
I WAS
BORN TO

CASE REPORT N^{0}1

- **Le Tuan Kiet, male , 3 years old, hospitalized in Children Hospital n^{0}2 on the first November 2010**
- **Reason for admission : thrombocytopenia**
- **History :**

- **In two months, sometimes his gums is bleeding for a moment. He is visited a dentist. The dentist figures out that the rest of his teeth are shaky. These teeth should be extracted to stop gums 's bleeding.**
- **However, his platelet is too low to extract his teeth.**
- **Hence, he is hospitalized.**

- **Past medical history:**
- **Osteopetrosis was diagnosed.**
- **His older brother had osteopetrosis disease and died in his forth year.**
- **Clinical features:**
- **Pale**
- **Splenomegaly grade IV**
- **Hepatomegaly**
- **Dental caries , no bleeding at gums**
- **Nystagmus**

- Labs results

- WBC 12.25 K/µL

  Neu 61.3%

- Hb 8.1 g/dL

  MCV 82.5 fL

  MCH 25.8 pg

  MCHC 31.2 g/dL

- PLT 49 K / µL

CASE REPORT N^{0}2

- Patient: Phan thi N. T.
- Date of birth: 9/1995
- Date of admission: 9/10/1999
- Reason for admission: transported from a province hospital to Children Hospital n^{0}1 with diagnosis: Osteomyelitis of the mandible /thalassemie

- **Symptoms: severe anemia and transfused many times, hepatomegaly (5 cm), splenomegaly (grade 4), pus discharging of mandible**
- **Labs results:**
- **Cell blood counts:**

  WBC: 7700/mm^3,

  Hct: 15% (MCV: 92 fl, MCH: 27,4 pg, MCHC: 29,8%,RDW: 18,6%)

  PLT: 40.000/mm^3

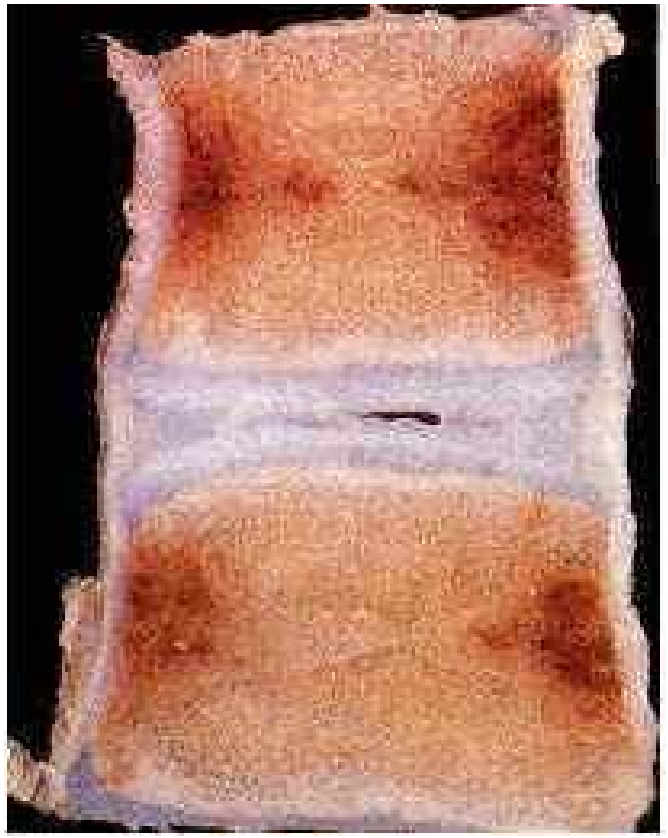
- Hb electrophoresis: normal
- Ultrasound through fontanel: hydrocephalus
- Skull Xray and chest X ray: dense
- Diagnosis: osteopetrosis

What is osteopetrosis?

