
International Foundation for Pediatric Imaging Aid

Pediatric metabolic bone diseases

Classification and overview of clinical and radiological findings

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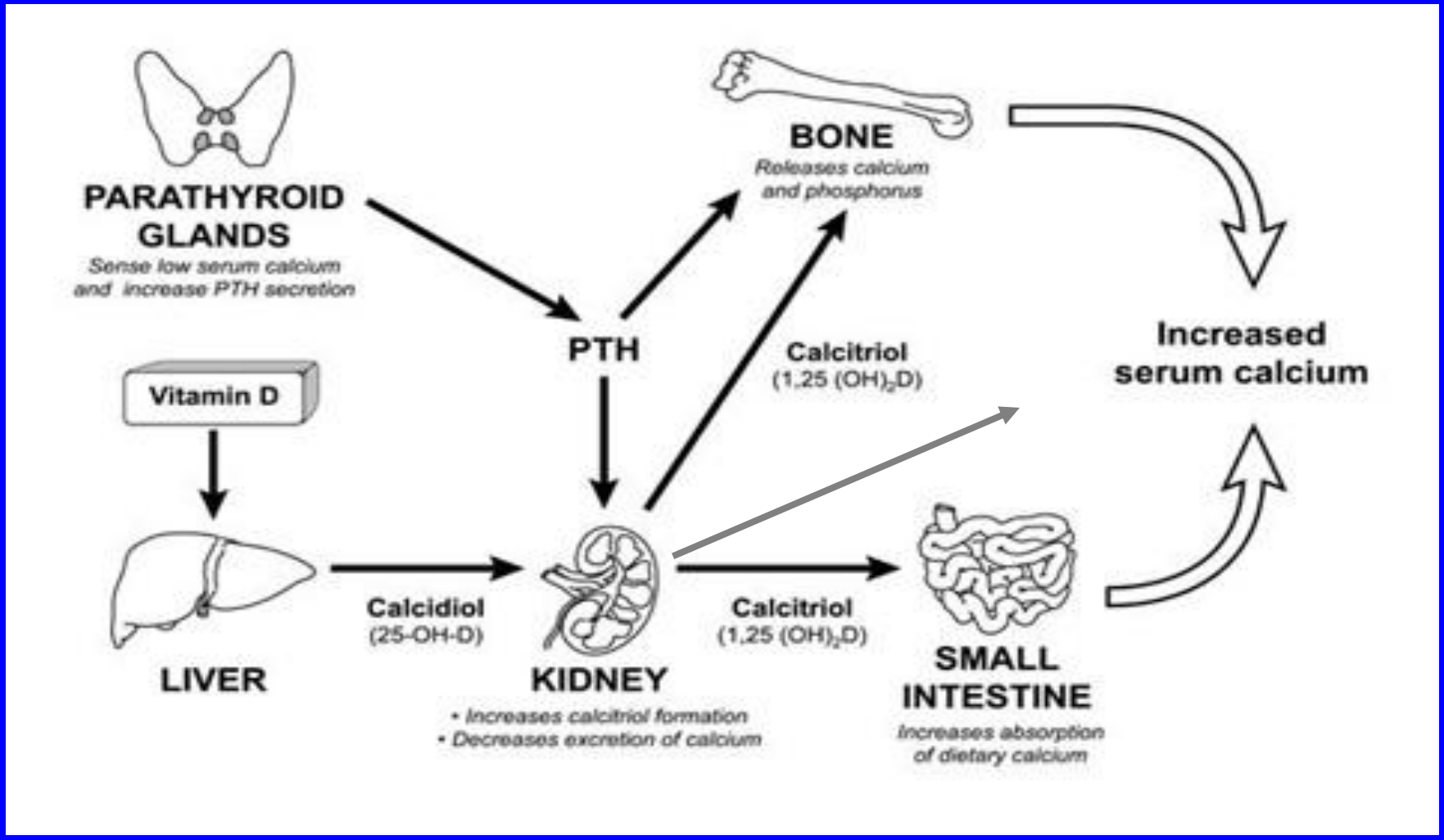
Introduction

Metabolic bone disease is categorized etiologically in 4 groups.

A. Diseases with insufficient mineralization of organic matrix including different types of vitamin D abnormalities, genetic and non-genetic, phosphopenic rickets and others.
B. Disorders of matrix formation (osteoid) functioning as organic framework for mineral deposition.
C. Abnormalities of decreased or increased bone resorption.
D. Pharmacologic and toxic changes in the skeleton.

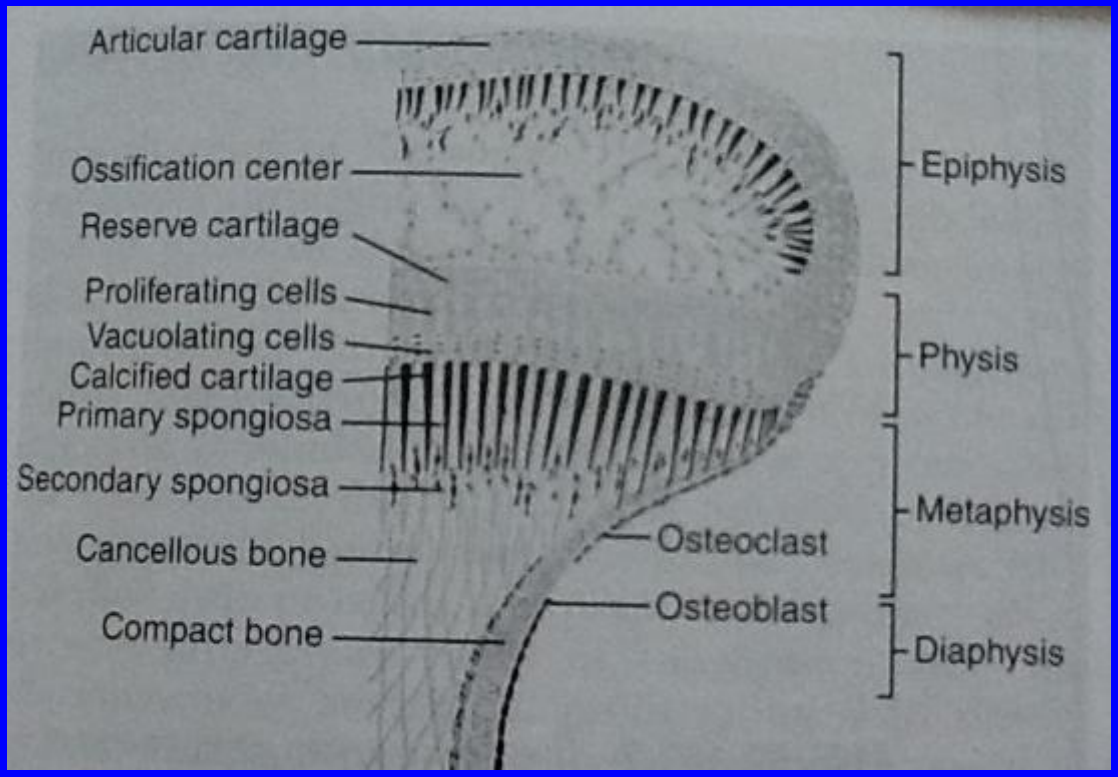

PARATHYROID GLANDS
Sense low serum calcium and increase PTH secretion
BONE
Releases calcium and phosphorus
PTH
Calcitriol
(1,25 (OH)2D)
Increased serum calcium
Vitamin D
LIVER
Calcidiol
(25-OH-D)
KIDNEY
• Increases calcitriol formation
• Decreases excretion of calcium
Calcitriol
(1,25 (OH)2D)
SMALL INTESTINE
Increases absorption of dietary calcium

Group A

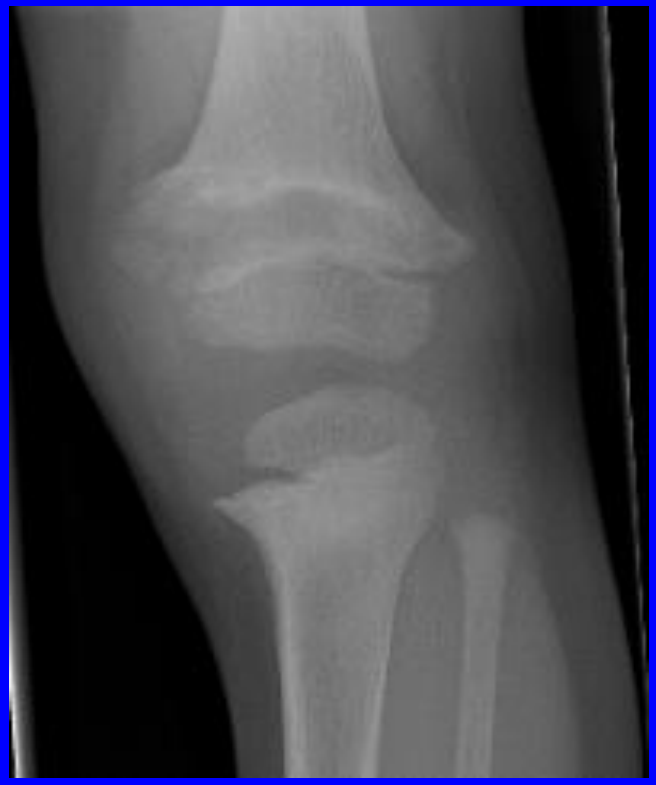
Diseases with insufficient mineralization of organic matrix including different types of vitamin D abnormalities, genetic and non-genetic, phosphopenic rickets and others.

Group A: Rickets

- The radiographic changes depend on the age and severity of rickets.
- Changes are most pronounced in the rapidly growing skeletal region.
- The initial finding is demineralization of the zone of provisional calcification.
- Metaphyseal cupping, fraying, flairing with diffuse coarse demineralization are all classical signs.
- Osteomalacia and rachitic rosary are frequent findings. Other skeletal deformities are incidental findings in treated or non-treated rickets.



Normal functional components of growing and tubular bone

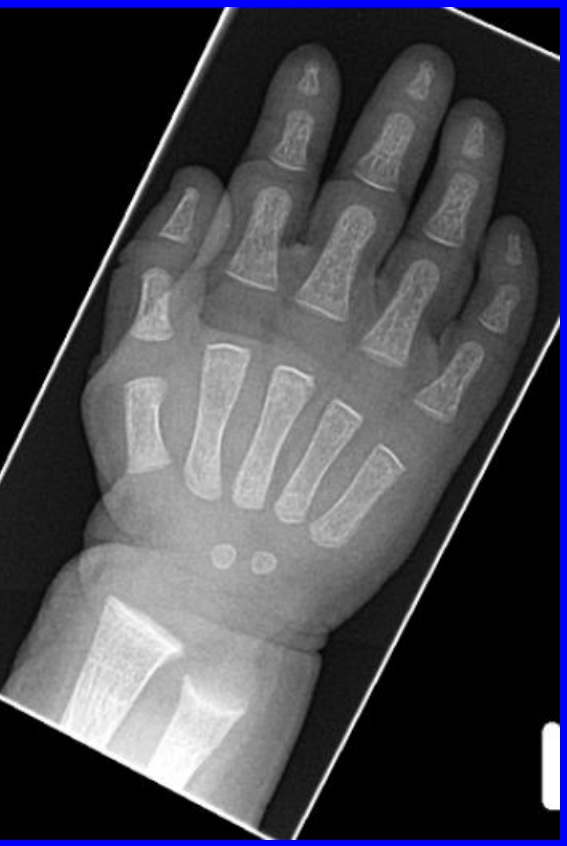


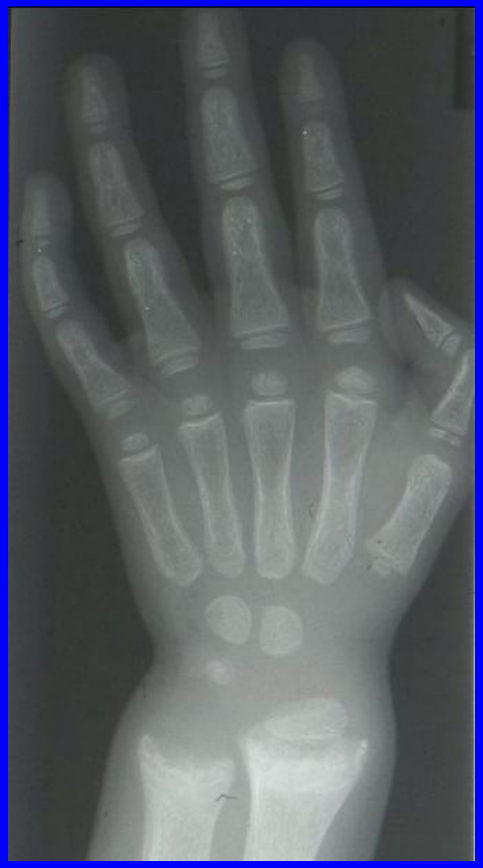
Metaphyseal changes in rickets

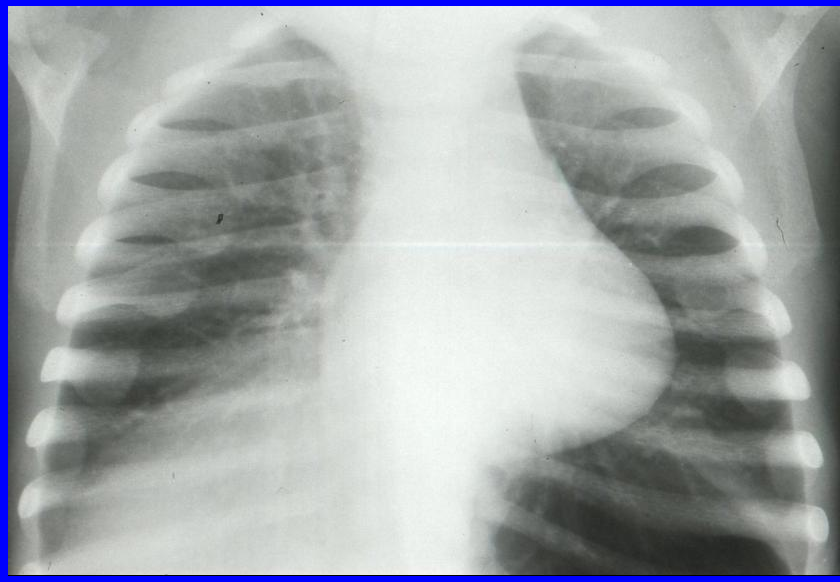
Group A1: Rickets – vit D deficiency

- Rickets and osteomalacia arising from calcium and phosphate insufficiency due to abnormalities of vitamin D.
- The most frequent causes of vitamin D deficiency are nutritional, hepatic and renal diseases.

