# RICKETS IN CHILDREN

Cracea Angela, Department of Pediatrics

# RICKETS IN CHILDREN

**DEFINITION**: Rickets is consequence of the vitamin D deficit and may occur due to calcium and phosphorus metabolic disorders.

- Blood analysis shows hypocalcemia and hypophosphatemia.
- Histology- Failure in mineralisation of the bone and cartilaginous tissues .
- Clinical- manifests as skeletal growth disorder.

# Hystory

- Rickets ( from Greek word meaning spinal column ) was known since the first years of the
- human generation. It is described by Soran Efess (A.D) and by Galen (134-211 A.D).
- It is described in detail by a British anatomist and orthopedician, Glisson in 1650.
- Incidence:
- Rickets is frequently in premature children and the children fed only wheat floor.
- In Moldova diagnosis was confirm in 35.5%, X-Ray -21.5% (A.Voloc, M.Garabedian, 1996)

# Risk factors

- Living in northern latitudes (>30o);
- Black children- inadequate skin penetration of sunlight;
- Decreased exposure to sunlight ( polluted geographical areas, humid climate);
- Maternal vitamin D deficiency;
- Diets low in calcium, phosphorus and vitamin D, e.g. exclusive breast-feeding into late infancy, toddlers on unsupervised “dairy-free” diets;
- Macrobiotic, strict vegan diets;
- Phytates of cereals, stearic and palmitic acids decrease calcium absorption;
- Prolonged parenteral nutrition in infancy with an inadequate supply of intravenous calcium and phosphate;

- Intestinal malabsorption: defective production of 25(OH)D3 – liver disease. Increased metabolism of 25(OH)D3 – enzyme induction by anticonvulsants;

Defective production of 1,25(OH)2D3

- Hereditary type I vitamin D-resistant (or dependent) rickets (mutation which abolishes activity of renal hydroxylase);
- Familial (X-linked ) hypophosphataemic rickets – renal tubular defect in phosphate transport;
- Chronic renal disease;
- Fanconi syndrome (renal loss of phosphate)
- Target organ resistance to 1,25(OH)2D3- hereditary vitamin D-dependent rickets type II (due to mutations in vitamin D receptor gene).