Osteopetrosis

DEFINITION

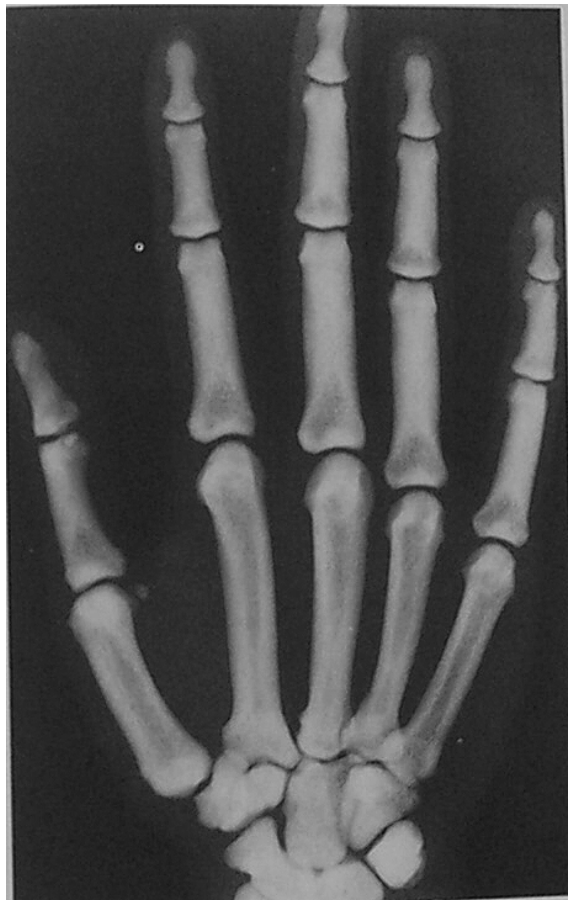
- **A German radiologist, Albers-Schönberg, first described osteopetrosis in 1904.**
- **Osteopetrosis or marble bone disease, is a heterogeneous group of disorders characterized by a generalized increase in bone density caused by defective osteoclastic bone resorption.**
- **Inherited in an autosomal dominant, autosomal recessive or X-linked manner**



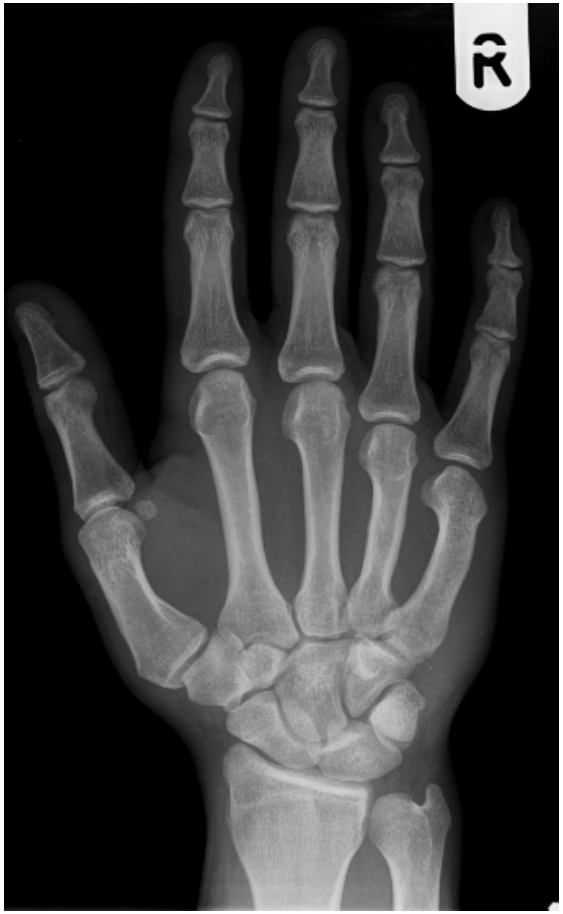
DEFINITION

- As a consequence, bone modeling and remodeling are impaired. The defect in bone turnover characteristically results in skeletal fragility despite increased bone mass, and it may cause hematopoietic insufficiency, disturbed tooth eruption, nerve entrapment syndromes, growth impairment, and a tendency for severe osteomyelitis of the jaws.

Osteopetrosis



Normal



EPIDEMIOLOGY

- It is a rare disease.
- Autosomal recessive osteopetrosis (ARO) has an incidence of 1 in 250,000 births, with a particularly high incidence reported in Costa Rica (3.4:100,000).
- Autosomal dominant osteopetrosis (ADO) has an incidence of 5:100,000 births.