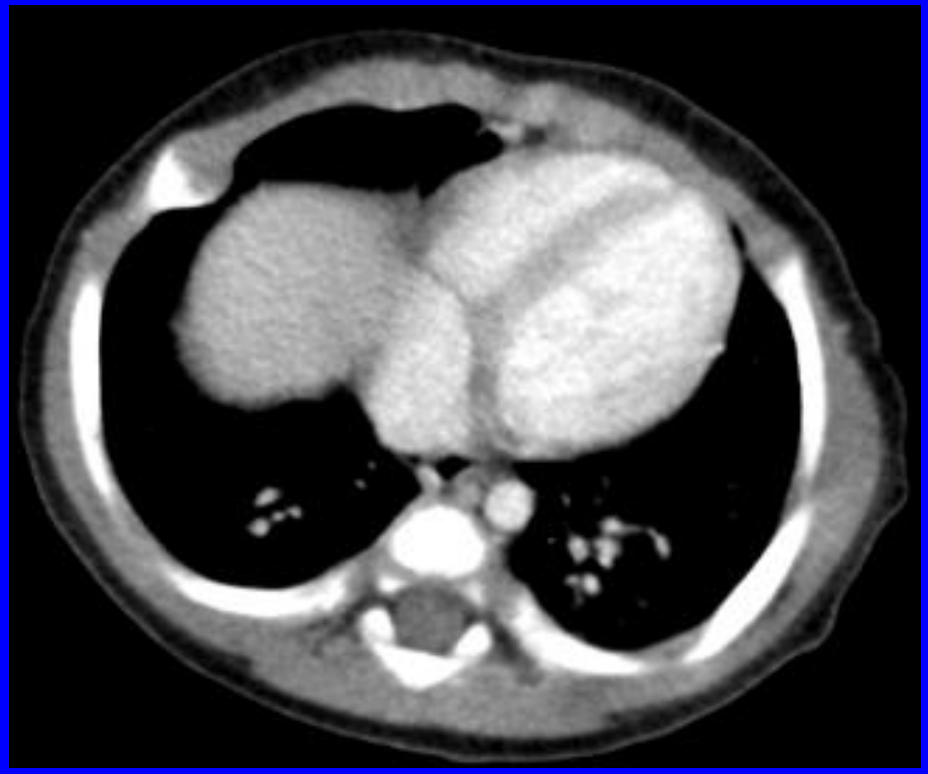
Group A1: Rickets – vit D deficiency

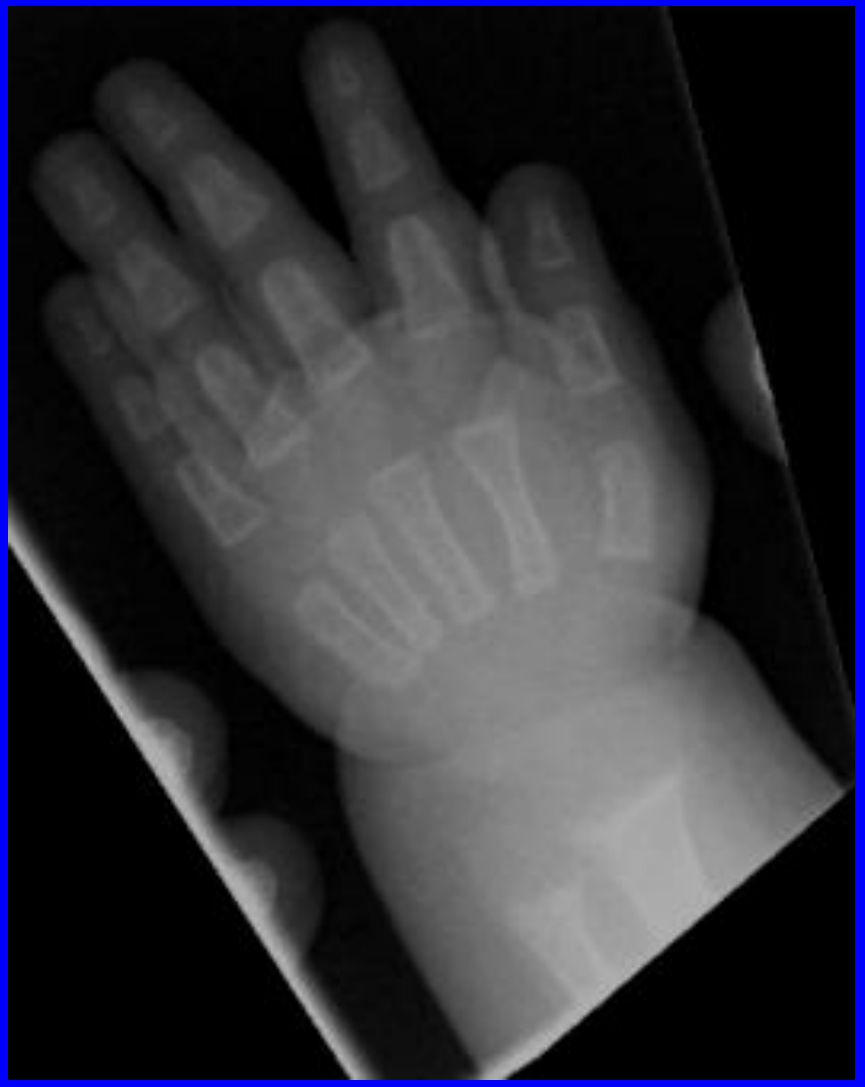




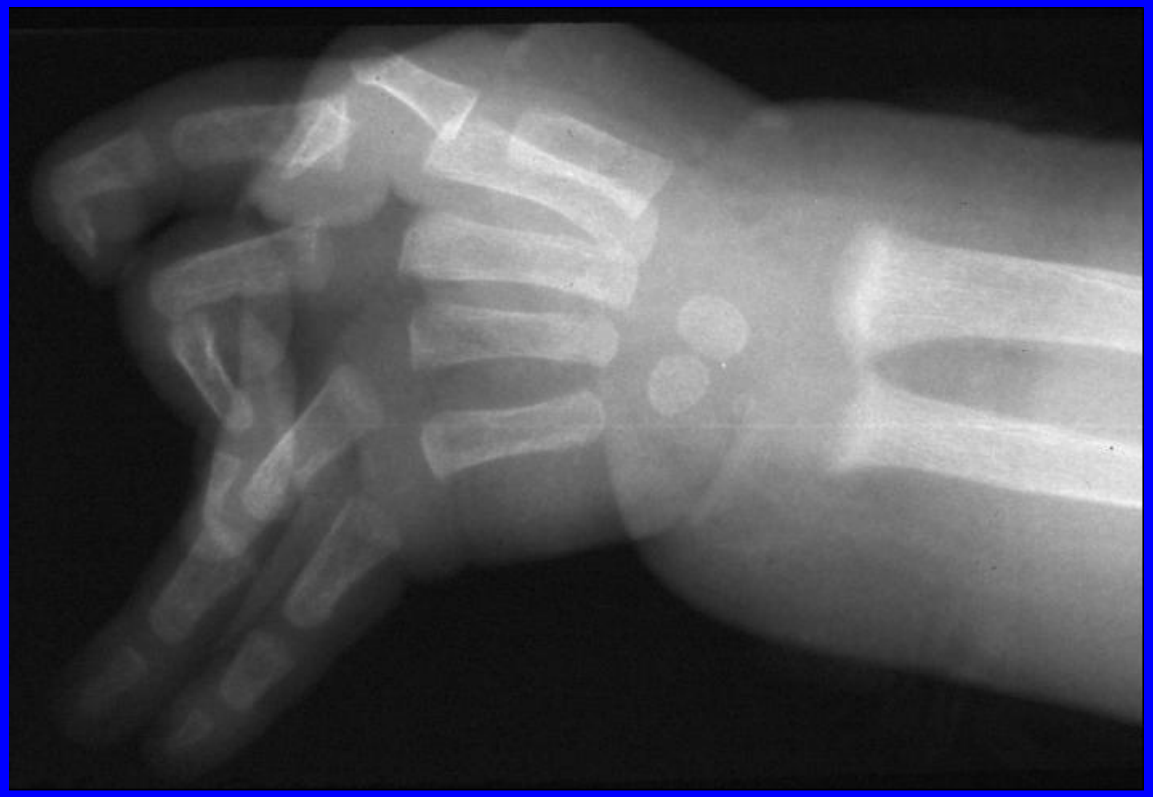


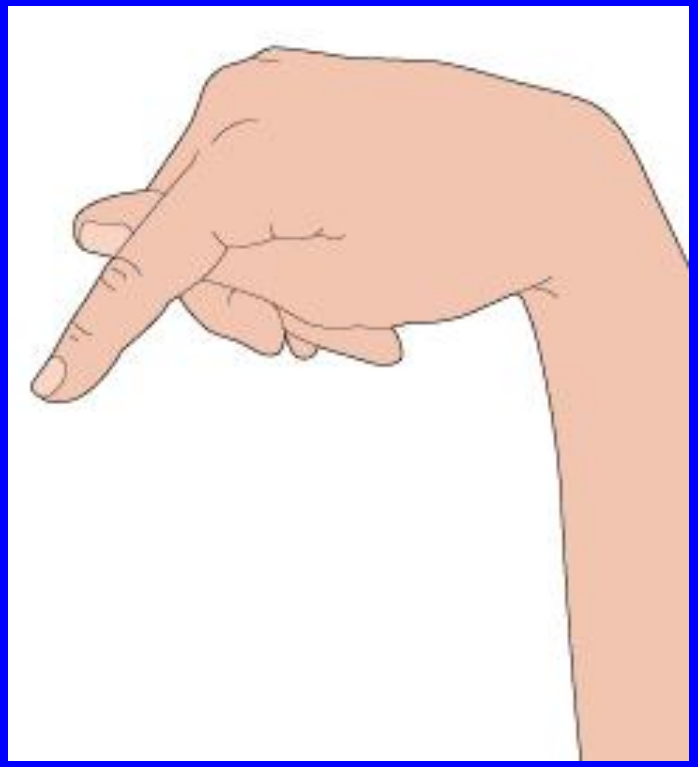
Rachitic changes of skeleton with different severity with osteopenia.



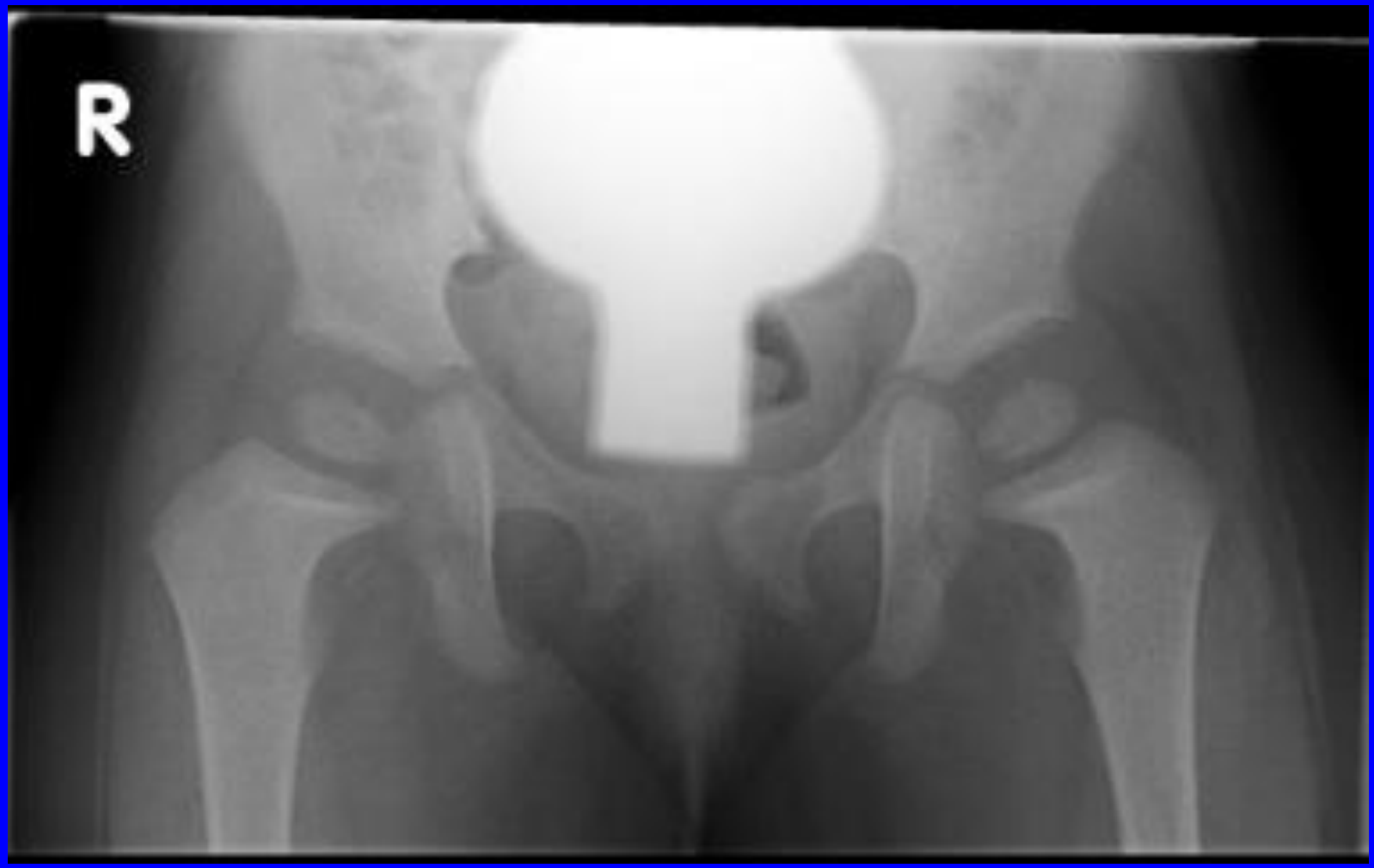


A case of rickets: 7 months old boy suffering from pulmonary infection and apnea. Rachitic metaphyseal changes, note rosary ribs on CT.





A case of rickets with cramping hand. This 7 months old girl had a diet of antroposophical food without vitamin D. Low total calcium was found.