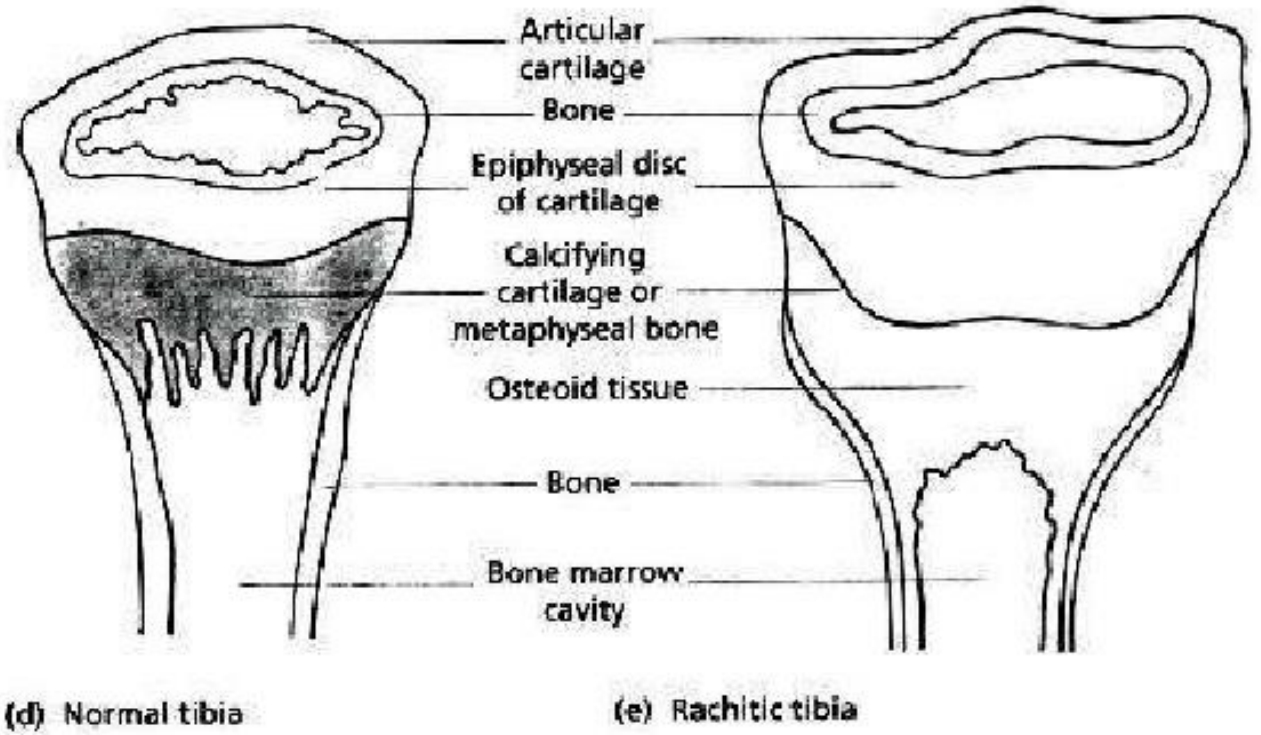
# ETIOLOGY

- Rickets is due to partial deficiency, rarely complete deficiency of vitamin D.
- Vitamin D exist  in 2 forms in the human body.
- Vitamin D2, exogenous form (calciferol), from ergosterol in the food
- Vitamin D3, endogenous form (cholecalciferol or provitamin stage 7-dehydrocholecalciferol , naturally present  in human  skin), activated by UV rays of 296-310nm wave length.
- Natural alimentation does not supply the daily requirement of 400-500IU of vitamin D in a baby.
- Breast milk contains 30-50IU/liter, cow's milk 20-30IU/l, egg yolk contains 20-50IU/10gr.
- 80% of the vitamin D is absorbed in the small intestine in the present of normal biliary secretion.
- Vitamin D reaches the blood through thoracic duct along with chilomicrons.

# Pathogenesis of rickets

In Ricket cartilage cells fail to complete their normal cycle of proliferation and degeneration;

subsequent failure of capillary penetration occurs in a patchy manner(Fig)



- Calcium regulation in the blood is as follows:
- Vitamin D2 in the food (exogenous) + vitamin D3 (skin, endogenous) =>liver microsomal hydroxylate =>25(OH) D3
- In the renal cortical cells => activated from 1alpha-hydroxilase in 3 forms:
- 24,25 (OH)2 D3; 1,24,25 (OH)2 D3; 1,25 (OH)2 D3 end product considered a hormone.
- In placental macrophage of pregnancy women are present 1,25(OH)2 D3

# FUNCTIONS OF VITAMIN D

Intestine- 1,25(OH)2D3 promote:

- Increases calcium binding protein
- Active transport in the jejunal cells
- Phosphorus ions absorption through specific phosphate carrier
- Alkaline phosphatase (AP) synthesis
- ATP-ase sensibility to calcium ions

# Bones

- Mineralization of the bone and osteoblasts differentiation in presence of adequate calcium and phosphorus
- Deposition and reabsorption of calcium and phosphorus, normal calcification
- Skeletal growth and mineralization involve vitamin D-PTH-endocrine axis, growth hormone via somatomedins, thyroid hormones, insulin, androgens and estrogens in puberty

# Kidney

- 1.25(OH)2D3 increase tubular re-absorption of calcium and phosphorus
- In rickets PTH blocks phosphorus reabsorption in kidney, elevated serum phosphatase due to increse osteoblastic activity
- Hypophosphatemia blocks PTH secretion and promotes 1,25(OH)2D3 synthesis, the most active metabolite of vitamin D

# Muscles

- Vitamin D increase the muscular protein and the ATP in myocyts

- Improve tonicity and the normal contraction of the muscles

# Parathyroid glands

- 1,25(0H)2D has direct feedback to PTH synthesis
- Low plasma calcium=> PTH secretion restore Ca from bone demineralization
- Secretion of PTH stimulate synthesis of 1,25(OH)2D3, increase calcium intestinal absorption, renal calcium reabsorption
- Calcitonin (secretion of C cells of thyroid gland) increase bone calcium deposition

# Other effects of vitamin D

- Cellular metabolism: citric acid oxidation
- Formation of soluble complex of citrate and Ca in the blood
- Skin differentiations in the local treatment of Psoriasis
- Pulmonary differentiation (increases the surfactant in preterm infants)
- Immunomodulatory action in autoimmune disorders

# Biochemical stages of rickets

- Stage 1: Low serum Ca level, normal serum P; normal serum PTH, little raise AP, Ca and P tubular re-absorption are normal, no amino acid loss in the urine.

# Biochemical stages of rickets

**Stage 2**. Raised PTH in the serum, serum Ca is normalized by bone demineralization.

Change in the ratio of Ca : P ( N=2:1), in this stage become 3:1 or 4:1, high serum AP.

Raised Ca tubular re-absorption and decrease phosphate tubular re-absorption.

As a result => hyper-aminoaciduria. Phosphates are lost in the urine, alkaline Ph.

X-ray findings: Osteoporosis and metaphyseal-epiphyseal changes.

# Biochemical stages of rickets

**Stage 3**. Severe deficiency of vit.D for a long duration. Laboratory reports:

Hypocalcemia, hypophosphatemia, serum elevated of AP, PTH; hyperaminoaciduria, Radiological changes more expressive.

