

Metabolic disorders

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Metabolic disorders- osteopathy

- Osteoporosis
- Osteomalatia
- Primary hyperparathyreoidisms
- Secondary hyperparathyreoidisms:
 - renal osteodystrophy
 - gastrointestinal osteodystrophy

Composition of bone

50 % anorganic material (hydroxyapatit crystals)

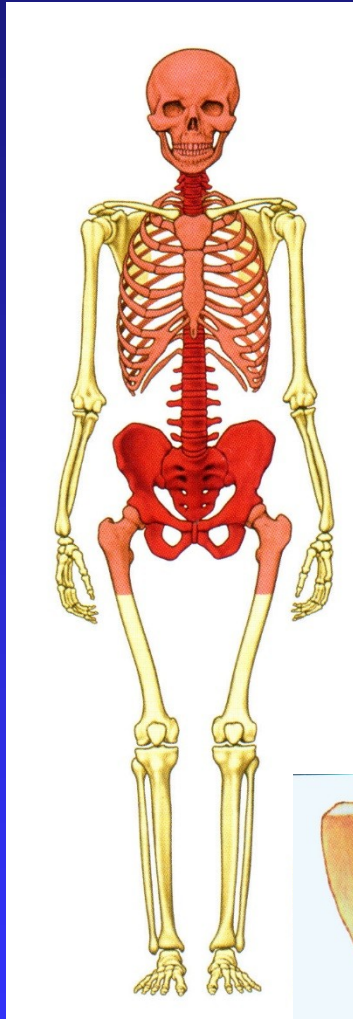
25 % organic bone matrix (osteoid):

90 % collagen type I

10 % other proteins (osteocalcin,
osteonectin, proteoglycans, enzymes)

25 % water binding on collagen and proteoglycans

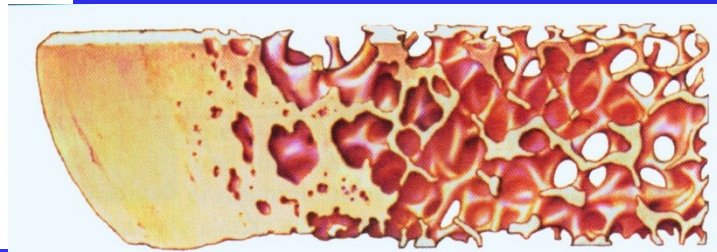
Skeleton



Weight 5 kg

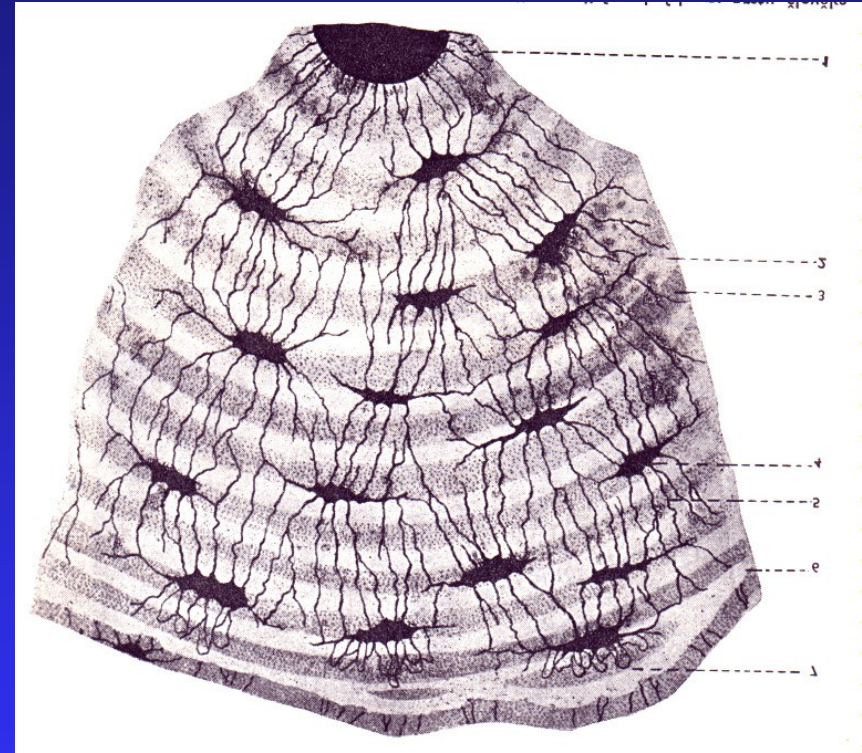
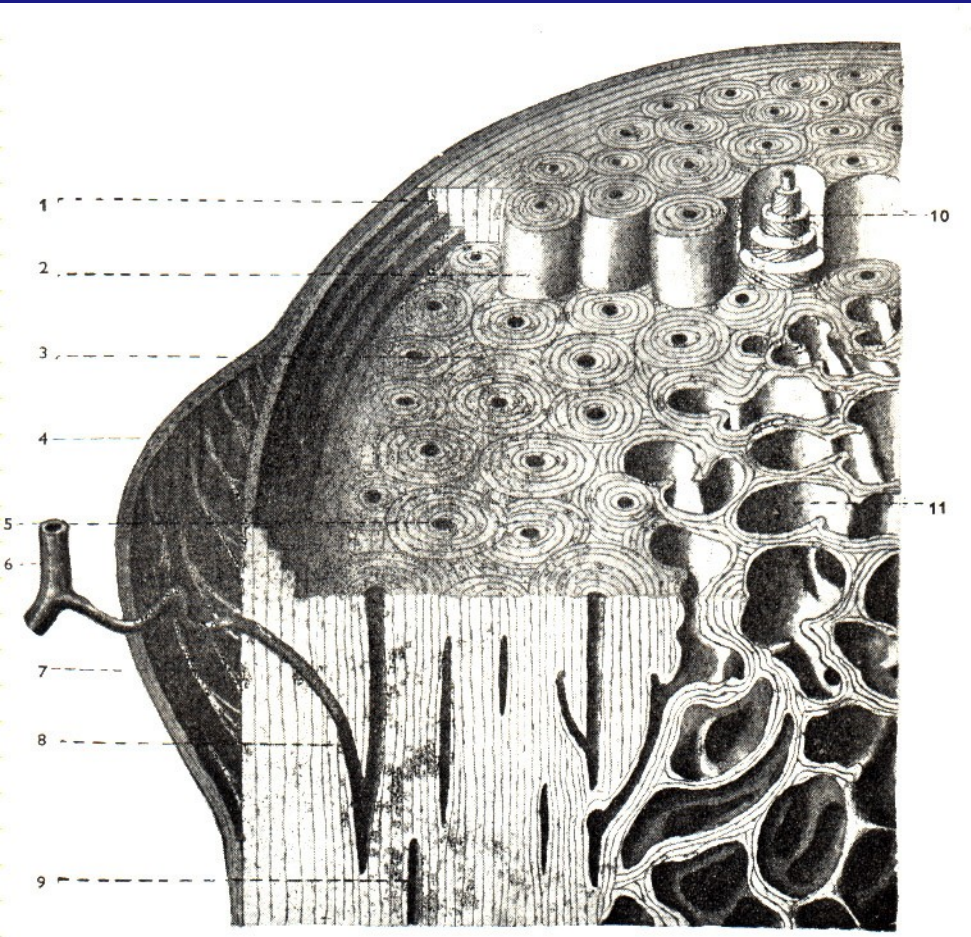
Cortical bone 4 kg

Trabecular bone 1 kg

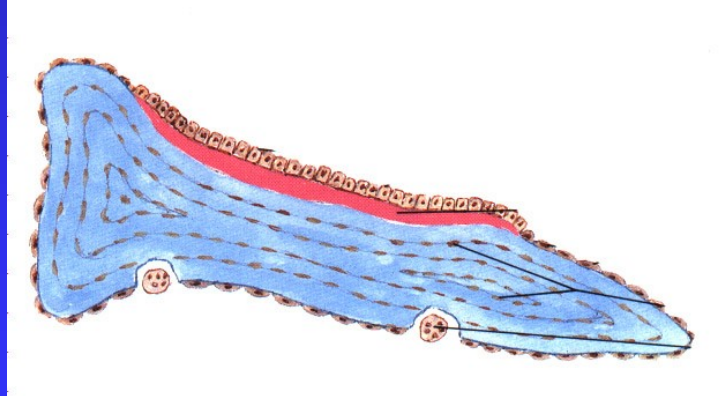
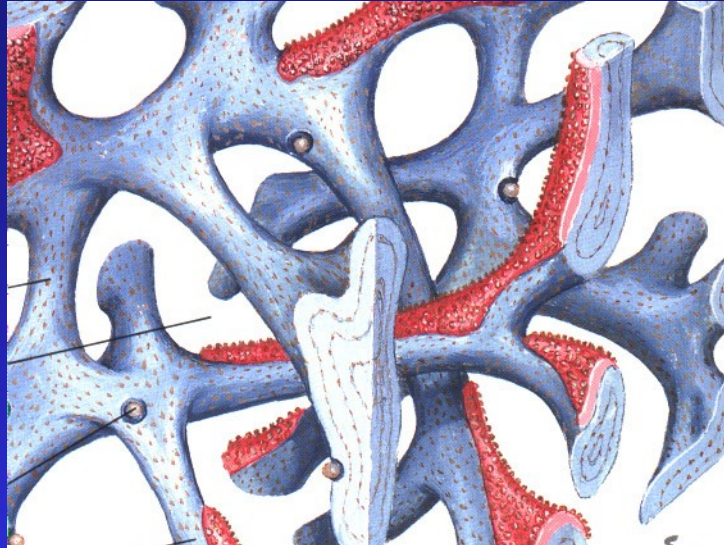


Cortical bone Trabecular bone

Cortical bone- Haversian system



Trabecular bone

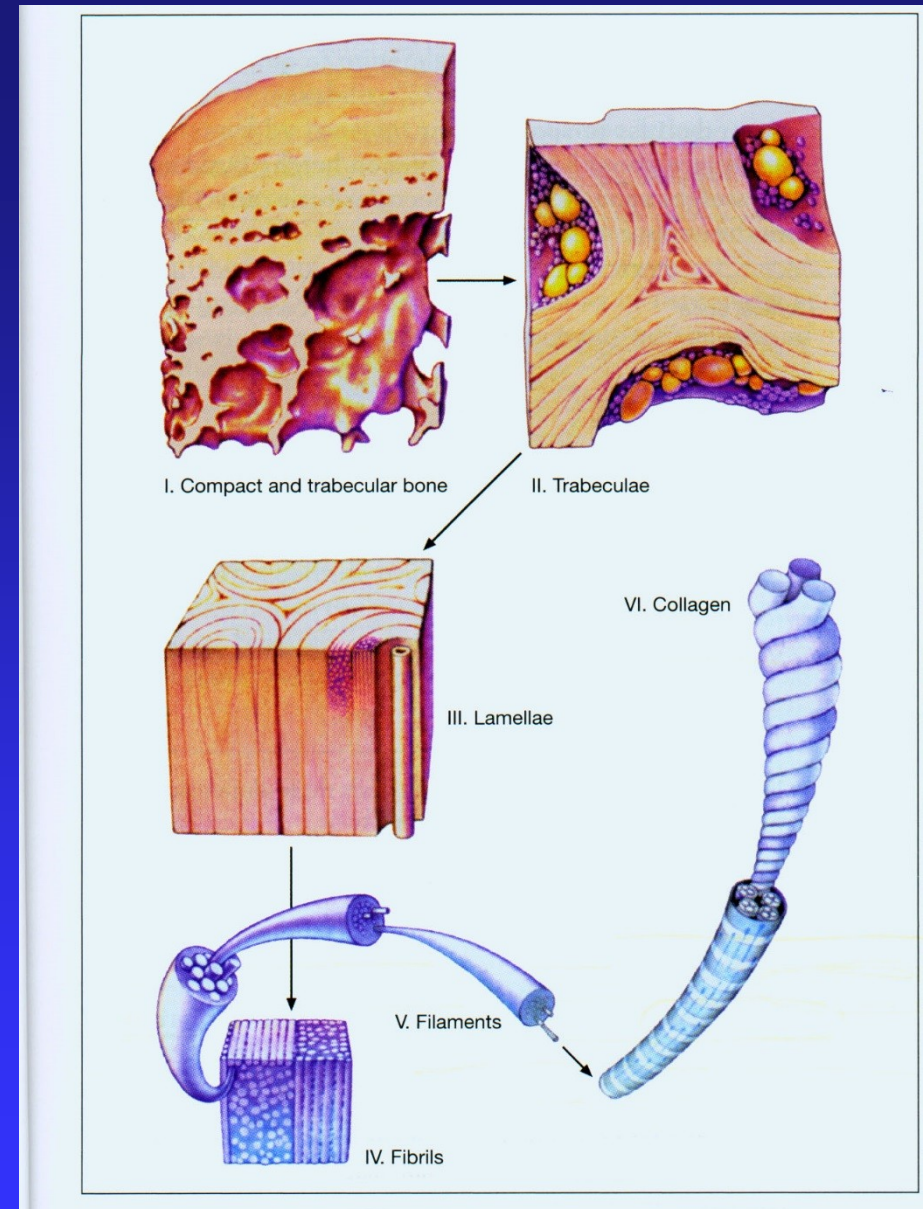


Trabecular bone:

- 20% of the skeleton
- 80% of remodelling

Cortical bone:

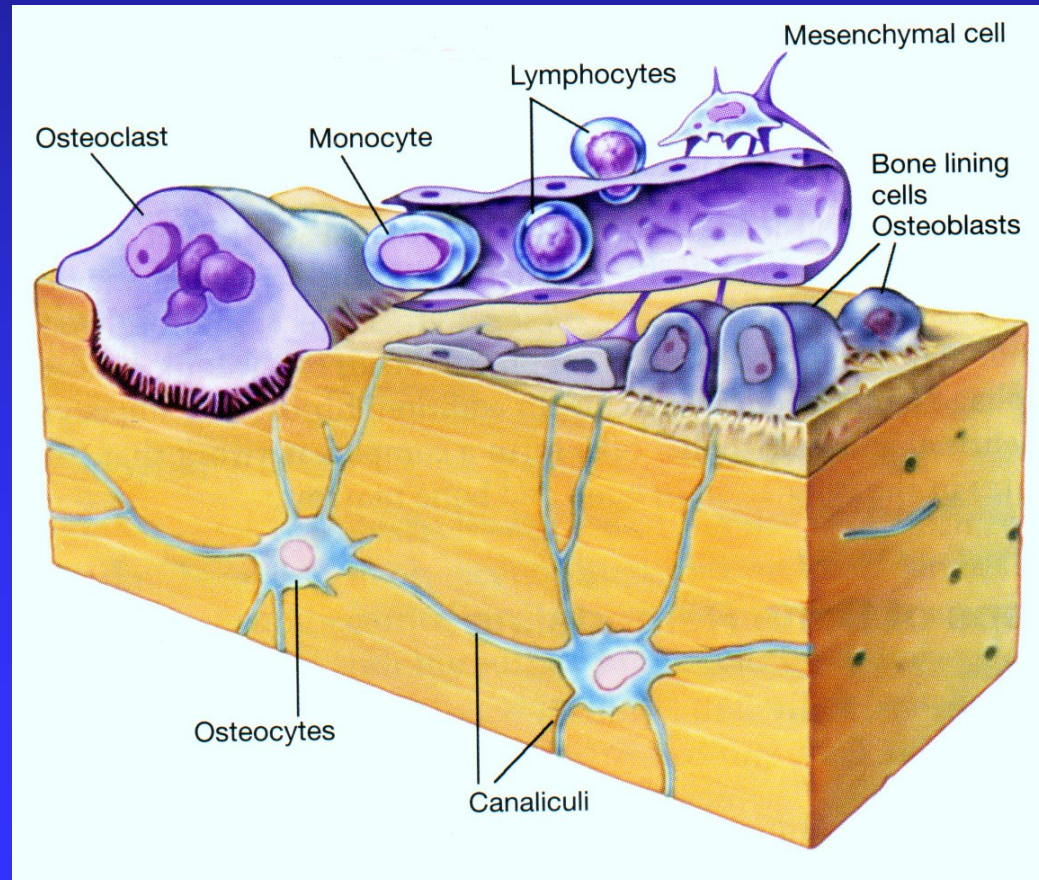
- 80% of the skeleton
- 20% of remodelling



Collagen type I.

Osteoblasts:

- They produce osteoid- organic part of matrix
- They provide mineralisation of bone
- They produce alkaline phosphatase
- indicator of the synthesis of proteins



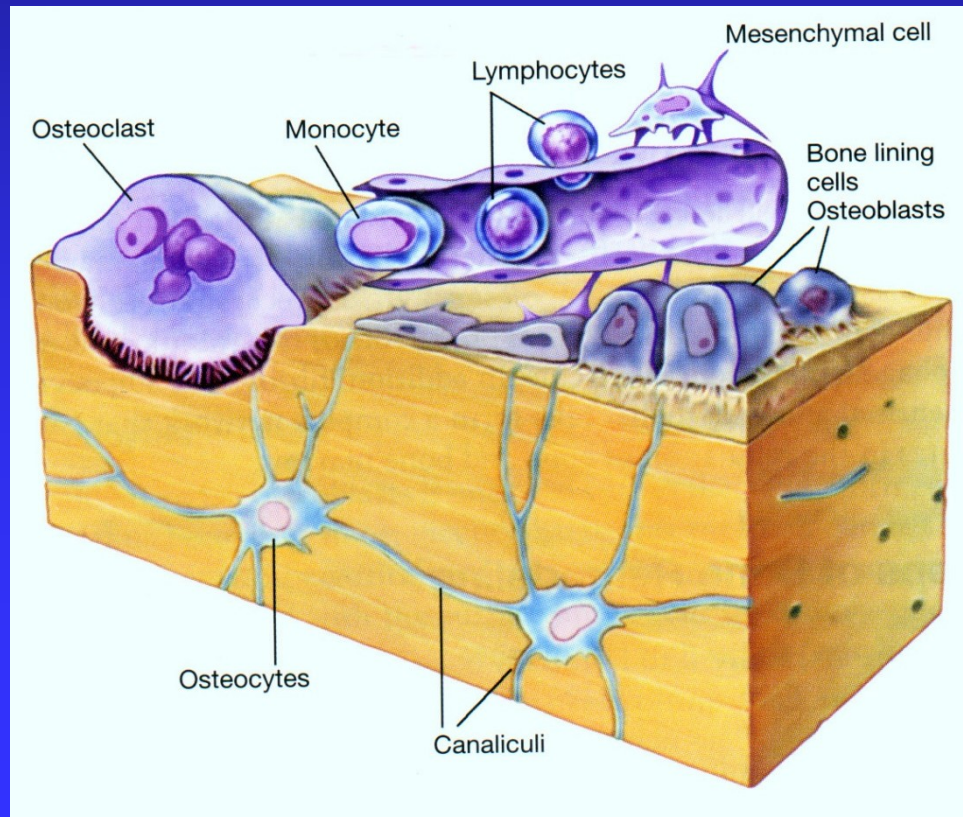
Osteoclasts:

