

Causes of Hypocalcaemia

Hypoparathyroid	Nonparathyroid	PTH Resistance
Postoperative	Vitamin D deficiency	Pseudo-hypoparathyroidism
Idiopathic	Malabsorption	Hyperproduction of calcitonin (medullary thyroid cancer).
Post radiation	Liver disease	
	Kidney disease	
	Vitamin D resistance	

Hypocalcaemia other causes

Drugs

Furosemide (increases renal excretion).

**Enzyme induced drugs e.g.
Phenytoin (induces hepatic enzymes that inactivate Vit.D).**

Hypoparathyroidism

Commonly occur accidentally after surgical removal of the thyroid gland → Latent or overt **tetany**.

Characterized by hypersensitivity (Low threshold) of nerves and muscles.

Can be demonstrated by two signs:

Chvostek's sign:

Tapping the facial nerve as it emerge from the parotid gland In front of the ear → Contraction of the facial muscles.

Trousseau's sign:

Arresting blood flow to the forearm for few minutes → Flexion of the wrist, thumb and metacarpophalangeal joints.

Hypocalcaemia – Clinical Features

- **Neuromuscular excitability**
- **Paraesthesia (tingling sensation) around mouth, fingers and toes**
- **Muscle cramps, carpopedal spasms**
- **Tetany**
- **Seizures – focal or generalised**
- **Laryngospasm, stridor and apneas (neonates)**
- **Cardiac rhythm disturbances (prolonged QT interval)**
- **Chvostek's and Trousseau's signs – latent hypocalcemia**

Tetanus → ↑ influx of sodium ions at motor neurons and interneurons → ↑ conduction of impulses → reflex muscle contraction causing:

- 1- Spasm of larynx and bronchus → asphyxia and death.**
- 2- Muscle cramps.**
- 3- Coronarospasm (cardiotetanus) → angina → infarction**

Hyperfunction

- hypercalcemia
- hypophosphatemia
- hyperphosphaturia
- osteoporosis
- Accumulation of Calcium in tissues

Hypofunction

- hypocalcemia
- hyperphosphatemia
- hypophosphaturia
- tetanus



Pseudohypoparathyroidism

- **Symptoms and signs**

- Hypocalcemia
- Hyperphosphatemia
- Characteristic physical appearance: short stature, round face, short thick neck, obesity, shortening of the metacarpals
- Autosomal dominant

- **Resistance to parathyroid hormone**

- The patients have normal parathyroid glands, but they fail to respond to parathyroid hormone or PTH injections

- **Symptoms begin in children of about 8 years**

- Tetany and seizures
- **Hypoplasia** of dentin or enamel and delay or **absence** of eruption occurs in 50% of people with the disorder

