  
 I.D.: Sex: F  
 S.S.#: - - Ethnic:  
 ZIP Code: Height: ' "  
 Operator: Height:  
 BirthDate: 09/03/58 Age: 36  
 Physician:  
 Image not for diagnostic use

TOTAL BMD CV FOR L1 - L4 1.0%

C.F. 1.017 0.992 1.000

Region	Est.Area (cm <sup>2</sup> )	Est.BMC (grams)	BMD (gms/cm <sup>2</sup> )
L1	13.93	12.48	0.896
L2	16.18	15.97	0.987
L3	18.50	18.70	1.011
L4	19.67	20.97	1.066
<b>TOTAL</b>	<b>68.29</b>	<b>68.12</b>	<b>0.998</b>

# T scores







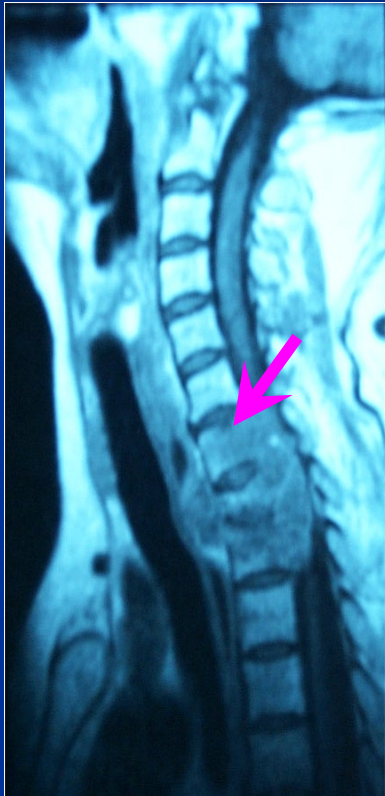
# Diagnosis Based on BMD (WHO)

BMD	T-score
Normal	0 - (-1)SD
Osteopenia	(-1) - (-2.5)SD
Osteoporosis	<(-2.5)SD
Established OP	“ + fracture

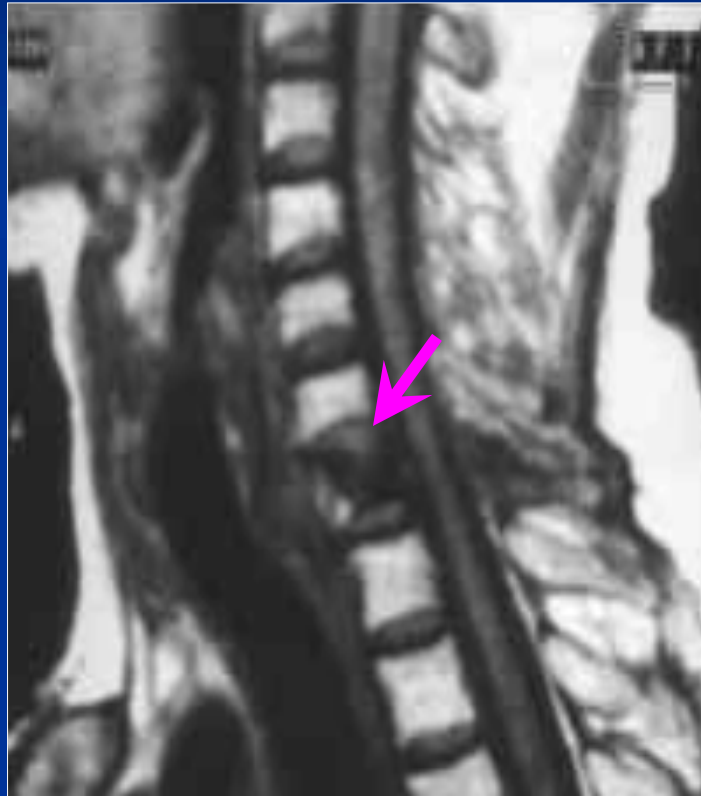
# Recommendations Based on BMD

<b>BMD</b>	<b>Risk of Fx</b>	<b>Action</b>
Normal	Very low	Prevention
Osteopenia	Low	Prevention
OP	High < (-2.5)SD	Treatment
Establ OP	Very high	Treatment