# CLASSIFICATION

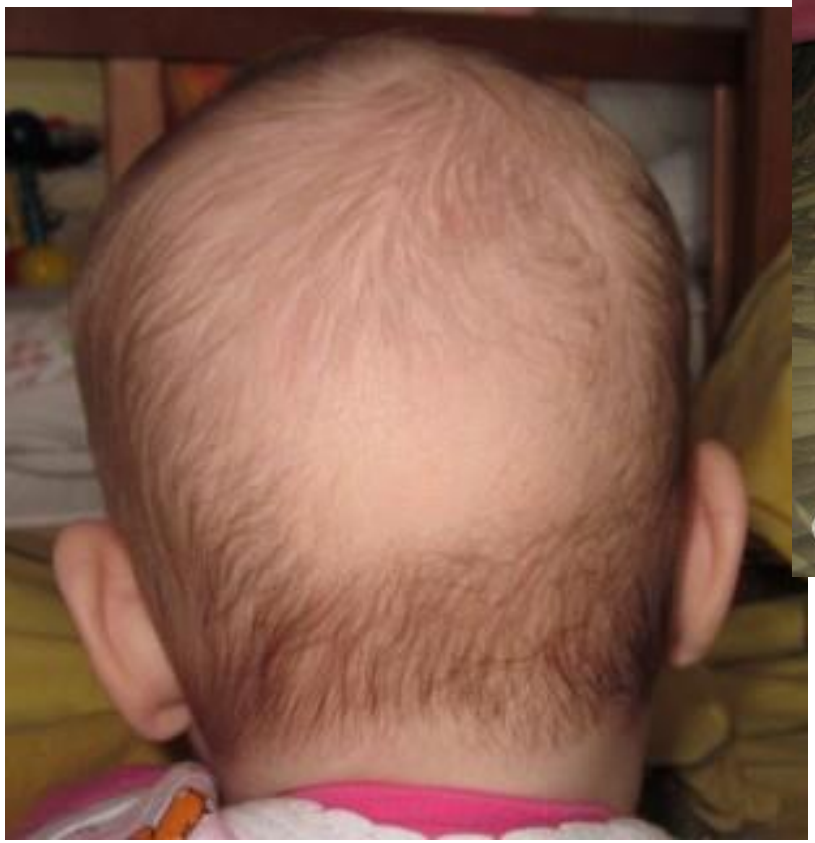
Calcium deficiency rickets can be classified in to 3 grades- I, II, III,

Depending on the duration, evolution and the complication:

1. Grade I, II, III; evolution acute, subacute, recurrent.
2. Depending on vitamin D insufficiency:
   A) Diet
   B) Infections
   C) Food diversification
   D) Habitual
   E) No prophylaxis
   F) Prophylaxis with low dose
   G) Phenobarbital induced

# COMPLICATIONS

- Rickets tetany
- Convulsions
- Respiratory disorders
- Cardiac disorders
- Skeletal deformation
- Frequent illness

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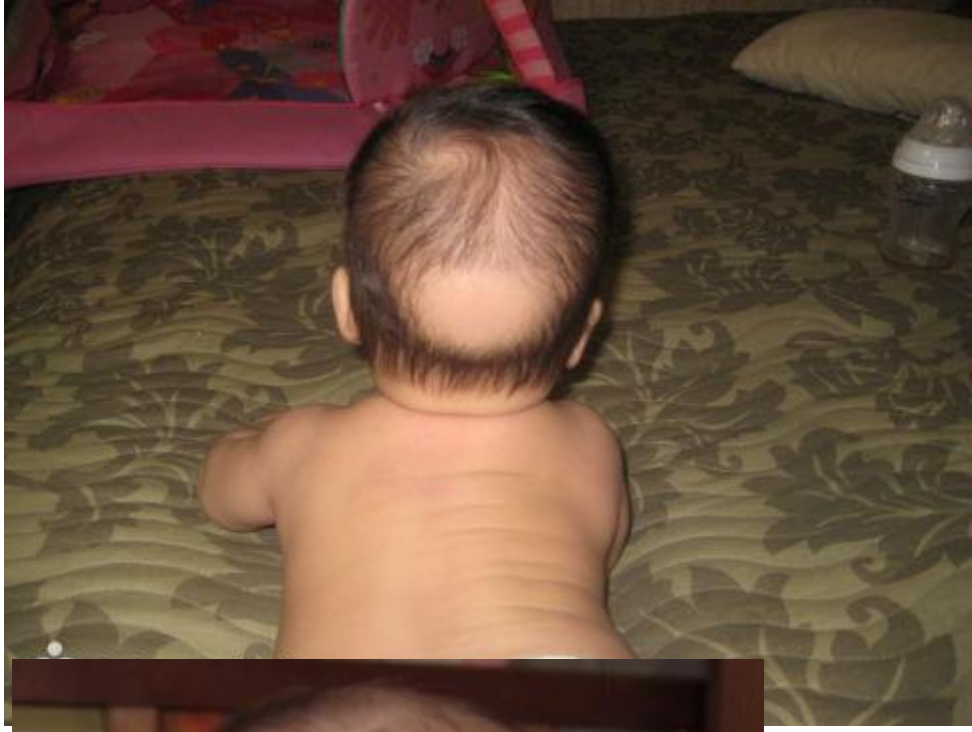
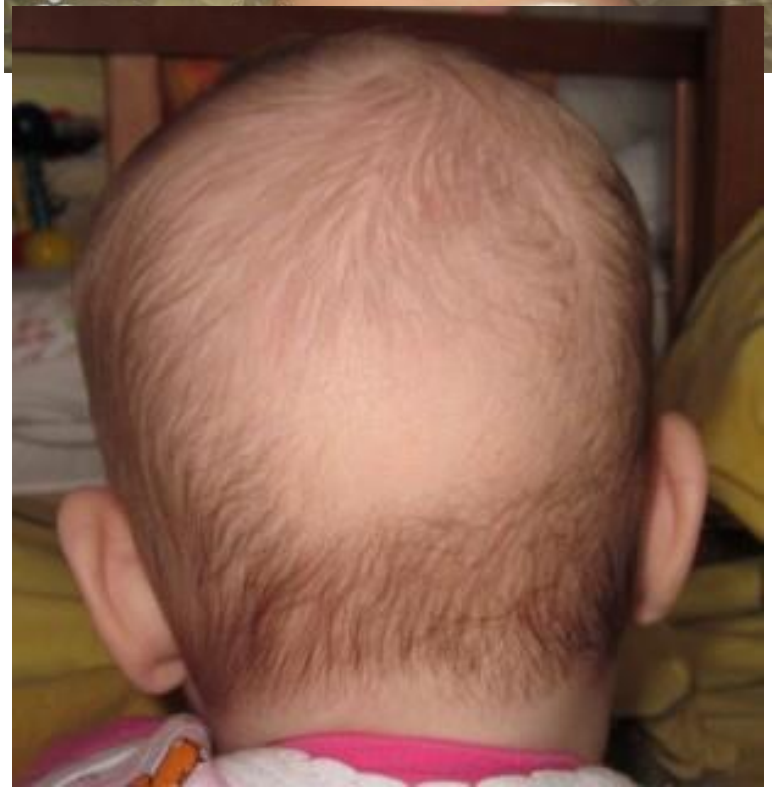


