Paraclinicl evaluation secondary osteoporosis

- INTRODUCTION — Osteoporosis is the most common bone disease.

- DEFINITION — Osteoporosis is a skeletal disorder characterized by two elements:

- low bone mass

- and microarchitectural disruption.

Secondary Osteoporosis

- It occurs in

 - 20% to 30% of postmenopausal women

 more than 50% of men

The condition mainly affects premenopausal women or younger men who are not usually targeted in routine screening for osteoporosis.

Secondary Causes of Osteoporosis

Secondary osteoporosis may be due to a large and diverse group of disorders:

- **Lifestyle Factors**

- **Medications**

- **Underlying Diseases**

- **Organ Transplantation**

- **Miscellaneous Causes**

Selected secondary causes of diminished bone density

- Endocrine disorders
  - Cushing's disease, hyperparathyroidism, hyperthyroidism, prolactinoma, hypogonadism
- Celiac disease and other causes of malabsorption
- Vitamin D deficiency
- Hepatic or renal dysfunction
- Genetic disorders, e.g., osteogenesis imperfecta
- Systemic inflammatory disease, e.g., rheumatoid arthritis
- Malnutrition, anorexia nervosa
- Malignancies, e.g., multiple myeloma

Drug causes of osteoporosis

- Glucocorticoids

- Excessive thyroid replacement

- Anticonvulsants

- Gonadotropin agonists(leuprolide….)

- Depot progestational contraceptives

- Heparin   ppi

Corticosteroids-effect on bone
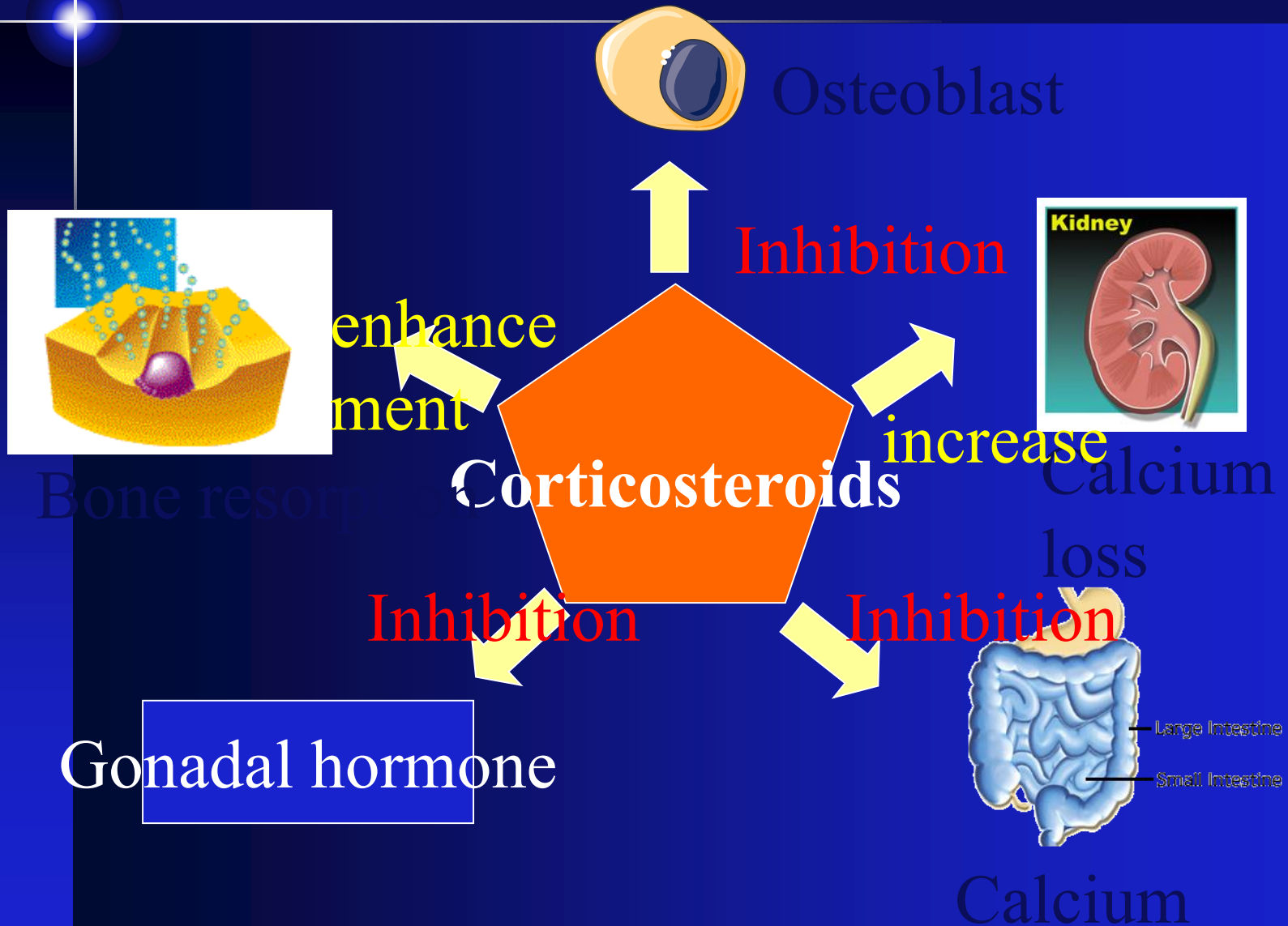
GLUCOCORTICOID-INDUCED OSTEOPOROSIS

- Therapeutic use of glucocorticoids :most common form of glucocorticoid-induced osteoporosis.