Classification

- ***Severe (malignant or infantile osteopetrosis):*** autosomal recessive form, mutations in a gene encoding an osteoclast-specific subunit of the vacuolar proton pump.
- ***Mild (Benign or aldult osteopetrosis, Albers-Schönberg Disease):*** autosomal dominant form, mutations of the gene encoding the chloride channel protein.

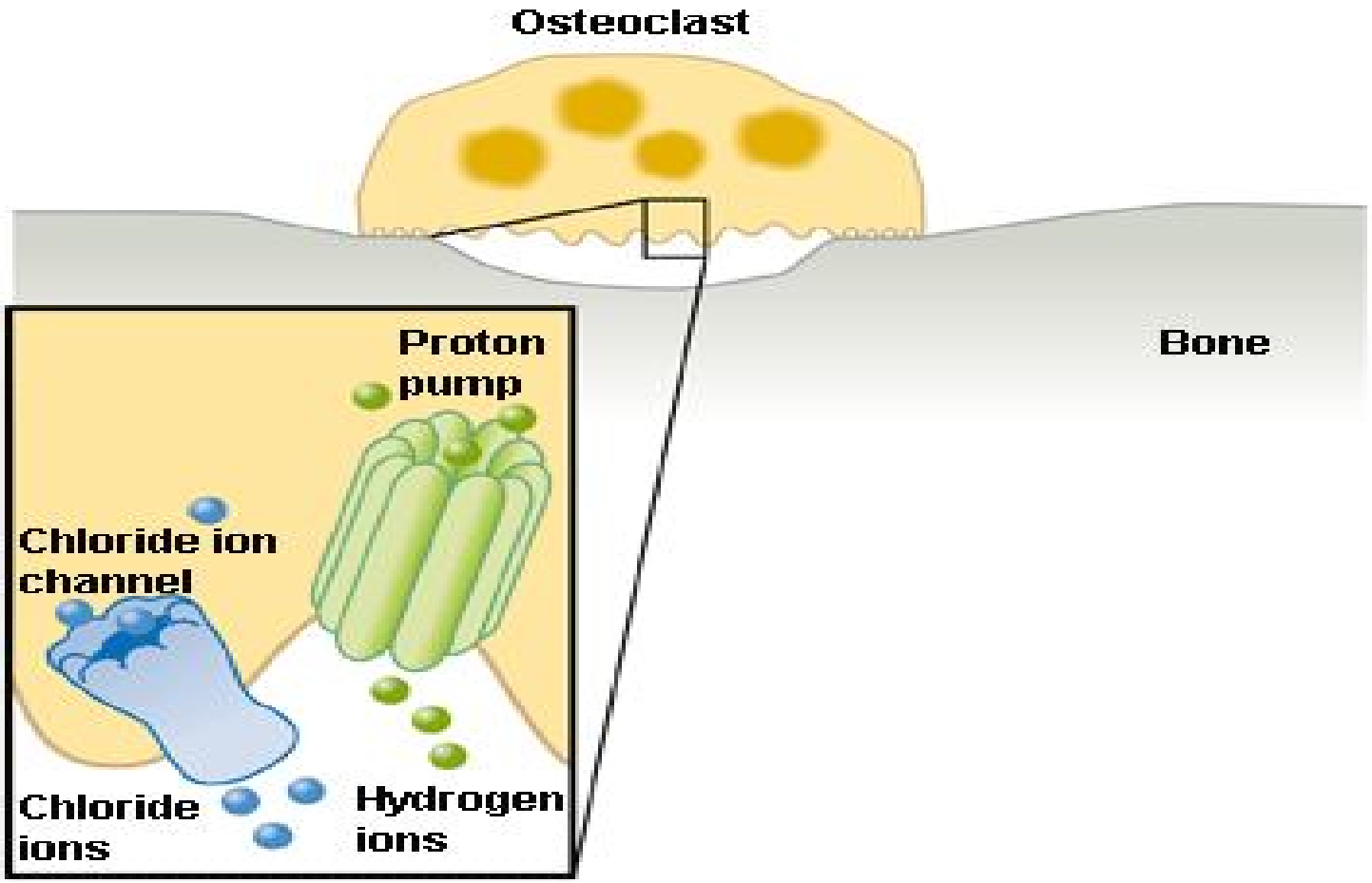
Classification

- ***Intermediate:*** autosomal recessive form
- ***Osteopetrosis accompanied by renal tubular acidosis:***

  Nonlethal autosomal recessive disorder, associated with a complete deficiency of the type II carbonic anhydrase that provides carbonic acid for hydrogen ion secretion by osteoclasts and by the distal tubules. It may involve both distal and proximal lesions. Affected individuals are shorter than their siblings and may have calcification of the basal ganglia. Bone marrow transplantation can correct the skeletal abnormalities.