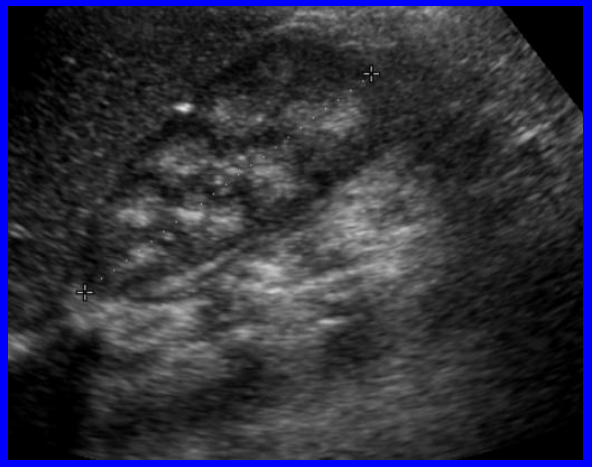


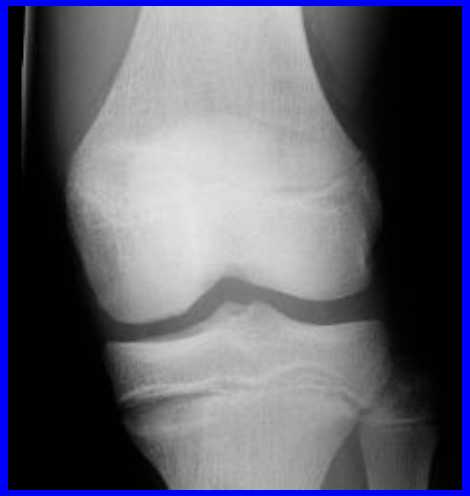
2 year old girl. Clinically suspected to have hip dysplasia because of gait abnormality. The X-ray pelvis however shows demineralization and rarefaction by rickets.

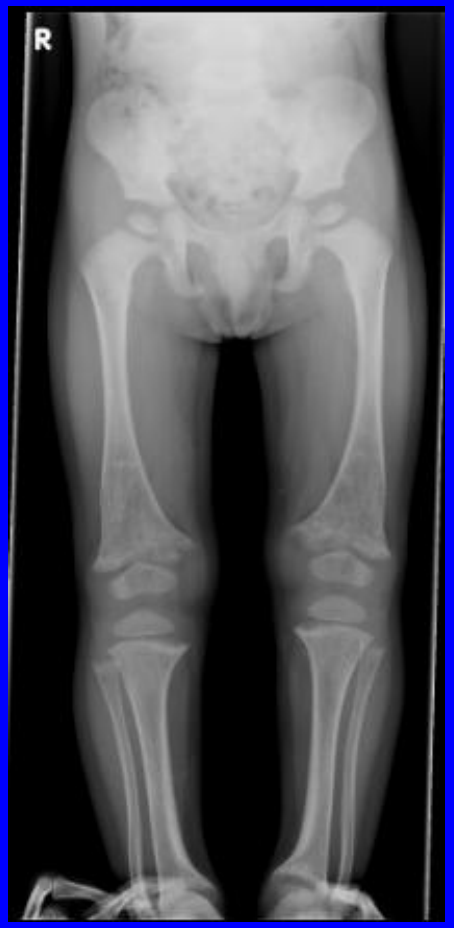
Group A2: phosphopenic rickets X-linked hypophosphatemia

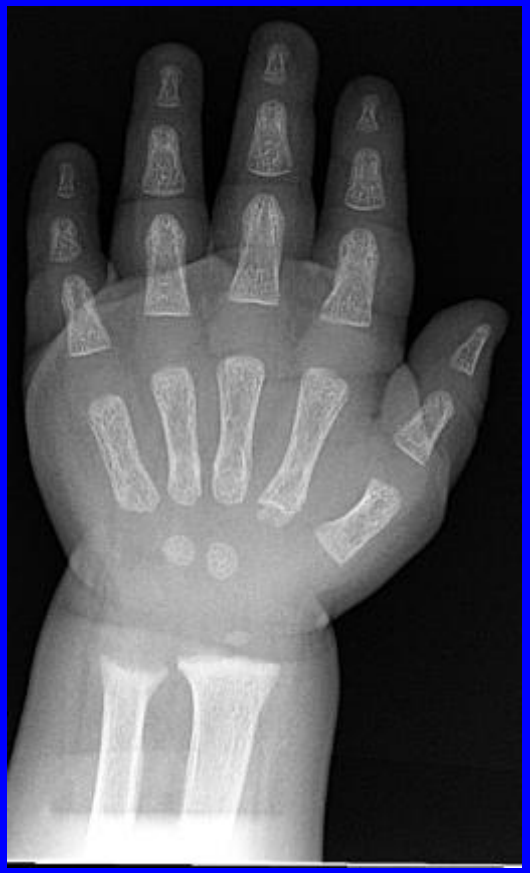
- Autosomal dominant mutation of PHEX (phosphate-regulating endopeptidase on the X-chromosome)
- Excessive renal phosphate wastage
- Low serum phosphate
- Normal calcium
- Elevated alkaline phosphatase

Group A2: phosphopenic rickets
X-linked hypophosphatemia







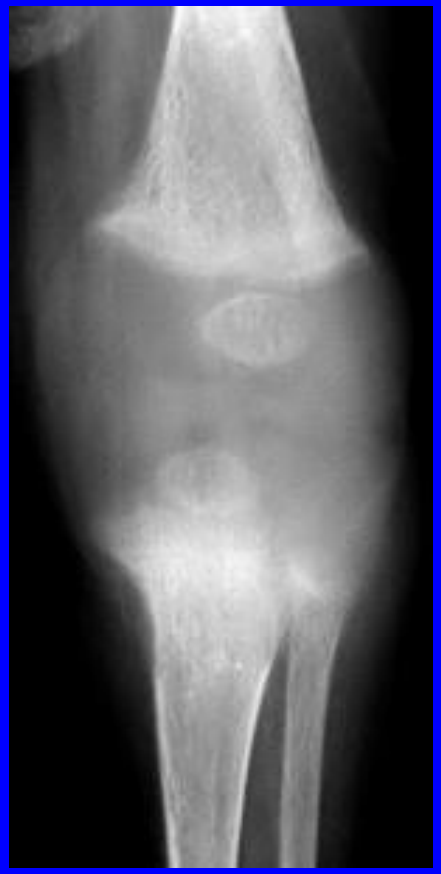


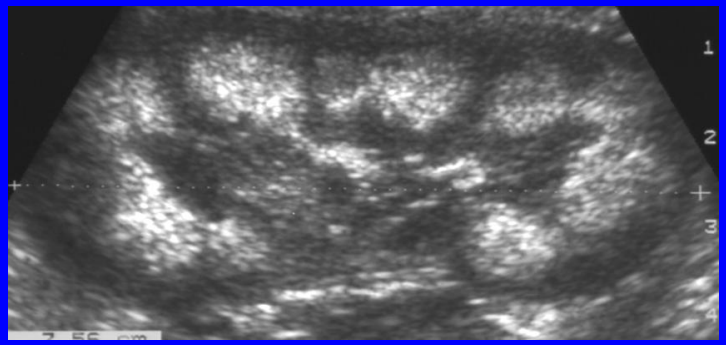
Renal calcification, metaphyseal changes and osteomalacia.

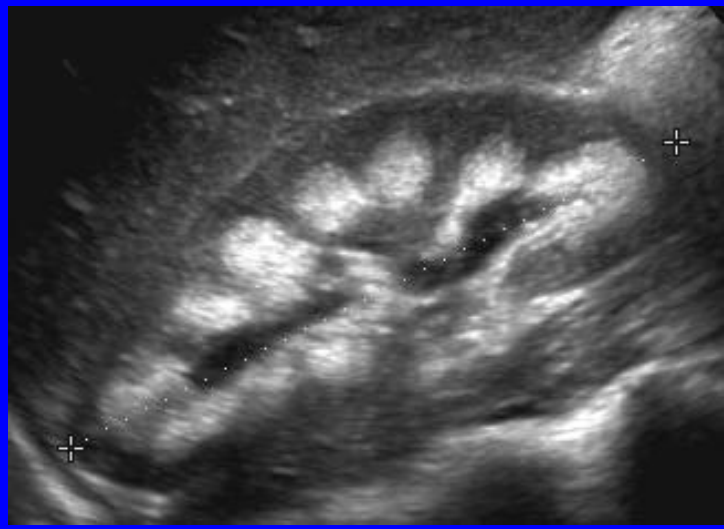
Group A3: Rickets
Renal tubular disease

- Tubular acidosis and glycosuria known as Fanconi syndrome.
- Not a specific entity, but may point to several diseases such as cystinosis, galactosemia and others.
- Hyperphosphaturia
- Amino-aciduria
- Rachitic changes are not distinguishable from disorders with another etiology.

Group A3: Rickets
Renal tubular disease

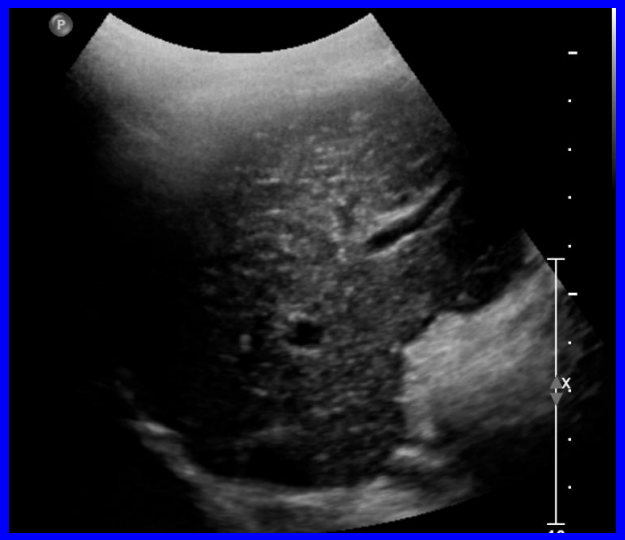


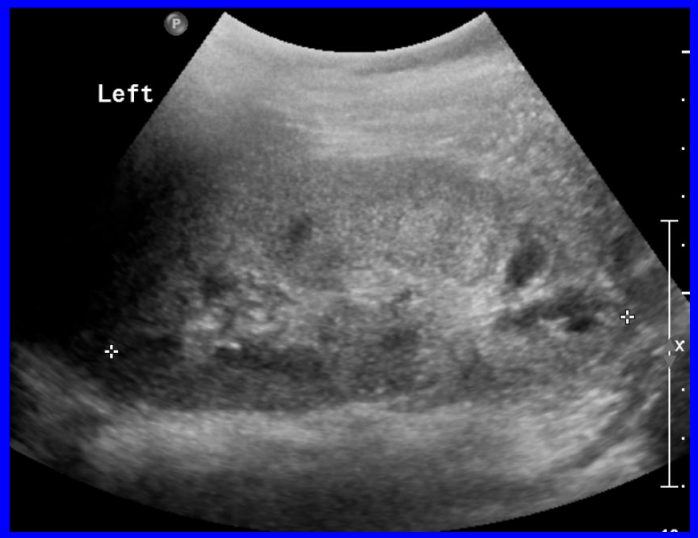


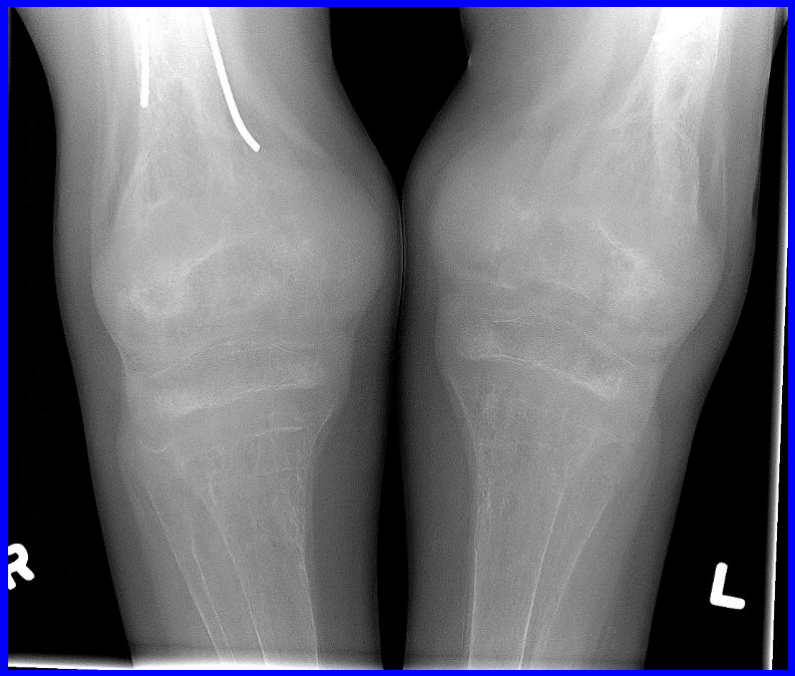


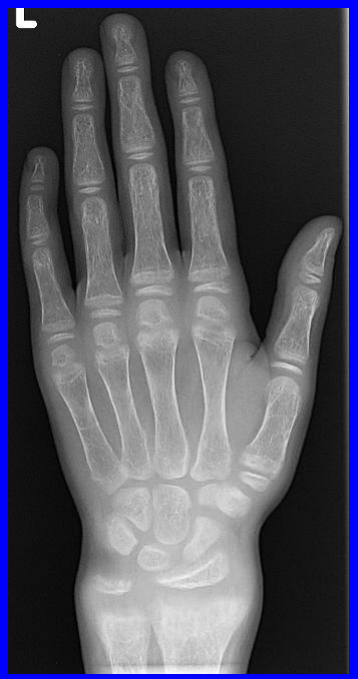
Fanconi syndrome with severe metaphyseal rachitic changes and nefrocalcinosis.