# Differential Diagnosis



**Metastasis**



**Multiple Myeloma**



**Osteoporotic  
Fx**

# 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

# Approaches for Management of Osteoporosis: Pharmac&Nonpharmacolo

- **Prevent fractures**

- Medical therapy
- Prevention of falls



- **Improve physical function**

- **Improve quality of life**



# Calcium – Vitamin D

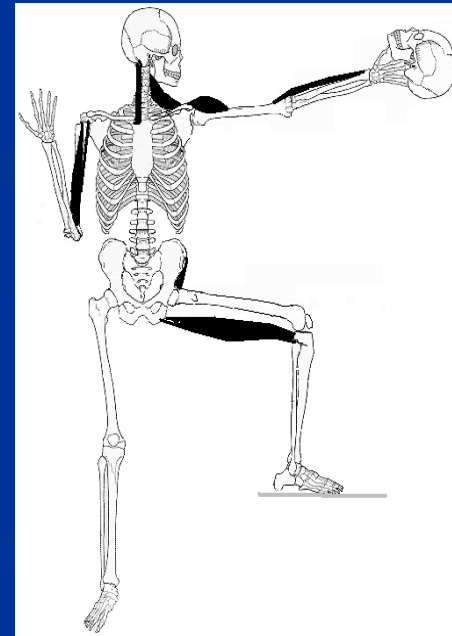
**Calcium - Adults : 1000 mg**

Increased: Over 65 years, after menopause,  
pregnancy, stiling

**Vitamin D :**

Adults : 400-800 IU

Over 70 years: >800 IU



# Stimulators of Bone Formation

- **Parathyroid hormone injections**



# HRT: Estrogen

- Reduces the rate of bone loss
- Reduces fracture risk in postmenopausal women

# Calcitonin

- Reduces bone loss in postmenopausal women- bone quality
- Effective on **spinal fractures**
- Opt.dose: **200 IU/daily nasal spray**
- High tolerability

# **Bisphosphonates: *Gold Standard***

**Decrease fracture incidence**

**Contraindication: Oesophageal  
irritation**

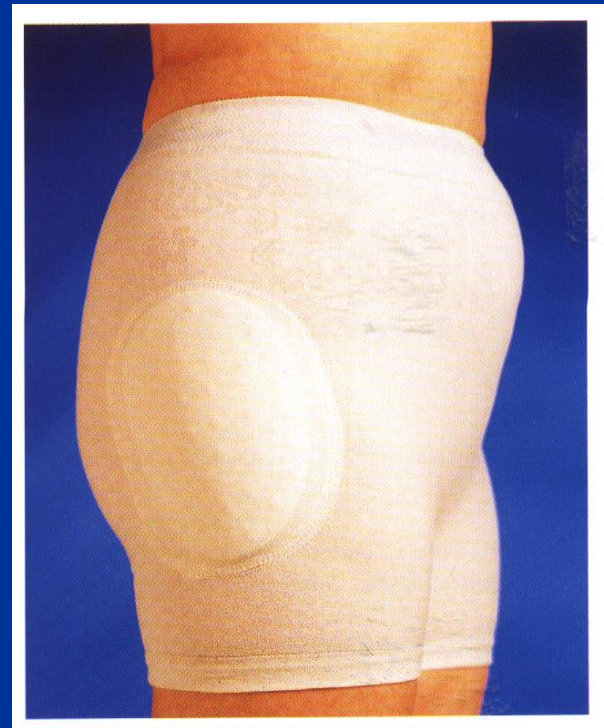
# Strategies for Reducing Falls and Fractures

- Maintain physical activity
- Provide a safe home environment
- Balance training
- Ambulatory support when appropriate
- Avoid sedative medications
- Hip pads in the frail elderly



# Hip Protectors

- Padding that fits under clothing
- Multiple studies demonstrate effectiveness at preventing hip fractures
- Likely cost effective
- Problem: adherence!