Large multinuclear cells

They are localised in Howship lacunae on the surface of bone

They produce acid phosphatase and lytic enzymes

They dissolve hydroxyapatite crystals and bone matrix

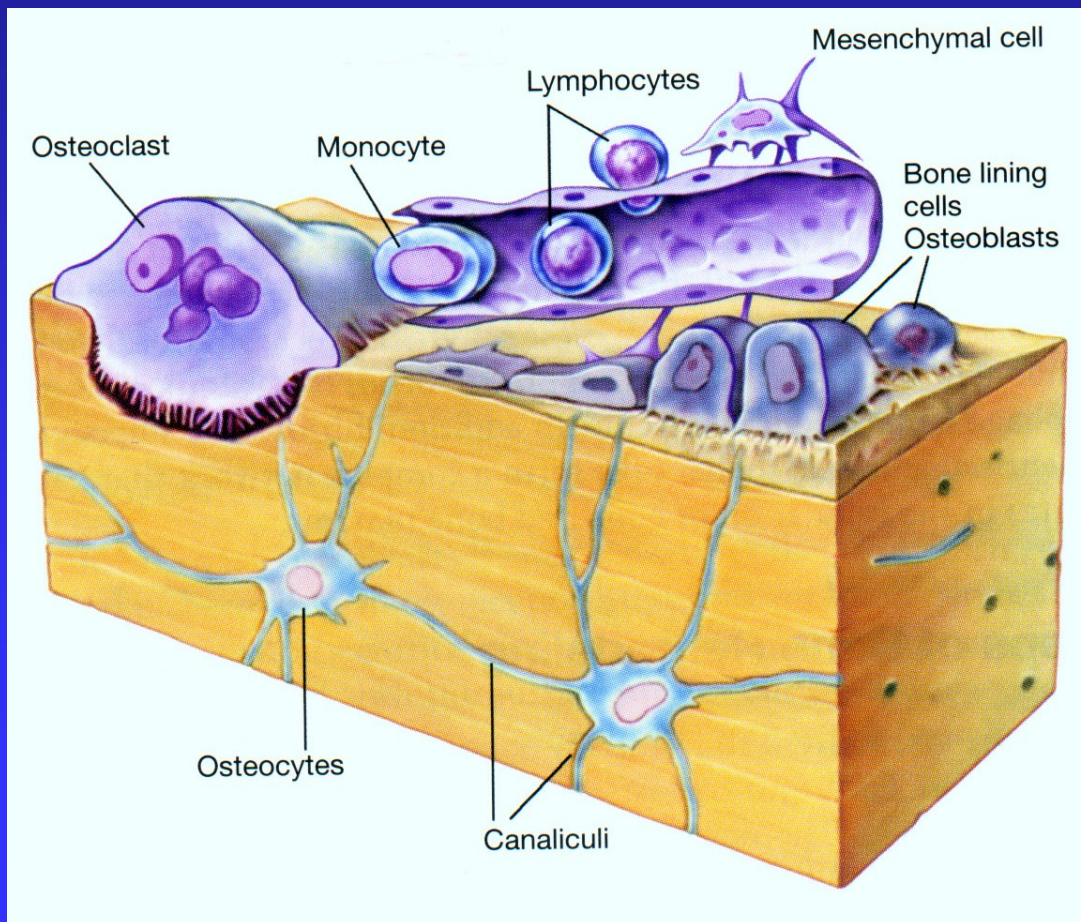


Osteocytes

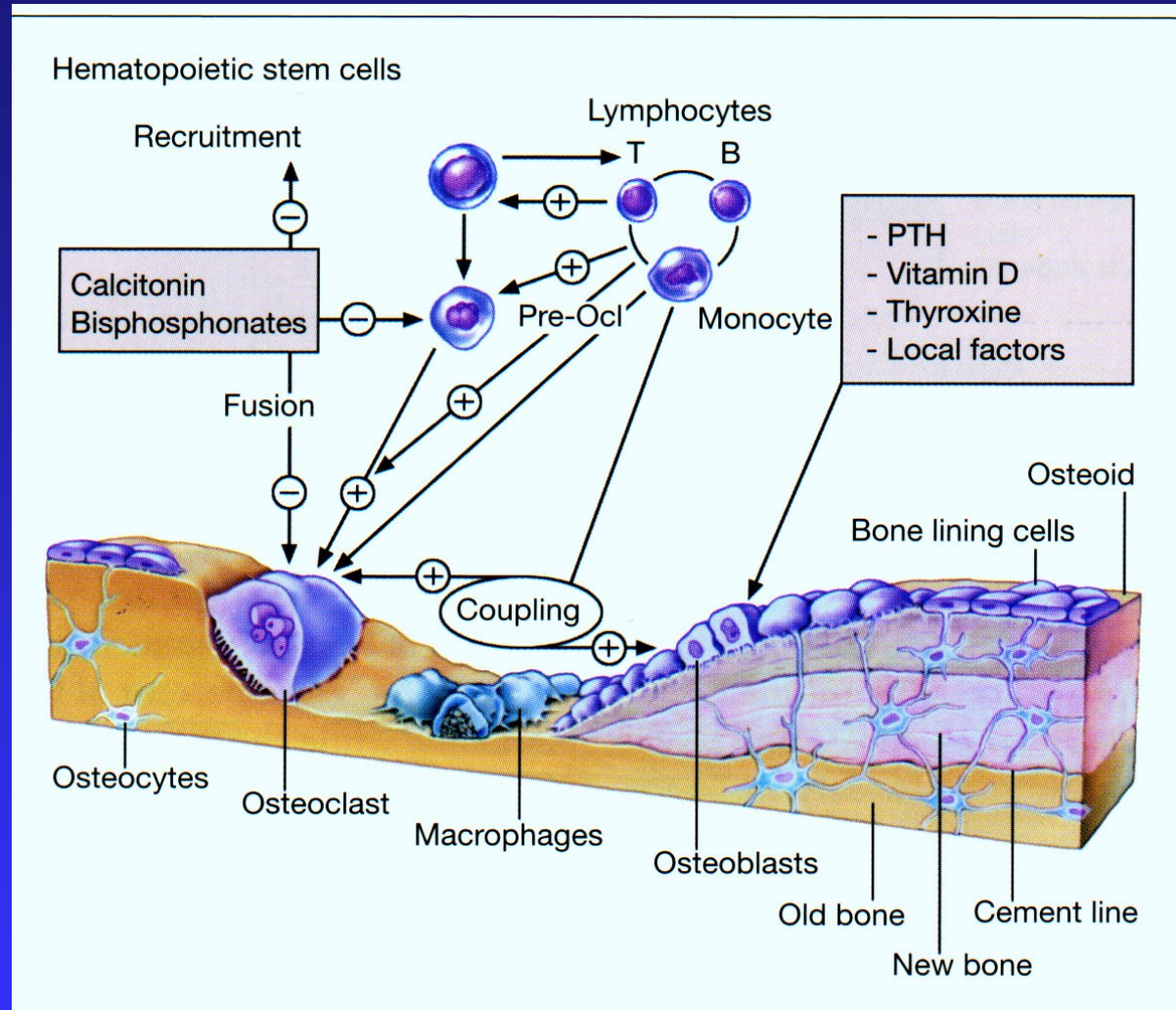
They lie in lacunae of corticals and trabecular bone

They are connected with canaliculi

They maintain metabolism of bone



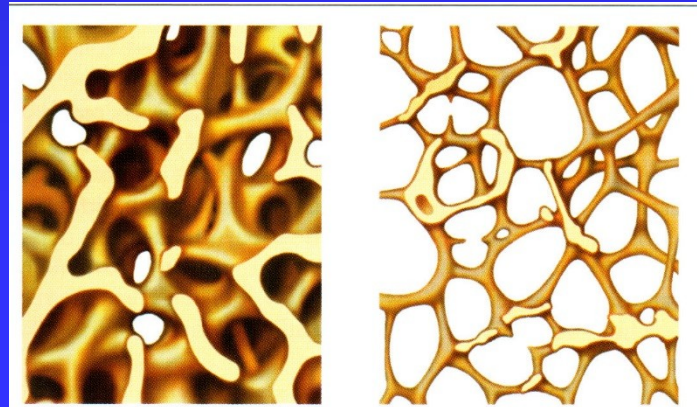
Remodelling of bone



Resorption is finished in 2 weeks
Mineralisation up to six months

Osteoporosis is a systemic disorder of the skeleton

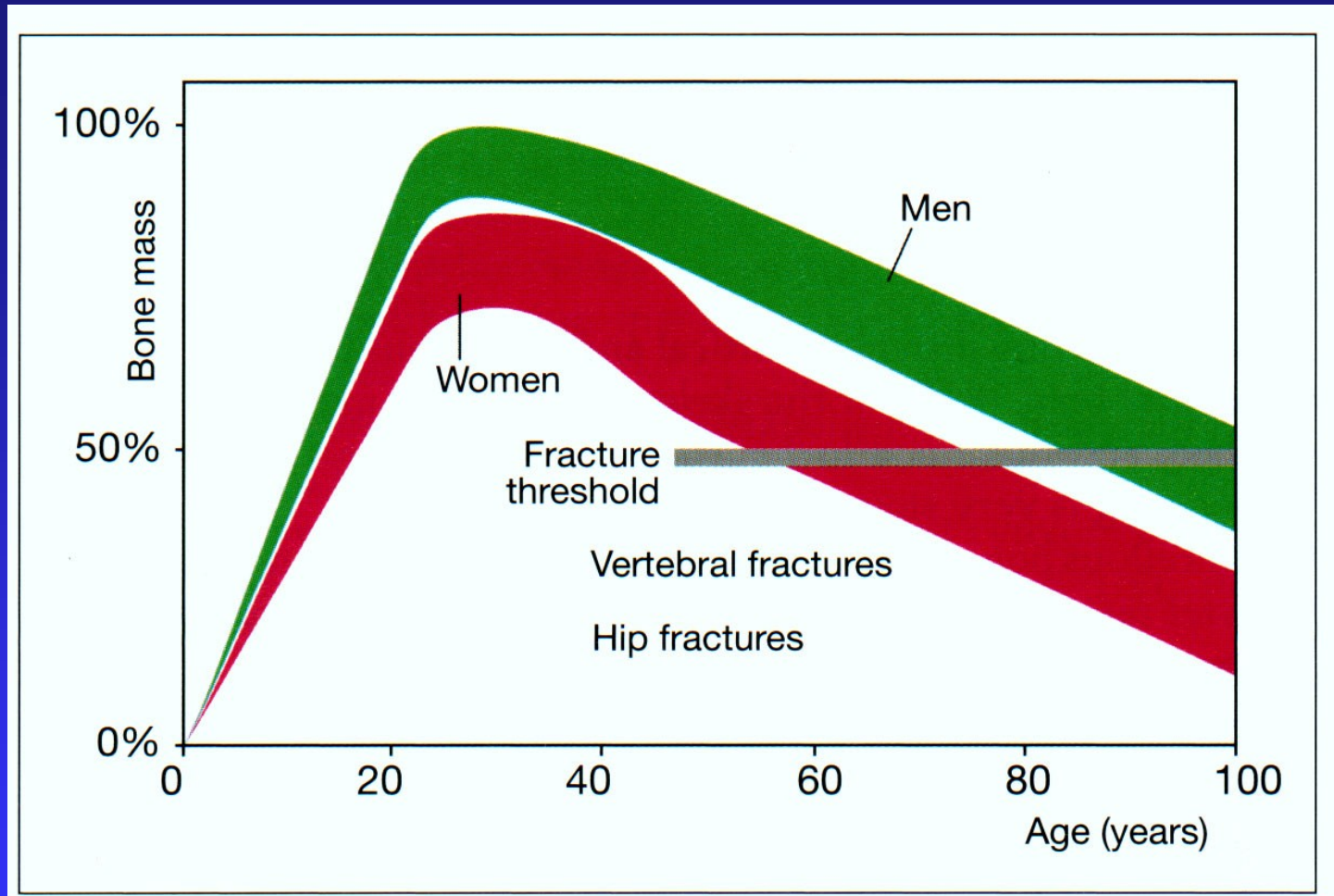
- Diminished strength of bone
- Low bone density
- Impaired microarchitecture
- Tendency to fractures
- Loss of organic and anorganic bone



Osteoporosis

- primary:
 - idiopathic
 - postmenopausal - type I.
 - involutional (senile) - type II.
- secondary - type III.

Peak bone mass – at 30 years of age



Bone loss:

Before menopause 0,3 % / year

After menopause 3 % / year

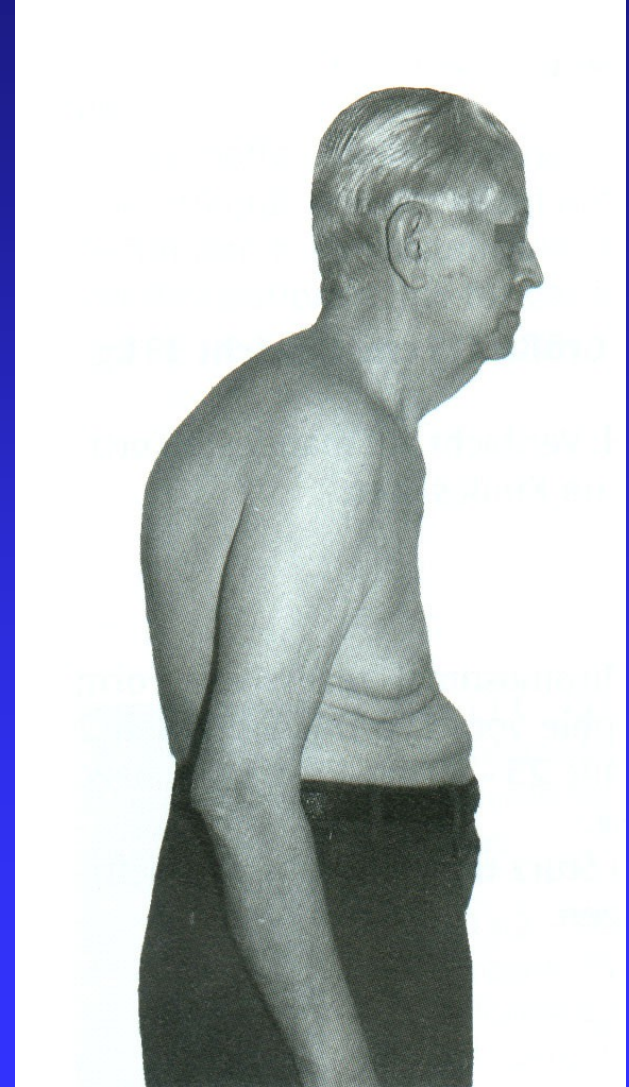
Clinical symptoms

- Back ache
- Diminished ability to work
- Problems with walking and standing
- Problems with lifting heavy objects
- Sharp pain- in a case of fracture

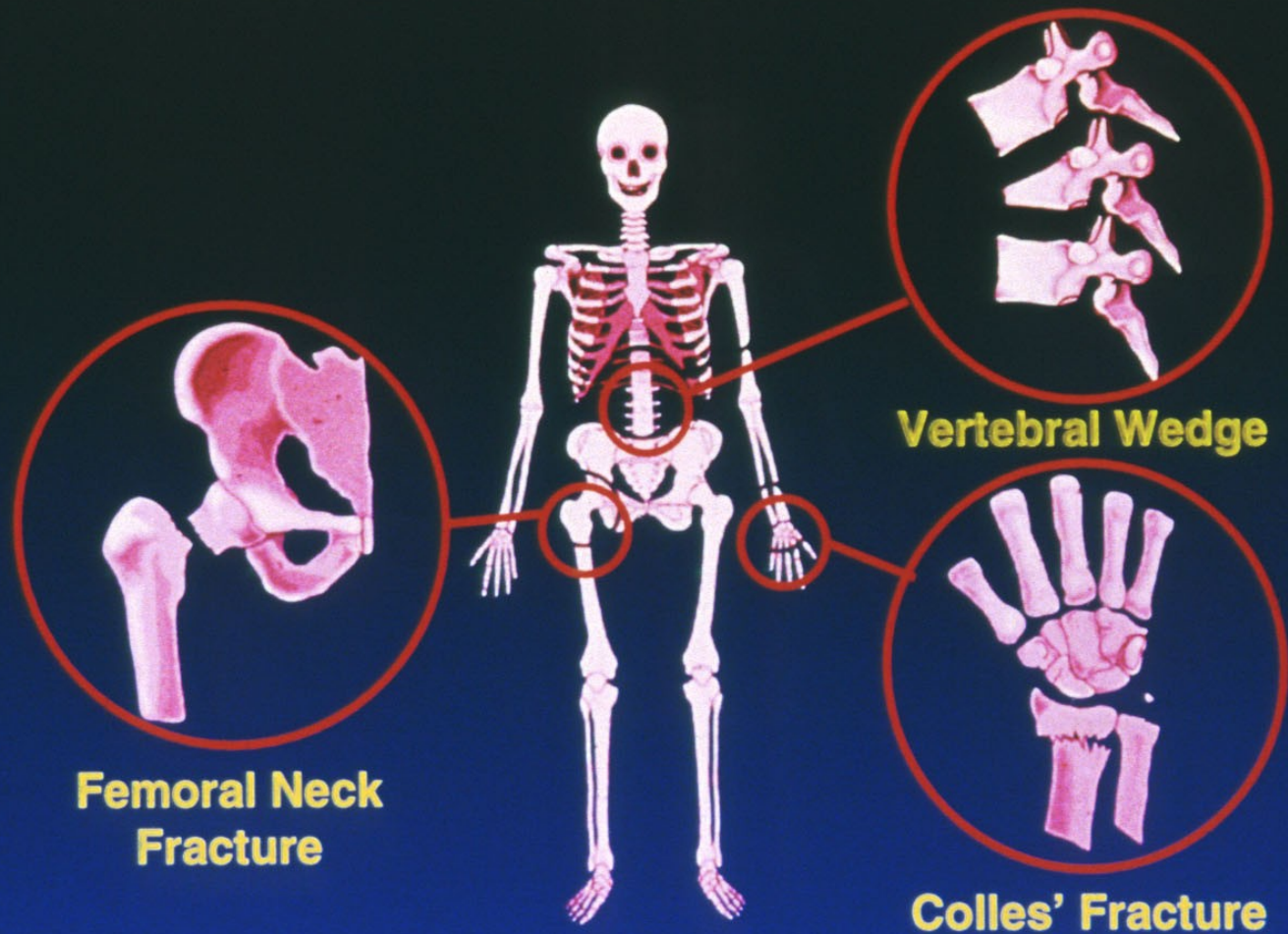


Examination

- Tenderness on spinous process
- Limited movements of the spine
- Paravertebral spasm
- Thoracic kyphosis
- Widow's hump
- Lower length of the stature



THE COMMON FRACTURES OF OSTEOPOROSIS



Postmenopausal osteoporosis

- 80% of all cases
- 25 % of female are involved
- Between 50- 65 years
- Loss of estrogens- high activity of osteoclasts
- Trabecular bone most often affected

Senile osteoporosis

Over 70 years, ratio female: male = 2 : 1

The cause: no production of osteoblasts in bone marrow

Cortical and trabecular bone



Secondary osteoporosis

- Corticosteroids
- Hyperthyreosis
- Malabsorption
- Alcoholisms
- After trnsplantations

Osteoporosis in men

- Primary
- Hypogonadism

Risk factors

- Low stature
- White and yellow ethnics
- Low physical activity
- Low nutrition with calcium

Risk factors

- Higher age
- Low BMI
- Occurrence in family

Hypogonadal conditions

- premature amenorrhoea
- surgery of ovaria
- oligomenorrhoea, amenorrhoea
- nullipara
- low endogen estrogen
- mental anorexia

Risk factors- drugs

- corticosteroids
- anticonvulsives
- diuretics
- heparin

Risk factors

- malabsorption
- chronic disorders of liver
- chronic disorders of kidney
- alcohol