- Risk of fractures depends on the dose and duration Bone loss is more rapid during the early months of treatment,

- Trabecular bone is affected more severely than cortical bone.

- As a result, fractures have been shown to increase within 3 months of steroid treatment.

Hormonal regulation of calcium
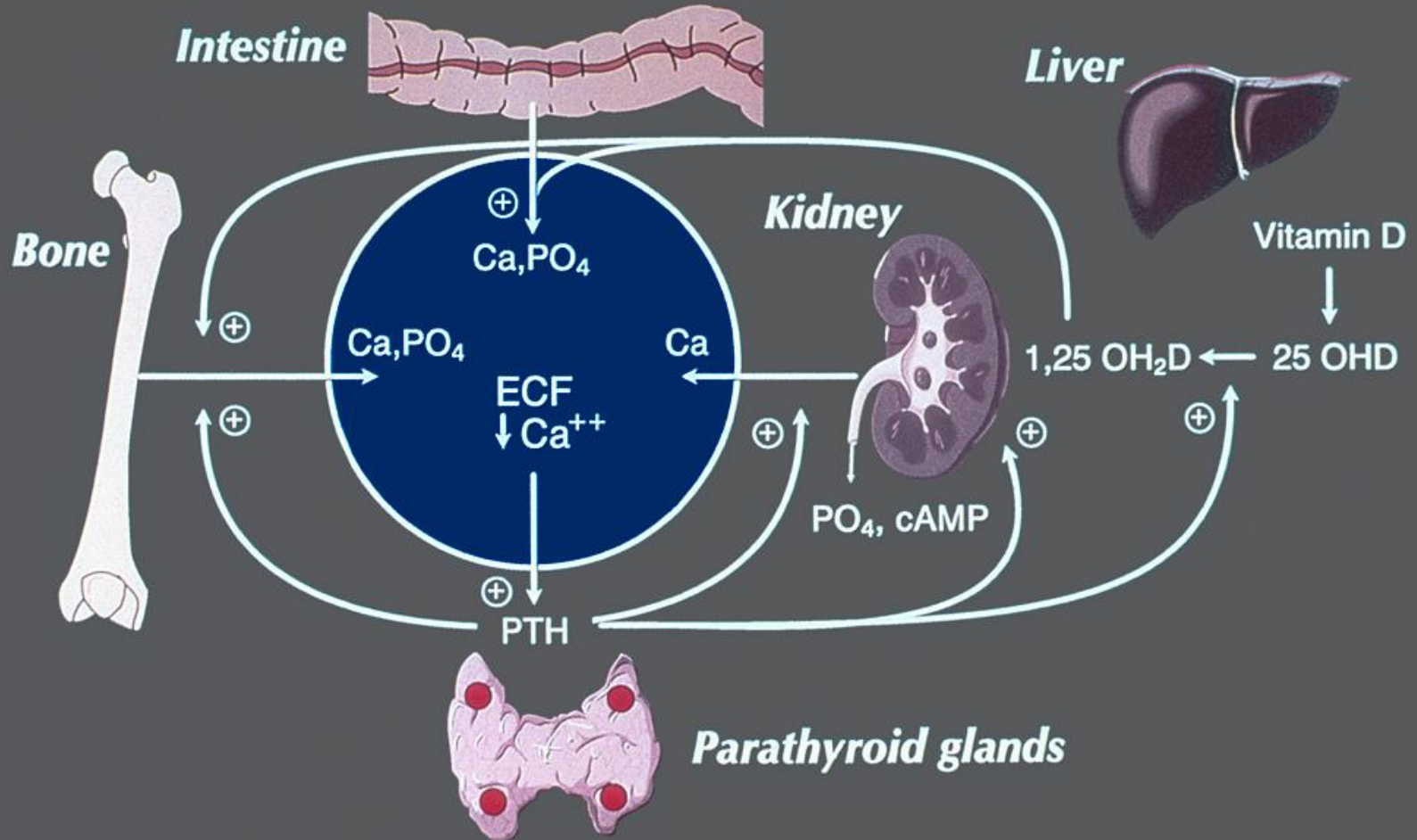
Paraclinicl Secondary Osteoporosis

History&PMH

Laboratory

Biomarker

Xray

DXA

QUS

QCT

Biopsy

Fracture risk assessment tool(FRAX)

SCREENING FOR SECONDARY CAUSES: Recommended Laboratory Tests

Cushing's disease Electrolytes**, 24-hour urinary cortisol**

Hyperthyroidism TSH**, T$_4$**

Hypogonadism Bioavailable testosterone

Multiple myeloma CBC, serum electrophoresis, **urine electrophoresis**

Osteomalacia Alkaline phosphatase**, 25(OH)D**

Paget's disease Alkaline phosphatase

Primary hyperparathyroidism Calcium, PTH

Biochemical Markers in Clinical Use

Marker	Bone formation	Bone resorption

Urine
 	
• **Urinary collagen crosslinks**
   – **Pyridinoline (u-PYD)**
   – **Deoxypyridinoline (u-DPD)**
   – **N-telopeptide crosslinks**
   – **C-telopeptide crosslinks**
		X
		X
		X
		X