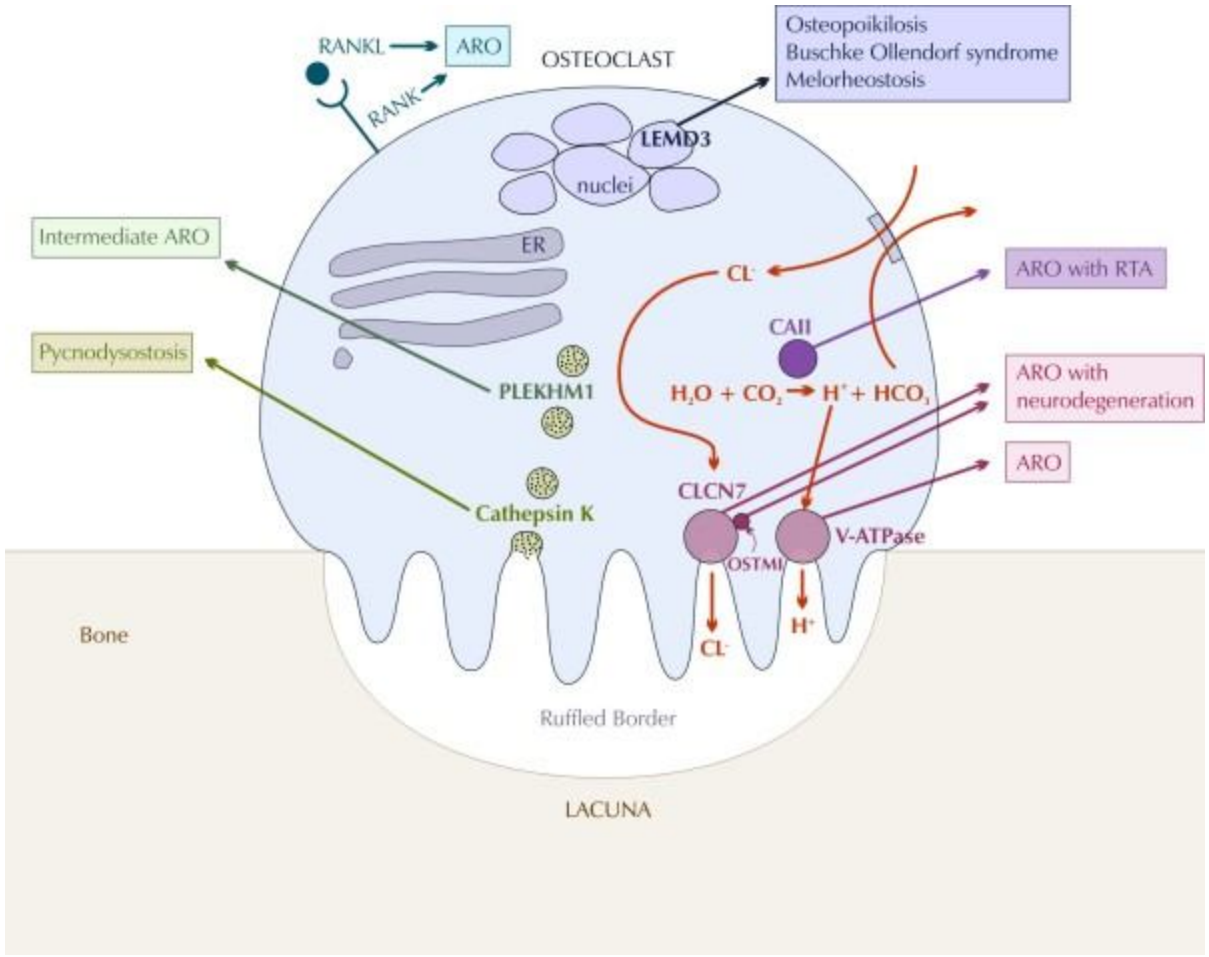
The osteoclast proton pump and chloride ion channel

The figure shows an osteoclast attached to the surface of the bone. The inset image is a magnified osteoclast cell membrane showing a schematic proton pump and chloride ion channel.