Diagnostic tools

DEXA

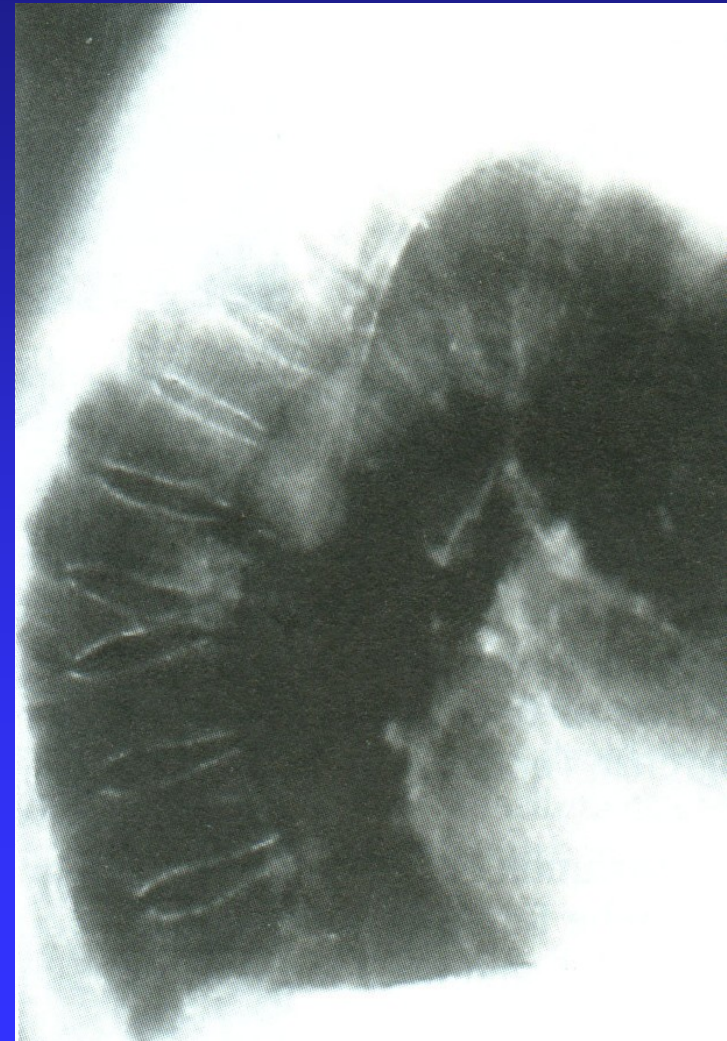
QCT

FRAX

Imaging methods

Laboratory tests

X- ray shows bone loss of
30 % or more



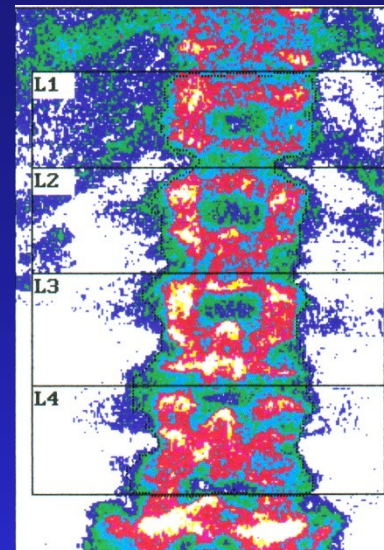
DXA – Dual Energy Absorptiometry

BMD v g/cm^2

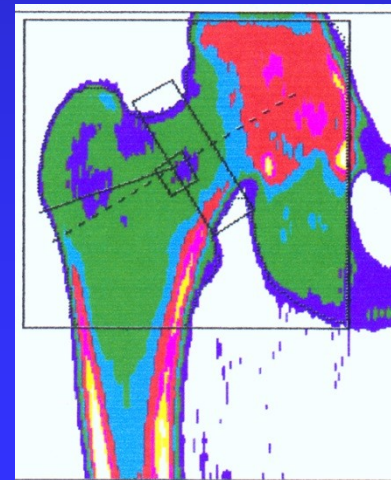
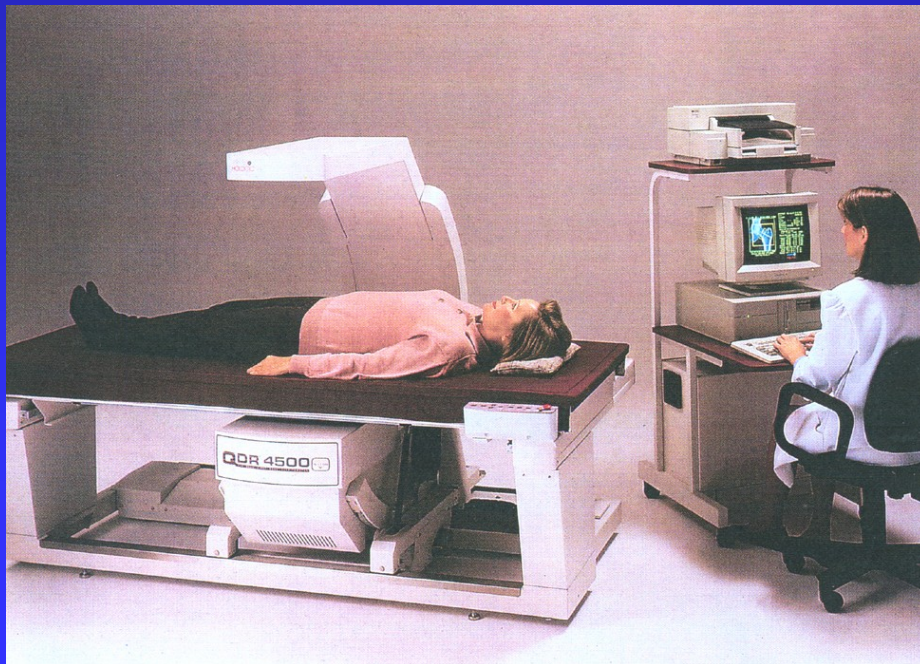
T score

Z score

Change



L1-L4

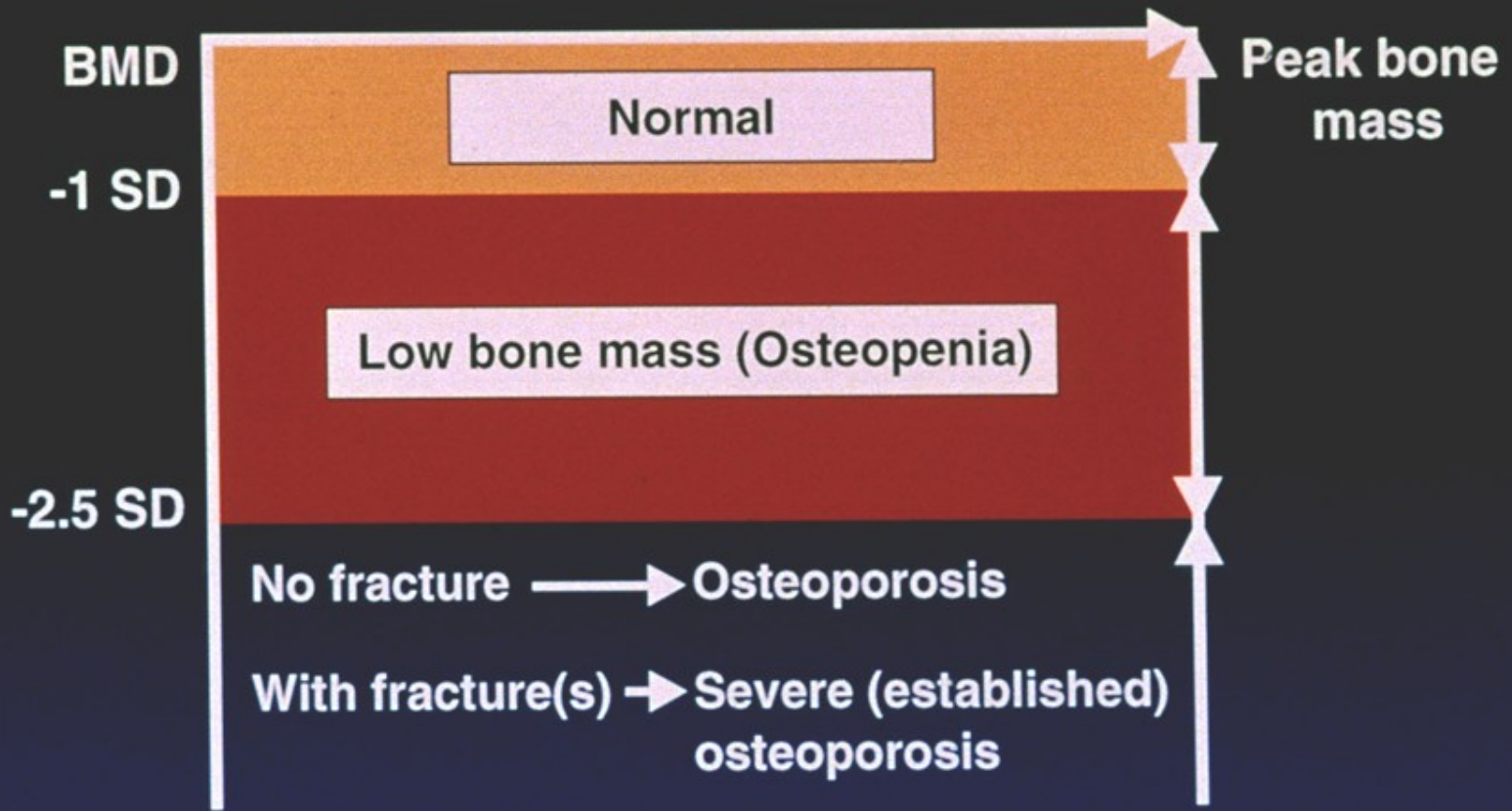


Hip Total

Hip neck

Wrist

WHO DEFINITION OF OSTEOPOROSIS



FRAX

FRAX

- fracture risk assessment tool
- 10 year risk of a major fracture

FRAX[®] 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

Country: UK **Name / ID:** [About the risk factors](#) ⓘ

Questionnaire:

1. Age (between 40-90 years) or Date of birth
Age: Y: M: D:

2. Sex Male Female

3. Weight (kg)

4. Height (cm)

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 per day No Yes

12. Femoral neck BMD (g/cm²)
T-Score

BMI: 20.2
The ten year probability of fracture (%)

with BMD

■ Major osteoporotic	23
■ Hip fracture	5.5

Weight Conversion:
pound:

Height Conversion:
inch:

Clinical data

Age

Sex

Weight

Height

Sustained fractures

Fracture in parents

Smoking

Alcohol 3 or more units/day

Corticosteroids

Rheumatoid arthritis

Secondary osteoporosis

Combination DXA + FRAX

Diagnostic tools

HR- pQCT

Pair biopsies- histology, histomorfometry
2 D micro CT, microindentation
SEM

Finite element analysis

Raman microspectroscopy

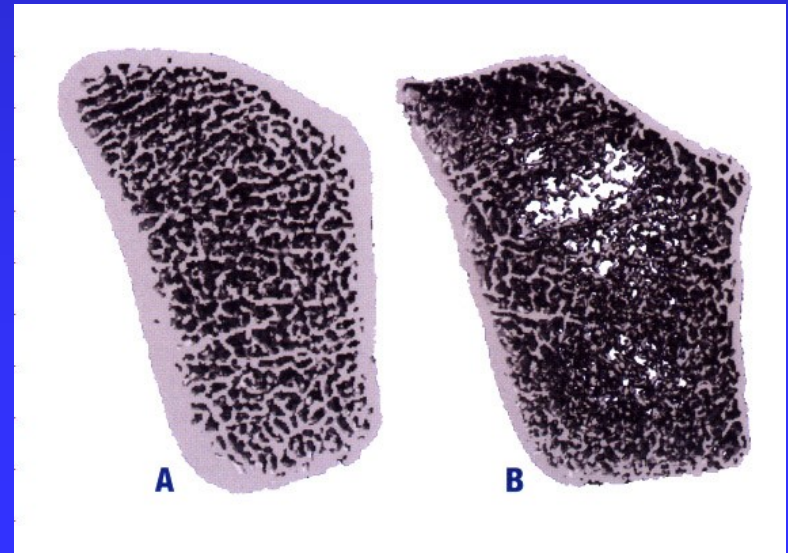
HR- pQCT

High resolution, peripheral, quantitative CT

Noninvasive measurement of bone morphology

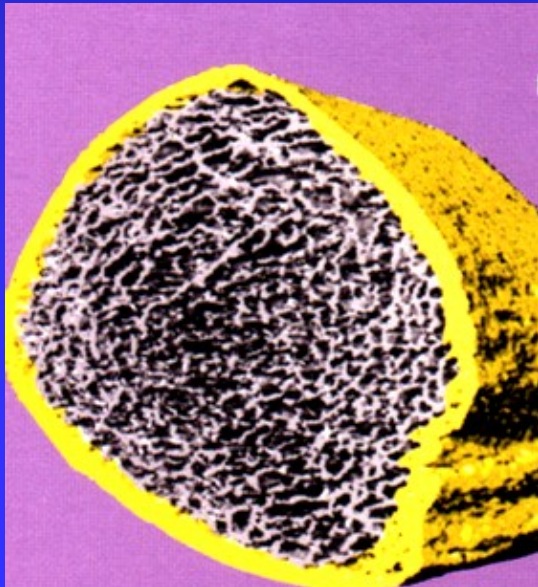
Virtual biopsy

Assess microarchitecture up to 82 μm



Xtreme CT

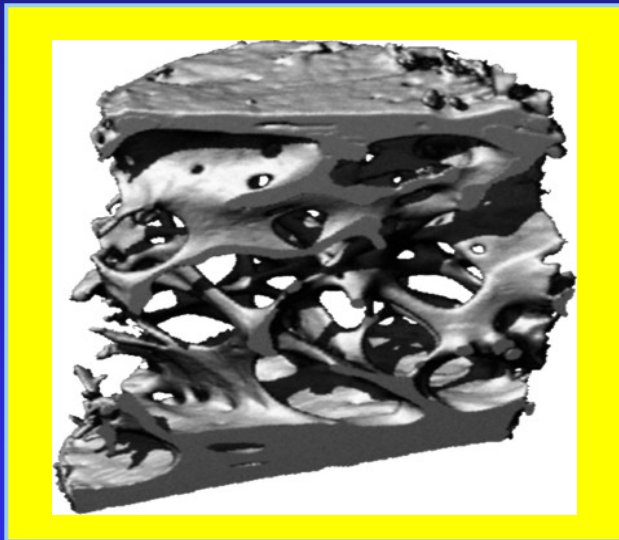
Assess thickness
of cortical bone



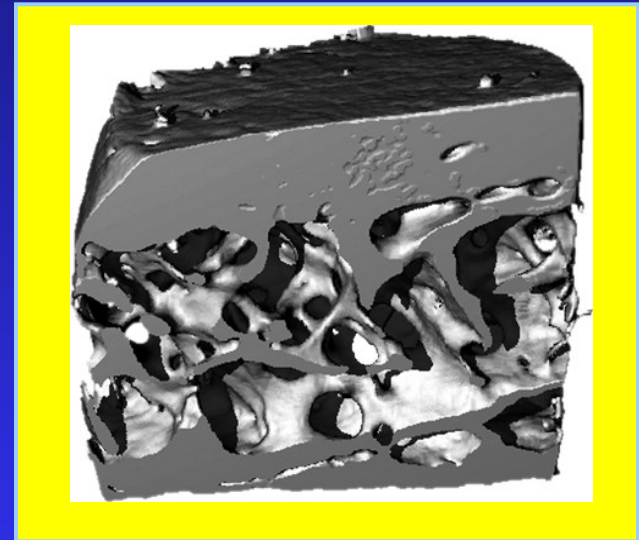
SCANCO
Xtreme CT
HR qCT

Pair biopsies- before and after treatment

Placebo 36 months



PROTELOS 36 months



Thickness of cortical bone	+ 18 %	$p=0,008$
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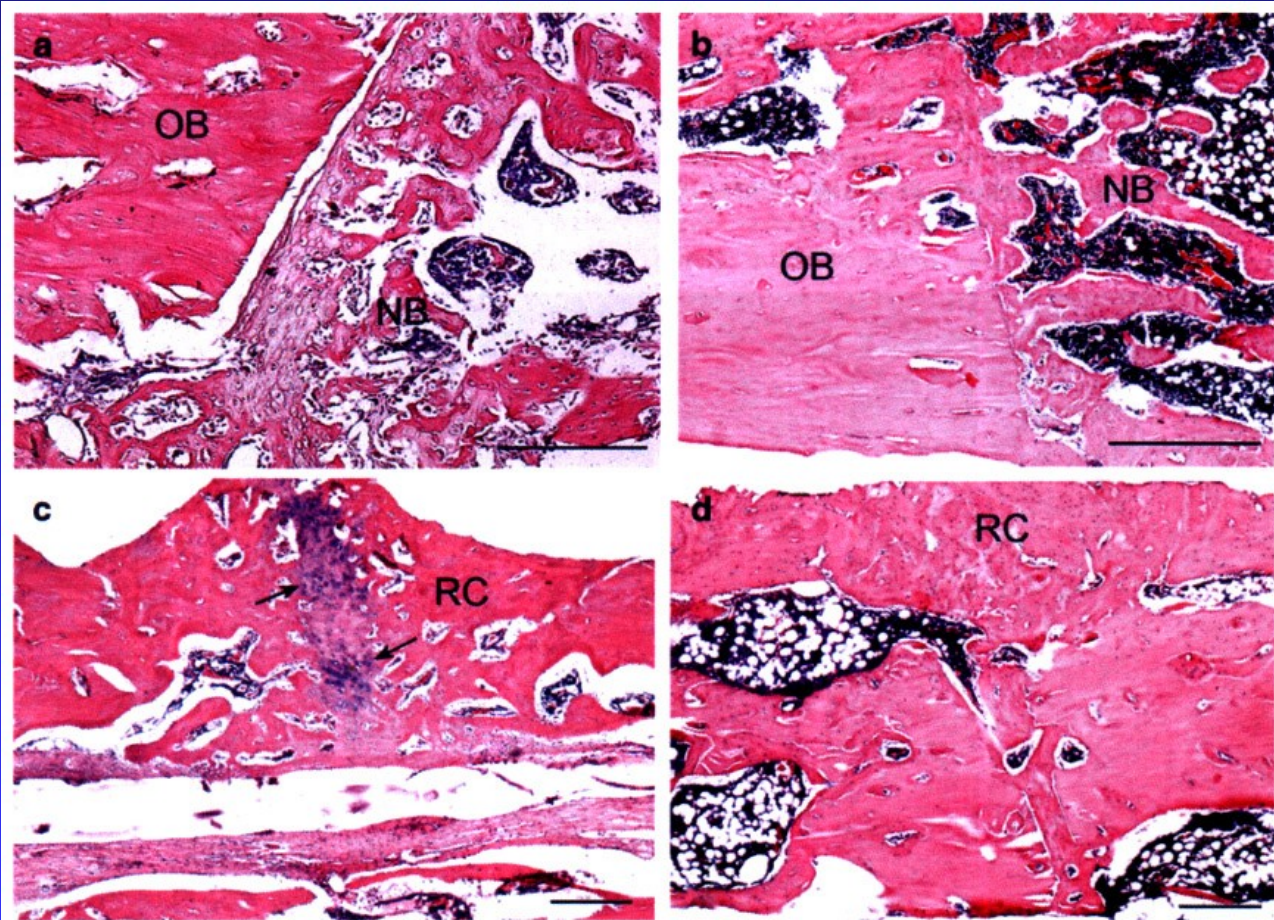
Number of trabeculae	+ 14 %	$p=0,05$
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Histology

Kontrola

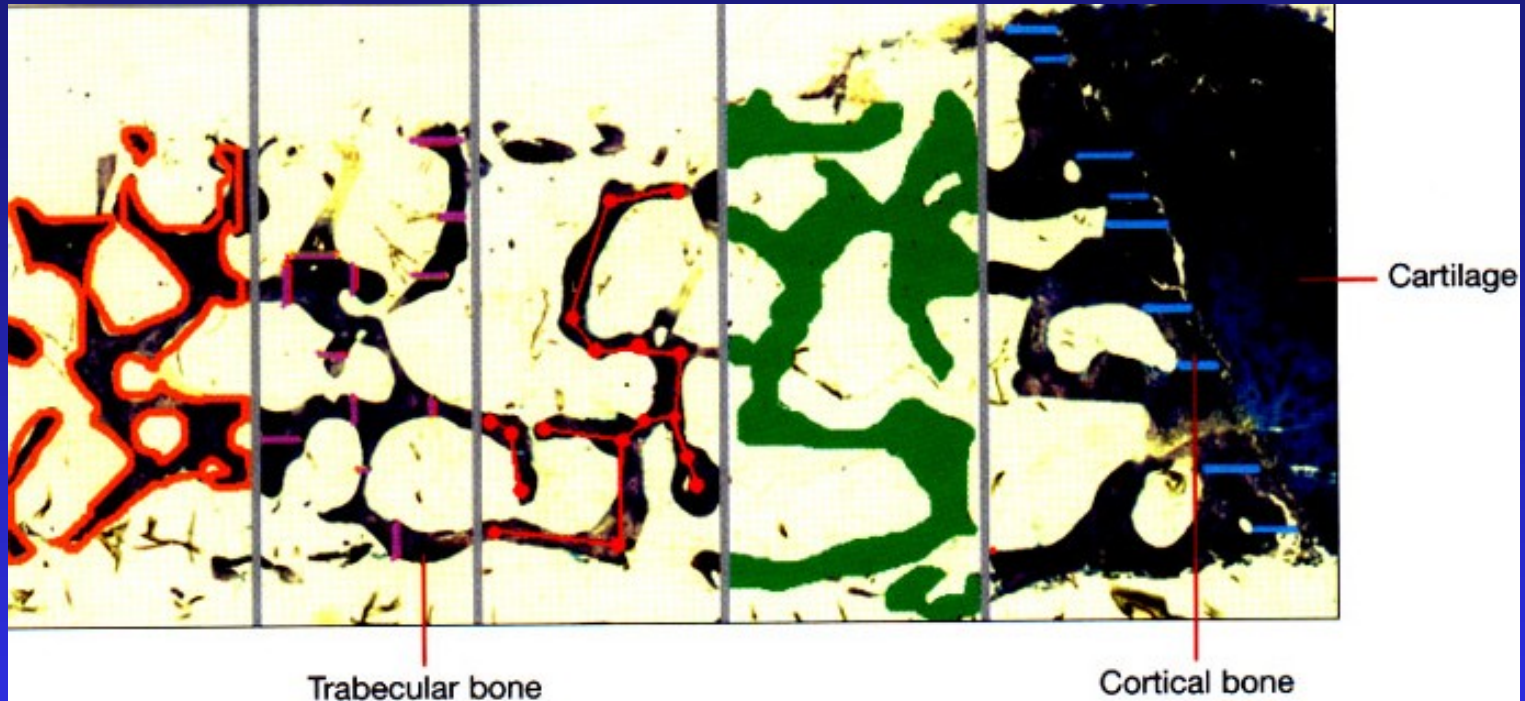
OVX a SR

4 t.