Group A3: Rickets
Renal tubular disease







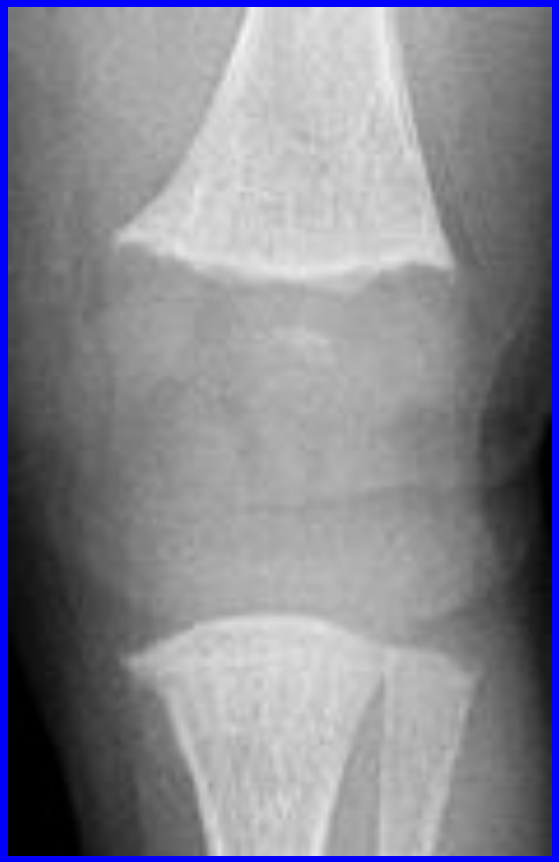


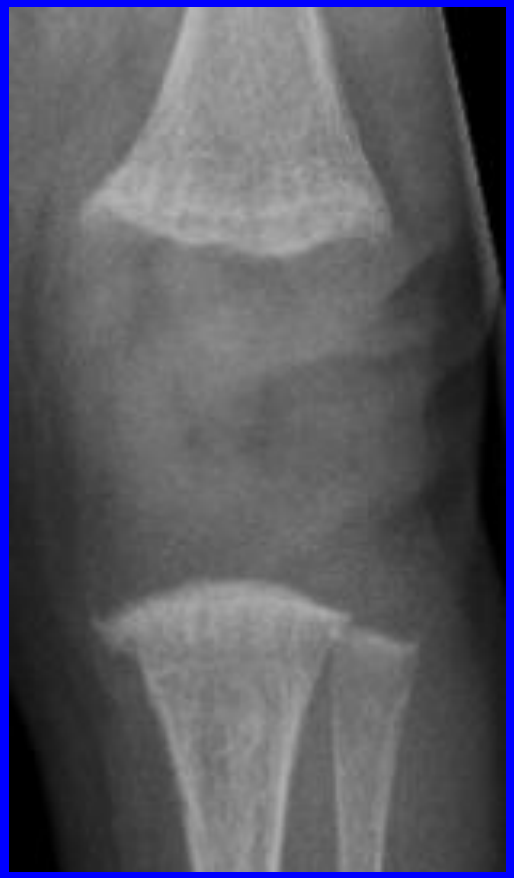
8 years old girl with tyrosinemia type I (Fanconi syndrome).

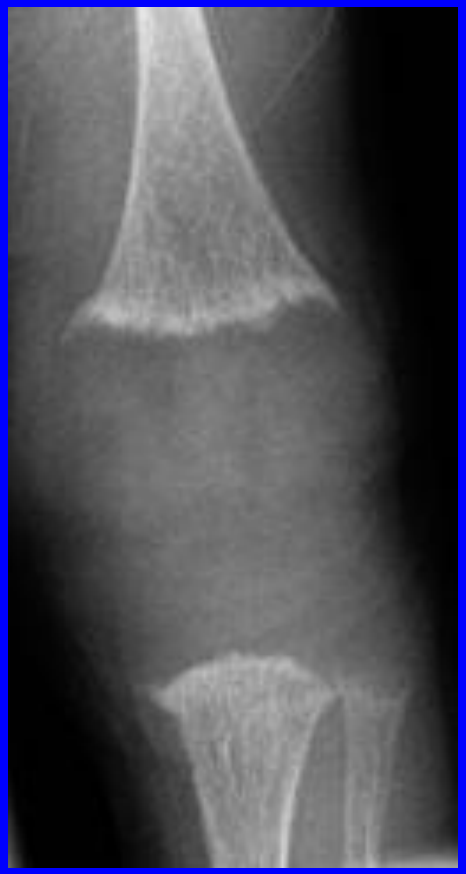
Group A4: Rickets of prematurity

- Most common in infants with birth weight below 1000 g.
- Primarily due to inadequate nutrition, with low intake of calcium and phosphorus.
- High incidence of fractures in this group.

Group A4: Rickets of prematurity





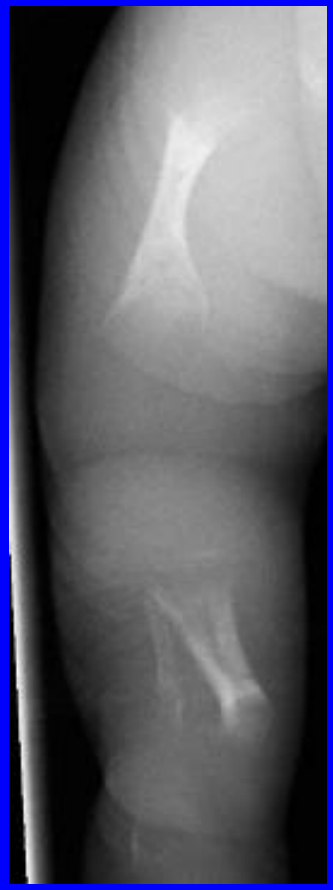


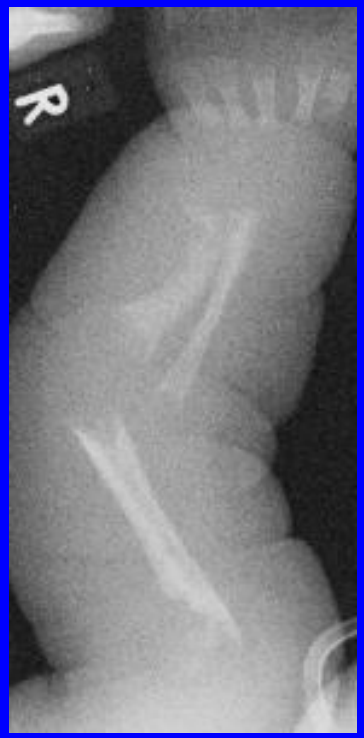
Osteopenic bones and rachitic metaphyseal changes.

Group A5: Hypophosphatasia

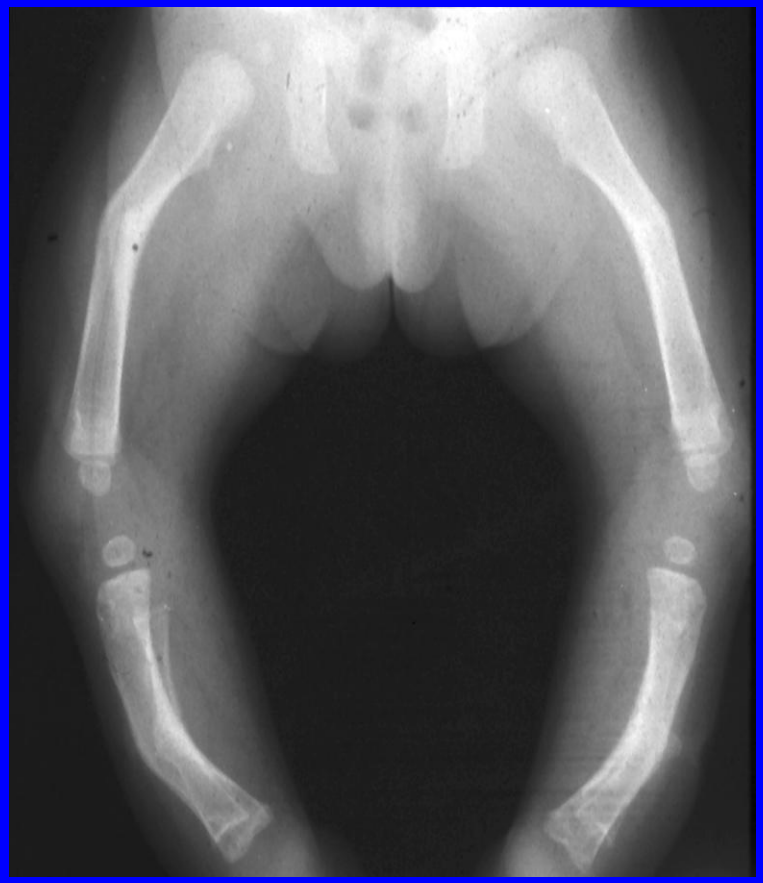
- Mineralization defect due to deficiency of tissue non-specific alkaline phosphatase.
- Laboratory findings: low or absent phosphatase activity, increased blood and urine level of phospho-ethanolamine and inorganic pyrophosphate.

A5: Hypophosphatasia

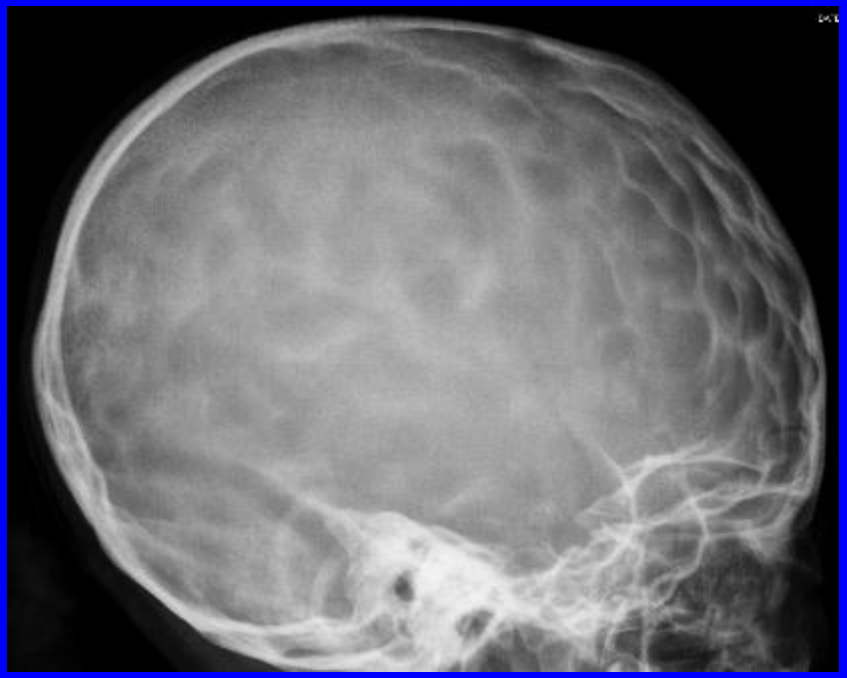


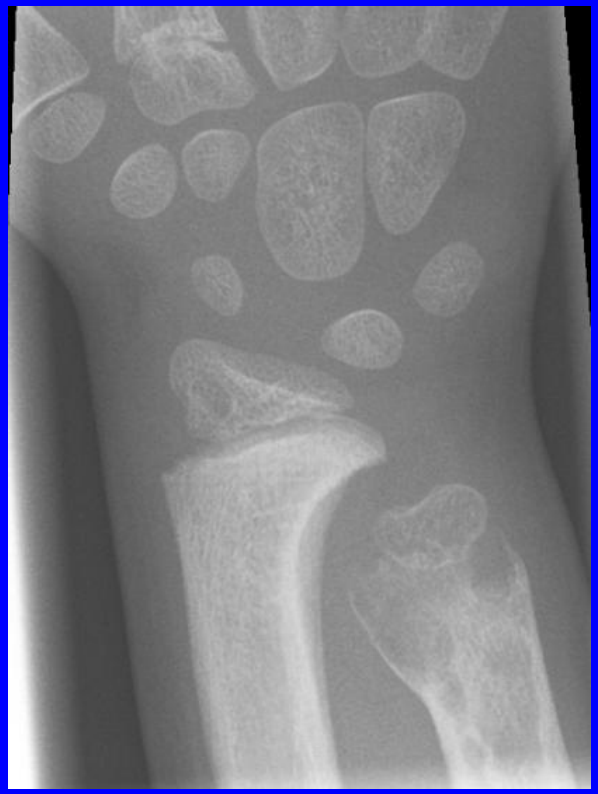


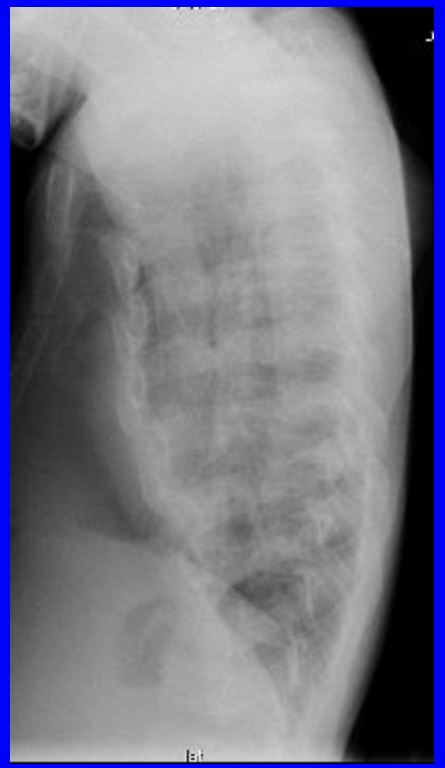
Perinatal form of hypophosphatasia.

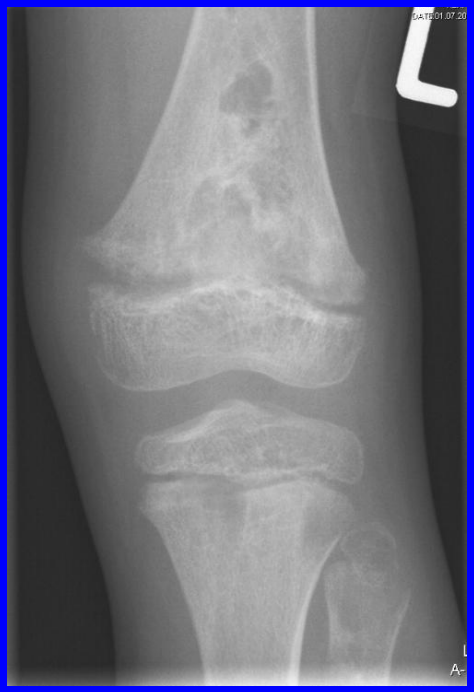


Infantile form of hypophosphatasia.