- **Treatment: vitamin D and calcium**

Pseudohypoparathyroidism

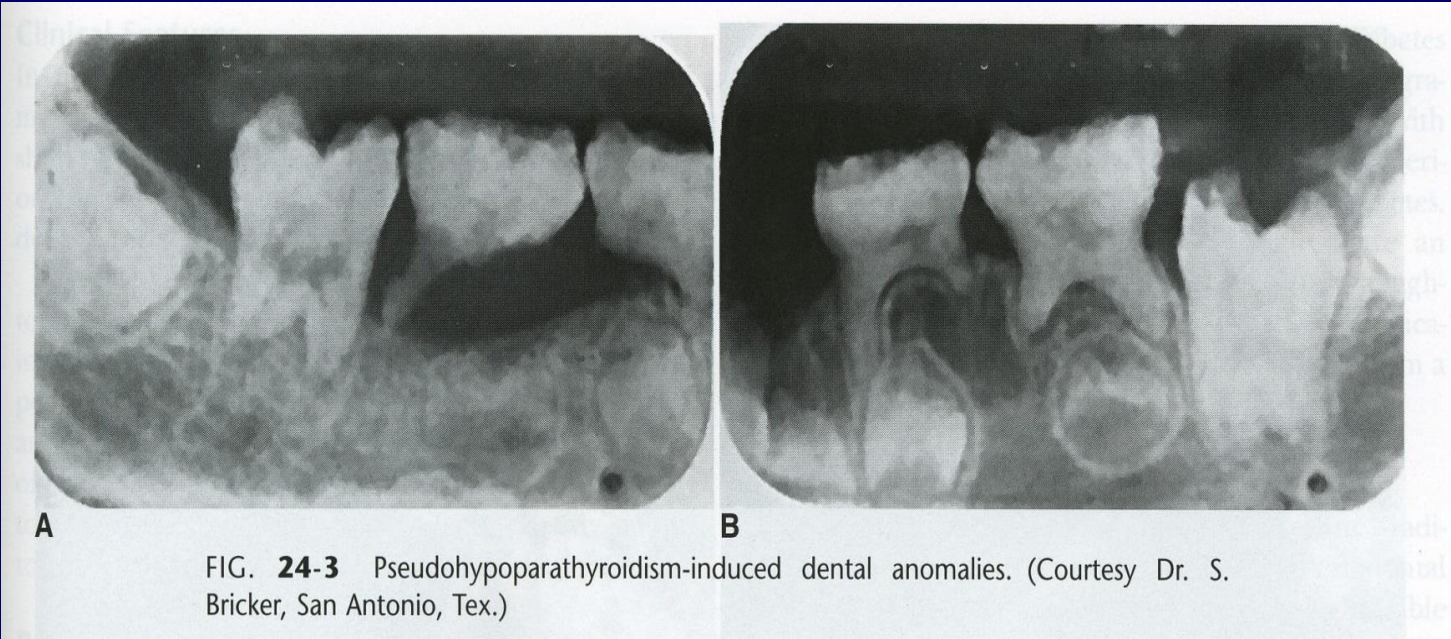
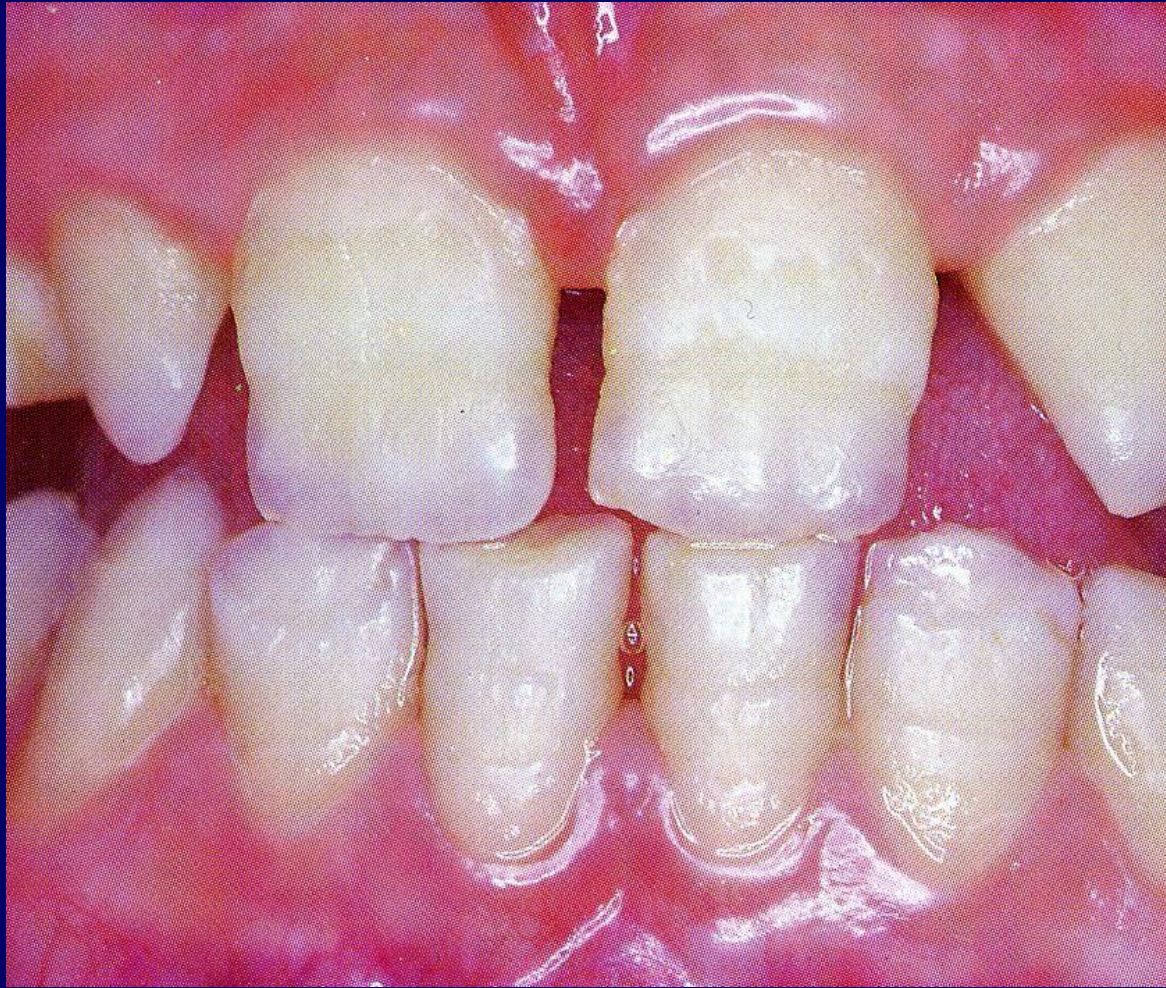