8 t.

Histomorfometry



Povrch kosti

Mineralizovaný povrch

Erodovaný povrch

Tloušťka trabekul

Konektivita trámců

Trabekulární objem

Kortikální tloušťka

FEA- finite element analysis

Trabecular bone (upto 82 μm)

Healthy bone



Plates

Osteoporotic bone

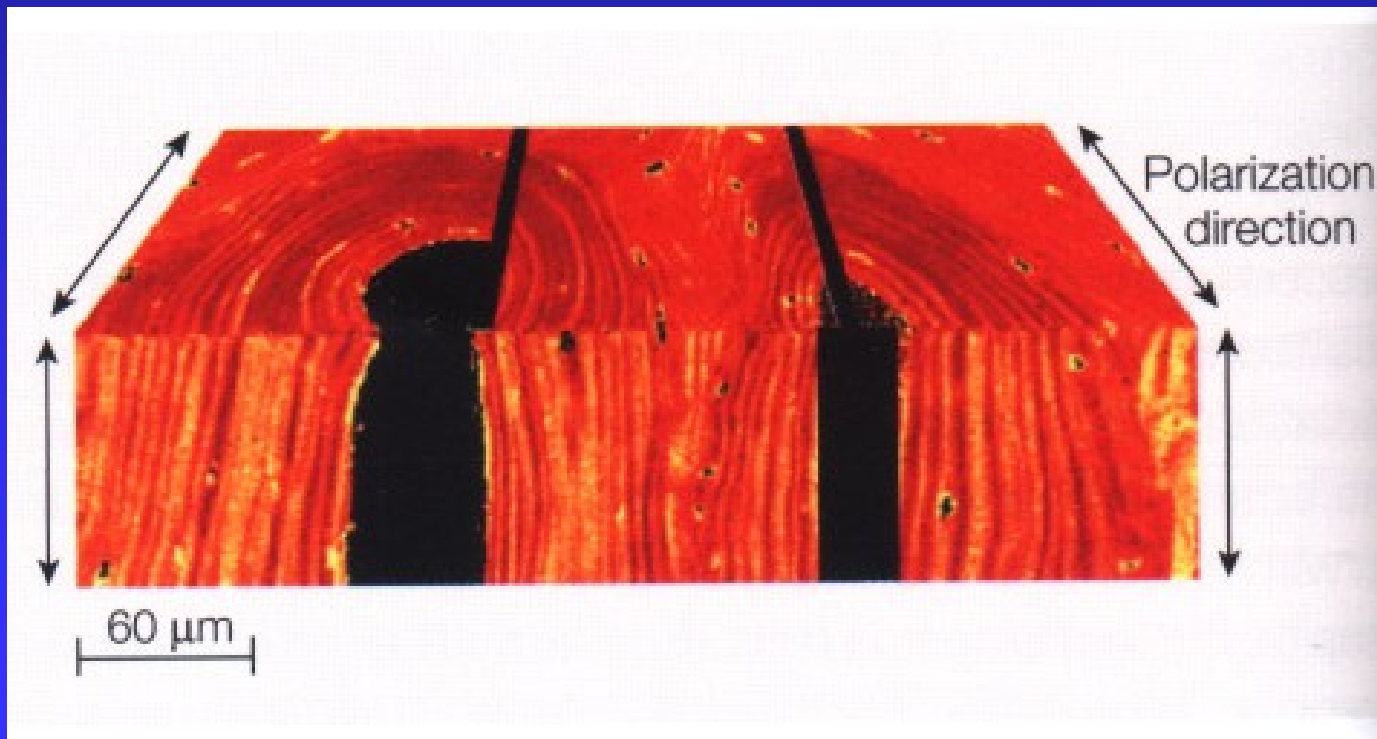


Rods

Raman microspectroscopy - cortical porosity

Increases after 40 years of age

- begins with resorption around Havers canal



Raman microspectroscopy

Laboratory tests

Calcium (Normal calcium 2,0 – 2,75 mmol/l)

Phosphorus (Normal phosphorus 0,7- 1,5 mmol/l)

ALP, bone isoemzyme of ALP

Vitamin D normal level: 20-80 ng/ml

Parathormon

Osteocalcin

CTX- C terminal peptid of collagen

NTX- N terminal telopeptid of collagen

Pyridinolin, deoxypyridinolin

Acid phosphatase

Bone formation

ALP normal level 2,7 ukat/l in man and 2,3 ukat/l in woman.
- indicator of osteoblasts function. Marker of bone formation.
High levels in osteomalacia !!

Bone isoenzyme ALP- marker of bone formation.

Osteocalcin 3,4- 11,7 ng/ml in men, and 2,4- 10,0 ng/ml in women.

C terminal propeptide of collagen I (PICP)

N terminal propeptide of collagen I (PINP) - products of collagen synthesis

Bone resorption

Tartrate resistant acid phosphatase – marker of bone resorption

Pyridinolin and deoxypyridinolin (crosslinks)
- marker of collagen degradation

CTx- (C terminal peptid of collagen I)

NTx (N-terminal peptid of collagen I)

- products of proteolytic resorption of collagen in bone

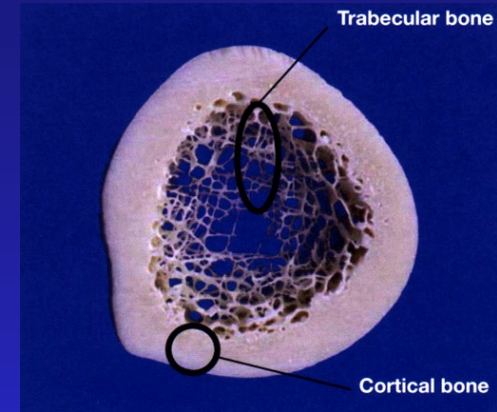
Vitamin D 40-80 ng/ml, under 20 ng/ml (severe hypovitaminosis)

Parathormon normal level 10-65 ng/ml.

Strength of bone

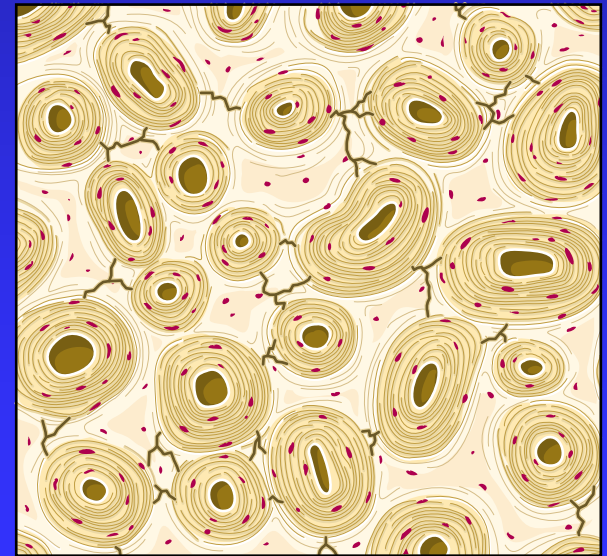
Density from BMD predicts only
60-75 % of mechanical power of bone

Quality of cortical and trabecular bone,
collagen and bone mineral



Cumulation of microdamage
and microfractures

Remodelation of bone:
-permanent removal of old
and damaged bone



Microcracks

Prevention of osteoporosis

- Maximal peak bone mass
- Management of disorders in children
- Removal of risk factors
- Management of gastrointestinal disorders
- Nutrition with calcium and vitamin D
- Physical activity

Management

Analgetics

Physiotherapy

Nutrition (proteins, calcium)

Calcium - 1300 mg/day

Vitamin D - 800 I.U./day

Drugs

Orthesis

Surgery



Physioterapy:

Bone crystals are orientated according the forces

Piesoelectric efect activates osteoblasts for more production of bone osteoid

Nutrition

BMI 23-25

Proteins 1,0 g/kg/day

+ 30g of proteins /day

IGF-1 – insulin like growth factor

Calcium

1,5 g / day

Application in the evening

Calcium

- Calcium eff. Pharmavit 500, 1000 mg
- Calcium Sandoz forte 500 mg eff.
- Calcium Slovakofarma eff.
- Maxi-Kalz eff tbl, 100, 500 mg.
- Vitacalcin pulvis, tablety
- Biomin H plv.- Ca, Mg + IGF-1.



Calcium

- Kombi-Kalz pulv, 1000Ca+ 880 IU vit D.
- Osteocare tbl.
- Caltrate plus tbl
- Calcium 500 + vit D3 eff.
- Calcium D forte cps
- Calcicew



Vitamin D

7-dihydrocholesterol

In the skin -UV beams -cholecalciferol

In liver conversion to 25-OH vit. D₃

In kidneys conversion to 1,25 dihydroxy-vit. D₃

Active agent is calcitriol 1,25 (OH) D₃.

80-90% of daily use is covered by sun radiation

Vitamin D

60 % of seniors have hypovitaminosis of vitamin D

Optimal level in blood is 80 nmol/l

Hypovitaminosis - below 20 nmol/l

Dosage: 800 IU/day

Vitamin D

- Infadin gtt, vit D cps., Vigantol oel, gtt
- Rocaltrol cps, Vitamín D Slovakofarma cps
- Calciferol inj.
- 1 alfa (OH) D3 – alfakalcidol - Alpha D3
- 1 alfa (OH) D2 – doxercalciferol (Hectorol)
- 22 oxakalcitriol (OCT)
- 19 nor 1,25 (OH)₂ D2 – parikalcitriol (Zemplar)

Management of osteoporosis

Inhibition of bone resorption
Stimulation of bone formation

Bisphosphonates- Alendronát (Fosavance)

Risedronát (Actonel)

Ibandronát (Bonviva)

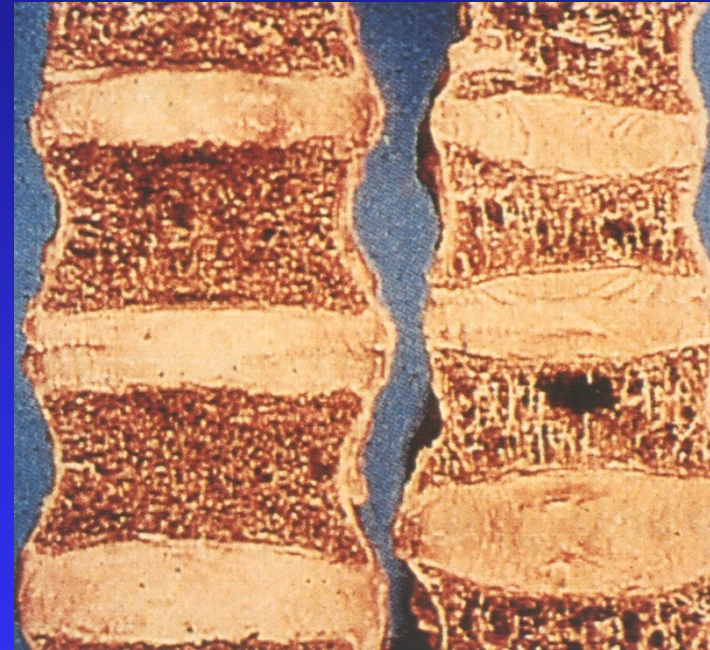
Zolendronát (Aclasta)

Denosumab (Prolia)

Parathormon, teriparatid

– syntetic parathormon 1-34 fragment
(Forsteo)

SERM- bazedoxifen

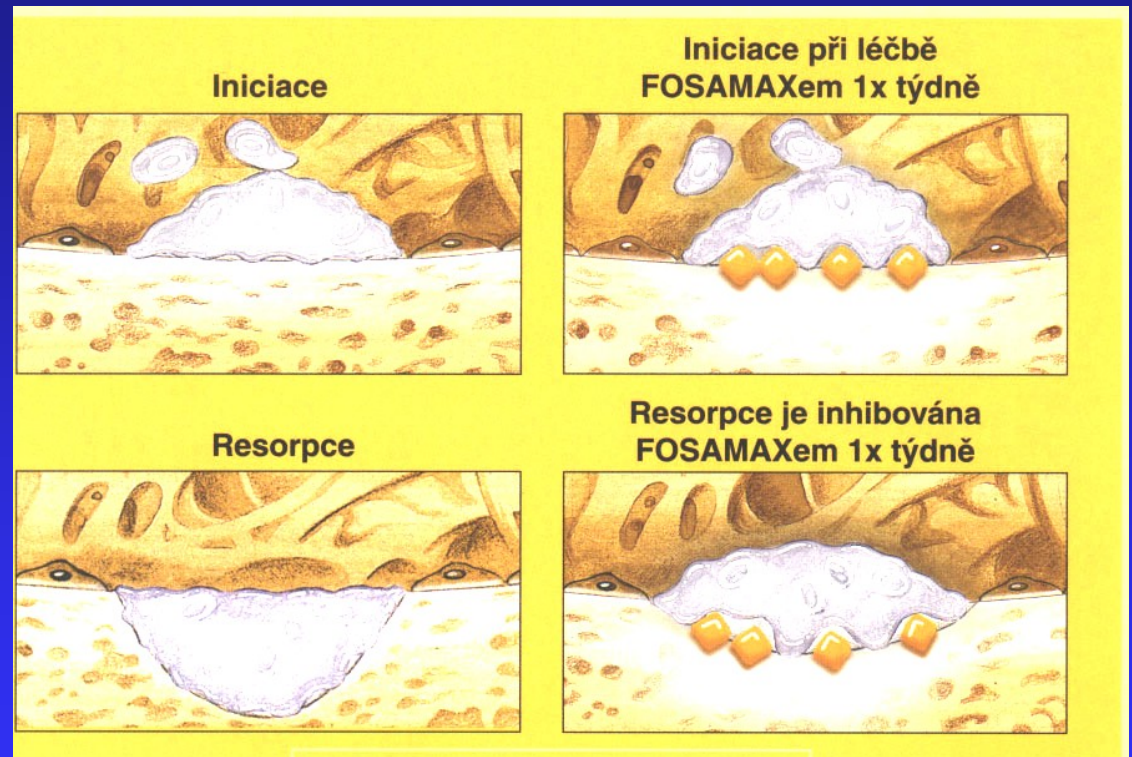


Bisphosphonates

Incorporation in HA
crystals and matrix

Inhibition of formation,
agregation and
dissolution of crystals

Inhibition of bone
resorption



Fosamax

Bisphosphonates

- Reduction of activity of osteoclasts
- Induction of apoptosis of osteoclasts

Bisphosphonates - indications

Osteoporotic fractures

All forms of osteoporosis

Paget 's disease of bone

Hypercalcemia in carcinomas or myeloma

Bisphosphonates

Pamidronate - Aredia inj.

Clodronate – Bonefos inj, cps., Lodronat inj, cps.

Ibandronate – Bonviva tbl., Bondronate inj.

Alendronate – Fosamax 70 mg tbl., Alendros tbl.

Risedronate - Actonel tbl.

Zoledronate – Aclasta inj.