Current model of the pathogenesis of osteopetrotic conditions in relation to normal osteoclast function

(ER: endoplasmic reticulum, ARO: autosomal recessive osteopetrosis, RTA: renal tubular acidosis).



Clinic classification

Characteristic	Adult onset	Infantile	Intermediate
Bone marrow failure	None	Severe	None
Prognosis	Good	Poor	Poor
Diagnosis	Often diagnosed incidentally	Usually diagnosed before age 1 y	Not applicable

Symptoms

MALIGNANT OSTEOPETROSIS

- Growth retardation
- Macrocephaly and frontal bossing develop within the first year
- Fracture easily.
- Bony defects occur: Nasal stuffiness due to mastoid and paranasal sinus malformation
- Dentition delayed
- Neuropathies related to cranial nerve entrapment: deafness, proptosis, and hydrocephalus.
- Osteomyelitis of the mandible due to an abnormal blood supply.

Symptoms

MALIGNANT OSTEOPETROSIS

- Defective osseous tissue tends to replace bone marrow, causing bone marrow failure with resultant pancytopenia: anemia, easy bruising and bleeding (due to thrombocytopenia), and recurrent infections (due to inherent defects in the immune system). Extramedullary hematopoiesis whith hepatosplenomegaly, hypersplenism, and hemolysis.
- Other manifestations: sleep apnea and blindness due to retinal degeneration, tetanic seizures (hypocalcaemia) and secondary hyperparathyroidism .

Symptoms

BENIGN

- Asymptomatic in one half of patients , diagnosed often in late adolescence because radiologic abnormalities appearing only in childhood. In other patients, the diagnosis is based on family history.
- Fractures: approximately 40% of patients having recurrent fractures
- Osteomyelitis: Osteomyelitis of the mandible occurring in 10% of patients.
- Scoliosis
- Bone pains.

BENIGN

- Bony defects are common and include neuropathies due to cranial nerve entrapment (eg, with deafness, with facial palsy), carpal tunnel syndrome, and osteoarthritis.
- Bone marrow function not compromised.
- Other manifestations: visual impairment due to retinal degeneration and psychomotor retardation

Symptoms

INTERMEDIATE

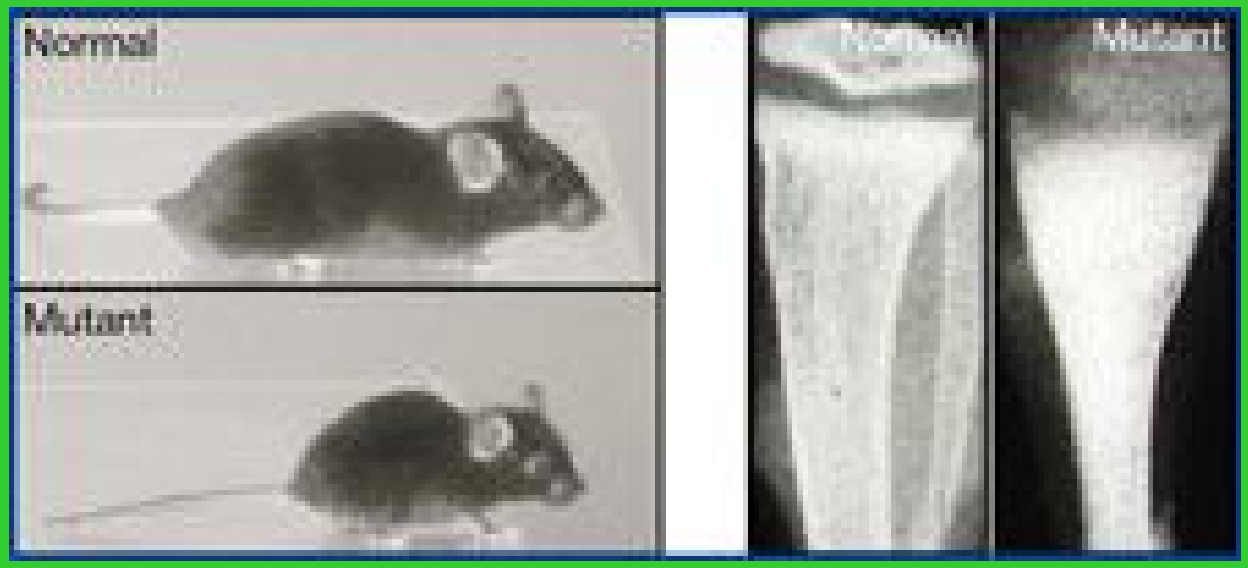
- Symptoms not fit clearly in two recognizable categories, more severe than those described as benign
- Diagnosed in the first decade of life
- Will be no family history