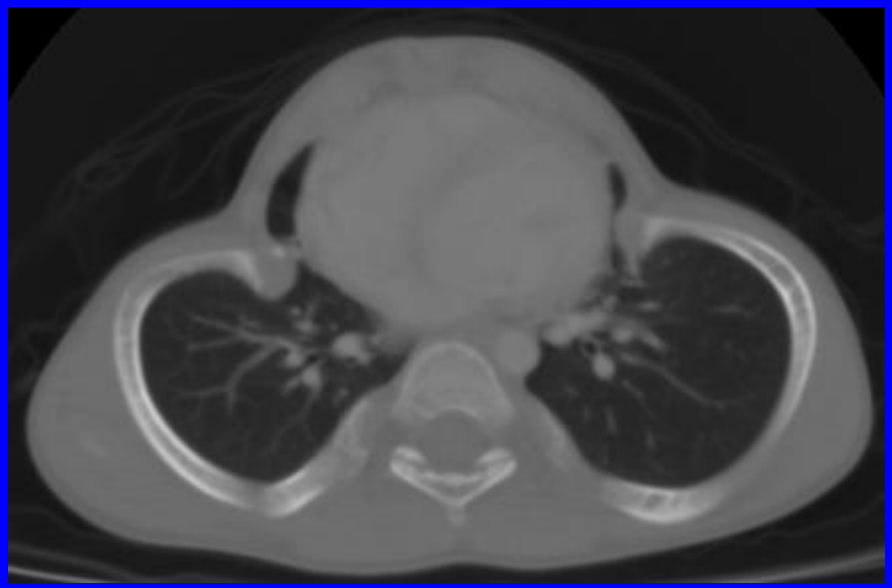








Late form of hypophosphatasia in a 7 year old girl.



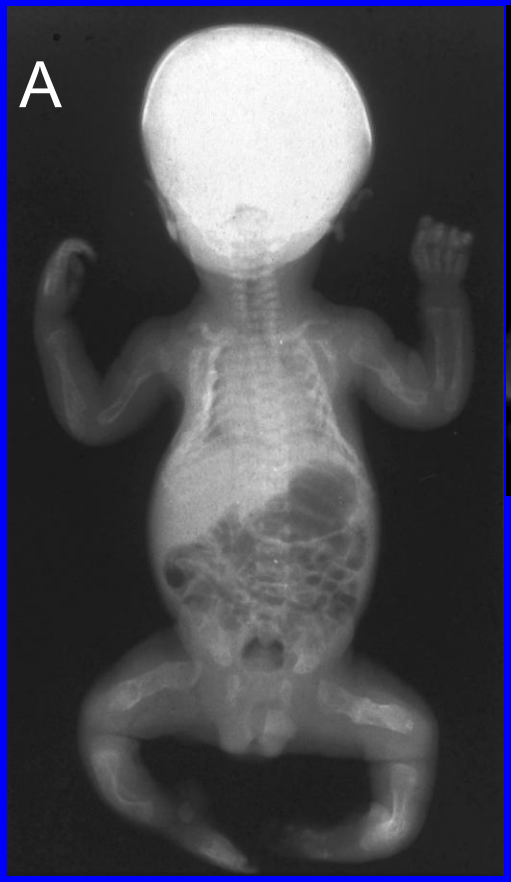
Group B

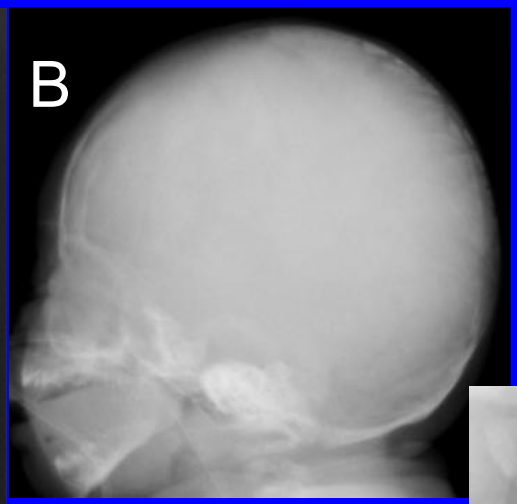
Disorders of matrix formation (osteoid) functioning as organic framework for mineral deposition.

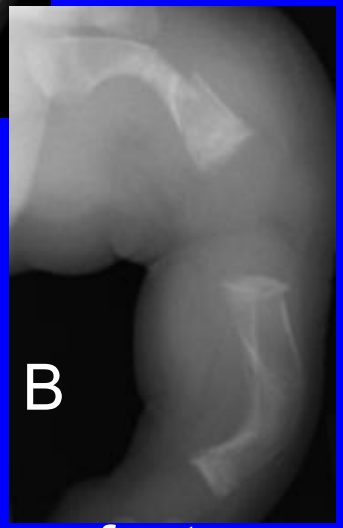
Group B1: Osteogenesis imperfecta

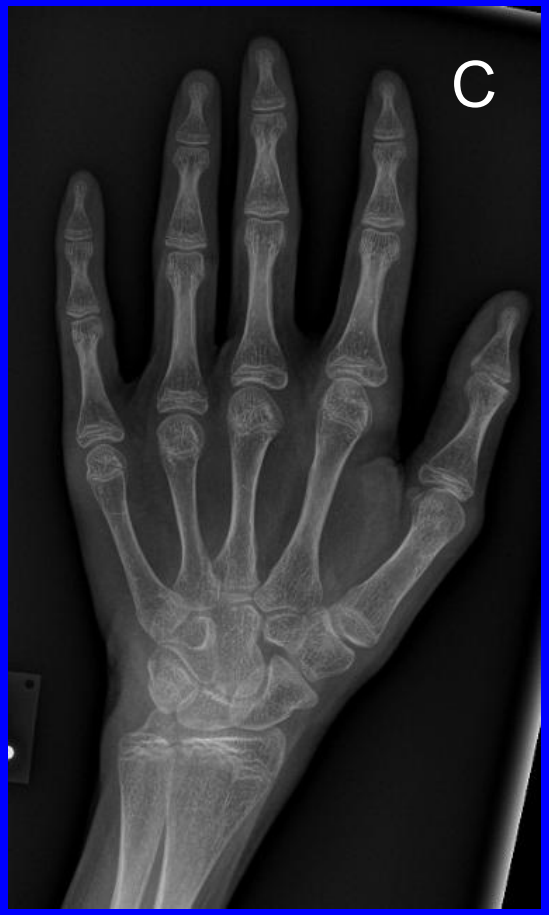
- Abnormal formation of bone matrix (osteoid) as frame work for mineral deposition.
- Qualitative and quantitative defects in the synthesis of type 1 collagen.
- Classified in 6 types depending on inheritance, severity and prognosis.
- Radiographically most severe changes in type II, rather mild changes in type I.

Group B1: Osteogenesis imperfecta









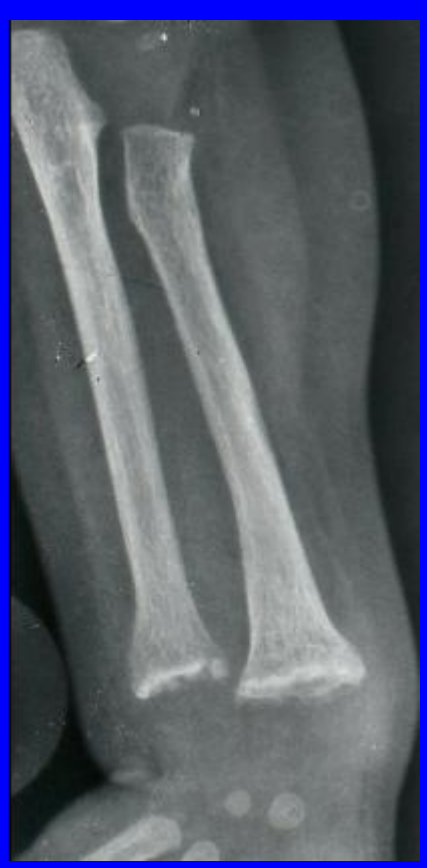
Three cases of osteogenesis imperfecta.

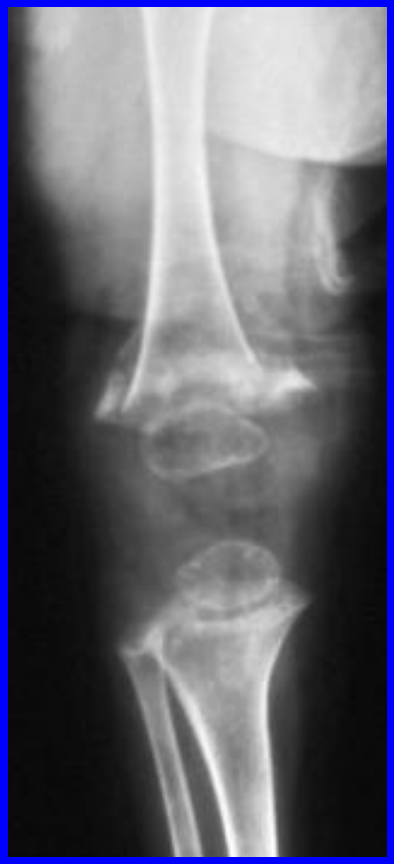
A. Type IIa, B. Type IIb, C. Type I.

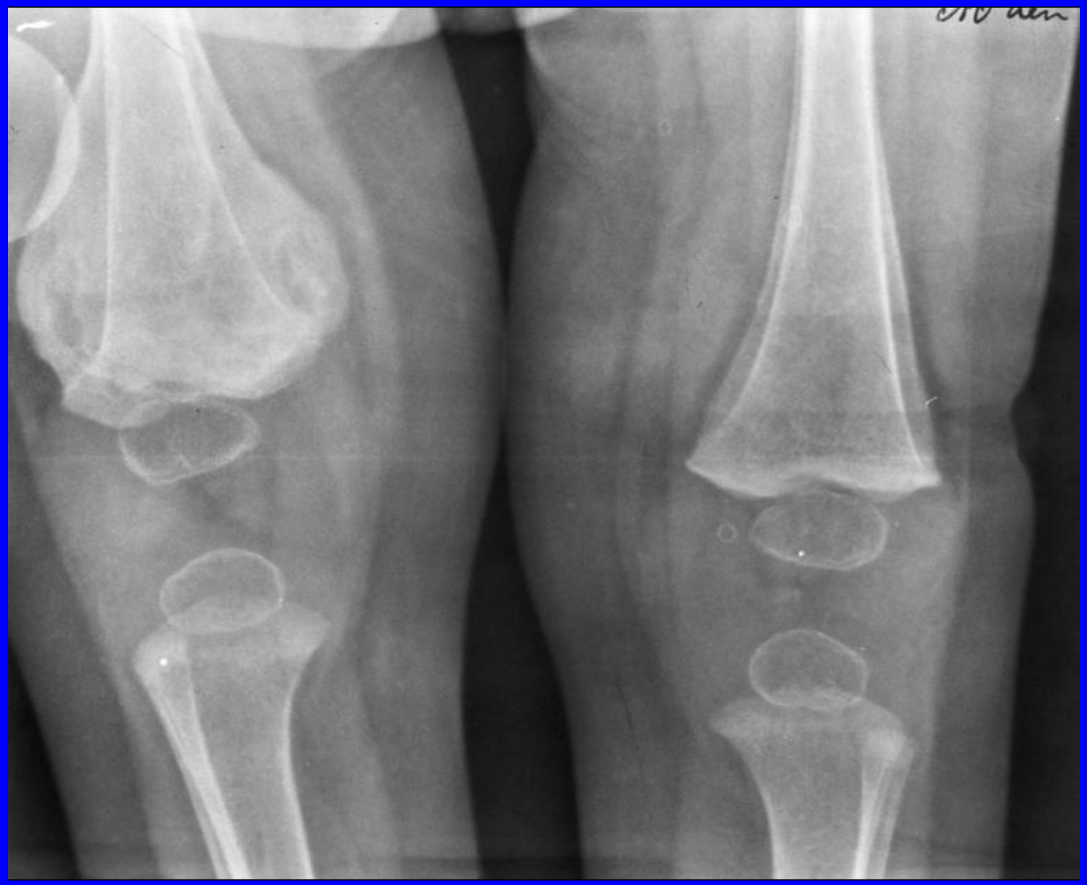
Group B2: Scurvy

- Diminished collagen synthesis, needed for osteoid formation.
- Radiographic findings depend on severity, advance and healing stages.

Group B2: Scurvy





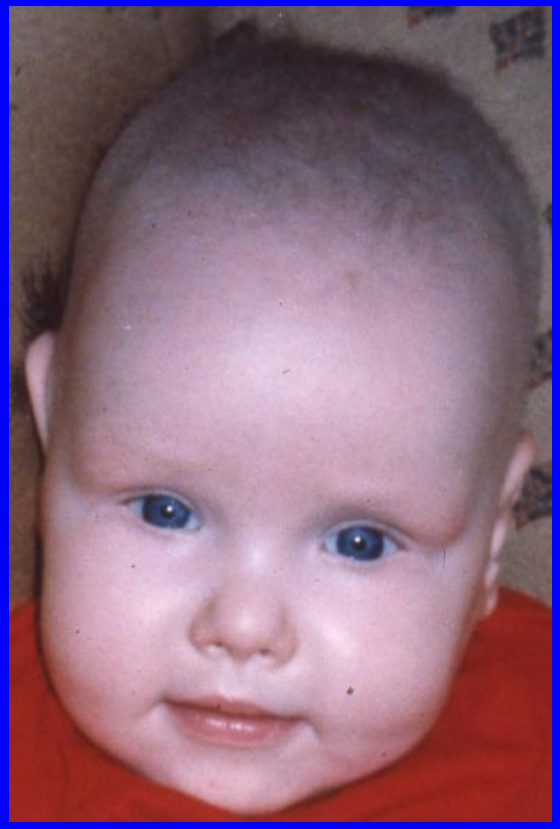


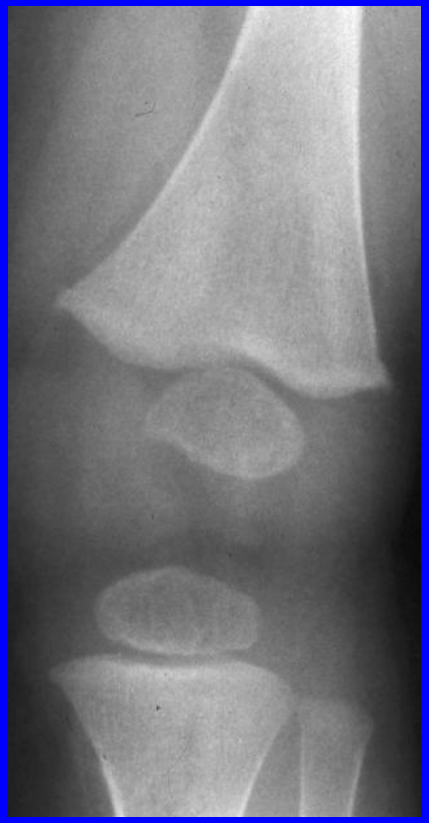
Three cases of scurvy with different changes of the zone of provisional calcification, severities and healing stages.