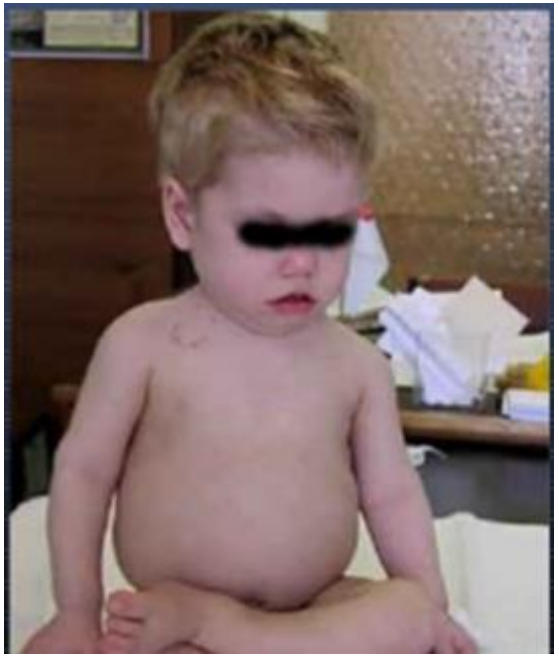


# Muscular hypotonia

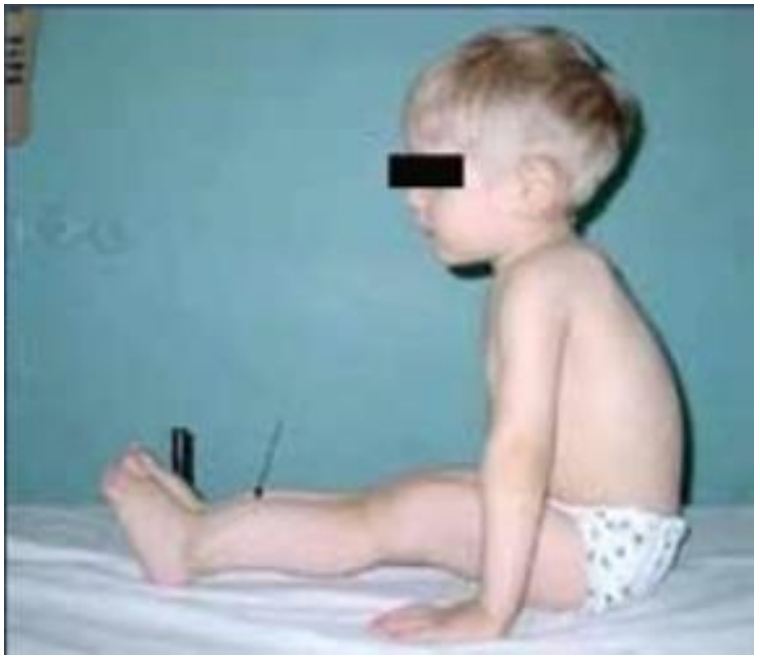
## Increased lability of articulations
## «Pocket knife» symptom

# Clinical manifestation of rickets

Muscular hypotony



Tibia convexity



# CLINICAL MANIFESTATIONS

Rickets may develop in any age of an infant, more frequent at 3-6mo, early in premature infants.