FIG. 24-3 Pseudohypoparathyroidism-induced dental anomalies. (Courtesy Dr. S. Bricker, San Antonio, Tex.)

**Short stature,
enamel hypoplasia**

Congenital Hypoparathyroidism



- Hypoplasia of the teeth, shortened roots, and retarded eruption

Case Study

- A 27 years old man presents to his physician 3 weeks after his thyroid surgically removed for a thyroid cancer.
- However, since he went home from the hospital, he noticed painful, involuntary muscular cramping.
- He also felt numbness and tingling around his mouth & in his hands and feet. His parents said that he was irritable for the last 2 weeks.
- He is on levothyroxine medication.

On examination

- He has a well-healing thyroidectomy scar & no palpable masses in the thyroid bed .
- Blood pressure cuff inflated above the systolic pressure induces involuntary muscular contracture in the ipsilateral hand after 60 seconds (Trousseau`s sign(
- Tapping on the face interior to the ears cause twitching in the ipsilateral corner of the mouth (**Chevostek`s sign**)

Lab Investigations:

Calcium: 5.6 mg/dl (N: 8.5 – 10.2)

Albumin: 4.1 g/dl (N: (3.5 – 4.8)

PTH: < 1 pg/ml (N: 11- 54)

DIAGNOSIS

The parathyroid glands were removed during thyroidectomy



PTH undetectable



Hypocalcemia



Clinical Manifestations of hypocalcemia
(increased reflexes & muscular cramping)

ETIOLOGY OF HYPERCALCEMIA

- **Increased GIT absorption:**
 - Vitamin D excess
 - Elevated PTH
- **Decreased urinary excretion:**
 - Thiazide diuretics
- **Increased loss from bone:**
 - Elevated PTH
 - Hyperparathyroidism
 - Malignancy (some lung cancers)

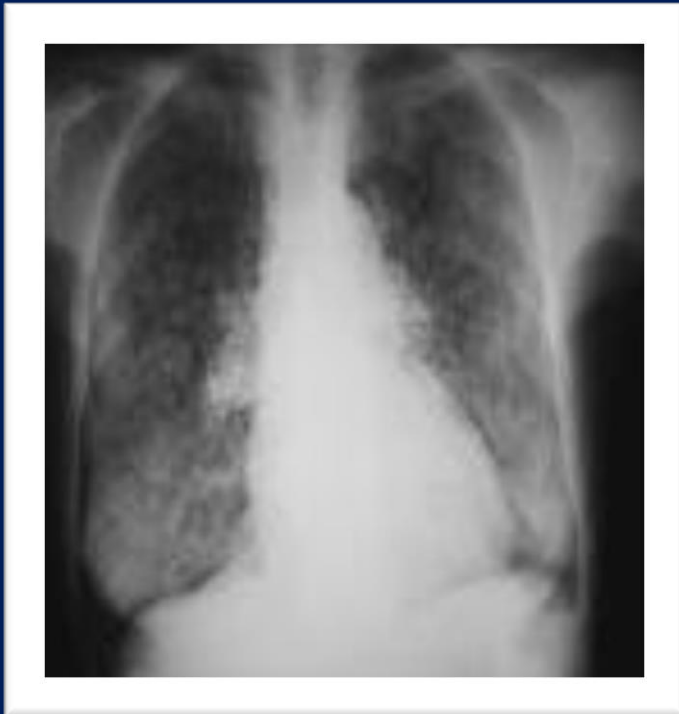
 - Osteolytic metastases

Hyperparathyroidism

- The disorder is characterized by hypercalcemia, hypercalcuria, hypophosphatemia, and hyperphosphaturia
- Parathyroid hormone causes phosphaturia and a decrease in serum phosphate
- Calcium rises and it is also secreted in the urine
- Most common complication are renal stones made of calcium phosphate
 - Stone chemistries: calcium, phosphate, urate
- Most serious complication is the deposition of calcium in the kidney tubules resulting in impaired renal function