# WHO fracture risk assessment tool FRAX<sup>®</sup>

FRAX<sup>®</sup>

10-year  
probability  
of fracture

Country

Bone mineral density

Age

Gender

Clinical risk factors

- Low body mass index
- Previous fragility fracture
- Parental history of hip fracture
- Glucocorticoid treatment
- Current smoking
- Alcohol intake (3 or more units per day)
- Rheumatoid arthritis
- Other secondary causes of osteoporosis

FRAX<sup>®</sup> WHO Fracture Risk Assessment Tool

HOME CALCULATION TOOL PAPER CHARTS FAQ REFERENCES

Calculation Tool

Please answer the questions below to calculate the ten year probability of fracture with FRAX

Country:  Name:

Questionnaire:

1. Age (Years)  11. Previous fragility fracture  YES  NO

2. Sex  Male  Female 12. Parental history of hip fracture  YES  NO

3. Height (cm)  13. Fracture  YES  NO

4. Weight (kg)  14. Current smoking  YES  NO

5. Parental history of hip fracture  YES  NO 15. Alcohol intake (units per day)  16. Rheumatoid arthritis  YES  NO

6. Current smoking  YES  NO 17. Other secondary causes of osteoporosis  YES  NO

7. Alcohol intake (units per day)  18. Fracture  YES  NO

8. Rheumatoid arthritis  YES  NO

9. Fracture  YES  NO

10. Fracture  YES  NO

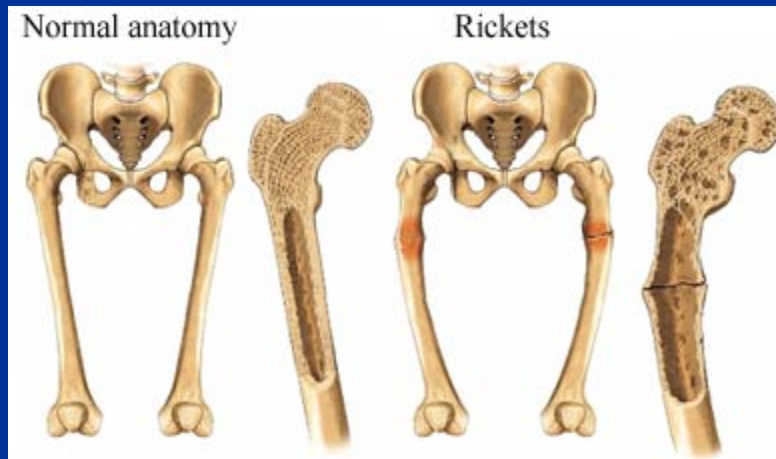
10-year probability of fracture (10%)

10-year probability of fracture (10%)

[www.shef.ac.uk/FRAX](http://www.shef.ac.uk/FRAX)

# RICKETS & OSTEOMALACIA

Reduction in bone mineralization !



# RICKETS, OSTEOMALACIA

## PATHOLOGY:

Sufficient osteoid, poor mineralization

(**Rickets** is found **only in children** prior to the closure of the growth plates, while **OSTEOMALACIA** occurs in **persons of any age**. Any child with rickets also has osteomalacia, while the reverse is not necessarily true).



# OSTEOMALACIA, RICKETS

## Normal bone metabolism

### ■ **CALCIUM**

99% in bone.

Main functions- muscle /nerve function, clotting.

Plasma calcium- 50% free, 50% bound to albumin.

### ■ Dietary needs-

Kids- 600mg/day,

**Adolesc.-1300mg/day,**

Adult-750mg/day,

**Pregnancy-1500mg/day,**

Breastfeeding-2g/day,

**Fractures- 1500mg/day**

### ■ Absorbed in duodenum (active transport) and jejunum (diffusion), 98% reabsorbed in kidney prox. tubule, may be excreted in stool.