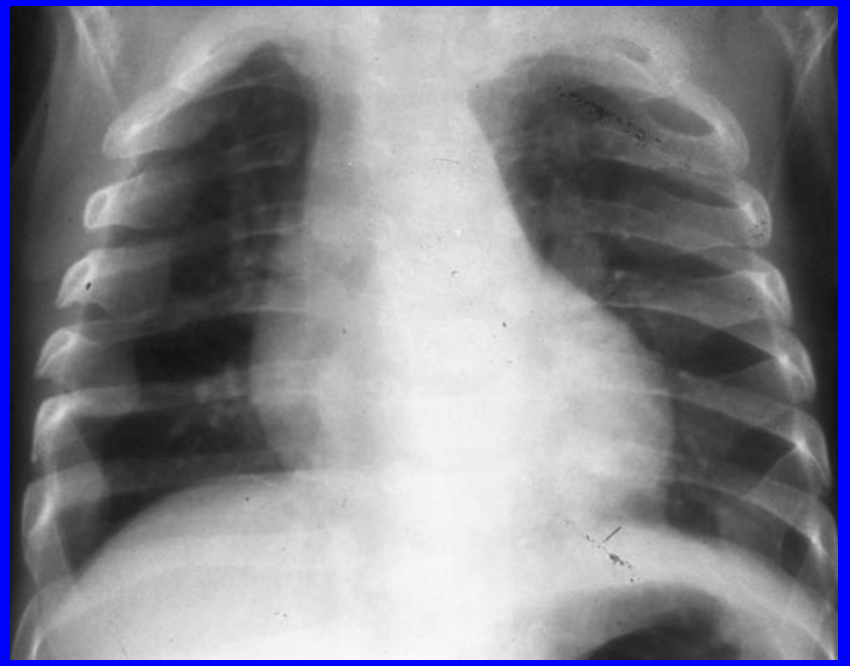
Group B3: Copper deficiency (Menkes disease)

- Deficiency of copper results in deficient matrix formation (collagen synthesis).
- Menkes disease is an x-linked recessive disorder.
- Clinical signs: kinky hair, bone fragility, mental retardation, seizures, intracranial hemorrhage.

Group B3: Copper deficiency (Menkes disease)







An infant with Menkes disease.

Note the kinky hair, metaphyseal spur, widening of rib ends and osteopenia.

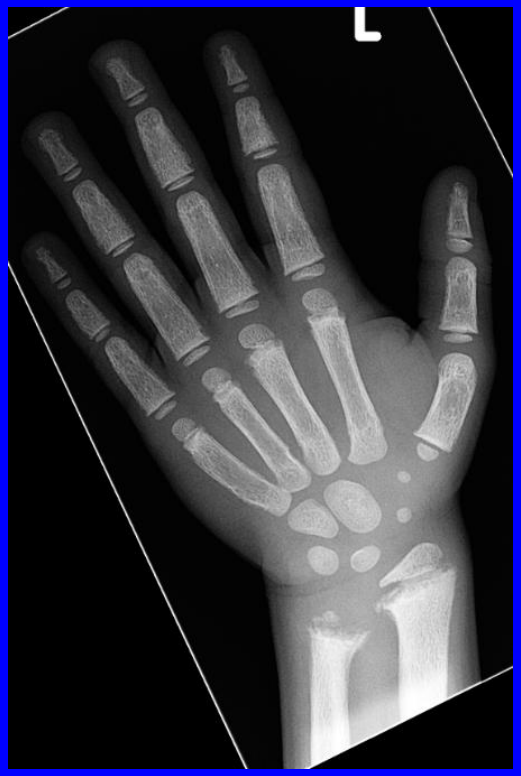
Group C

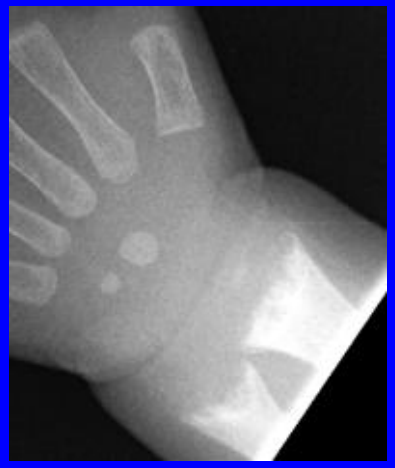
Abnormalities of decreased or increased bone resorption

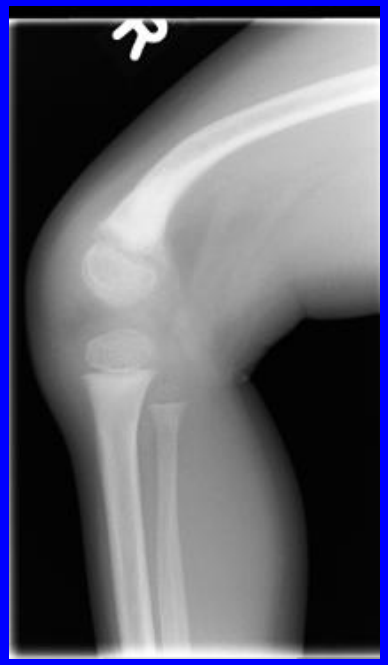
Group C1: Renal osteodystrophy (increased bone resorption)

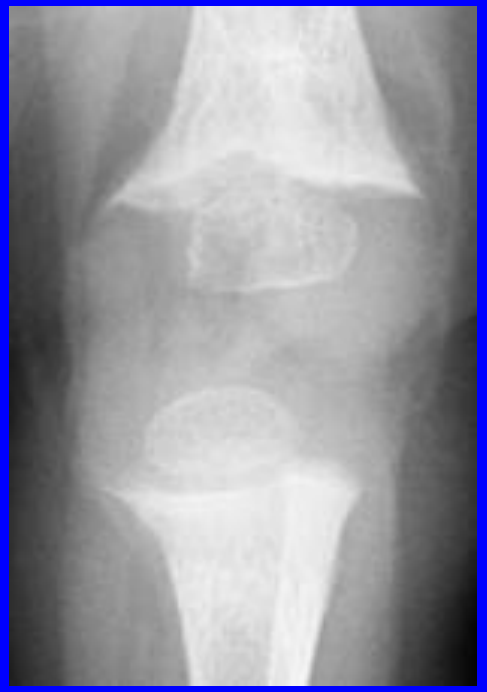
- Chronic renal failure by congenital and acquired renal diseases complicated with hyperparathyreoidism.
- Subperiosteal resorption is a frequent finding
- Excessive rachitic metaphyseal changes, osteomalacia and slipped epiphyses are more severe findings.

Group C1: Renal osteodystrophy (increased bone resorption)









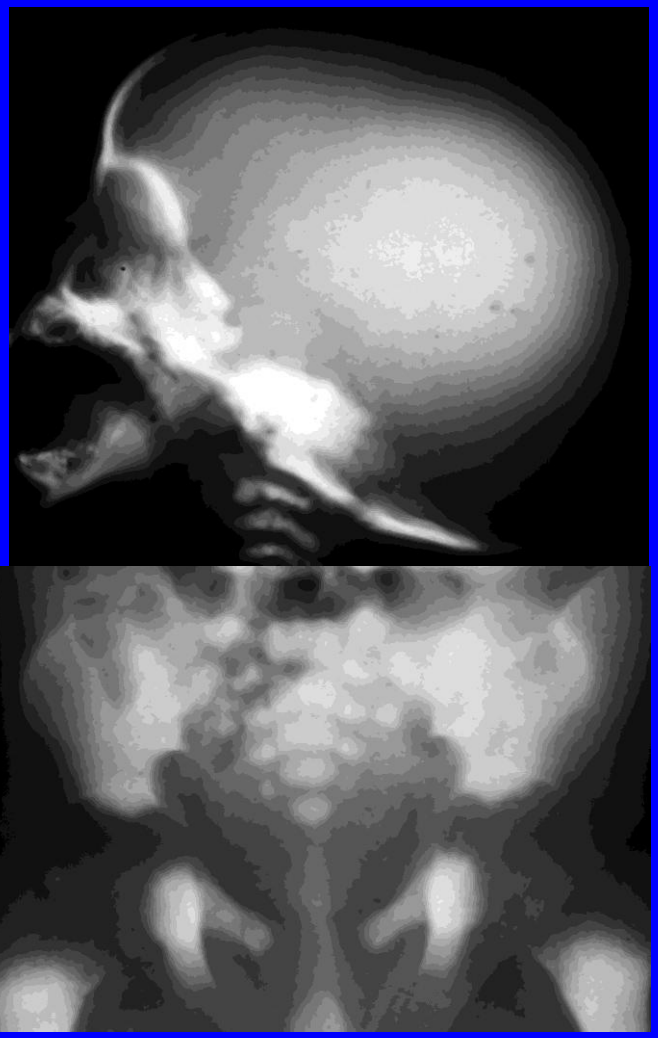
Example of several findings with metaphyseal changes and osteomalacia.

Group C2: Osteopetrosis (decreased bone resorption)

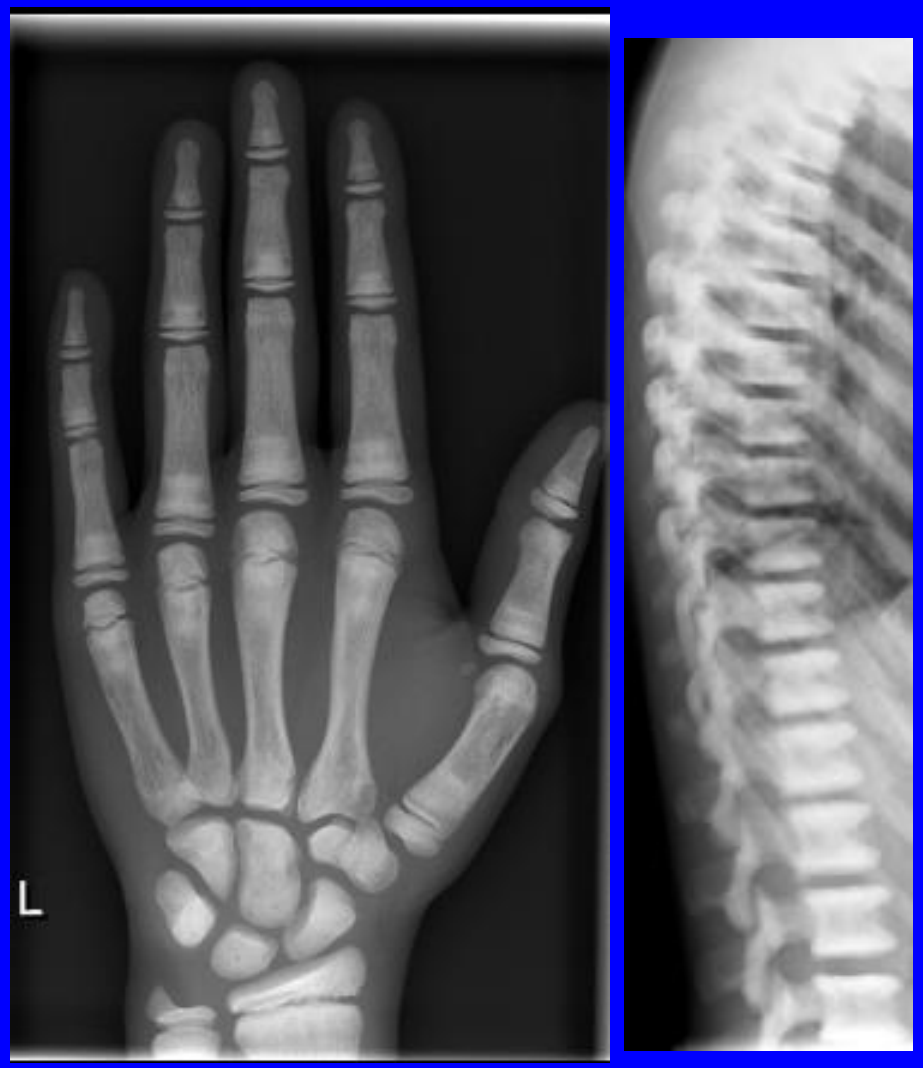
Divided into 3 types:

- Infantile malignant (autosomal recessive)
- Intermediate type (autosomal recessive)
- Benign autosomal dominant.

Group C2: Osteopetrosis (decreased bone resorption)



Infantile malignant type.

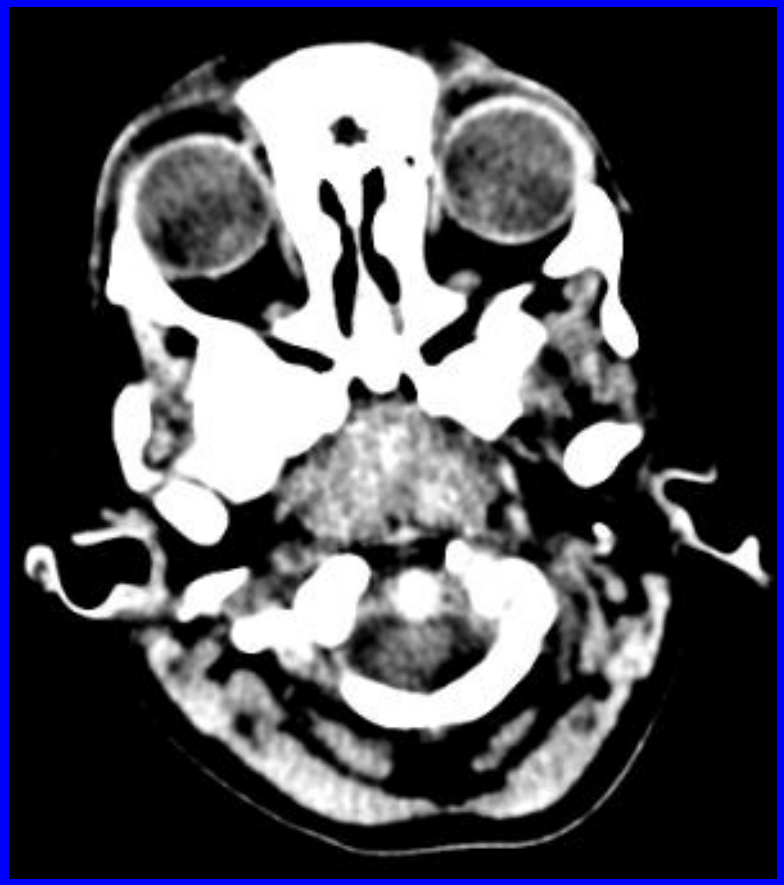


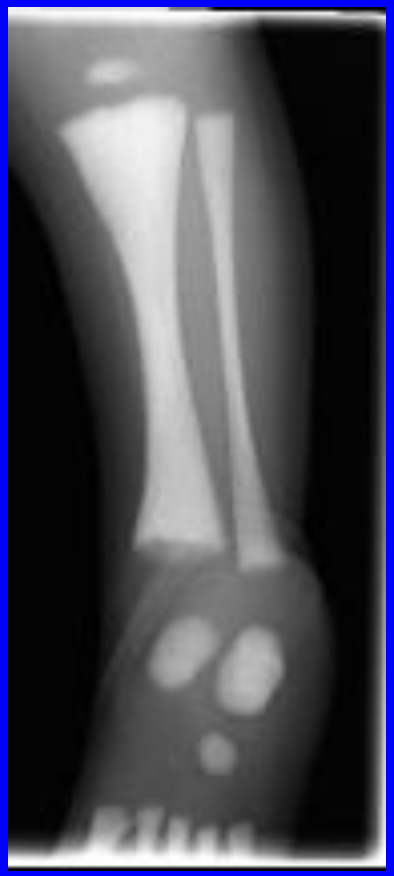
Intermediate type.