- The first signs of hypocalcaemia are CNS changes- excitation, restlessness, excessive sweating during sleep and feeding, tremors of the chin and extremities.
- Skin and muscle changes- pallor, occipital alopecia, fragile nails and hair, muscular weakness, motor retardation.
- Complications- apnea, stridor, low calcium level with neuromuscular irritability (tetany).
- CNS changes are sometimes interpreted as CNS trauma and the administration of the Phenobarbital which interfere in metabolism of vitamin D and after 1-2wk of treatment with Phenobarbital the clinical stage worsens.

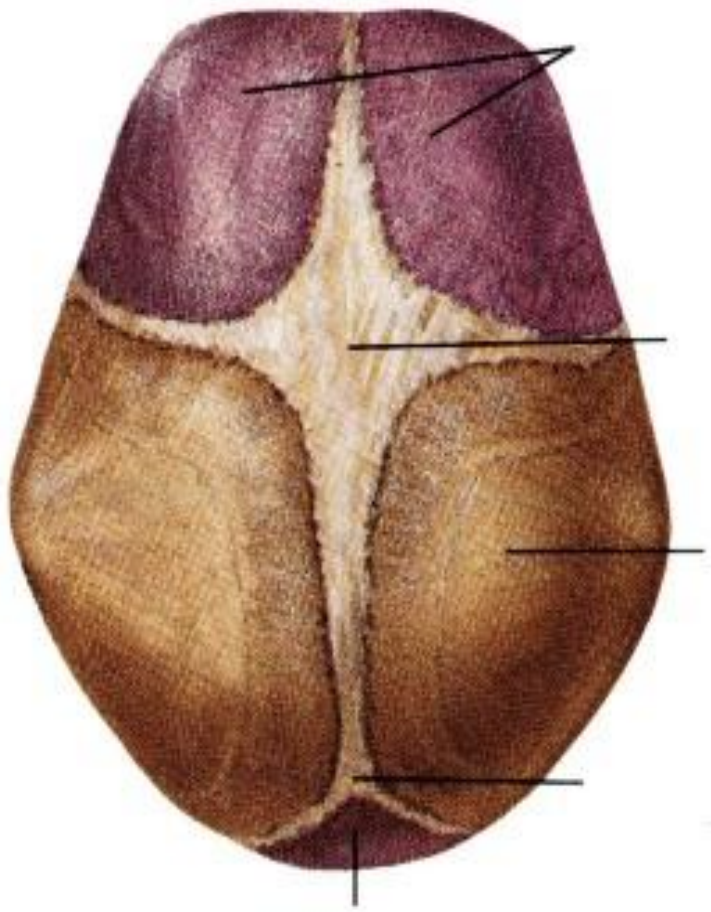
# ACUTE SIGNS

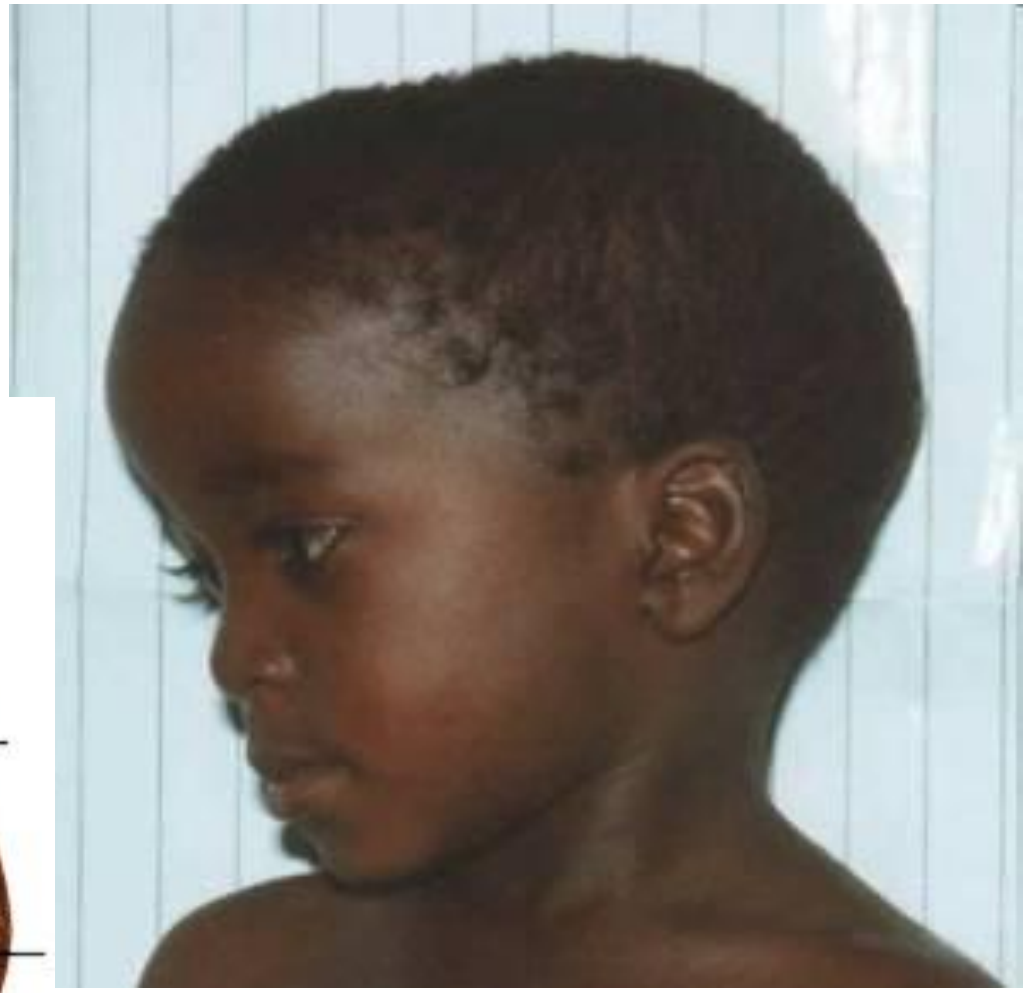
Florid (acute) rickets clinical signs:

- Craniotabes– osteomalacia, acute sign of rickets, detected by pressing firmly over the occipital or posterior parietal bones, ping-pong ball sensation will be felt. Large anterior fontanella, with hyperflexible borders, cranial deformation with asymmetric occipital flattening.

# SUBACUTE SIGNS

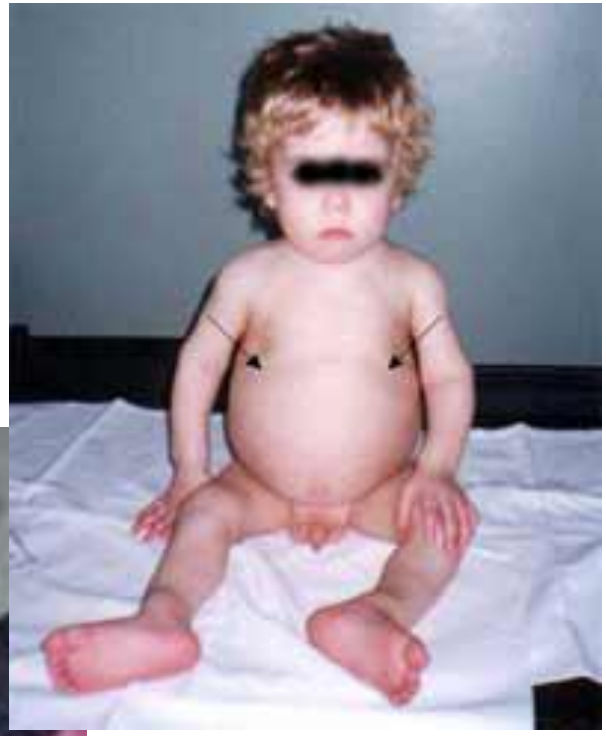
- Subacute signs are all the following: frontal and temporal bossing
- False closure of  sutures (increase protein matrix), in the X-ray craniostenosis is absent.
- Maxilla in the form of trapezium, abnormal dentition.
- Late teeth eruption, enamel defects in the temporary and permanent dentition.
- Enlargement of costo-chondral junctions-“rachitic rosary”
- Thorax, sternum deformation, softened lower rib cage at the site of attachment of the diaphragm- Harrison groove.