Symptoms

ARO with RENAL TUBULAR ACIDOSIS (RTA)

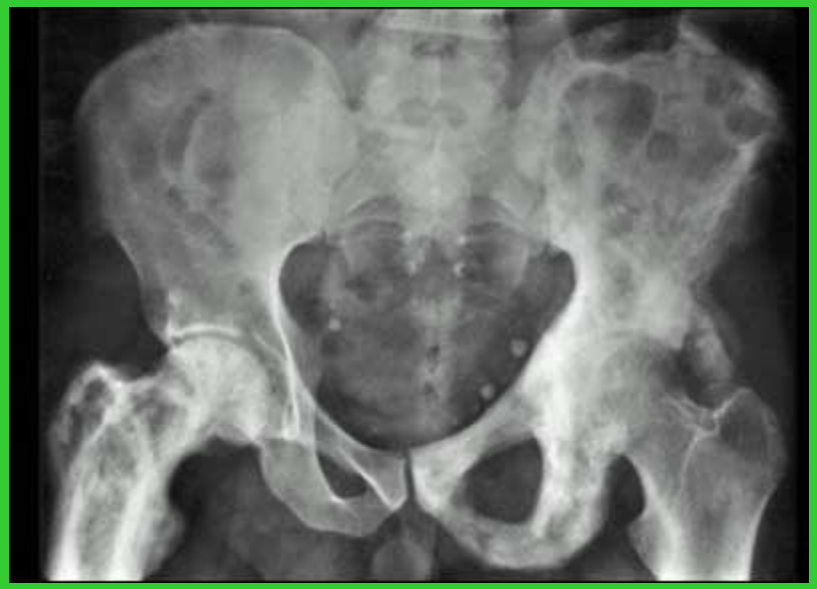
- Milder course
- Cerebral calcifications are typical
- Other clinical manifestations: fractures, short stature, dental abnormalities, cranial nerve compression and developmental delay

Malignant



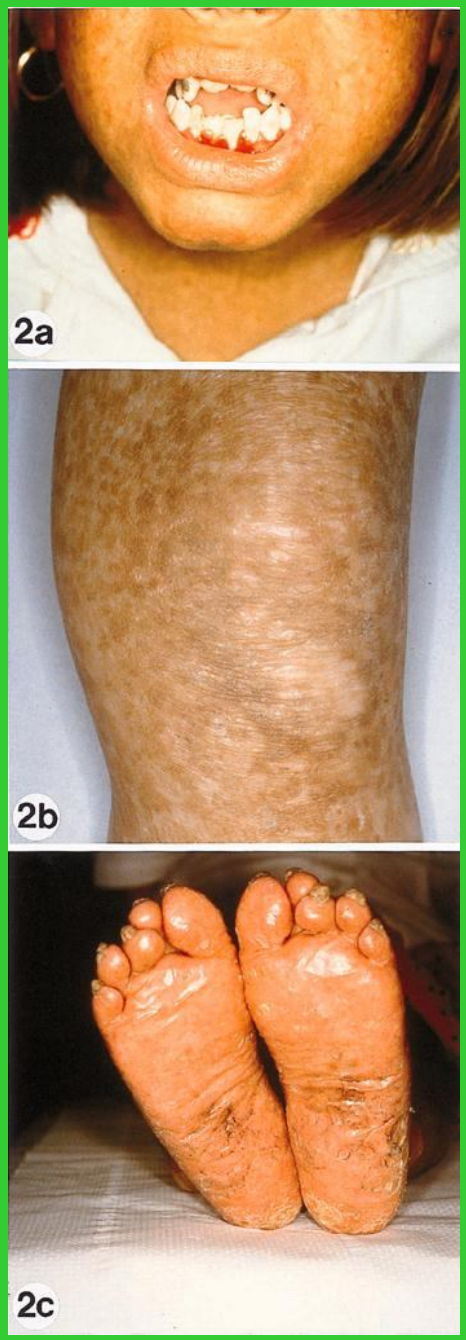
http://www.nature.com/nature/journal/v409/n6822/full/409778a0.html