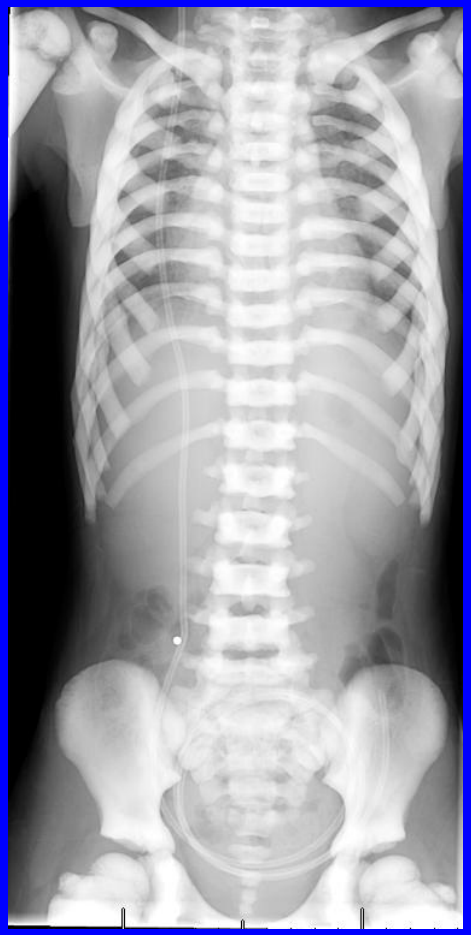
Group C3: Carbonic anhydrase II deficiency

- Clinical findings: osteopetrosis, cerebral calcification, development delay, short stature and fractures. Renal tubular acidosis, hyperchloremic metabolic acidosis.
- Autosomal recessive disease.

Group C3: Carbonic anhydrase II deficiency







Highly sclerotic skull , high density of other parts of skeleton and short limbs.

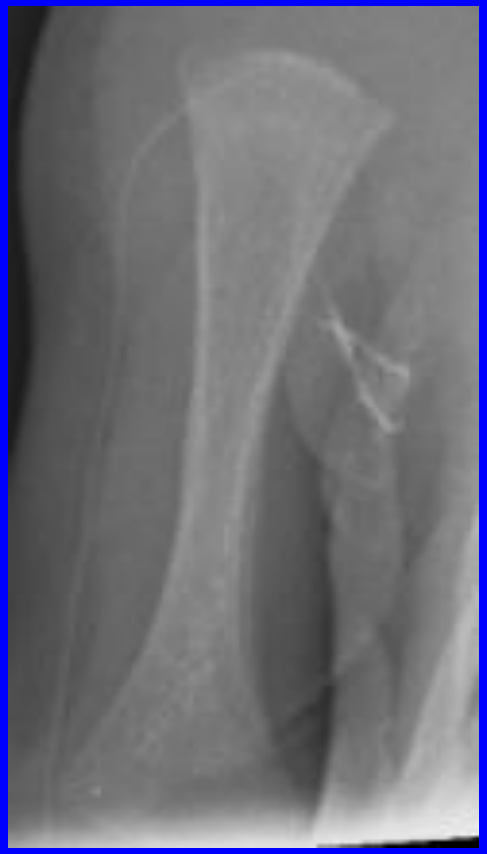
Group D

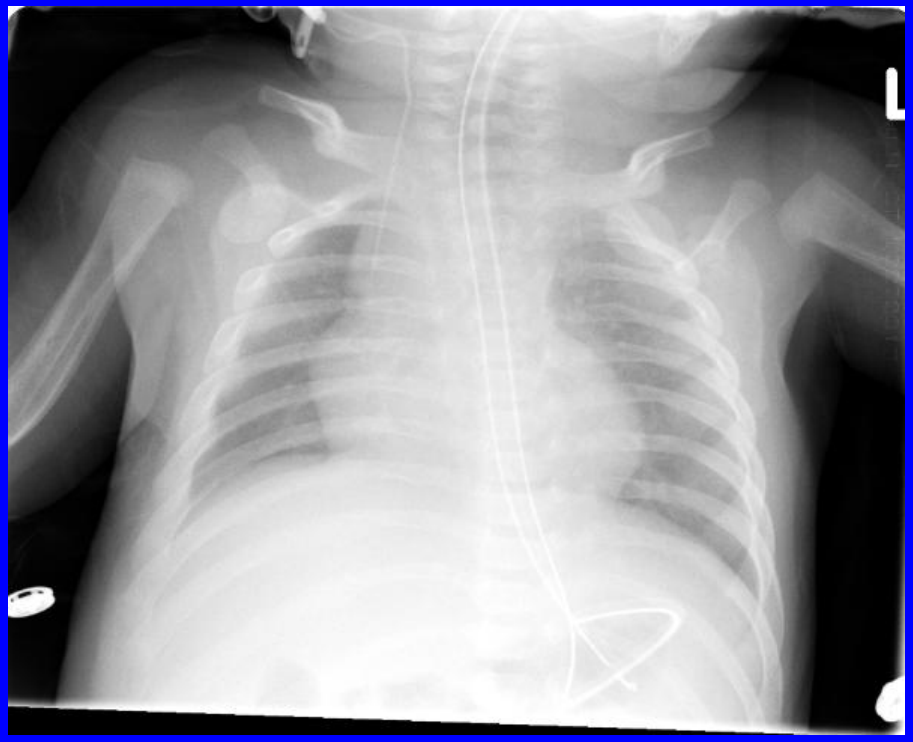
Pharmacologic and toxic changes in the skeleton

Group D1: Prostaglandine E

- Prostaglandine E maintains the patency of the ductus arteriosus in management of cyanotic congenital heart disease.
- By using it for a longer period cortical hyperostosis is expected.

Group D1: Prostaglandine E





Periostal reaction along the length of the humerus diaphyses in two infants.

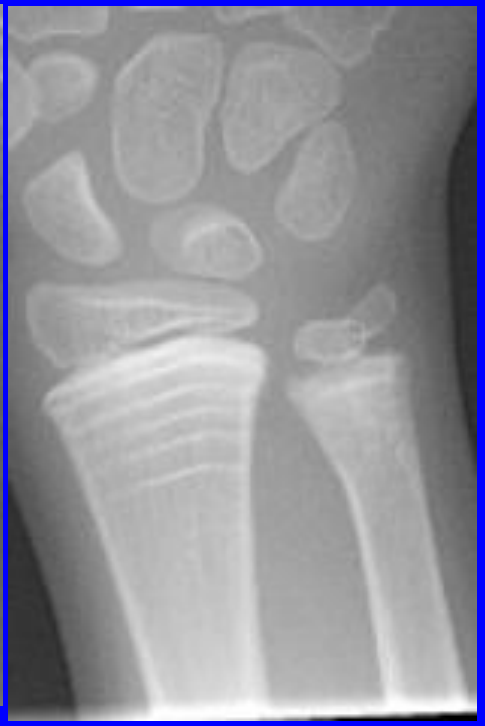
Group D2: Bisphosphonates

- Used in treatment of osteopenia mainly in osteogenesis imperfecta, leading to increased bone density and fracture incidence.
- Expected effect on radiographs are sclerotic metaphyseal lines.

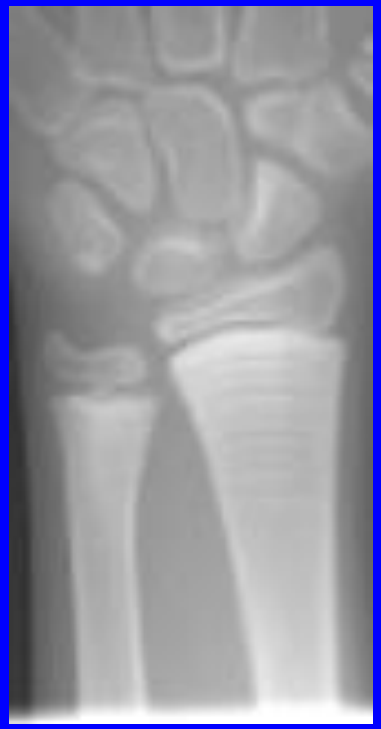
Group D2: Bisphosphonates

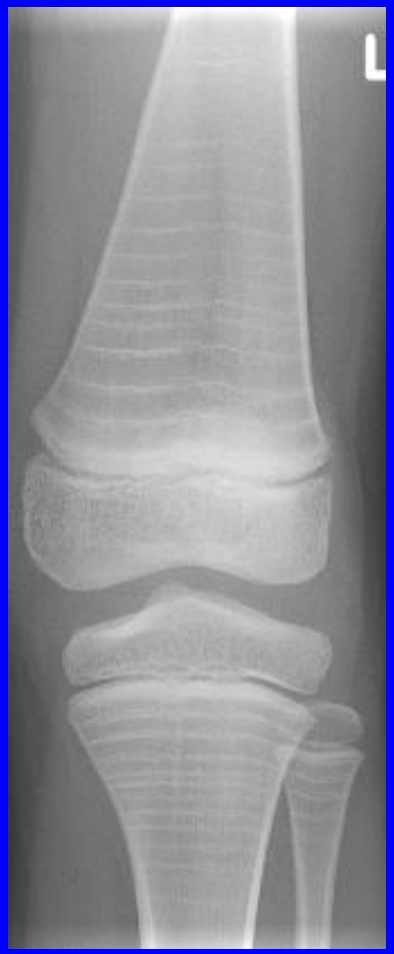
2006

2007



2009





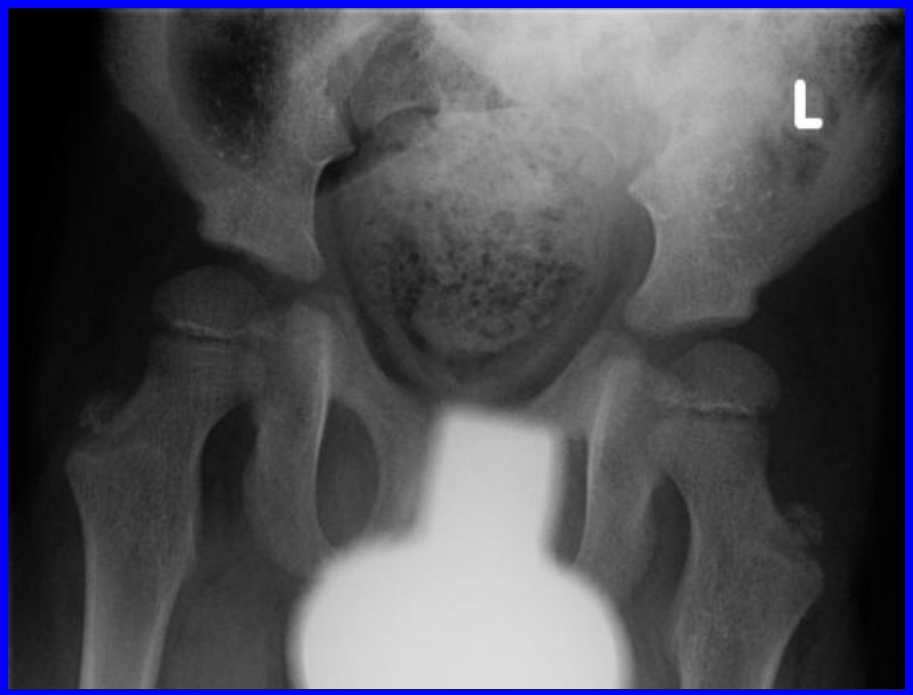
Case 2

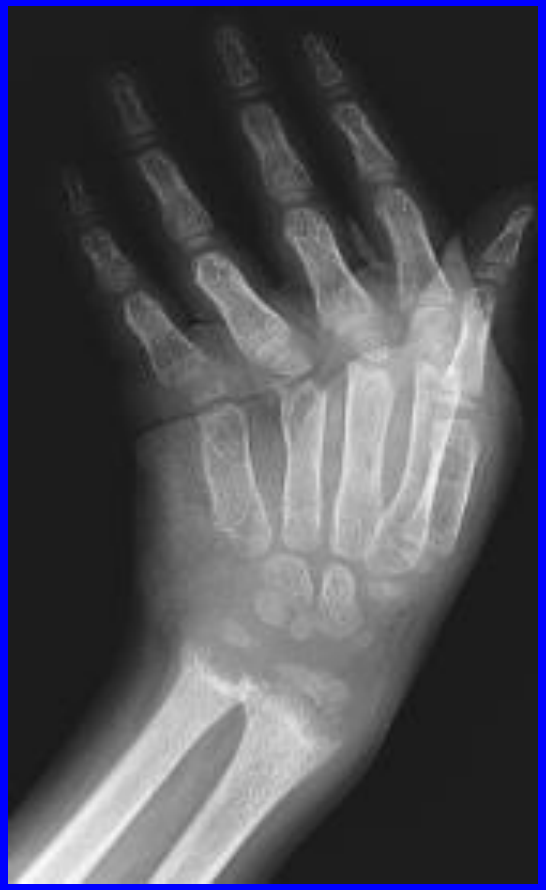
2 cases of osteogenesis imperfecta with sclerotic metaphyseal lines after bisphosphonate therapy.