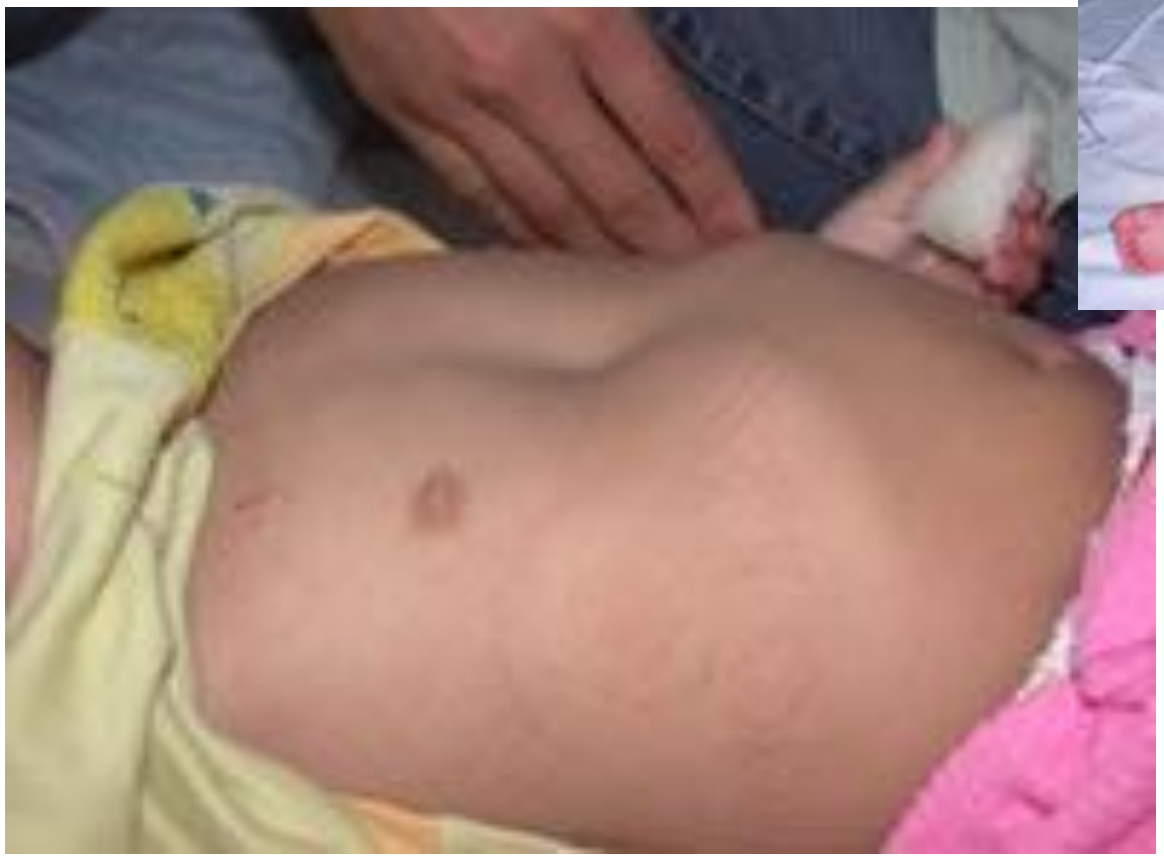




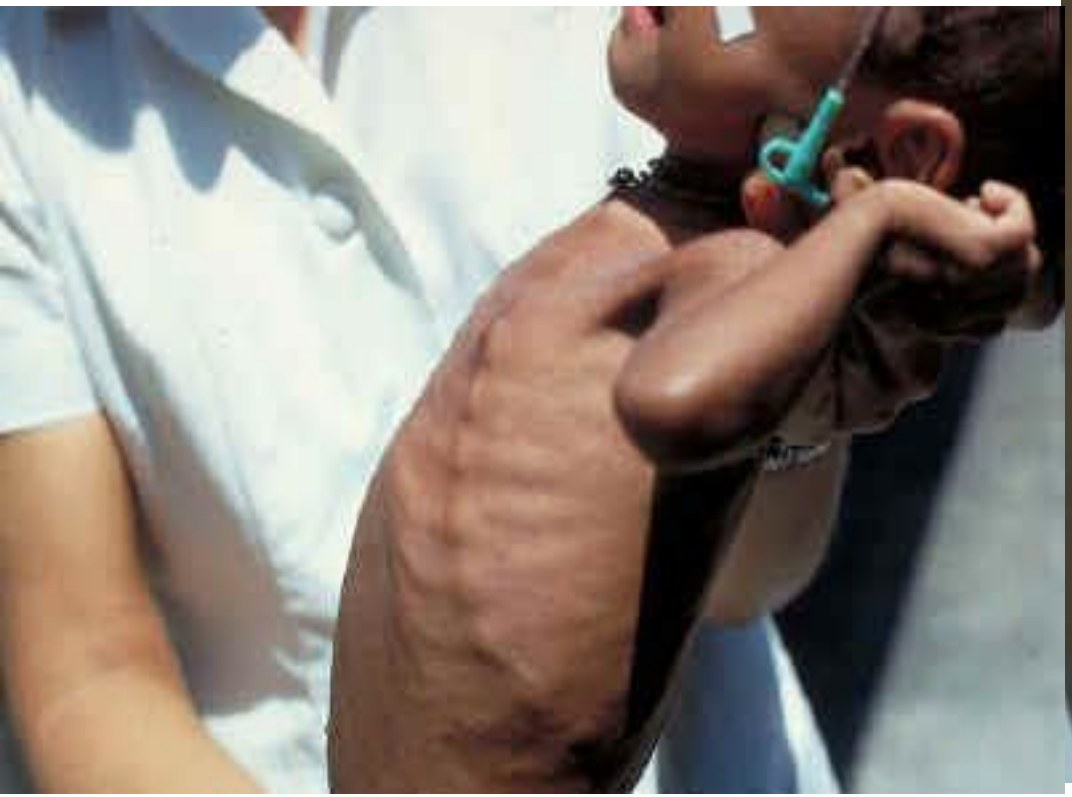
boxlike appearance

# Harrison fissure





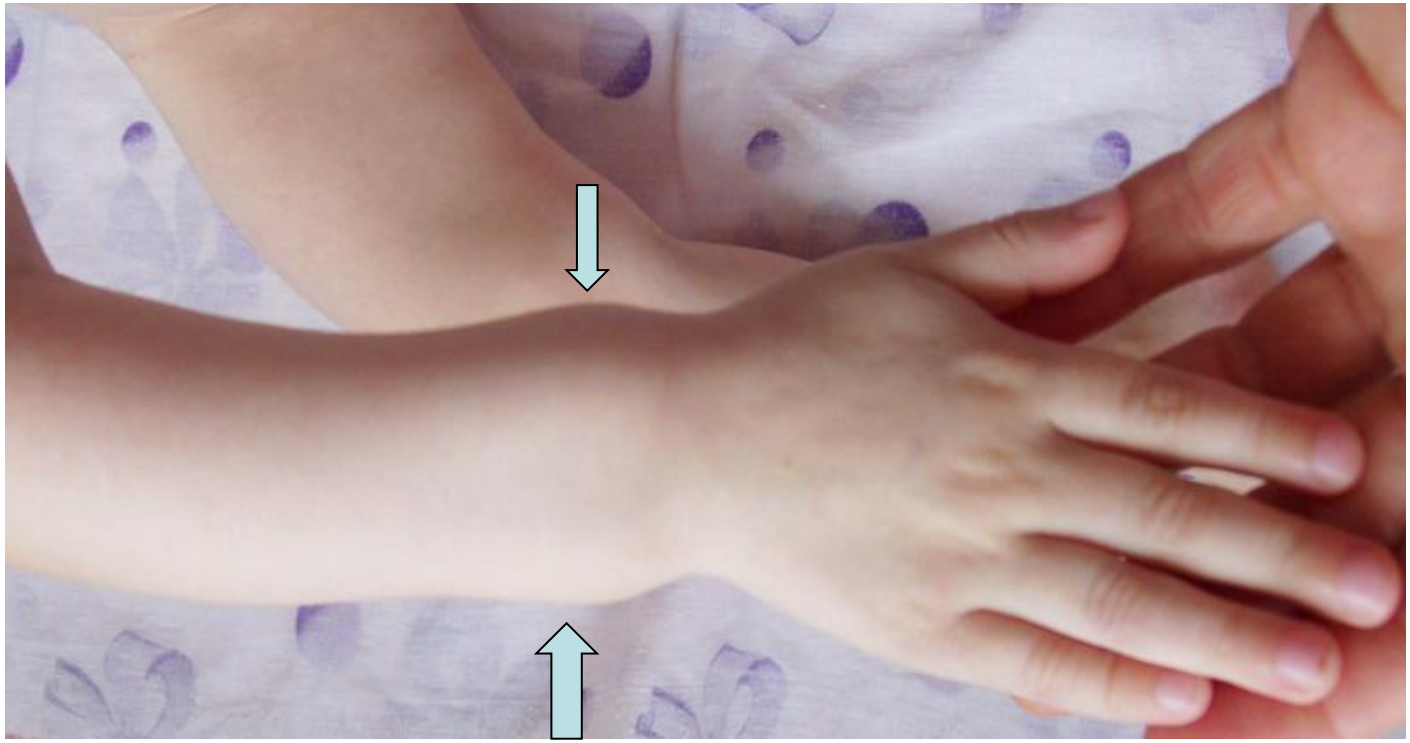