Benign



www.endotext.org/.../ figures15/figure4.jpg

Intermediate



Laboratory Studies

- ***Findings in infantile osteopetrosis***
  - Hypocalcemia
  - Parathyroid hormone (PTH) often elevated (secondary hyperparathyroidism).
  - Acid phosphatase increased due to increased release from defective osteoclasts.
  - Levels of creatinine kinase isoform BB (CK-BB) increased due to increased release from defective osteoclasts.

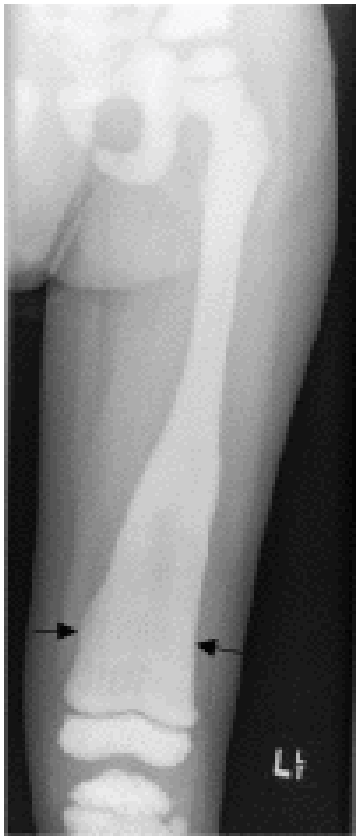
Laboratory Studies

- ***Findings in adult osteopetrosis***
  - Acid phosphatase and CK-BB concentrations increased
  - Serum bone-specific alkaline phosphatase values may also be increased
- ***Other findings***
  - Mutation screening of appropriate candidate genes
  - Knowledge of the molecular basis of the osteopetrosis allows clinicians to provide informed genetic counseling and, in some cases, to choose appropriate therapy

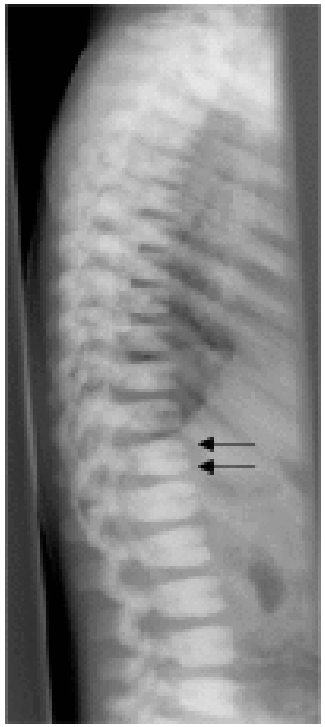
Imaging Studies

- *X ray:*
  - Generalized osteosclerosis
  - Skull thickened and dense
  - Small sinuses and underpneumatized
  - Fractures or osteomyelitis
- *MRI* used to assess bones over time after bone marrow transplantation