SERM - selective modulators of estrogen receptors

Bazedoxifen

- Agonists on bone and cardiovascular apparatus
- Antagonists on endometrium and breast
- They bind on the same place as estrogens (receptors α , β)

Teriparatid – synthetic parathormon 1- 34 fragment

Stimulates bone formation
Stimulates osteoblasts
and remodeling
Improves the strength
of trabecular and cortical
bone



New agents

1. Monoclonal sclerostin antibodies

Romosozumab, Blosozumab

Osteoformative effect

Sclerostin – inhibitor of osteoblasts

production from osteocytes

stimulates bone resorption via RANKL

2. Inhibitors of katepsin K- inhibition of bone resorption

Odanatocibe

HRT

no evidence of effect

Livial®

tibolone

**The tissue-specific therapy with
an estrogenic effect on bone¹**

enhances mood and
libido^{5,6}

treats climacteric
symptoms⁷

no proliferation of
breast cells (*in vitro*)⁸

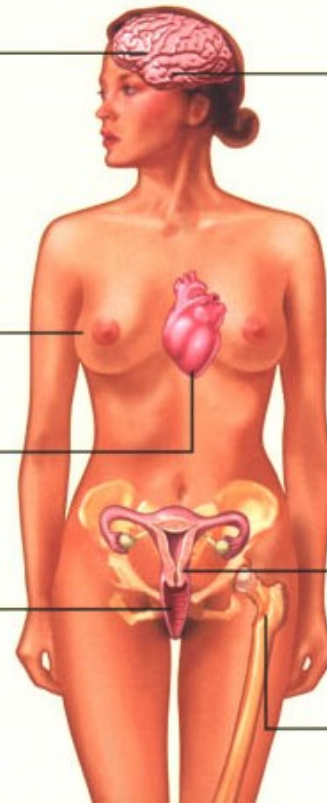
low incidence of
side effects
(eg breast tension)⁹

beneficial effects on the
cardiovascular system¹⁰

treats vaginal atrophy¹²

no endometrial
stimulation¹¹

prevents postmenopausal
bone loss⁴



Frailty syndrom

1. Loss of weight 4-5 kg/year
2. Exhaustion
3. Muscle weakness / handgrip more than 20 %
4. Lower velocity of gait less than 20 %
5. Lower physical activity less than 20 %

Frailty syndrom

Subclinicaly

Early frail

Late frail

Endstage frailty syndrom: terminal geriatric deterioration

Frailty syndrom

Disposition to falls

Disposition to organ decompensation

Worsening of cognitive functions

Need for help in daily activities

Sarcopenia

Osteoporosis

Low level of vitamin D

Occurrence

Advanced age

7 % persons over 65 years

25 % persons over 75 years

Loss of muscle power 20 % in 65-70 years

Loss of muscle power 60 % in 80 years

Cause: longlasting deficiency of vitamin D

Risk factors of frailty syndrom

Cardiovascular disease

Diabetes mellitus

Atherosclerosis

Renal failure

Neurologic disorders

Obesity

Hormonal dysfunction

Hypovitaminosis D

Prevention and treatment of frailty syndrom

Frailty syndrom is reversible

Nutrition and proteins 1,3 g/kg/day

Vit D 800 IU/day till 2000 IU/day

Vigantol 1 drop = 500 IU, alpha kalcidol 1 μ g

Strengthening of muscles, exercise, walking

Strengthening of stability, prevention of falls

Prevention of atherosclerosis

Management of other comorbidities

Aleviating of pain

Stop walking when talking

Sarcopenia

Loss of muscle substance more than 20-30 %

Dysbalance between synthesis and degradation of muscles
(myostatin, glucocorticoids, sexual hormones, insulin, IGF-I)

Osteopenia

Sedentary way of life

Sarcopenia

Muscle densitometry: below 2 SD – man under 7,26 kg/m²
- woman under 5,45 kg/m²

MRI

Hand grip- dynamometr

Flexion- extension of the knee

Maximal forced breathing out

Velocity of gait

Test of balance

Get up and go test

Walking on stairs

Medication

Vit D 800 IU/day till 2000 IU/day

Vigantol 1 drop= 500 IU

Alpha kalcidol 1 μ g

Testosteron

Ghrelin

GH secretogoga

Estrogens

Leptin

Consequenses of sarcopenia

Lower physical activity (myosteatorosis, sarcopenic obesity)

Sarcoporosis

Higher risk of falls

Risk factors for developing of sarcopenia:

Parkinson sy, multiple sclerosis, CVA, catarracta

Management

Farmacotherapy of osteoporosis
diminishes risk of fragility fractures
only 20-50 %

- + frailty syndrom
- + sarcopenia
- + osteoarthritis
- + other comorbidities
- + prevention of falls



Differential diagnosis

Osteoporosis with corticosteroids

Condition after transplantations

Cushing syndrom

Hyperthyreosis

Rheumatoid arthritis

Osteogenesis imperfecta

Fibrous osseous dysplasia

Osteomyelitis

Myeloma, tumors, osteolytic metastasis

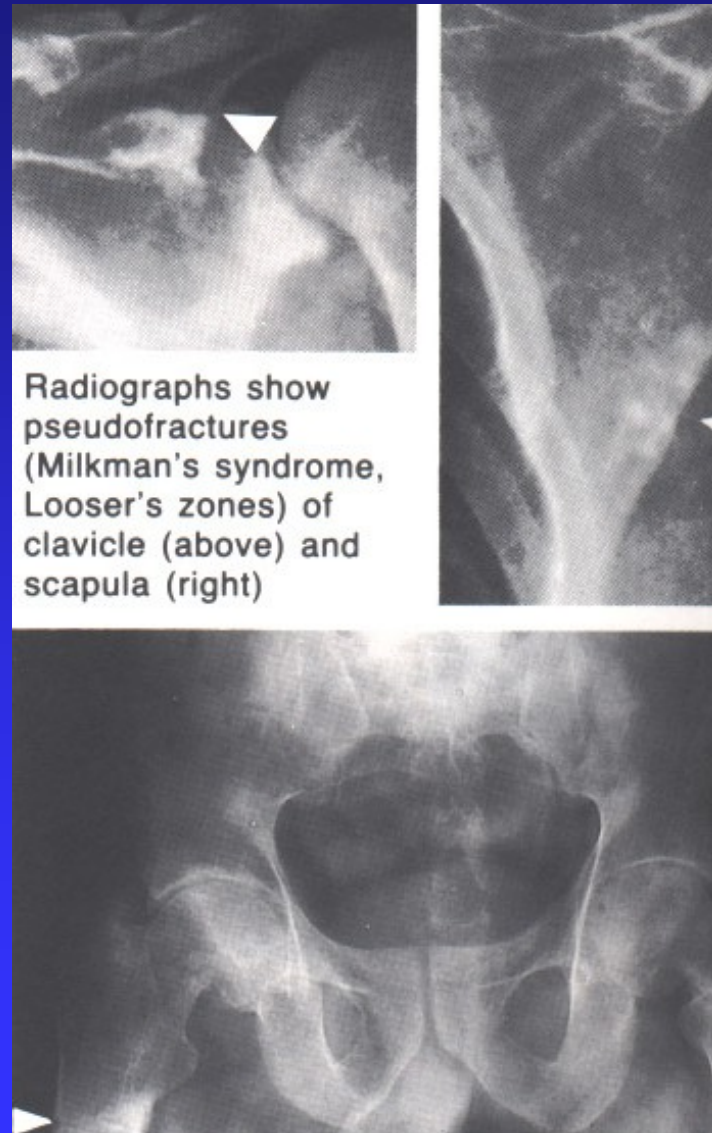
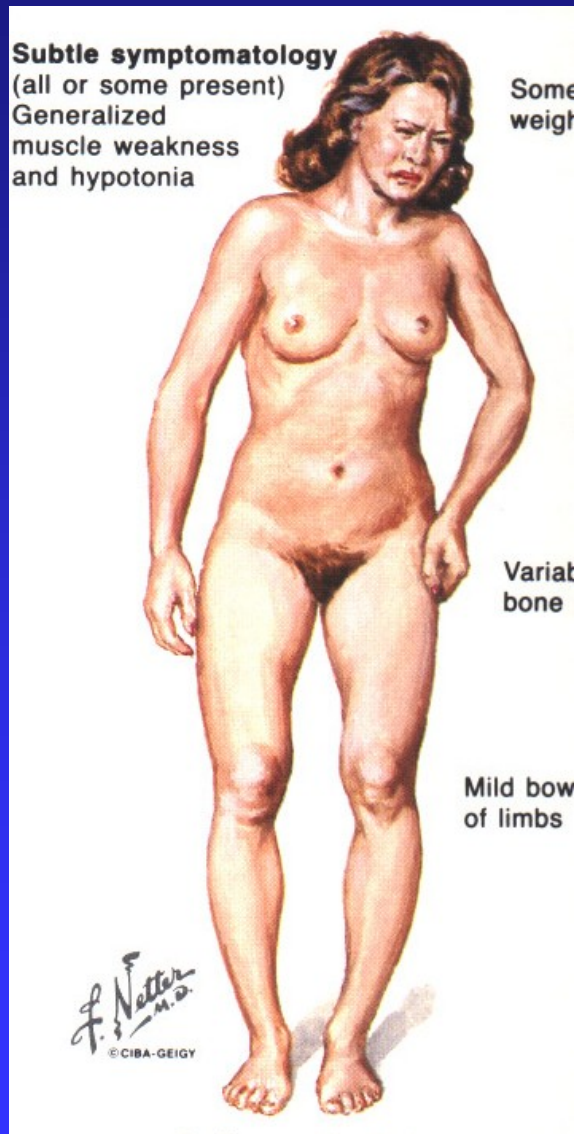
Malnutrition

Algoneurodystrophy

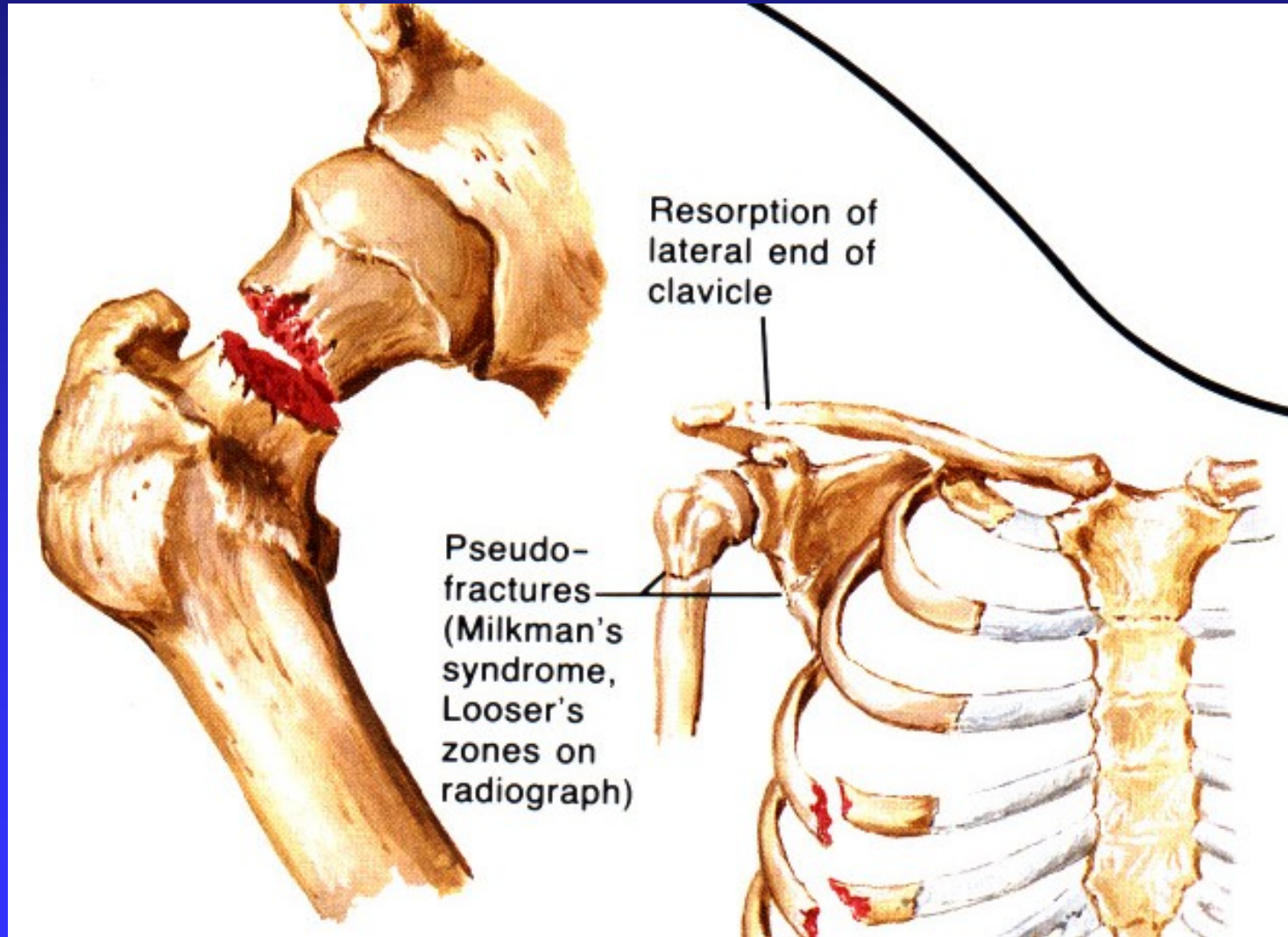
Osteomalatia

- Systemic disorders in adults
- Bone is in a form of nonmineralised osteoid
- Calcium is not layed in HA crystals
- Bone is soft
- The cause: lack of vitamin D

Osteomalatia



Osteomalatia



Symptoms

- Diffuse pain in skeleton
- Muscle weakness
- Tenderness of bones
- Deformities of bones
- Thoracic kyphosis

Laboratory tests

- High level of alkaline phosphatase
- High level of bone isoenzyme of ALP
- Low level of calcium
- Normal level of phosphorus

Radiological finding

Rarefaction of skeleton

Narrow cortical bone

Looser's zone of remodelling
- non mineralised osteoid

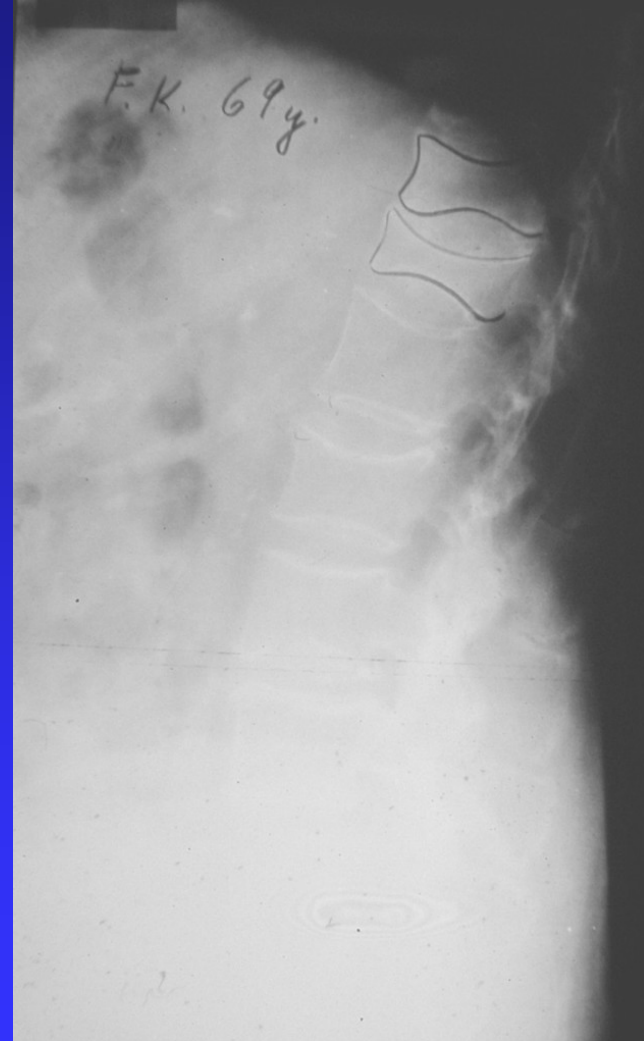
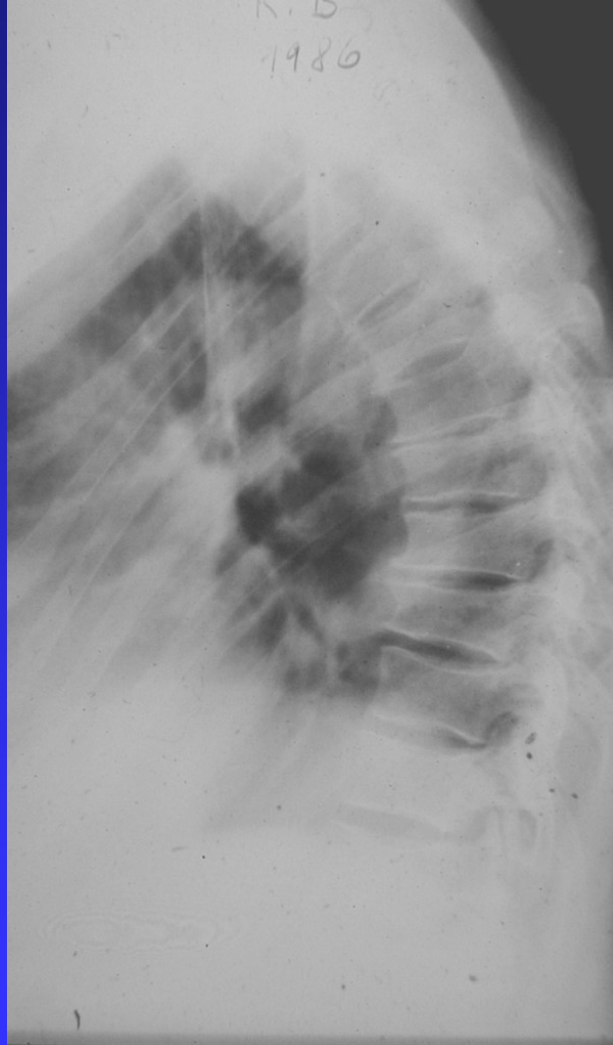
Biconcave shape of vertebrae
coxa vara

Protrusion of acetabulum

Thoracic hyperkyphosis



Osteomalatia



Prevention

- Vitamin D - sun radiation and in food
- Application of vitamin D in renal and liver disorders

Therapy

- Vit. D 10 000 IU per day i.m.
- Calciferol inj.
- Vit. D p.os 2000 IU daily
- Calcium 1000 - 2000 IU daily
- Food with milk, sea fish