COMPLICATION:

- **Metastatic calcification**
- **Renal stones**



Hypercalcemia

The quantity of calcium in blood more than 2.6 mmol/L

Causes:

- Hyperparathyroidism and Malignant neoplasms account for majority of hypercalcemia
- Neoplasms most frequently associated with hypercalcemia:
Breast cancer, lung cancer and multiple myeloma
- Most hypercalcemias in malignancy are caused by humoral hypercalcemia of malignancy (**↑PTHrP**).
- Single **adenomas** of the parathyroid gland account for **75%** of primary hyperparathyroidism associated with hypercalcemia.

Parathyroid Hormone related Peptide (PTHrP)

- Can activate the PTH receptor
- Plays a physiological role in lactation, possibly as a hormone for the mobilization and/or transfer of calcium to the milk
- May be important in fetal development
- May play a role in the development of hypercalcemia of malignancy
 - **Some lung cancers are associated with hypercalcemia**
 - **Other cancers can be associated with hypercalcemia**

Clinical Manifestations of Hypercalcemia

- “Stones”
- “Bones”
- “Abdominal moans”
- “Psychic groans”
- Neuromuscular
- Cardiovascular
- Other

Clinical Manifestations of Hypercalcemia

- **Renal “stones”**
 - **Nephrolithiasis**
 - **Nephrogenic DI: polydipsia and polyuria**
 - **Dehydration**
 - **Nephrocalcinosis**

Clinical Manifestations of Hypercalcemia

Skeleton “bones”

- Bone pain, arthralgias
- Osteoporosis of cortical bone such as wrist
- In primary hyperparathyroidism:
Subperiosteal resorption, leading to osteitis fibrosa cystica with bone cysts and brown tumors of the long bones

Clinical Manifestations of Hypercalcemia

- **Gastrointestinal “abdominal moans”**
 - Nausea, vomiting
 - Anorexia
 - weight loss
 - Constipation
 - Abdominal pain
 - Pancreatitis
 - Peptic ulcer disease

Clinical Manifestations of Hypercalcemia

- **“Psychic groans”**
 - Impaired concentration and memory
 - Confusion, stupor, coma
 - Lethargy and Fatigue

Clinical Manifestations of Hypercalcemia

- **Neuromuscular**

- Reduced neuromuscular excitability and muscle weakness
- Easy fatigability and muscle weakness more common in hyperparathyroidism than other hypercalcemic conditions

- **Clinical features of hyperparathyroid myopathy:**

- Proximal muscle weakness, wasting and mild nonspecific myopathic features on electromyogram and muscle biopsy

Clinical Manifestations of Hypercalcemia

- **Cardiovascular**
 - Shortened QT interval on electrocardiogram
 - Cardiac arrhythmias
 - Vascular calcification

Clinical Manifestations of Hypercalcemia

- **Other**

- Itching

- Keratitis

- Conjunctivitis

- Corneal calcification, band keratopathy

- Carpal tunnel syndrome has occasionally been associated with hyperparathyroidism

CASE REPORT

A 59 year old woman with a past medical history significant for hypertension who comes for a routine clinic visit. She initially states that she has no symptomatic complaints, but later in the interview describes chronic fatigue and a mildly depressed mood. Her exam is unremarkable. She used thiazide diuretics as treatment for hypertension, Labs results showed:

(normal ~ 8.5-10.2
mg/dL)

(normal ~ 2.0-4.3
mg/dL)

(normal ~ 3.5-5.0 g/dL)

(normal ~ 10-60
pg/mL)

Creatinine – 1.2 mg/dL

Calcium (total) – 11.9 mg/dL

Phosphate – 1.8 mg/dL

Albumin – 3.8 g/dL

PTH – 124 pg/mL

Metabolic Diseases of Bones

RICKETS

Normal formation of the collagen matrix

BUT

Incomplete mineralization (poor calcification)



Soft Bones



CLINICALLY: Bone Deformity (Rickets**)**

OSTEOMALACIA

Demineralization (poor calcification) of preexisting bones



CLINICALLY: More Susceptibility to Fracture

➤ **Rickets :**

is a softening of bones in children potentially leading to fractures and deformity. The predominant cause is a vitamin D deficiency, lack of calcium in the diet may also leads to rickets

(bow-legged) due to weight bearing on the legs.