Blood • **Bone-specific alkaline phosphatase** • **Osteocalcin** • **Serum collagen crosslinks**	X X X	

OP Biomarkers

- **Derived from cortical and trabecular bone.**

- **Rapid and noninvasive with proven use in therapeutic monitoring rather than diagnosis.**

- **Combined use of BMD measurement and biochemical markers is helpful in risk assessment, especially in those women who are not identified as at risk by BMD measurement alone.**

- **Major disadvantage = most are non-specific and levels are affected by many factors.**

Future Use of Biochemical Markers

- Which patients are suffering from **decreasing bone mass**?

- Is a particular patient at a **high risk** for fracture?

- What treatment would be **best** in a particular patient?

- What is the therapeutic **response level**?

Dual x-ray absorptiometry(DEXA)

- The two photons are emitted from an x-ray tube instead of a radioactive source.

- DXA is the most popular method for measuring bone density at the spine and hip and some times at distal of radious bone.

Indications for Bone Density Testing

Consider BMD testing in the following individuals:

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

- Younger postmenopausal women, women in the menopausal transition and men age 50–69 with clinical risk factors for fracture

- Adults who have a fracture after age 50

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

Dual x-ray absorptiometry(DEXA)

- Strong relationship between fracture risk BMD

- Best available clinical tool for diagnosis

- Tscore(-1to-1.49) follow-up DXA in10 to 15y

- MEN<50y Tscore<-2   evaluation risk

WHY THE WHO CHOSE T = -2.5

- "Such a cutoff value identifies approximately 30% of postmenopausal women as having osteoporosis using measurements made at the spine, hip, or forearm. This is approximately equivalent to the lifetime risk of fracture at these sites."

Image not for diagnostic use
k = 1.139, d0 = 43.5
116 x 150
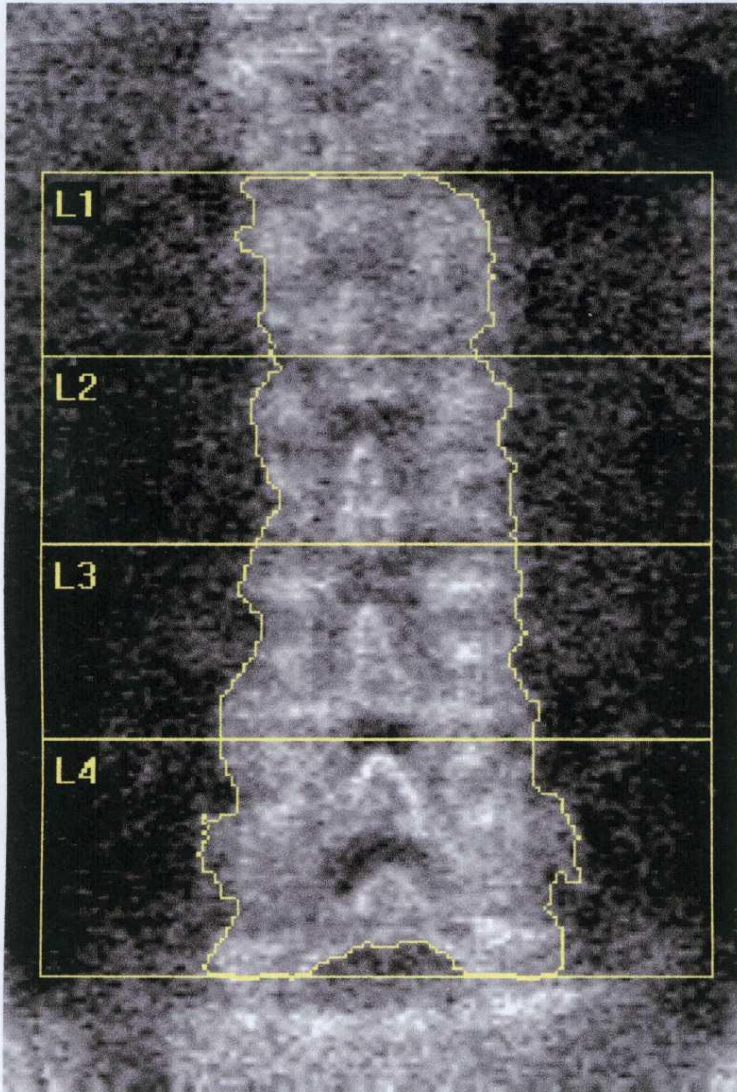
DXA Results Summary:

Region	Area (cm²)	BMC (g)	BMD (g/cm²)	T - Score	Z - Score
L1	13.17	9.12	0.692	-2.9	-1.0
L2	14.83	11.09	0.748	-3.5	-1.3
L3	17.67	15.83	0.896	-2.7	-0.4
L4	24.95	23.23	0.931	-2.7	-0.3
Total	**70.63**	**59.27**	**0.839**	**-2.8**	**-0.6**