Rickets

1. Lack of vitamin D
2. Lack of phosphates

Inability to calcify of matrix

Bone is soft

Bending of bone

Wide growth plates

Metaphysis is wide

Deformities of bones



Rickets

Fatigue

Enlargement of abdomen

Walking ability - worsened

Craniotabes

Large fontanels

Dentic disturbances

Caput quadratum

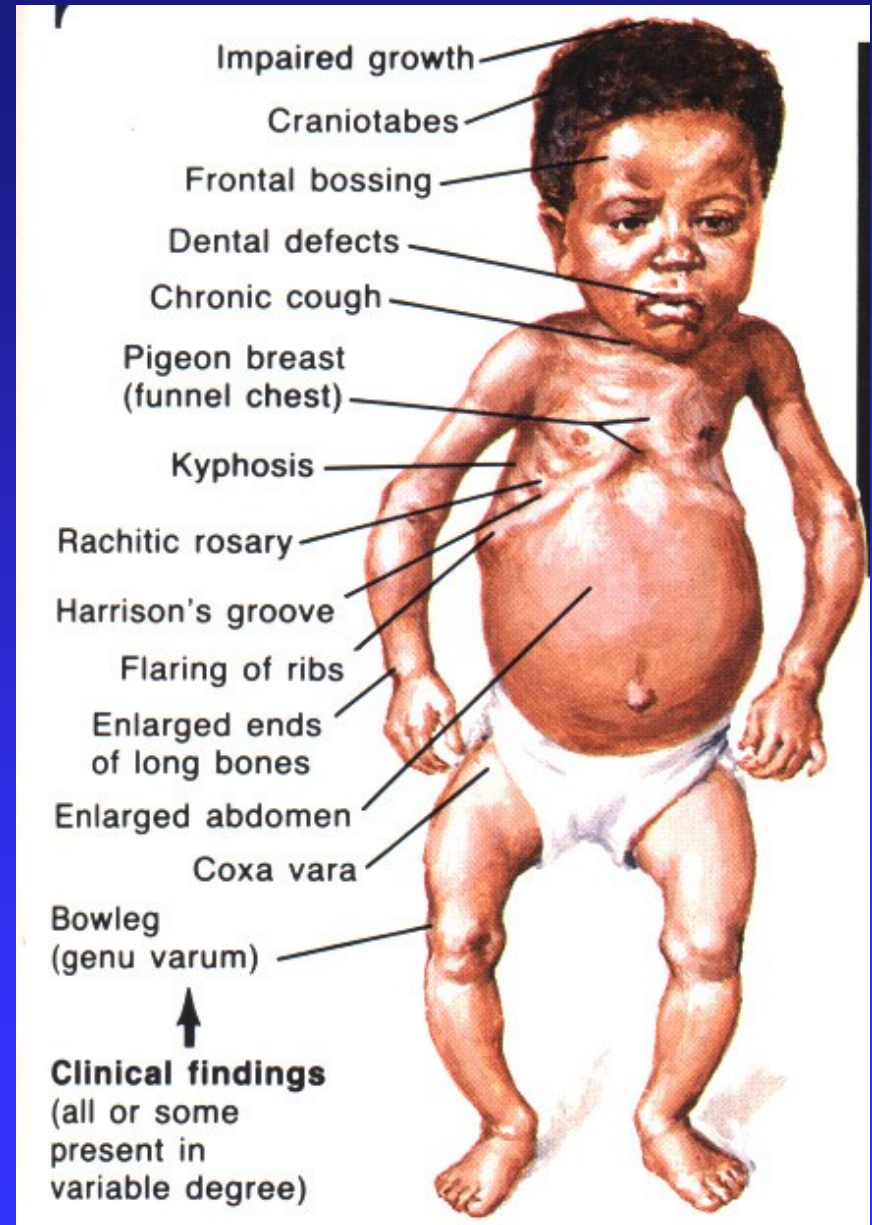
Harrison's groove

Rachitic rosary

Pectus carinatum

Crura et coxa vara

Pedes plani



Management

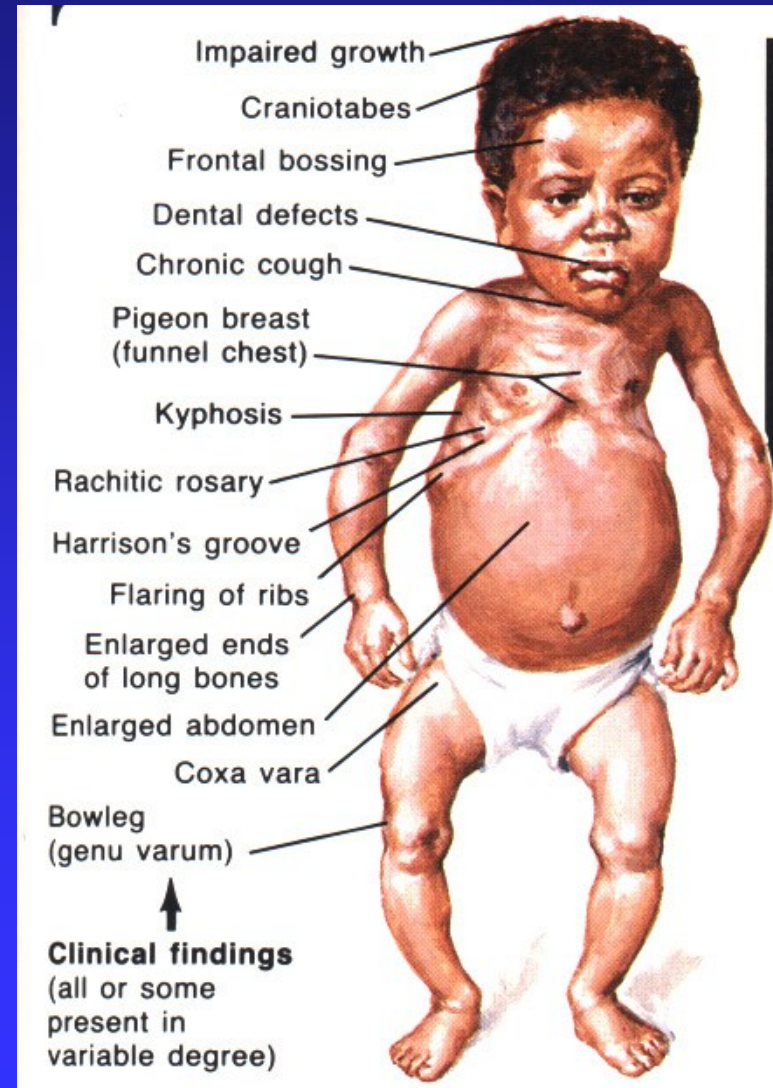
Vitamin D 500- 1000 IU/day 10 weeks

Sun radiation

Milk products with vitamin D

Orthosis

Osteotomies

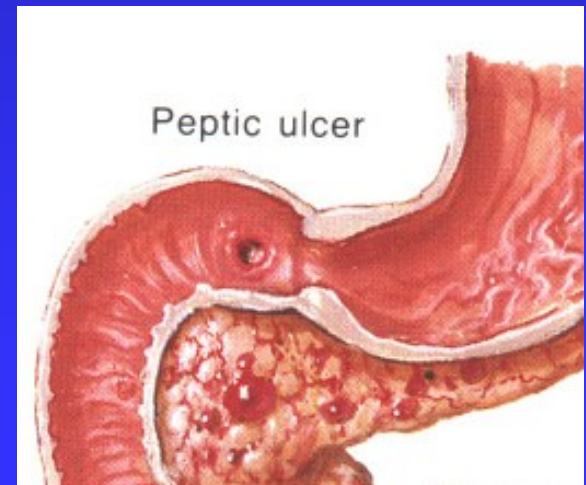
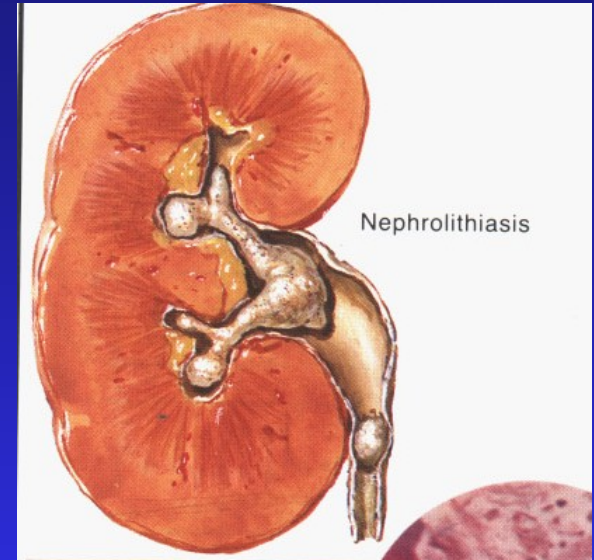


Hyperparathyreoidisms - HPT

- Adenoma of parathyroid glands
- Hyperplasia of parathyroid glands
- Carcinoma of parathyroid glands

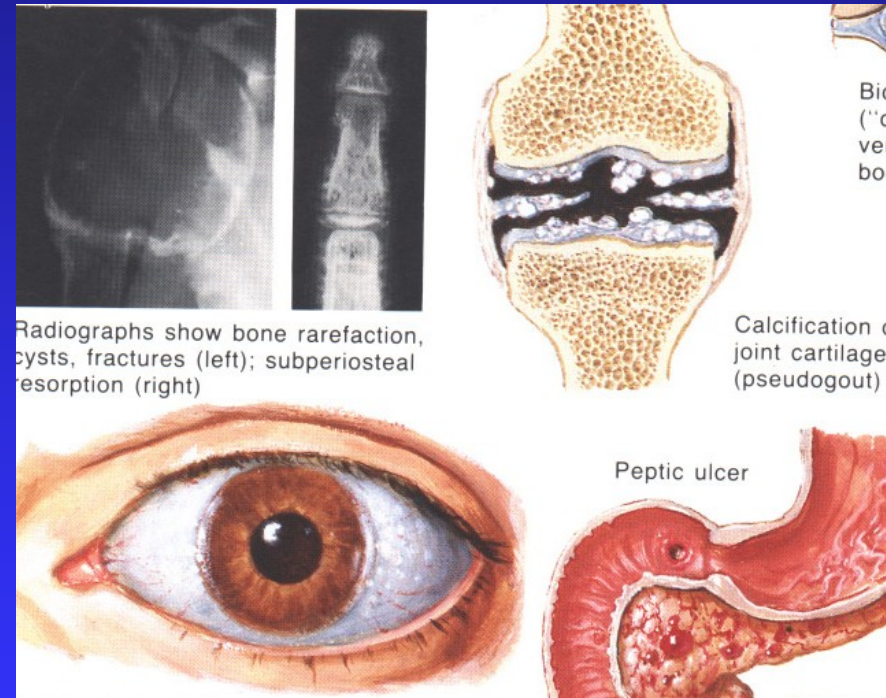
Primary HPT

- Nephrolithiasis, polyuria, polydypsia
- Osteodystrofia fibrosa cystica generalisata
- Gastrointestinal problems
- Acute pancreatitis, cholelithiasis
- Muscle weakness, fatigue, bone pain
- Chondrocalcosis, calcifications



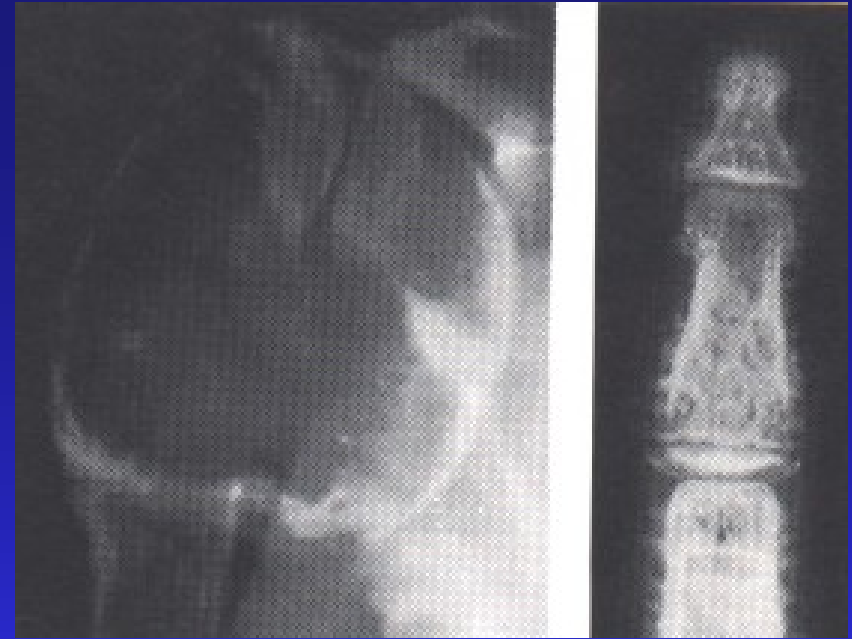
Primary HPT

- High level of calcium
- Hypofosfatemia
- Hyperfosfaturia
- High level of ALP
- High level of parathormon

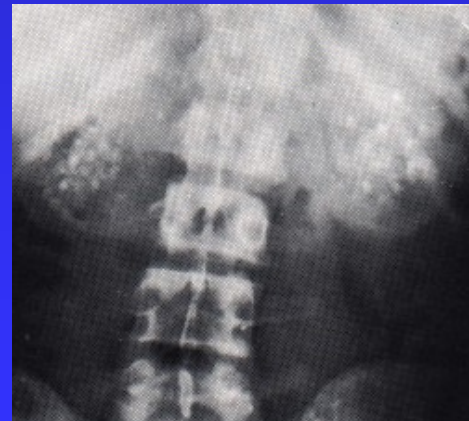


Radiological finding

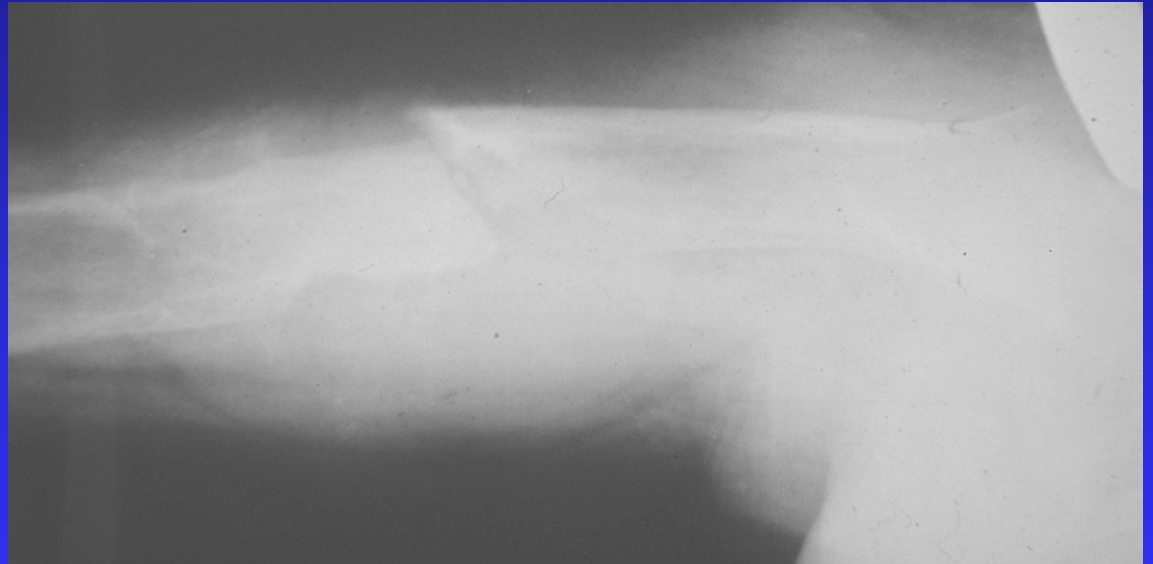
- Rarefaction in skeleton
- Narrow corticalis bone
- Resorption in phalangs
- Large cysts as bone tumors



- Kyphosis
- Coxa vara
- Fisures and complete fractures



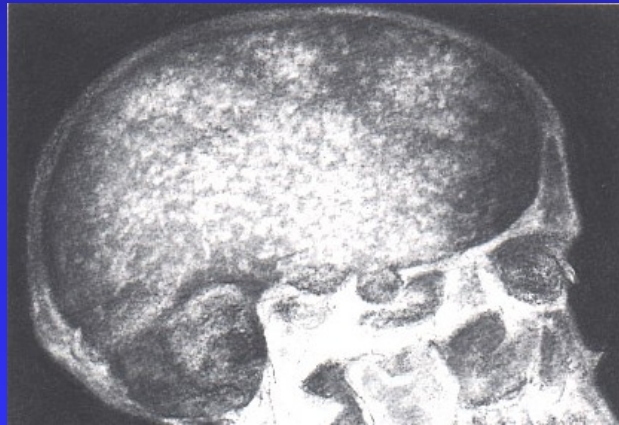
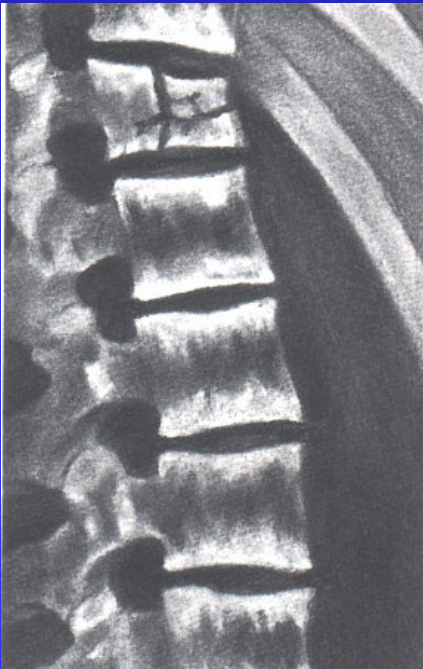
Primary HPT



Renal osteodystrophy

- secondary HPT in renal disorders

Secondary hyperplasia of parathyroid glands



Renal osteodystrophy

Fatigue, bone pain

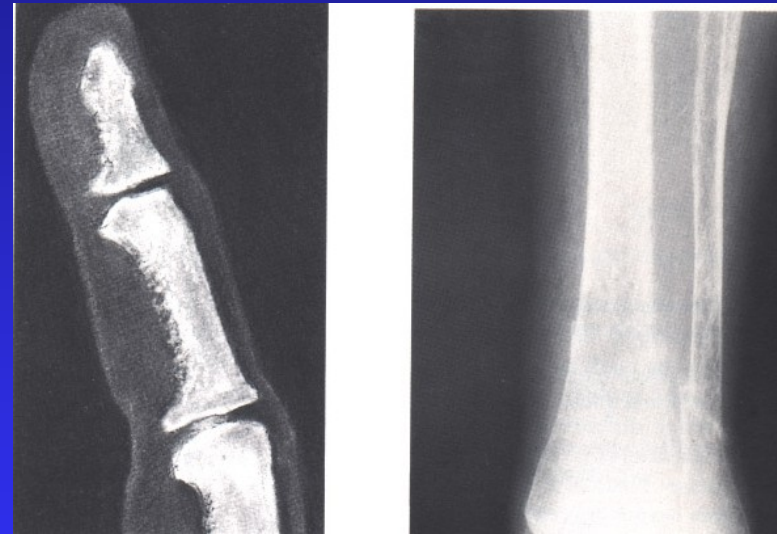
Muscle weakness

Fractures

Th: Treatment of renal disorders

vitamin D3

calcium



Secondary HPT

- Malabsorption of vitamin D

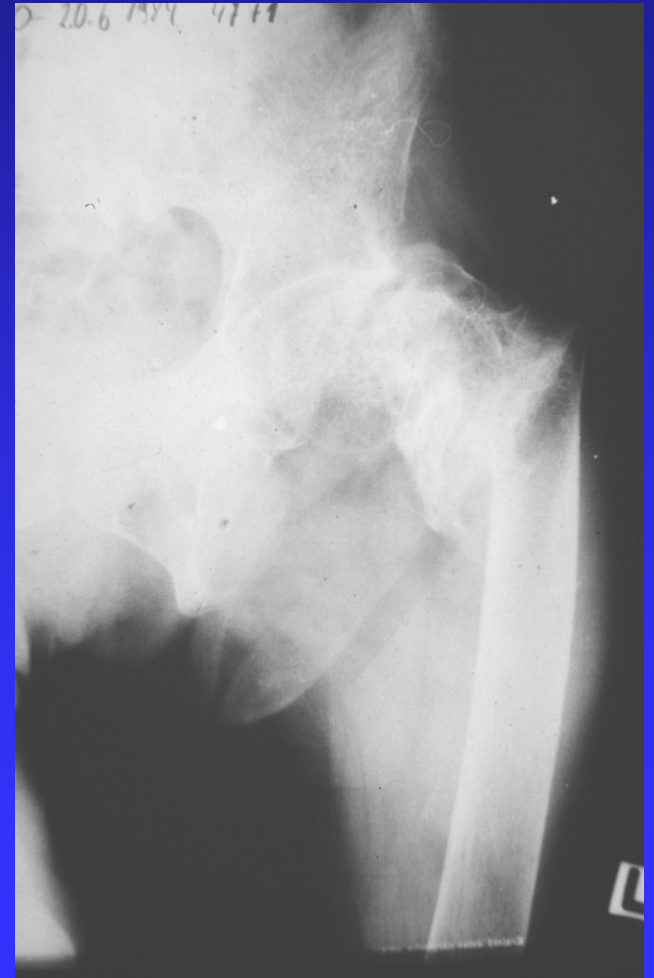
Resection of the stomach or intestine,
gall bladder problems, coeliakia,
pancreatitis

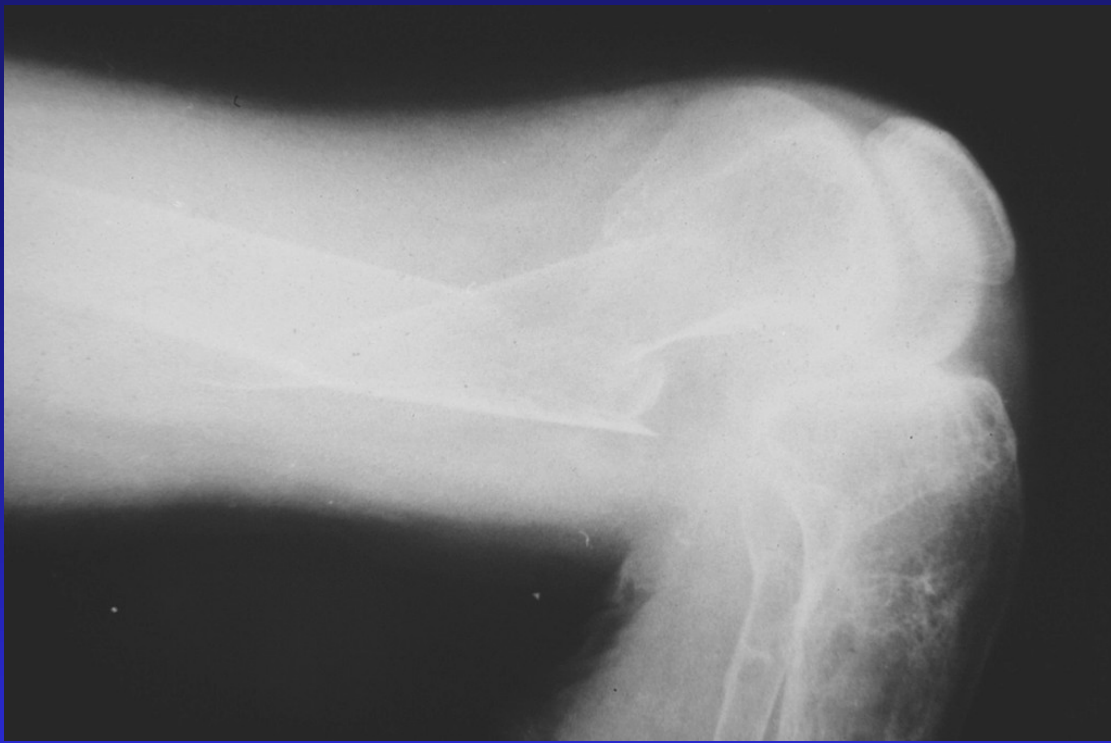
Pain in bones

Muscle weakness

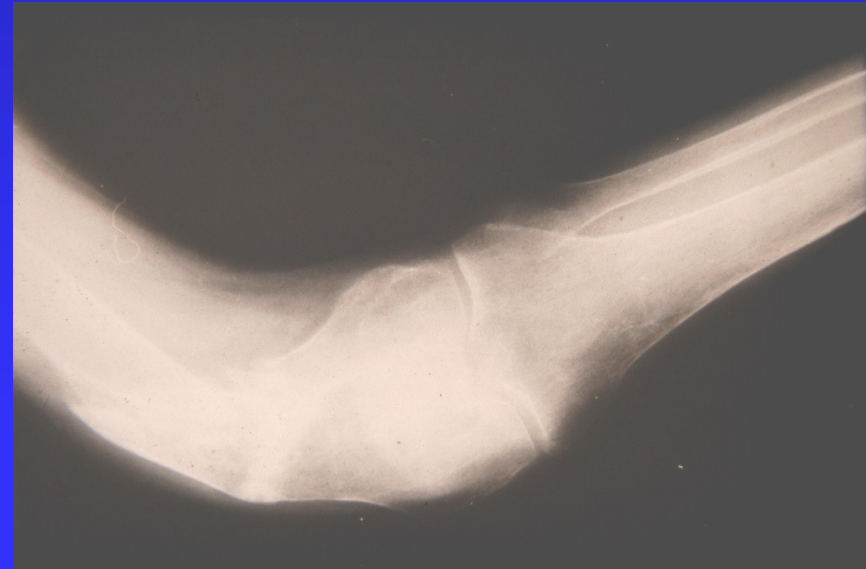
Pseudofractures

Deformities of bone





Secondary HPT
- malabsorption of vitamin D



Paget 's disease of bone

- Sir James Paget in 1876
- Chronic disease
- Slow viral infection (distemper virus from group of paramyxoviruses)
- GB, USA, Australia, New Zealand, France
Germany, Malta.