➤ **Osteomalacia :**

is the softening of the bones due to defective bone mineralization It may show signs as diffuse body pains, fragility of the bones. A common cause of the disease is deficiency in vitamin D, which is normally obtained from the diet and/or sunlight exposure

Rickets



Child with Rickets

Vitamin D-resistant rickets

A deficiency of renal 1α -hydroxylase enzyme produces **vitamin D-resistant rickets**

- Sex linked gene on the X chromosome
- Teeth may be hypoplastic and eruption may be retarded

Vitamin D-Resistant Rickets

- Above: Hypoplastic teeth
- Below: Minimal caries can produce pulpitis; periapical abscesses are thus common
- Lack 1α -hydroxylase in kidney
- Rx: Respond well to 1, 25-dihydroxy vit. D₃



Renal Rickets Renal Osteodystrophy

In Chronic Renal Failure



Low activity of Renal 1α -hydroxylase



Decreased ability to form the
active form of vitamin D

(1, 25 DHCC will be low)

Treatment: 1,25 DHCC (Calcitriol)

Vitamin D deficiency

Childhood

Rickets

- Bony deformity e.g. bowing of long bones
widening of cartilage at growth plate
- Bone pain
- Weakness



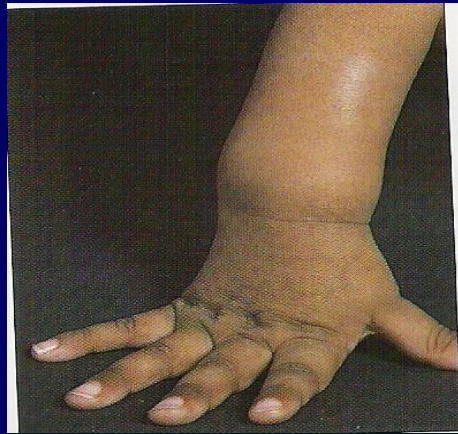
Before



After vit D



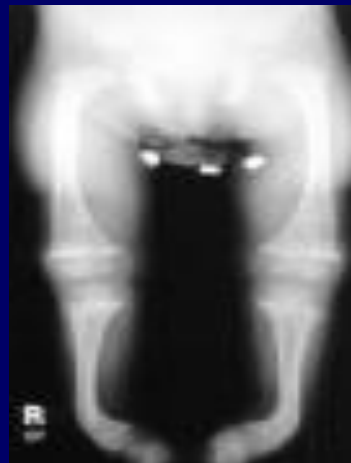
Images of Rickets



Wrist expansion: cupping and fraying of hypertrophied metaphyseal plate



Rachitic Rosary



Bone demineralization and deformity



Osteomalacia

- After closure of epiphyseal plates
- Impaired mineralization
- Fractures
- Lab tests
 - Low calcium & phosphate
 - High ALP
- X-rays
 - Looser's zones → Fractures

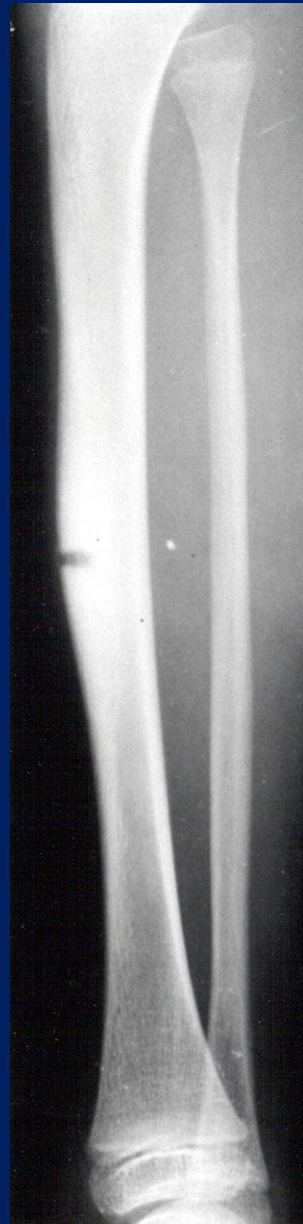
Vitamin D deficiency



Adulthood

Osteomalacia

- Bone pains
- Proximal myopathy
- Fractures e.g. through Looser's zones



Associated Clinical Conditions

- **Muscle Weakness and Falls**
 - **Proximal muscle weakness**
 - **Chronic muscle aches**
 - **Myopathy**
 - **Increase in falls**

Recent studies suggest that vitamin D supplementation at doses between 700 and 800 IU/d in a vitamin D-deficient elderly population can significantly reduce the incidence of falls.