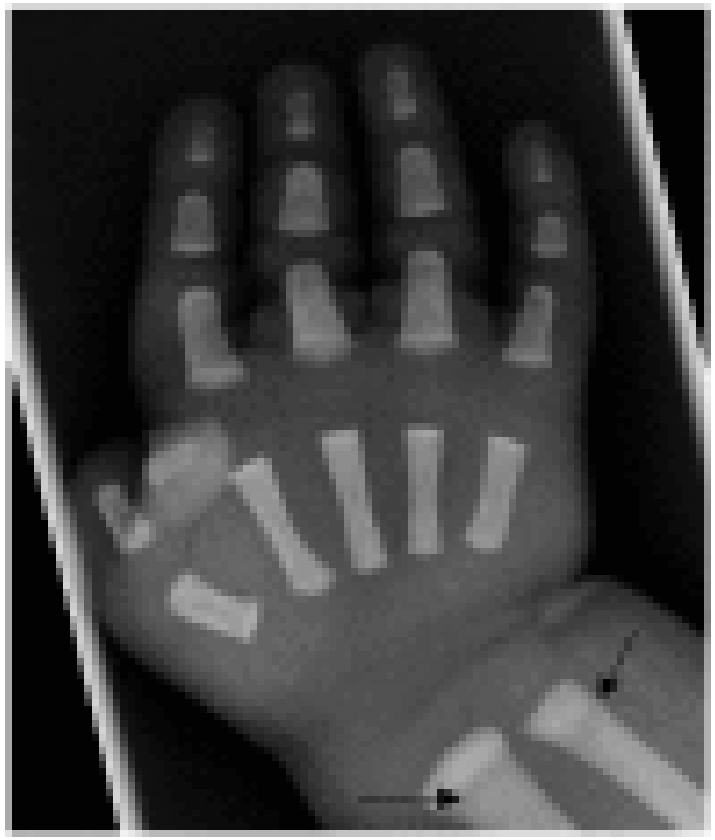
ADO: Radiograph of left femur, age 4 years.



- **ADO: lateral spine radiograph, age 4 years**.

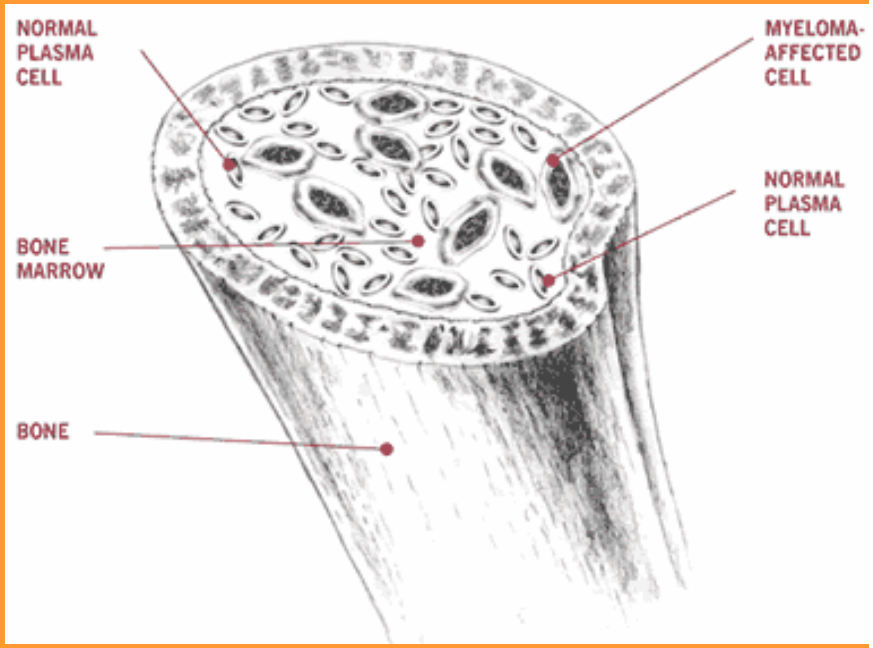


- **Severe ARO: Right hand radiograph, age 2 weeks**.



Treatment

- **Both the adult and childhood forms of osteopetrosis may benefit from Actimmune (interferon gamma) injections.**
- **Bone marrow transplant is the only complete cure available for malignant infantile osteopetrosis. This is used only in children severely, but if it is successful it saves the life of the child who would otherwise die from the disorder.**
- **Other treatments include calcitrol (stimulating dormant osteoclast), erythropoietine,**



Prognosis

- **Patients with the adult form of osteopetrosis have a normal life span.**
- **Less than 30 percent of all children with the severe malignant infantile form of osteopetrosis survive to their tenth birthday, unless they are treated with BMT or a combination of interferon gamma and calcitriol. Only 10 percent of infants who have blindness and anemia before six months old survive more than one year unless they are successfully treated.**