# OSTEOMALACIA, RICKETS

## Normal bone metabolism

- **PHOSPHATE**  
85% in bone.  
Functions-metabolite and buffer in enzyme systems.
- Plasma phosphate mainly unbound.  
**Daily requ. 1-1.5g/day**

# rickets, osteomalacia

## causes:

1. Nutritional deficiency
  1. Vit D
  2. chelators of calcium- phytates, oxalates, phosphorous
  3. antacid abuse : causing reduced dietary phosphate binding
2. GI Absorption defects
  1. Post gastrectomy
  2. Biliary disease (reduced absorption of Vitamins )
  3. Small bowel disease
  4. liver disease
3. Renal tubular defects
4. Renal osteodystrophy

# Causes of osteomalacia/rickets

## ■ Reduced availability of Vit D

- Diet: oily fish, eggs, breakfast cereals
- Elderly individuals with minimal sun exposure
- Dark skin, skin covering when outside
- Fat malabsorption syndromes
- Kidney failure
- malabsorption

## ■ Malabsorption of Vit D

- Coeliac
- Intestinal bypass
- Gastrectomy
- Chronic pancreatitis

■ Epilepsy: **phenytoin, phenobarbitones**

■ Genetic disease

# RICKETS, OSTEOMALACIA

## CLINICAL FEATURES:

- **Rickets** -

Tetany , convulsions,

restlessness, muscular flaccidity.

Flattening of skull (craniotabes),

Thickening of wrists from epiphyseal overgrowth,

Stunted growth,

Spinal curvature,

**Coxa vara, bowing, fracture of long bones**

- **Osteomalacia**, - Aches and pains, muscle weakness  
loss of height, stress fractures.

# RICKETS, OSTEOMALACIA

## X-RAY FINDINGS:

### RICKETS

Thickening and  
widening of physes,  
Cupping of metaphysis,  
Wide metaphysis,  
Bowing of diaphysis,  
Blurred trabeculae.



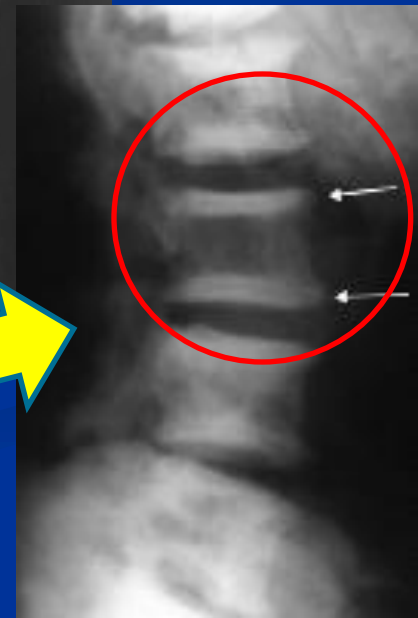
# RICKETS, OSTEOMALACIA

## XRAY FINDINGS:

### OSTEOMALACIA

**Loosers zones** - incomplete stress fractures with healing lacking calcium, on compression side of long bones.

Codfish vertebrae due to pressure of discs





# Loosers zones



# RICKETS, OSTEOMALACIA

## BLOOD TESTS

Calcium reduced,

Phosphate reduced

Alkalline Phosphatase increased

Urinary excretion of calcium diminished

# RICKETS, OSTEOMALACIA

## MANAGEMENT:

Depends on the cause

### Nutritional

Vitamin D deficiency

Dietary chelators of calcium

Phytates

Oxalates

Phosphorus deficiency (unusual)

Antacid abuse

- *Treatment- vitamin D (5000u) and Calcium (3g/day)*

# RICKETS, OSTEOMALACIA

## MANAGEMENT:

Depends on the cause

### Gastro-intestinal absorption defects

Post-gastrectomy

Biliary disease

Enteric absorption defects

Short bowel syndrome

Rapid onset (gluten-sensitive enteropathy)