At-Risk Groups

- **Elderly**
 - **Stores decline with age**
 - **Winter**
 - **House-bound or institutionalized**
 - **Poor nutritional intake**
 - **Impaired absorption**
 - **Chronic kidney disease**

Conclusion

- **Commoner than we think!**
- **Can be prevented:**
 - **Promote awareness, especially in high-risk groups**
 - **Sun-exposure**
 - **Safe, 10-15 minutes per day (longer with darker skin)**
 - **Adequate intake of fortified products in diet**

Laboratory Investigations for the Diagnosis of Rickets & Osteomalacia

Investigations to confirm the diagnosis of rickets:

- ↓ Blood levels of 25-hydroxycholecalciferol (25 HCC)
- ↓ Blood calcium ,(hypocalcemia)
- ↑ Blood Alkaline phosphatase (ALP)

Osteoporosis

- **Most prevalent metabolic bone disease in adults**
- It means **reduction in bone mass**.
i.e. bone matrix composition is normal, but it is reduced.
- **Typically silent** (without symptoms) until it leads to **fracture** at a minimal trauma.
Most affected: **vertebral compression** (may be asymptomatic) & **hip fractures** (requires surgery in most cases).
- **Post-menopausal** women lose more bone mass than men
)primary osteoporosis(

How does look osteoporotic patient



Osteoporosis



Fig. 2 **Crush fractures of vertebral bodies in a patient with osteoporosis.**

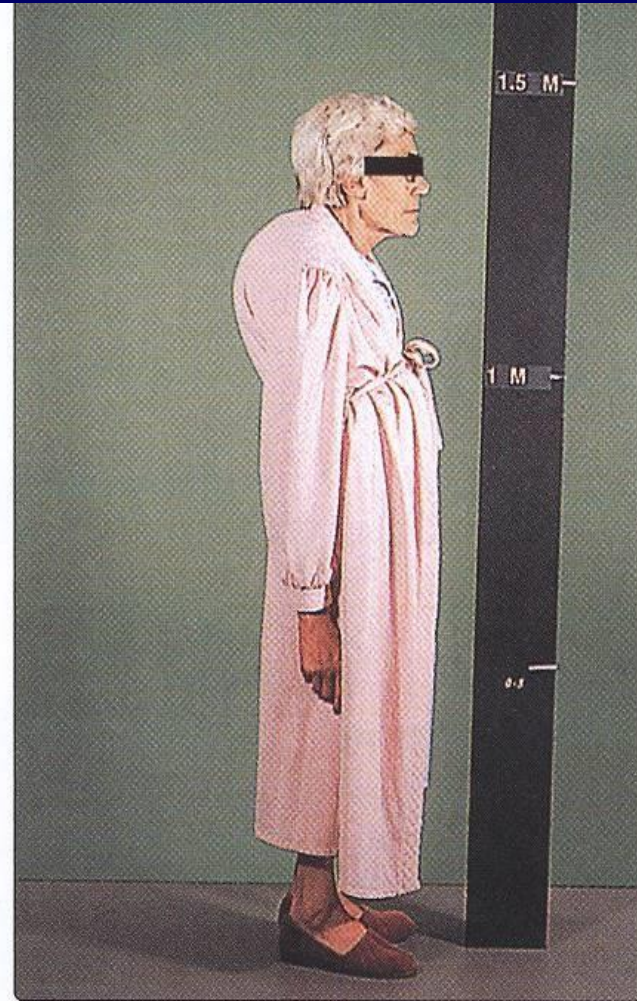
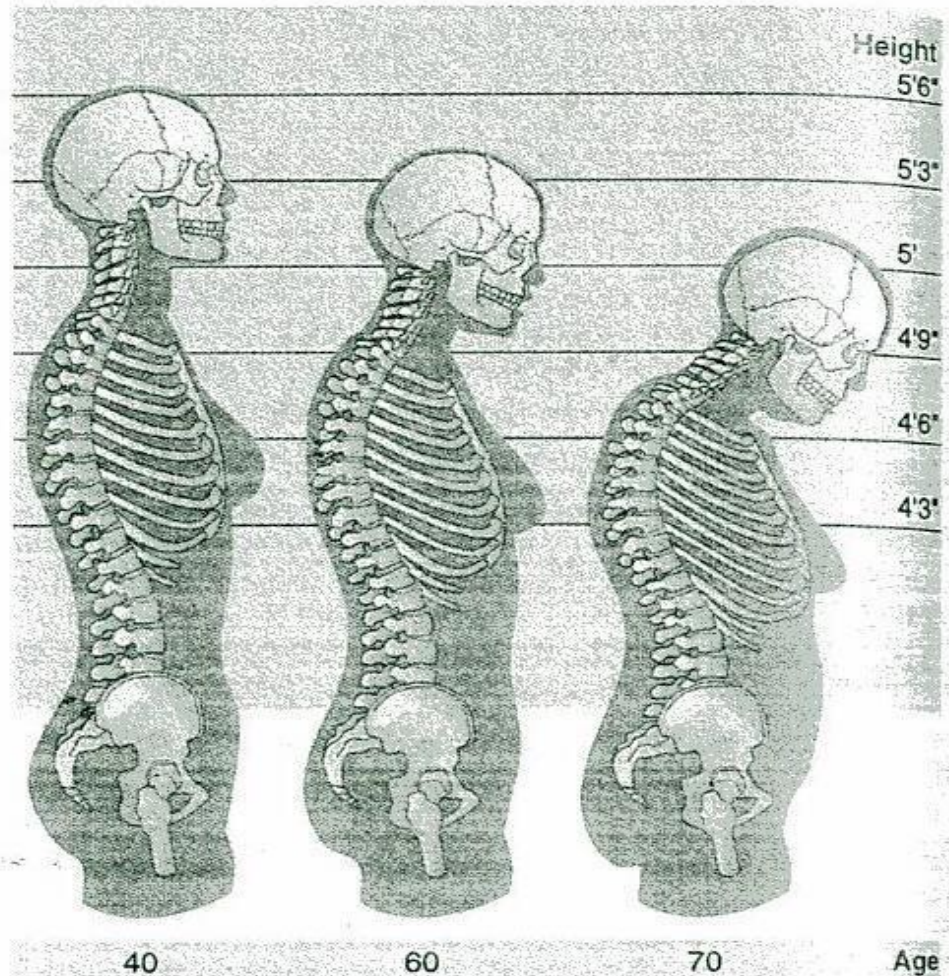