Morbus Paget

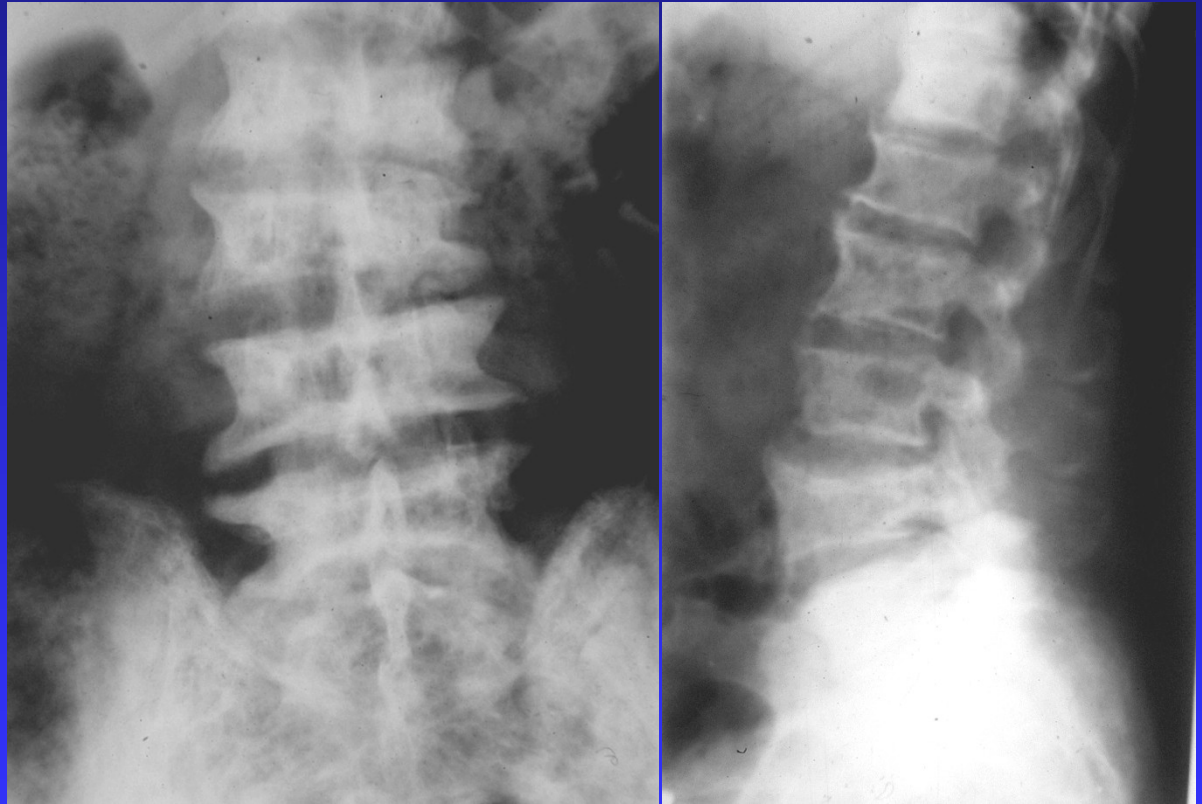
- 1. Osteolytic phase
- 2. Mixed phase
- 3. Osteoblastic phase

Morbus Paget

- Monoostotic form - 20 %
- Polyostotic form
- 95 % are asymptomatic
- 5% symptomatic

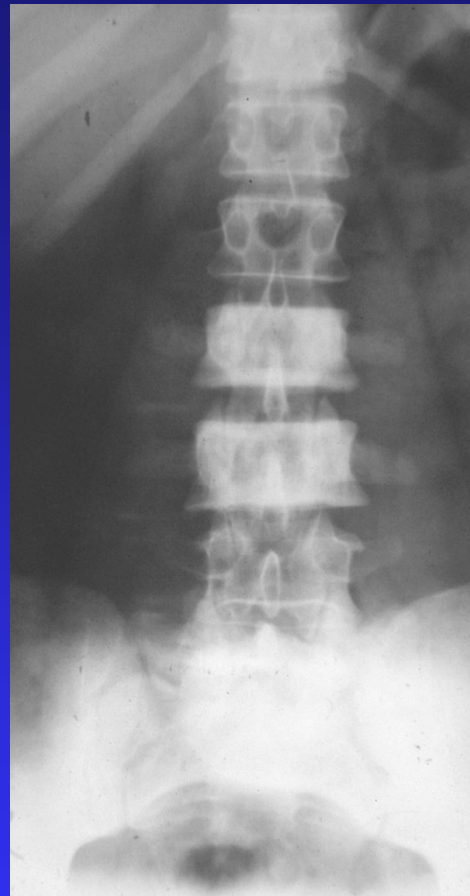
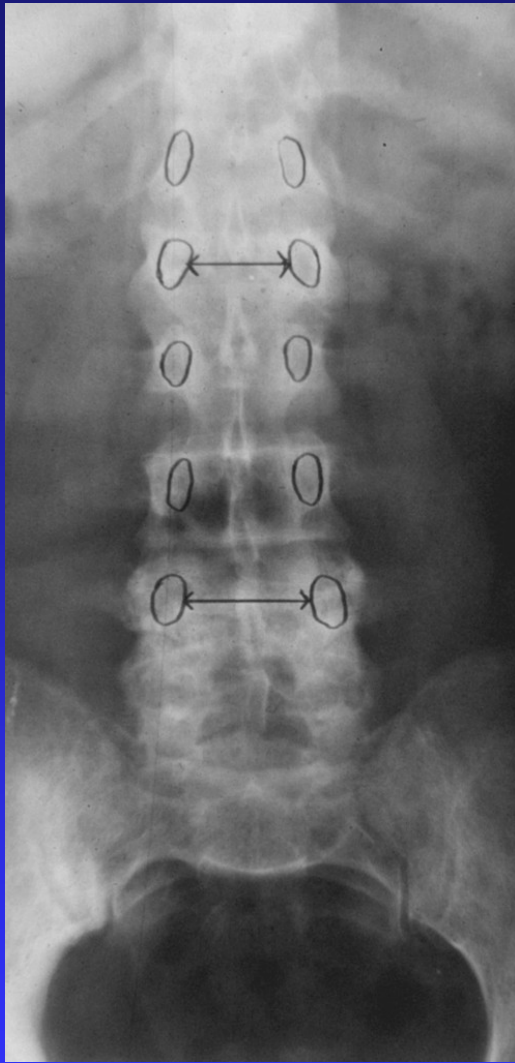
Symptoms

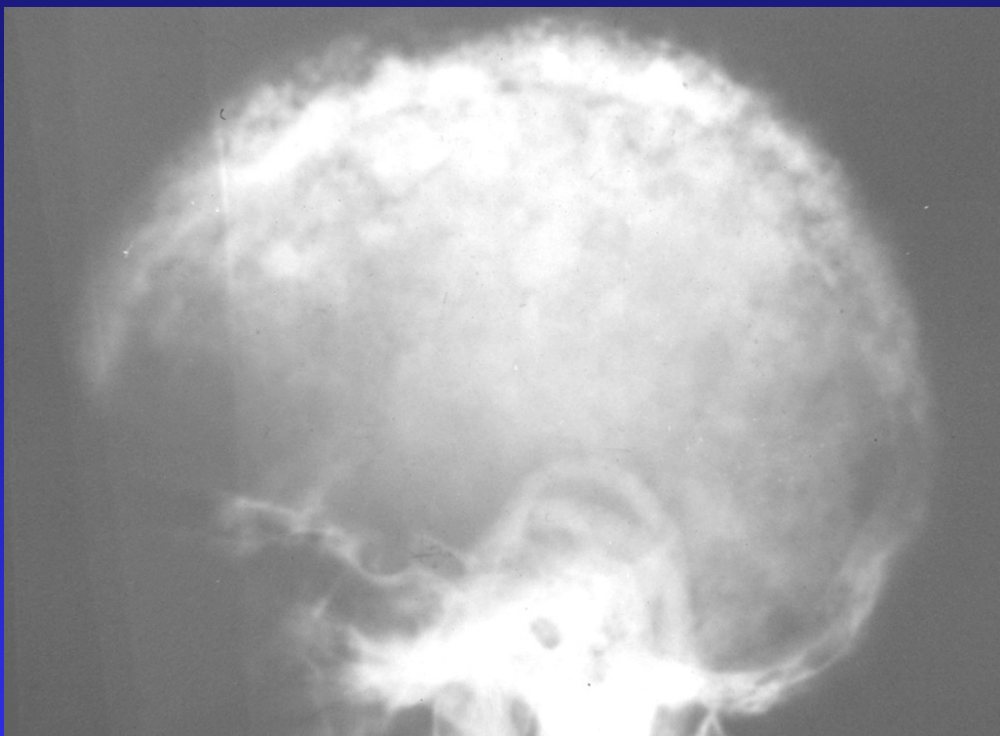
- Pain
- Fatigue
- Deformities
- Complications

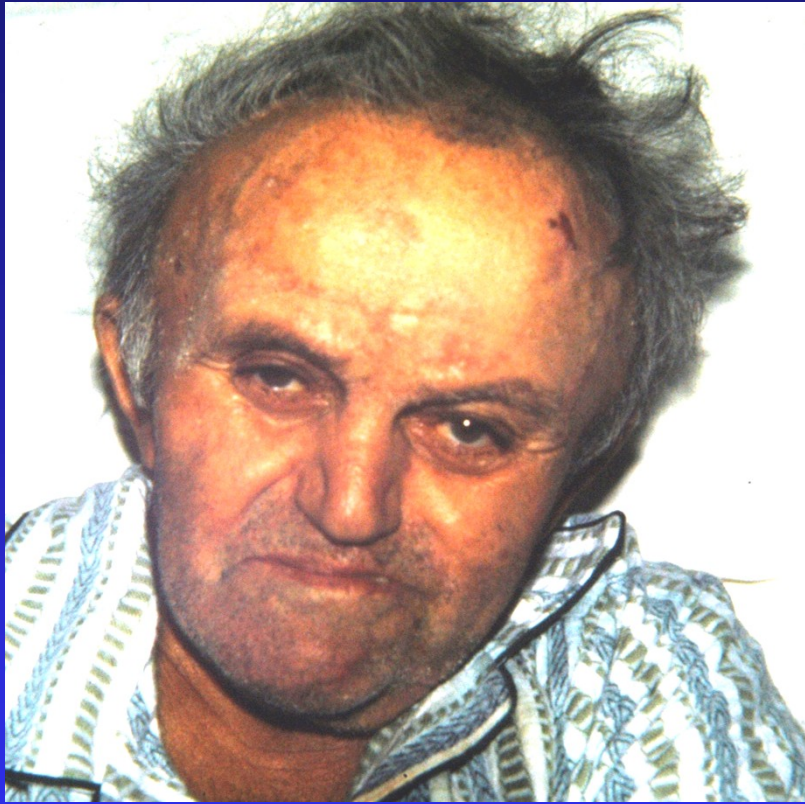


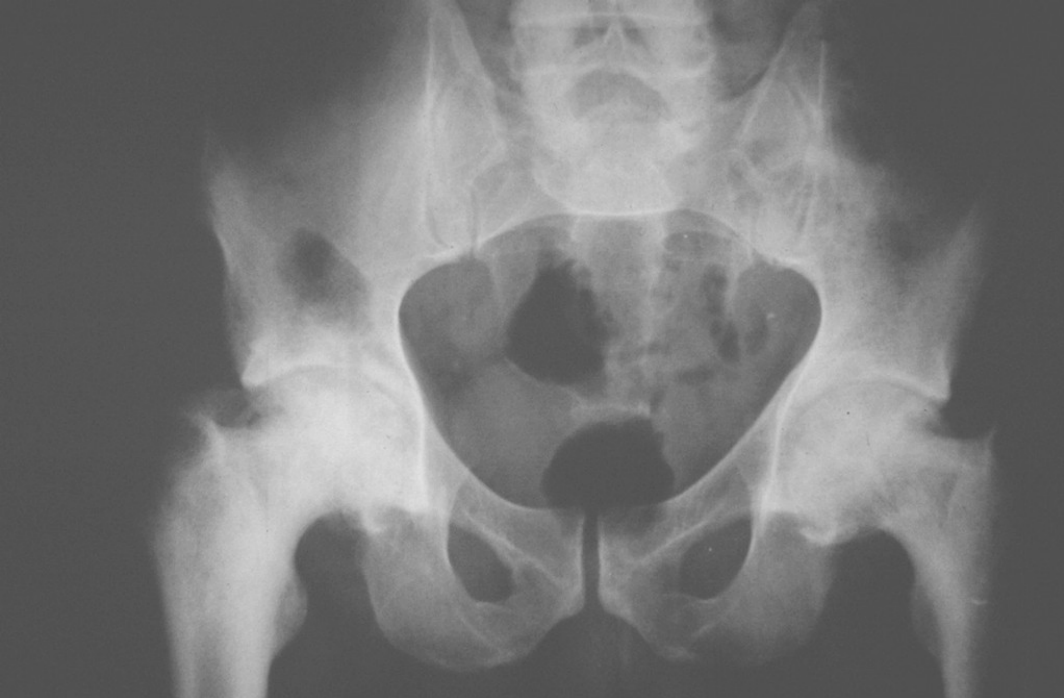
Clinical symptoms

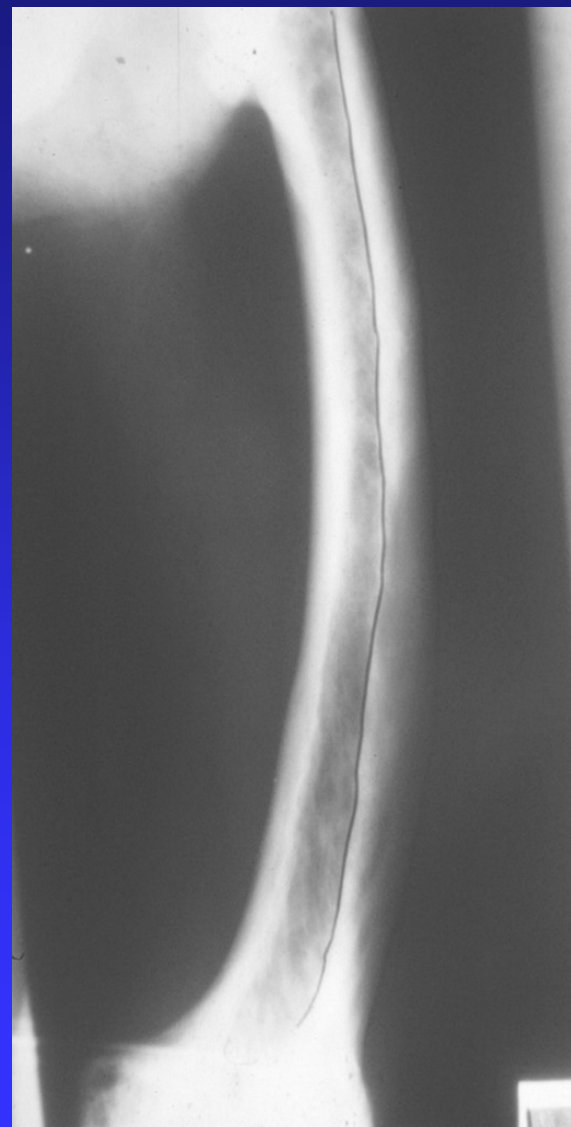
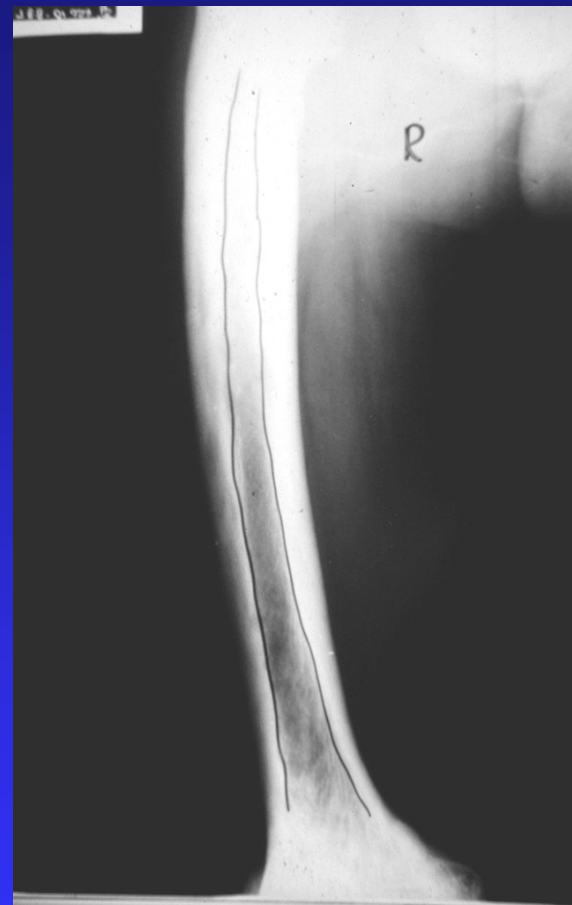
- Mild
- Moderate
- Severe