### Inflammatory bowel disease

Crohns

Celiac

# RICKETS, OSTEOMALACIA

## MANAGEMENT:

Depends on the cause

Renal tubular defects  
Vitamin D dependant

type I

type II

*Treatment; High levels of vit D*

Vitamin D resistant (familial hypophosphatemic rickets)

*Treatment; Phosphate 1-3 gm daily, Vit D3 high*



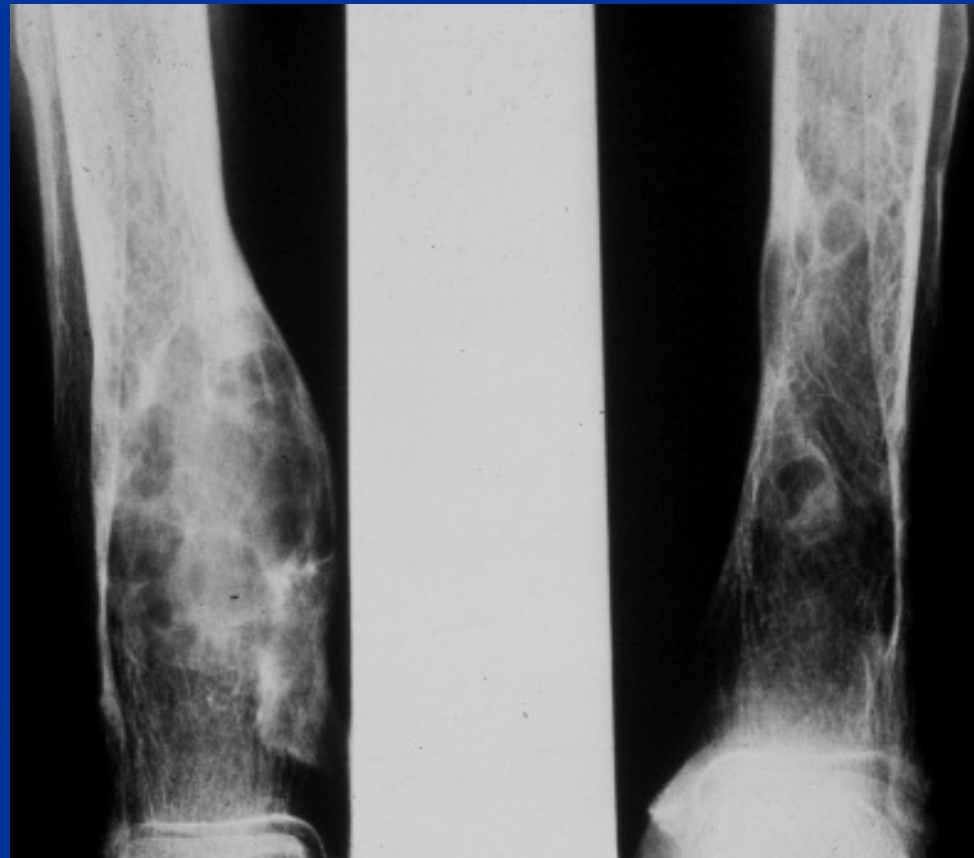
Thank you

# Symptoms of hypercalcaemia

- Stones: *Renal colic*
- Bones: *Joint, bone, muscle pain, Muscle weakness*
- **Moans:** *Constipation Abdominal pains*
- **Psychic Groans:** *Depression, confusion, altered mental state, Fatigue, lethargy*
- *Dehydration, polyuria*

# Causes of Hypercalcaemia

- Malignancy
- Hyperparathyroidism – primary or tertiary
- Increased intake
- Myeloma
- Sarcoid
- Adrenal failure







# Multiple endocrine neoplasia

- Aut dom
- MEN 1 parathyroid tumours, ant pituitary, pancreas
- MEN 2A thyroid tumour, phaeochromocytomas, parathyroid hyperplasia
- MEN 2B thyroid tumours and phaeos