Fig. 3 **Elderly woman with so-called 'Dowager's hump' from collapsed vertebrae due to osteoporosis.**

Sequelae of Osteoporosis



- Normal spine at 40 years of age and osteoporotic changes at 60 and 70 years of age. These changes can cause a loss of as much as 6 to 9 inches in height and result in the so-called dowager's hump (*far right*) in the upper thoracic vertebrae. (From Ignatavicius D, Bayne MV: *Medical-surgical nursing: a nursing process approach*, Philadelphia, 1991, WB Saunders.)



Radiology of hyperparathyroidism

Secondary Osteoporosis Risk Factors

Risk Factors for osteoporosis:

- **Advanced age (esp. in females)**
- **Certain Drugs**
- **Family history of osteoporosis or fractures**
- **Immobilization**
- **Smoking**
- **Excess alcohol intake**
- **Cushing's syndrome**
- **Long term glucocorticoids therapy**
- **Hyperparathyroidism**
- **Hyperthyroidism**
- **Vitamin D disorders**
- **Certain malignancies**

Treatment

- **Exercise, activity**
- **Calcium intake should be 1000-1500 mg/day**
 - Males and females should take in 1000-1500 mg/day
 - All adults greater than 65 years should take 1500 mg/day
 - Three glasses of milk or three cups of yogurt per day provide 1000-1500 mg/day
- **Estrogen treatment**
 - Estrogen inhibits osteoclastic activity
 - Estrogen may increase the incidence of breast cancer, heart attacks, stroke, blood clots
 - That it may exacerbate cardiovascular disease is controversial