Total BMD CV 1.0%, ACF = 1.029, BCF = 0.999, TH = 9.033
WHO Classification: Osteoporosis
Fracture Risk: High

BONE DENSITY MEASUREMENTS AT PERIPHERAL SITES

QUS

DXA

pQCT

ADVANTAGES

- Portable
- Less expensive than central DXA
- Ultrasound does not involve radiation

LIMITATIONS

- Less predictive for hip fracture than hip measurement
- Cannot be used for diagnosis with WHO criteria
- Cannot be used for monitoring (sites less likely to change)

Quantitative computerized tomography (QCT)

- **Advantage:**

  - **Provides real bone density per bone volume (mg/cm3) in the axial as well as the peripheral skeleton with high spatial resolution**

  - **Capacity for separate analysis of the BMD of the trabecular and cortical compartments.**

  - **Provides an accurate measure of trabecular BMD, with NO significant influence of osteophytes)**

QCT

- **With the availability of QCT, there is no need for Bone Bx for diagnosing Osteoporosis.**

- **Disadvantage:**
  - **Delivering a considerable radiation dose if applied to the central skeleton.**

- **Has good diagnostic performance in discriminating fracture among elderly females.**

- **CANNOT be used for diagnostic classification and is NOT clinically useful to monitor the effects of therapy.**

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Ultrasonography

- Potential advantages include:
- **Expense**, portability, and lack of **radiation** exposure.
- Measurements are usually made at the patella **or** calcaneus (heel).
- good predictor of fracture risk especially in pregnancy.

RADIOGRAPHIC FEATURES

- Plain radiographs show detectable changes when bone loss exceeds 30 percent.
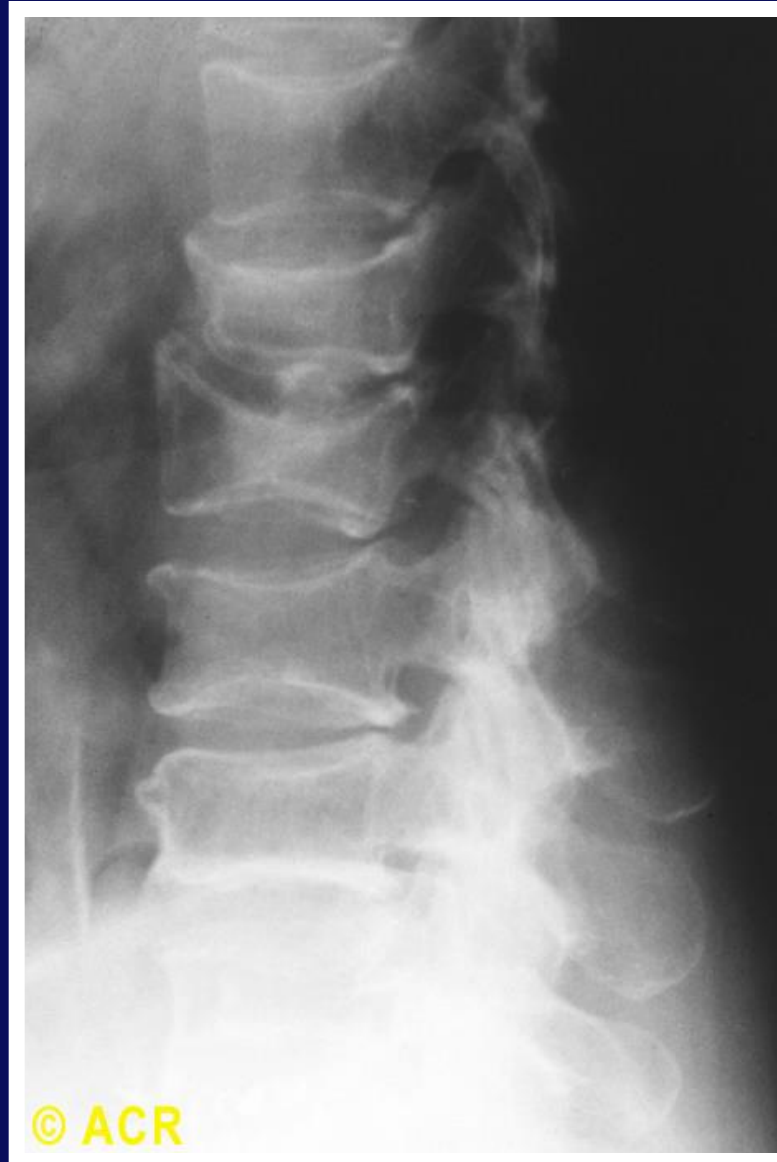
- An early manifestation is "codfish" vertebrae.