# Renal Osteodystrophy

- Effect on bone of **disordered calcium homeostasis**
- May be osteomalacia, hyperparathyroidism
- Leads to
  - Bone pain
  - Skeletal deformity
  - Muscular weakness
  - Ectopic calcification
  - Growth retardation

# Hypoparathyroidism

## Causes

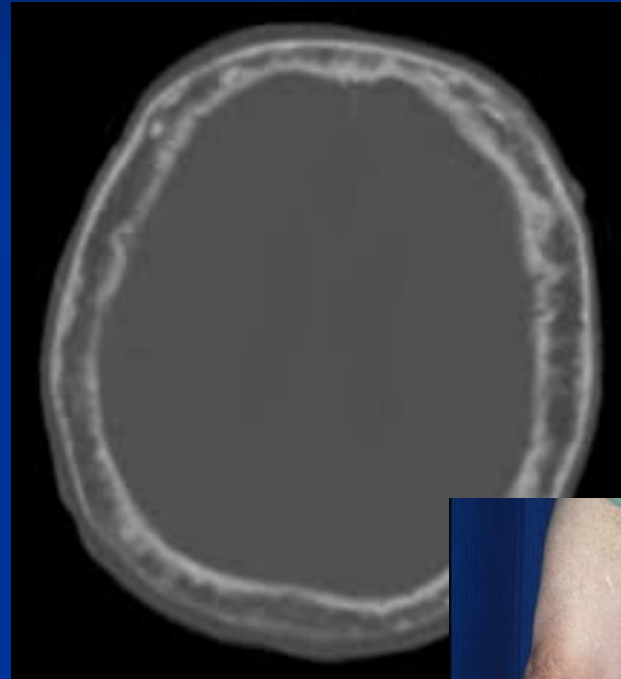
- Destruction of gland- surgical (thyroidectomy- may be transient)
- Autoimmune- polyglandular autoimmune glandular syndrome
- Irradiation or infiltration (cancer, wilsons)
- Abnormal gland development

# Paget's Disease

- Disease of bone remodeling
- **Accelerated bone resorption and formation**
- Disorganised mosaic pattern bone with increased vascularity and fibrosis
- Cause unknown
  - paramyxovirus, canine distemper
  - Genetics- susceptibility loci
- More common in caucasian
- M:F ratio 3:2      10% in over 70's