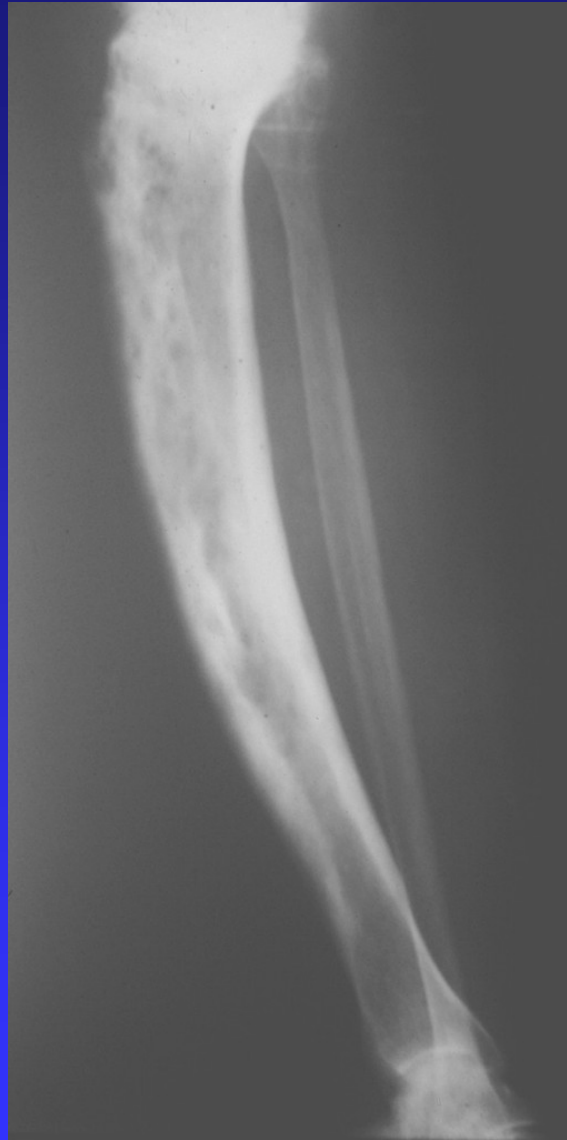
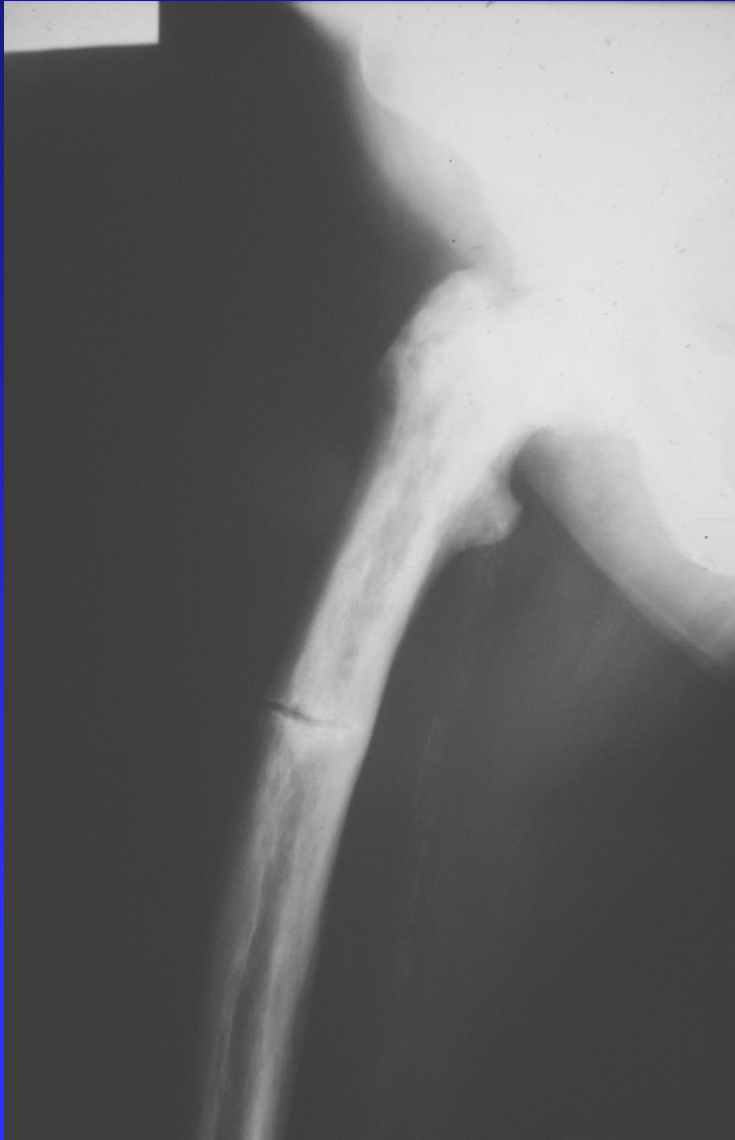


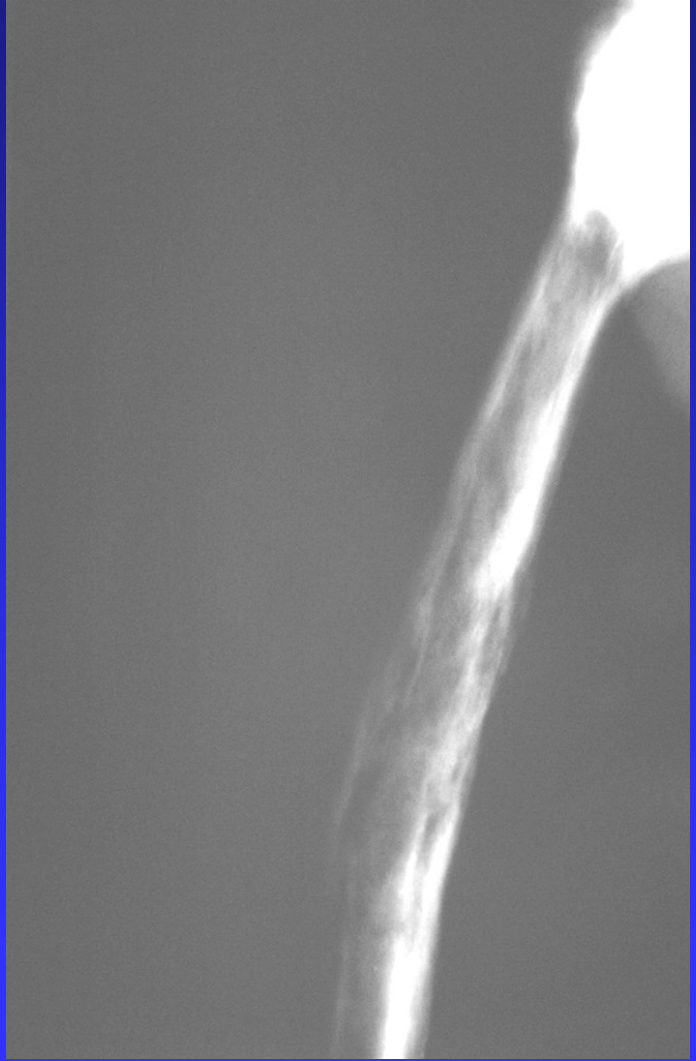
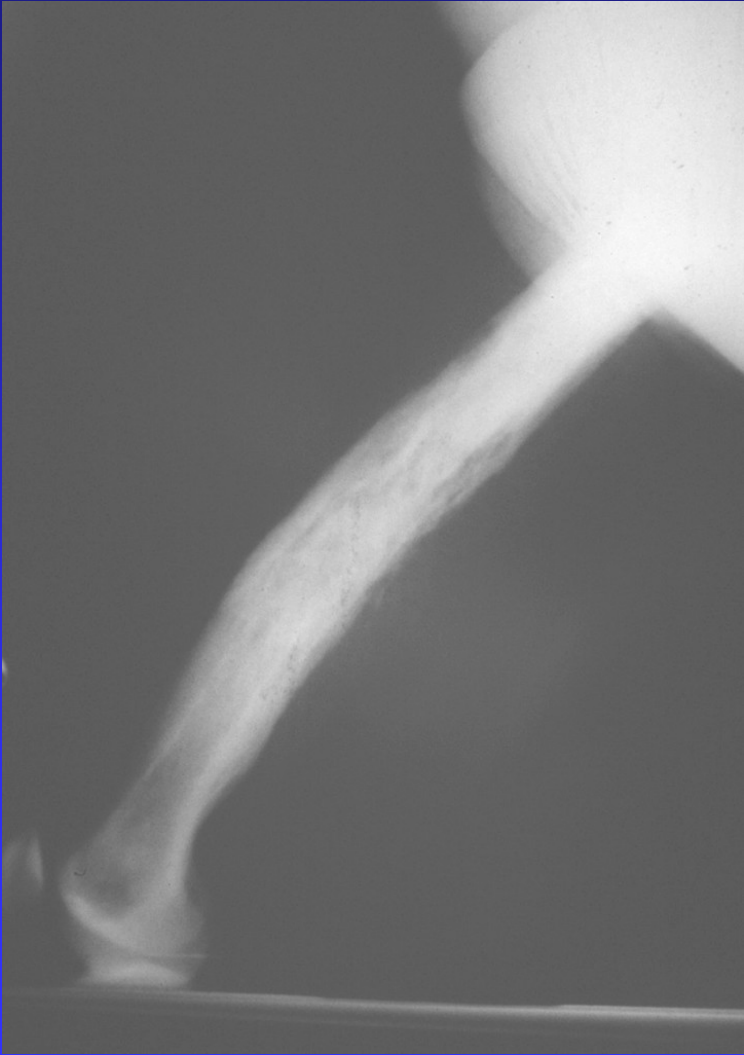














Gothic arch







Complications

Fissures

Fractures

Osteoarthritis

Deafness

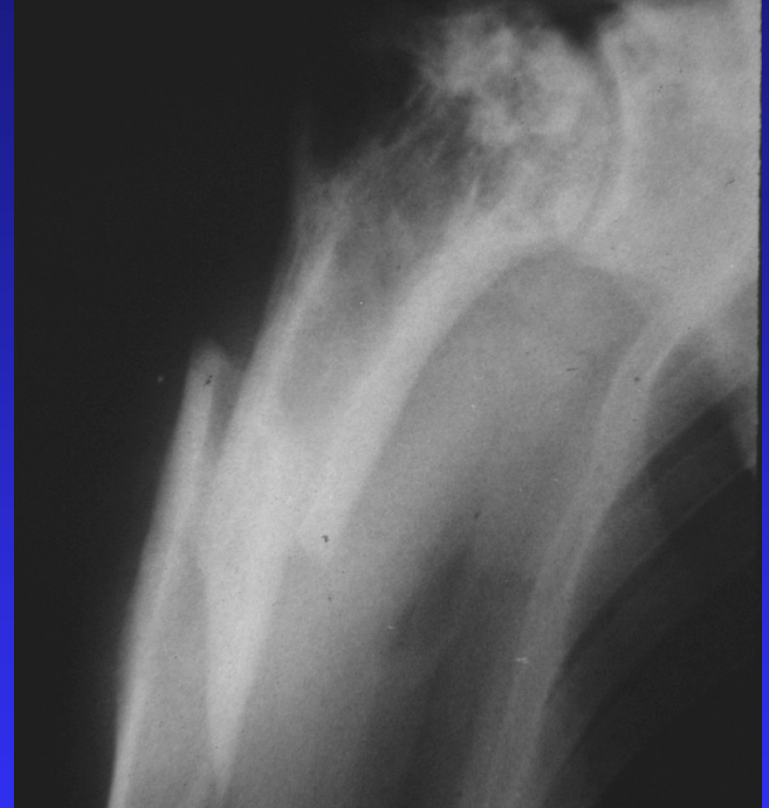
Neuralgia n. trigeminus

Basilar invagination

Vertebrobasilar insufficiency

Paraparesis, sciatica

Dental problems



Complications

Hypertension

Ischemic heart disease

Cardiomegaly

Neoplastic degeneration

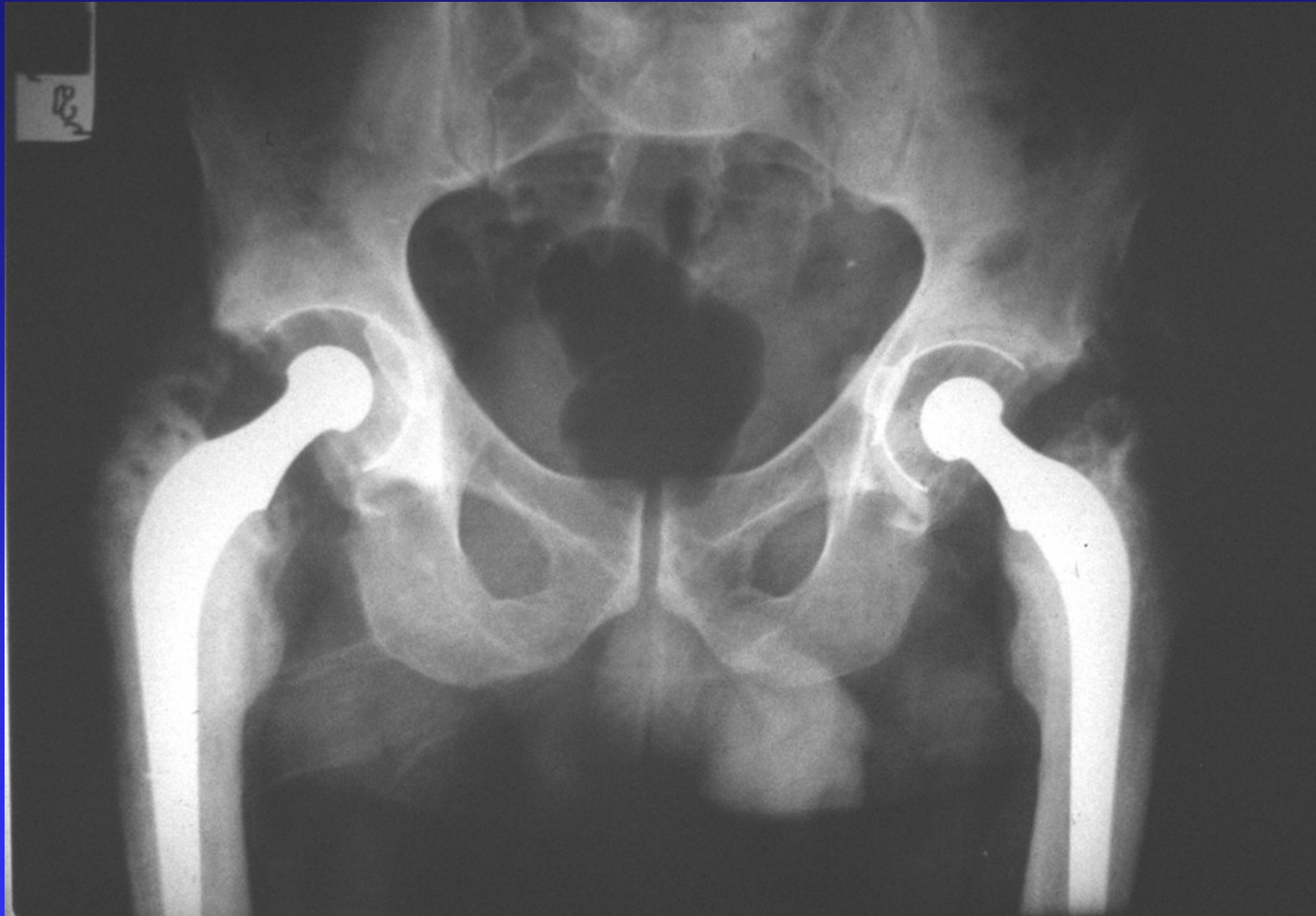
sarcoma

Nephrolithiasis

Calcifications

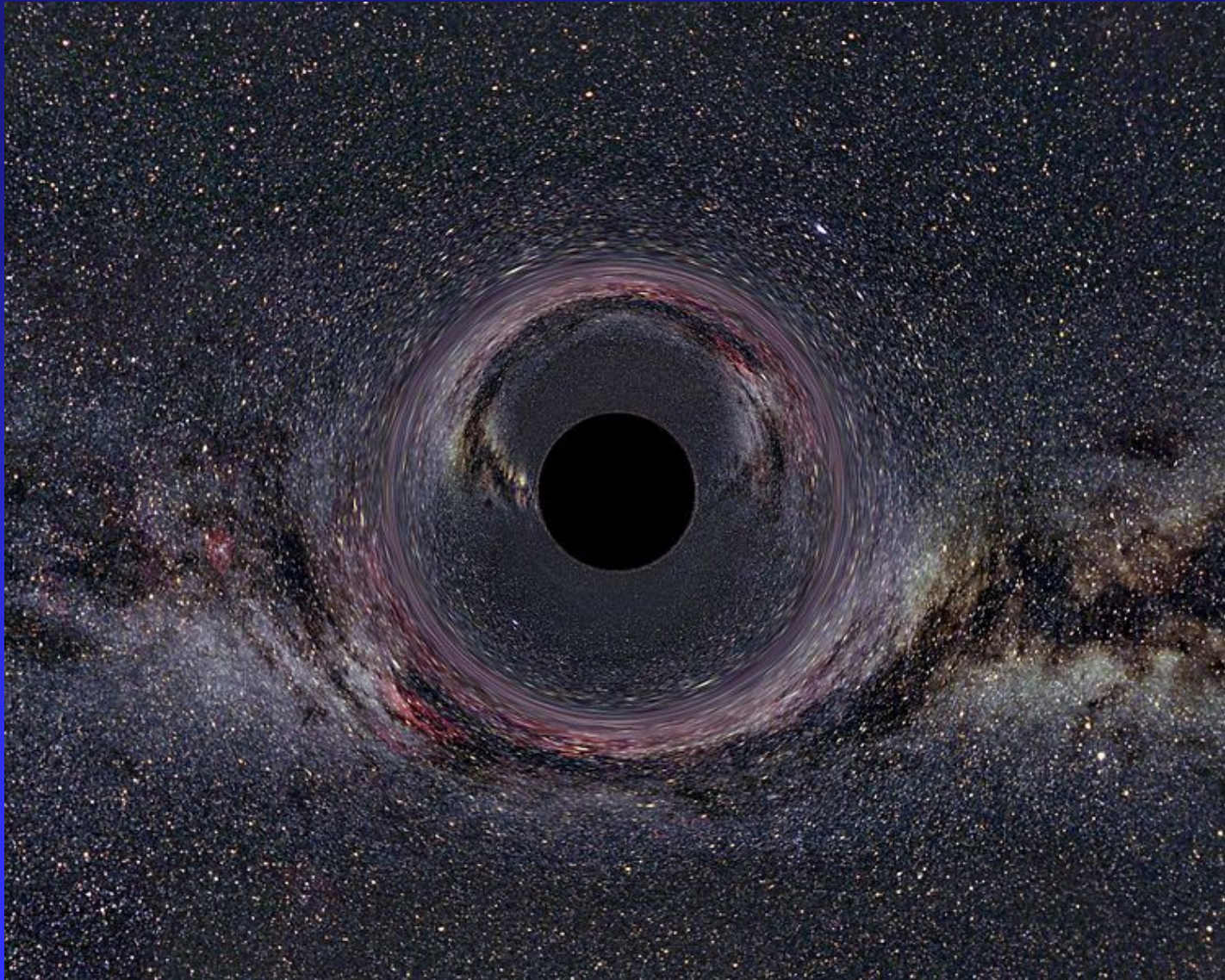
Management

- Bisphosphonates (Fosamax 40 mg daily three months, Pamidronate, Zoledronate)
- Calcium
- Therapy of complications
- Osteosynthesis of fx
- Total knee and hip replacement



Charnley total hip arthroplasty

Thank You for Your attention



Black Hole of the Milky Way