Normal

Biconcave (codfishing) deformity

Wedge fracture

Compression fracture

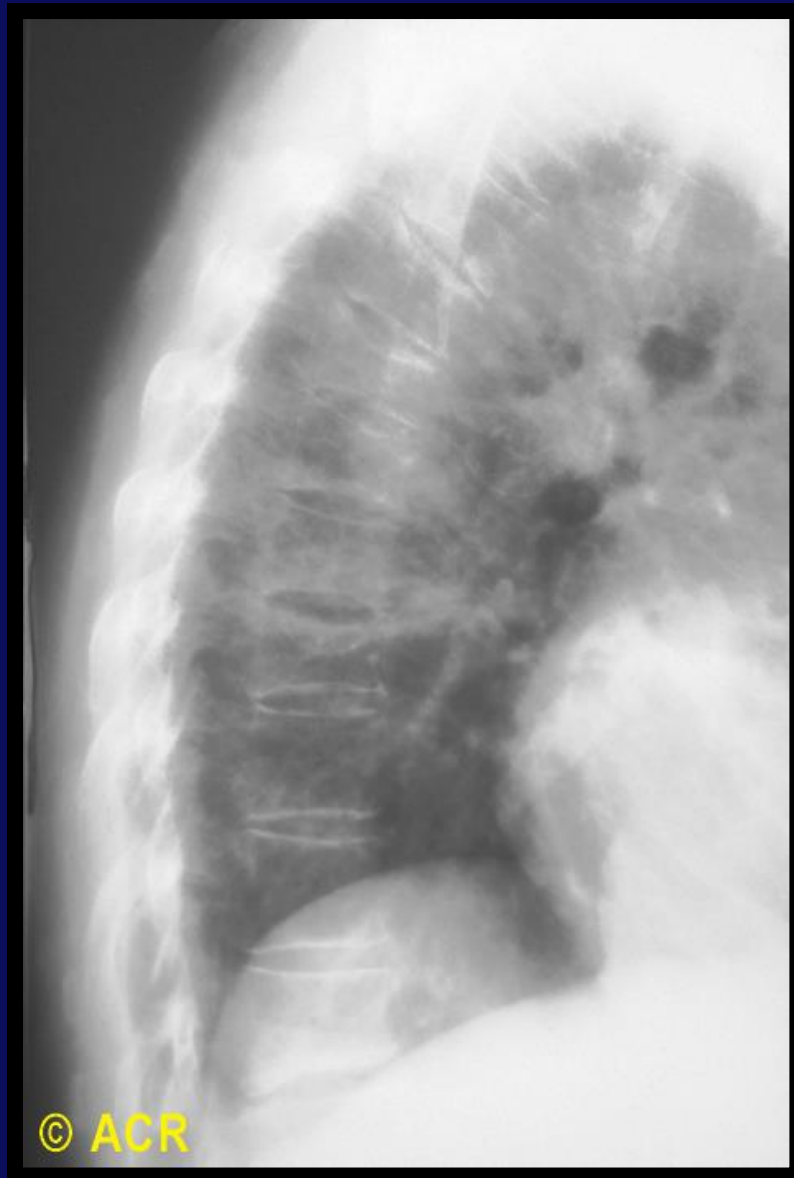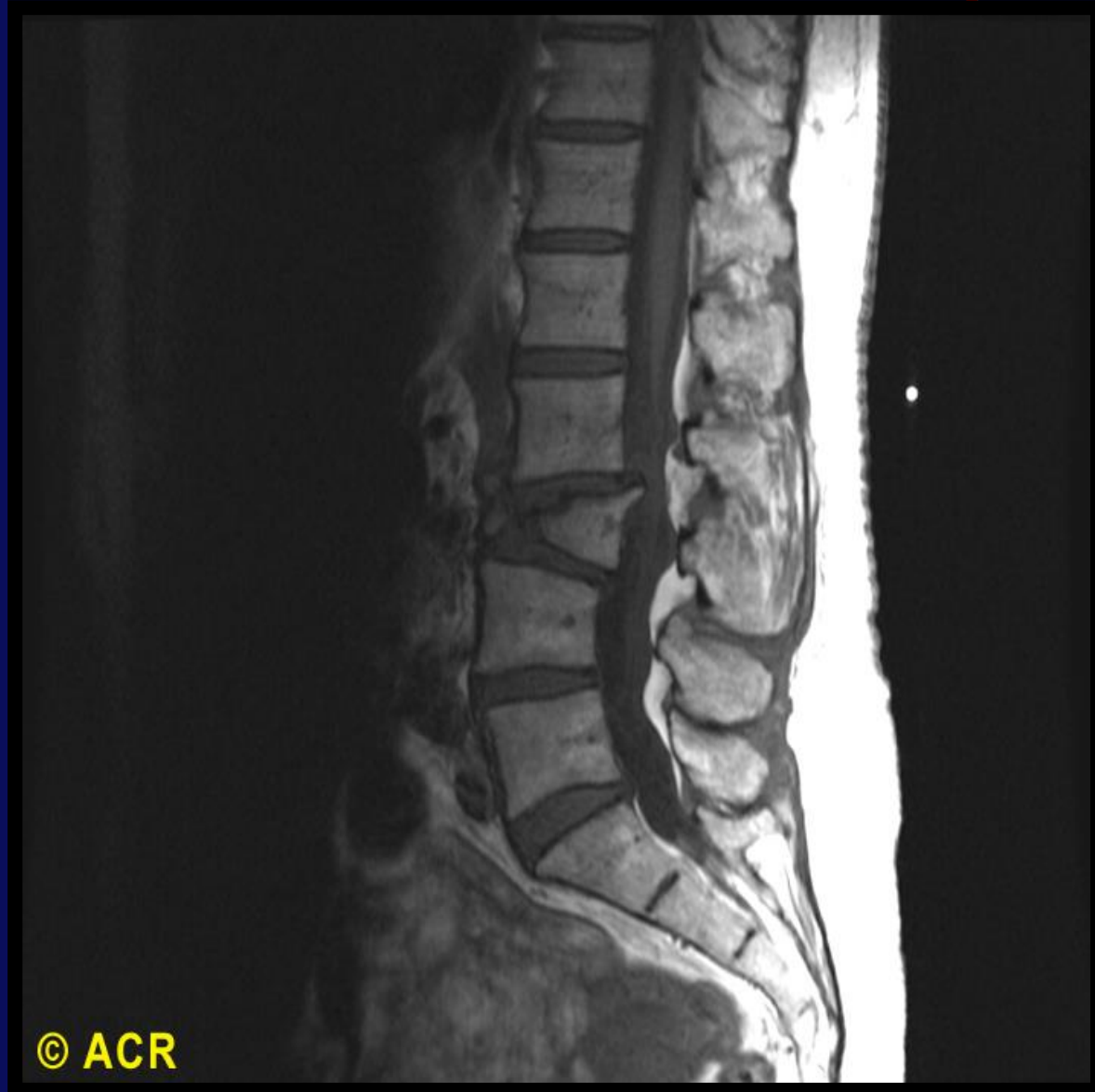# Osteopenia, compression fractures: lumbar vertebrae (radiograph)