# Paget's Disease: clinical manifestations

- Bone pain
- Joint pain
- Deformity
- Spontaneous fractures

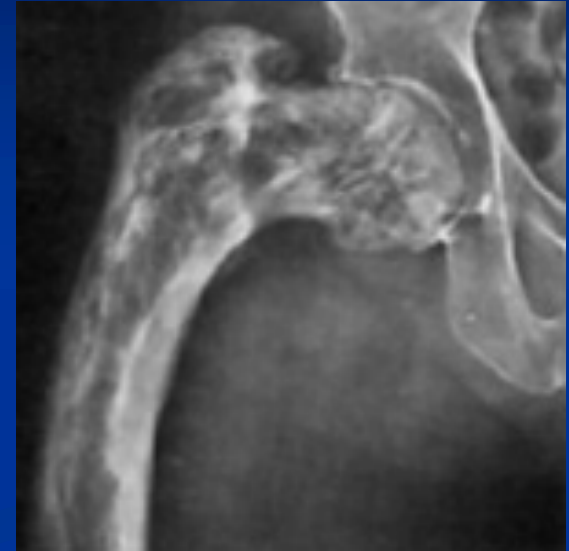


# Pagets Disease: complications

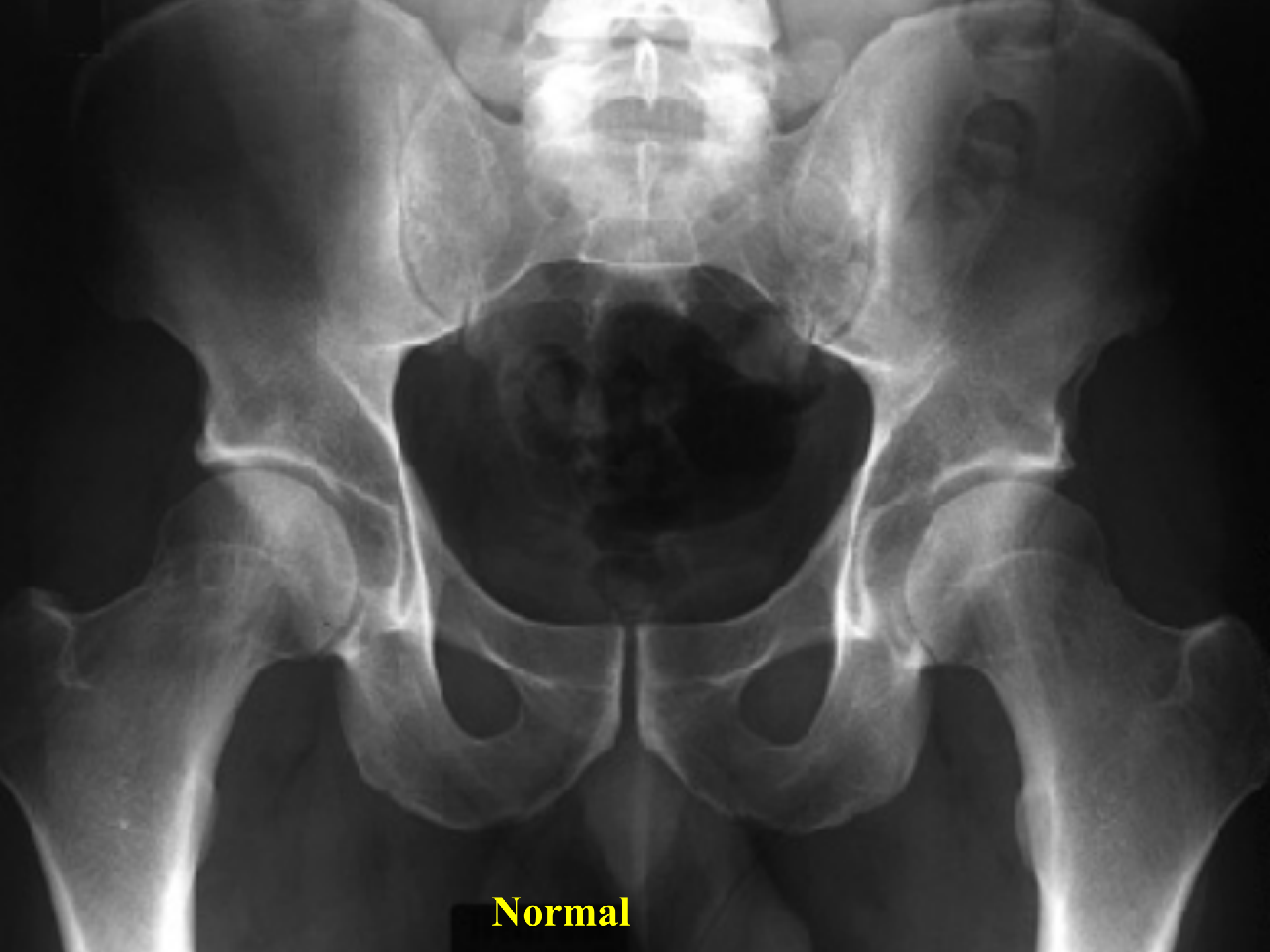
- Fractures
- Deafness
- Nerve entrapment
- Spinal stenosis
- Cardiac failure
- Osteogenic sarcoma
- Hypercalcaemia (only if immobilized)

# Paget's Disease: investigations

- Raised serum alk phos
- Radiology
  - cortical thickening
  - osteolytic, osteosclerotic and mixed lesions
  - osteoporosis circumscripta







**Normal**