Group D3: Drug-induced rickets

- Anticonvulsants, phenytorin, phenylbarbital are the most common causes of drug-induced rickets.
- Radiographic findings: florid signs and osteomalacia.

Group D3: Drugs induced rickets



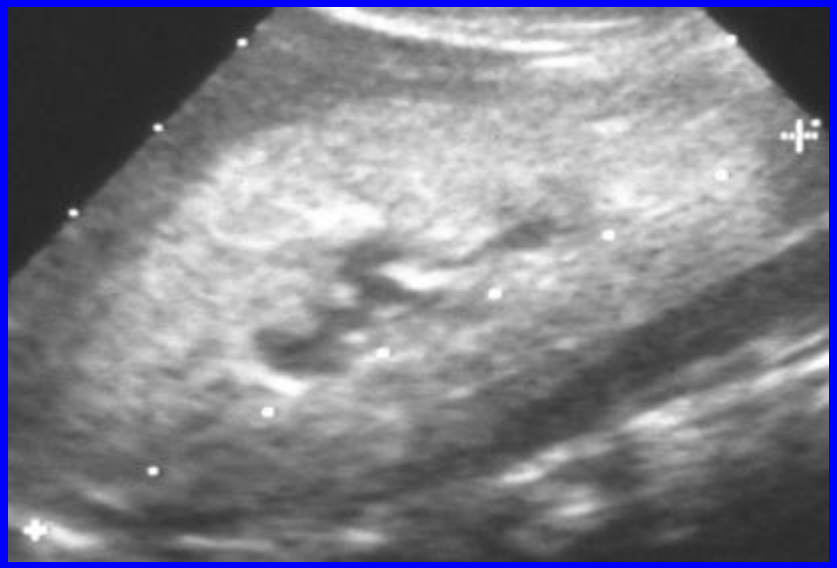


Osteopenic pelvis with typical rachitic changes of distal radius and ulna metaphysis, caused by anticonvulsant therapy.

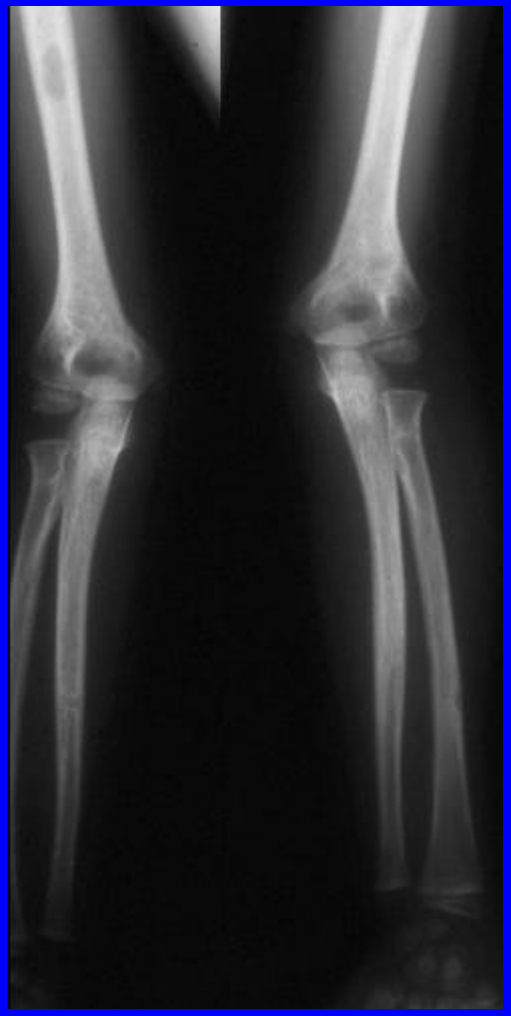
Group D4: Primary oxalosis

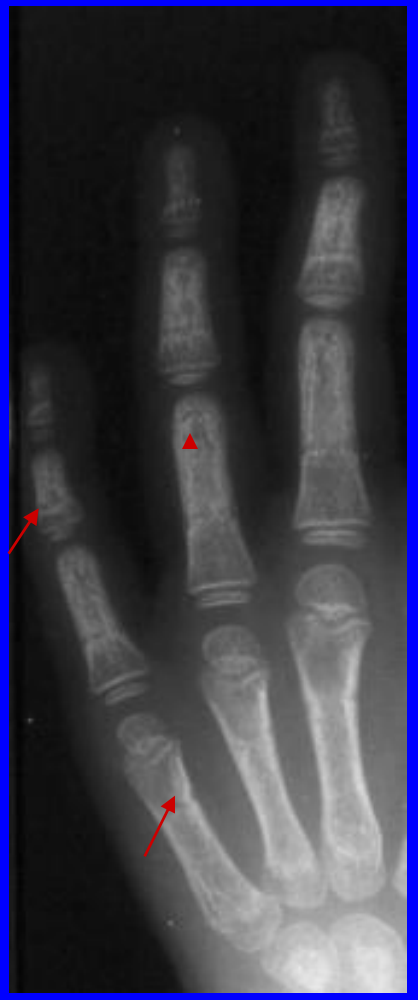
- Etiology: liver enzym defect with excessive production of oxalic acid and deposition of calcium oxalate crystals in kidneys, bone and other organs.
- Autosomal recessive disease.

Group D4: Primary oxalosis



A case of oxalosis with calcification of kidney and subperiostal and cortical defects.



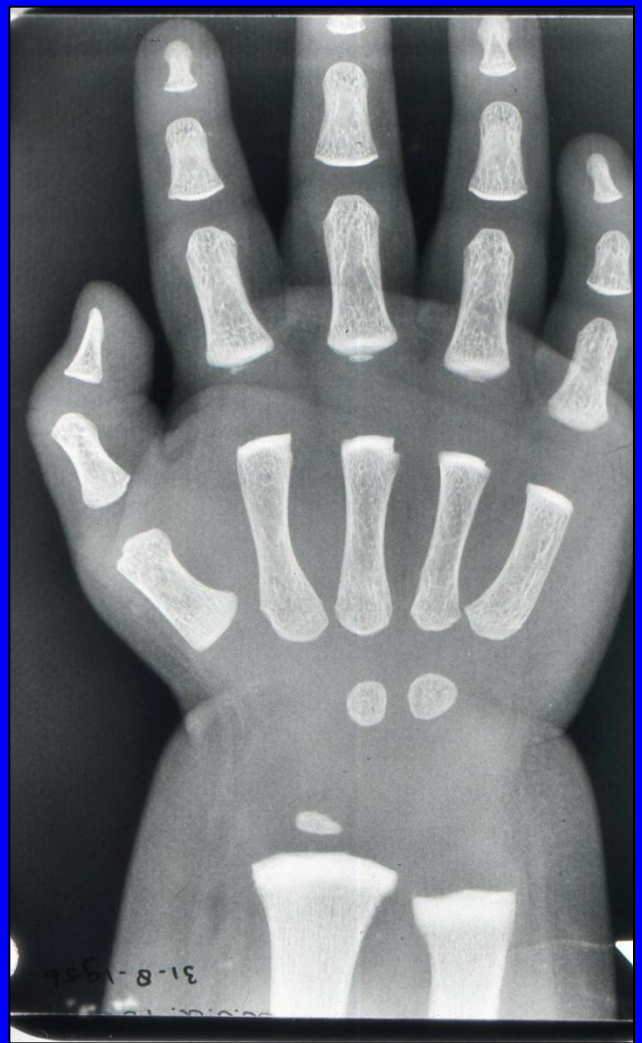


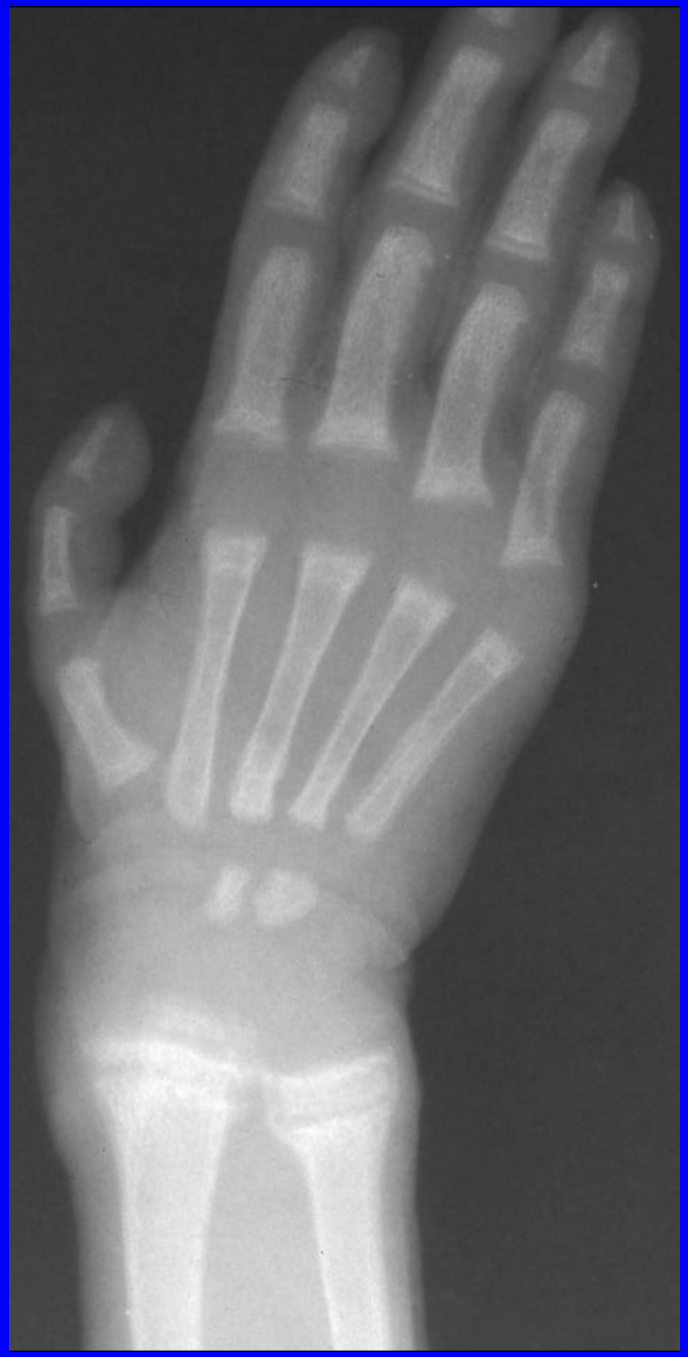
Group D5: Lead poisoning

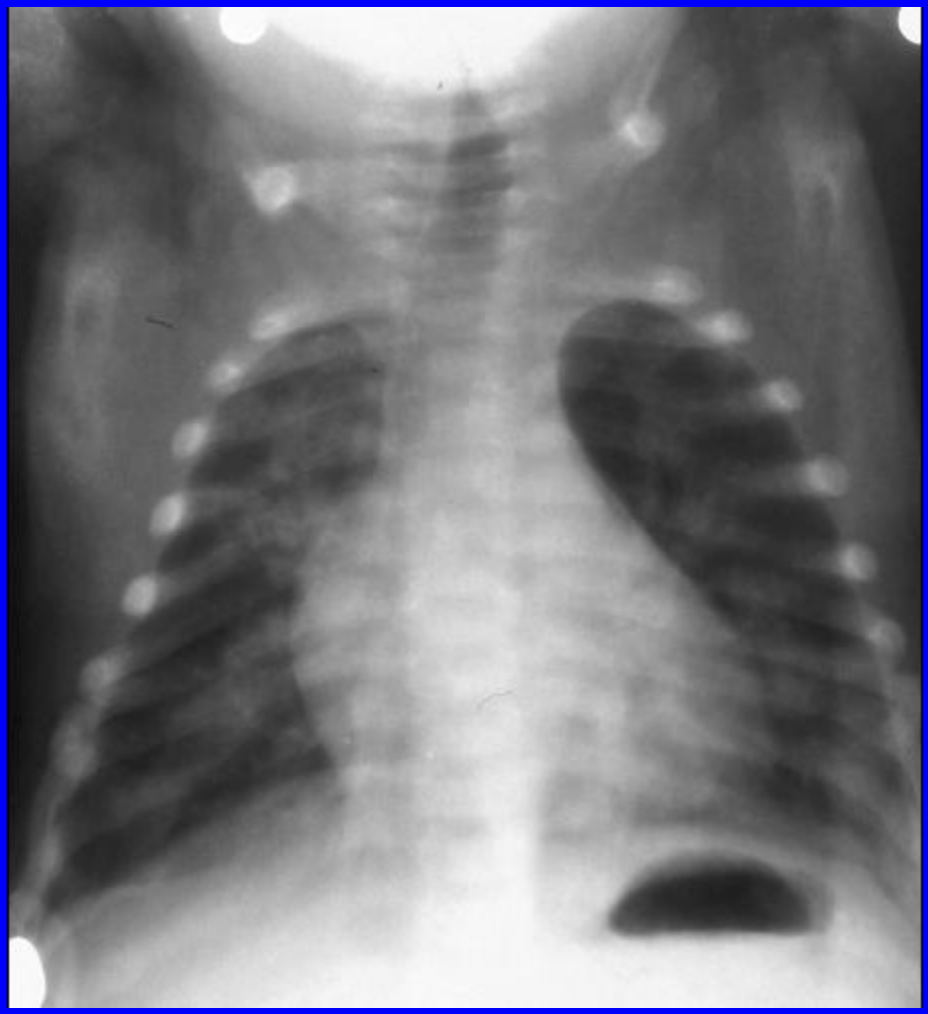
- Lead contained in paint chips is the most common cause of poisoning in children.
- Chronic lead poisoning is characterized by increased opacity in metaphyses representing calcium by defective resorption of calcified cartilage.

Group D5: Lead poisoning

Lead lines pronounced in distal metaphyses of radius, ulna, metacarpalia and proximal phalangies.







Diagnostic puzzle?

Conclusions

- Metabolic bone diseases include a large number of abnormalities.
- Etiological classification in three main groups of mineral, matrix and resorption disorders is practical in differentiation of metabolic disorders.
- Patient history, clinical and laboratory findings are crucial for an adequate diagnosis.
- Generally, genetic evaluation is needed in metabolic bone disorders.
- Skeletal survey should be performed, especially if deformity of other skeletal parts exists.
- Ultrasound, MRI or CT are indicated to exclude renal calcification or in cases with expected brain damage.