Compression fracture: lumbar spine (radiograph)
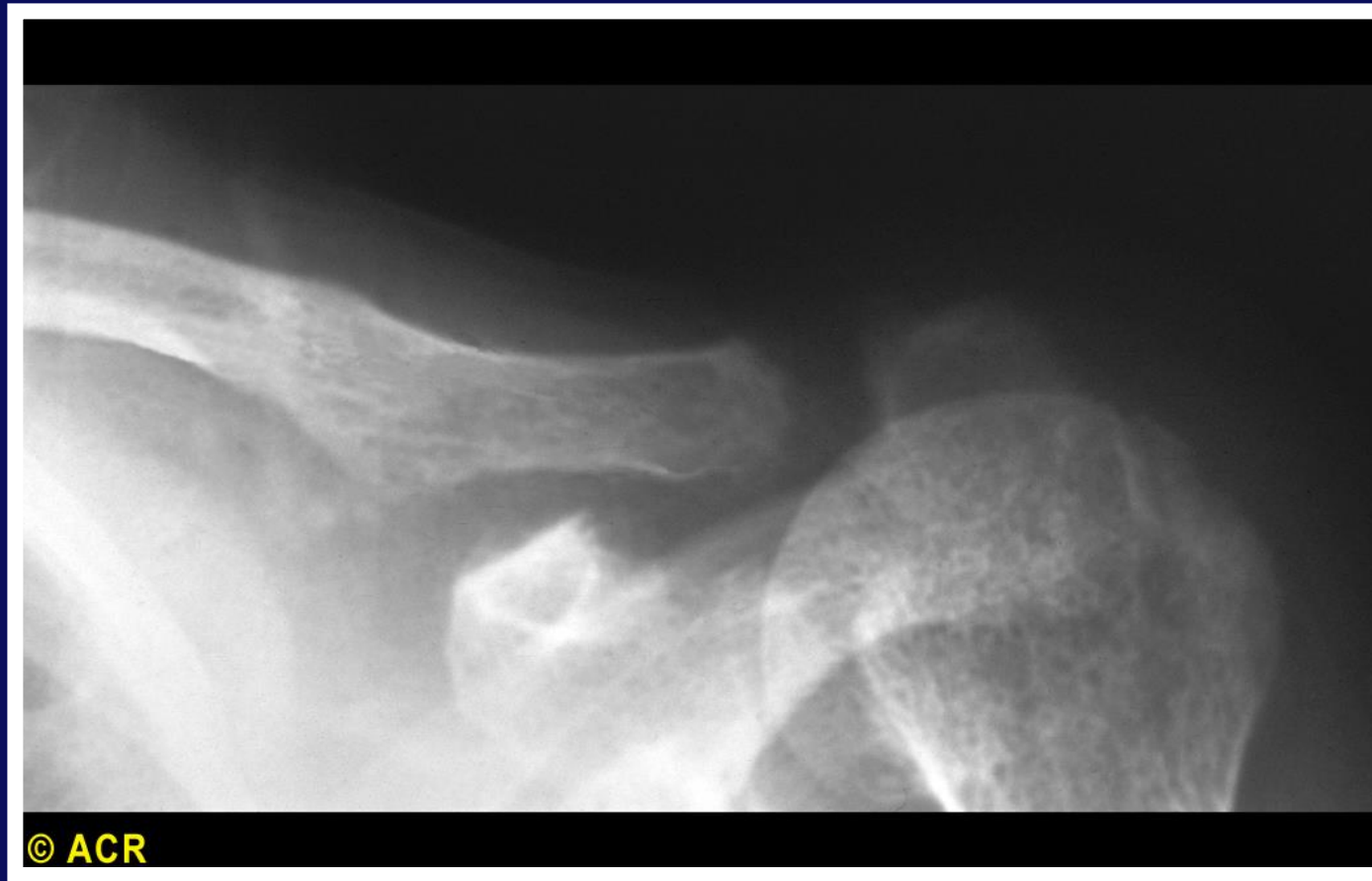
Osteoporotic spine (radiograph)

Compression fracture: lumbar spine (MRI)

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Hyperparathyroidism: clavicular resorption (radiograph)

Cortical resorption of the distal clavicle is present in this patient with secondary hyperparathyroidism due to chronic renal failure

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Hyperparathyroidism: hand (radiograph)

Note that the distal phalanges of the thumb and index finger exhibit subperiosteal bone resorption and acrolysis

Hyperparathyroidism: subperiosteal resorption, finger (radiograph)

Distal tuft and subperiosteal middle phalangeal bone resorption are seen in the right second finger of this patient

with hyperparathyroidism.

Paget's disease of bone: knee (radiograph)

Osteomalacia
Loosers zones

Osteomalacia

1- ca ↓   P = Nl   Alk ph ↑

2- ca = Nl   P ↓   Alk ph ↑

3- ca ↓   P ↓   Alk ph ↑

24 h Urinary ca < 100 mg / 24 h

24 h Urinary Hydroxyproline Excretion ↑

Vitamin D-dependent rickets, type I: spine (radiograph)

Vitamin D-dependent rickets, type I: spine (radiograph)
This lateral view of the thoracic spine of the patient in slide 52 shows the "rugger jersey" spine due to bands of osteosclerosis at the superior and inferior vertebral endplates. This can be seen in rickets as well as renal osteodystrophy and hyperparathyroidism.

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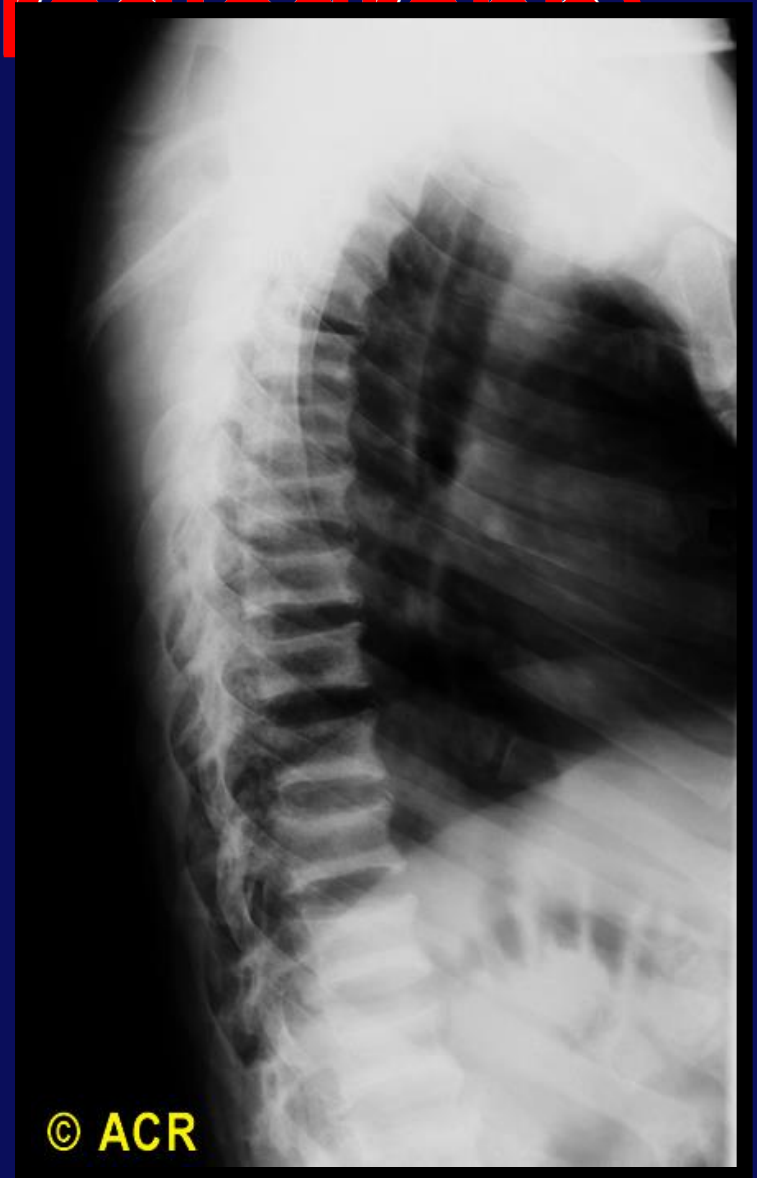
VITAMIN D

- **Severe vitamin D deficiency** causes rickets in children and osteomalacia in adults.
- **vitamin D insufficiency** may be **more** elderly , nutrition, malabsorption, or chronic liver or renal disease.
- **Dark-skinned individuals** are also at high risk of vitamin D deficiency.
- **optimal levels** of serum 25-hydroxy-vitamin D [25(OH)D], levels >20 ng/mL -30 ng/mL).
- most adults requires an intake of 800–1000 units/d,.
- **Vitamin D insufficiency** leads to compensatory secondary hyperparathyroidism and is an important risk factor for osteoporosis and fractures.
- **vitamin D levels decline** during the winter months.
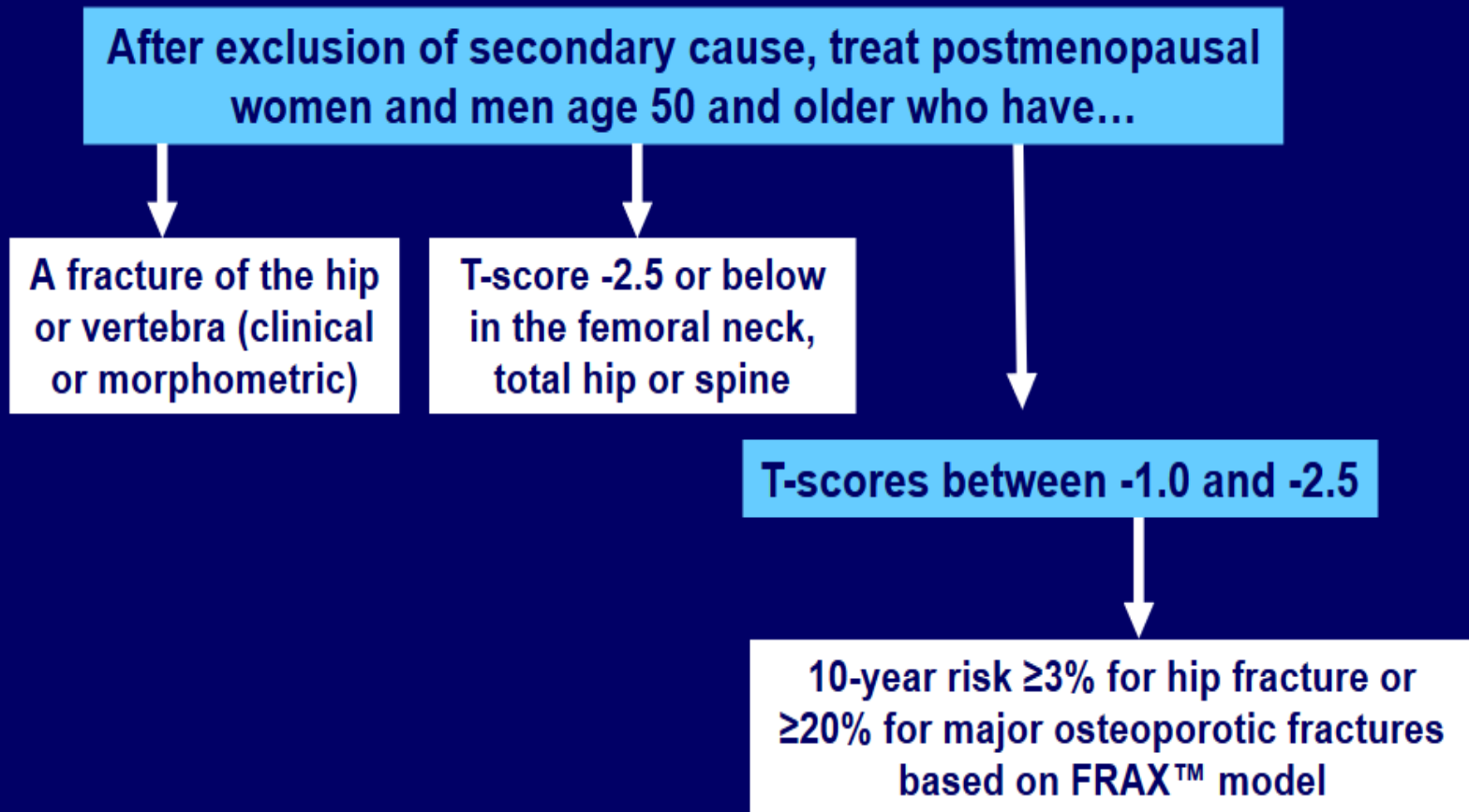
FOR PATIENTS WITH FRACTURE

Remember: not all fractures are due to osteoporosis.

- Consider bone scan if there is equivocal fracture or if fracture might be remote

- Consider MRI or biopsy if fracture might be due to metastatic carcinoma

- Consider MRI if there is question of lateral or posterior displacement

Iliac crest bone biopsy

- Patients with unusual features of osteoporosis
  - men
  - young women
  - patients with very low bone mass
  - patients who have fragility fractures but normal bone mass
- Patients failing conventional therapy

Fracture risk assessment tool(FRAX)

After exclusion of secondary cause, treat postmenopausal women and men age 50 and older who have…

- A fracture of the hip or vertebra (clinical or morphometric)

- T-score -2.5 or below in the femoral neck, total hip or spine

- T-scores between -1.0 and -2.5
  - 10-year risk ≥3% for hip fracture or ≥20% for major osteoporotic fractures based on FRAX™ model

Case

- Man 36y : with paresthesia
- Female 56y : with bone pain and Alkp
- Female 40y : with bone pain and diarrhea
- Man 42 y : cellulits and back pain