# Rickets rosary



# Subacute rickets signs

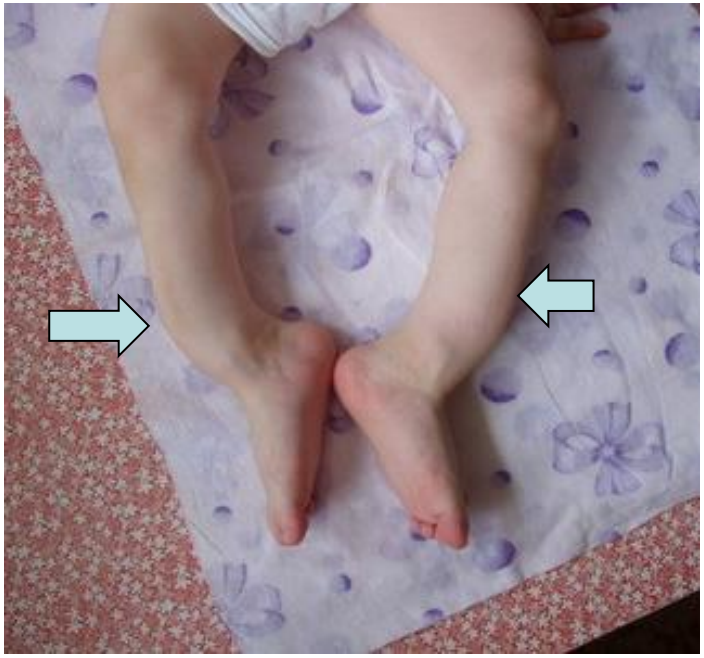
- Spinal column- scoliosis, lordosis, kyphosis.

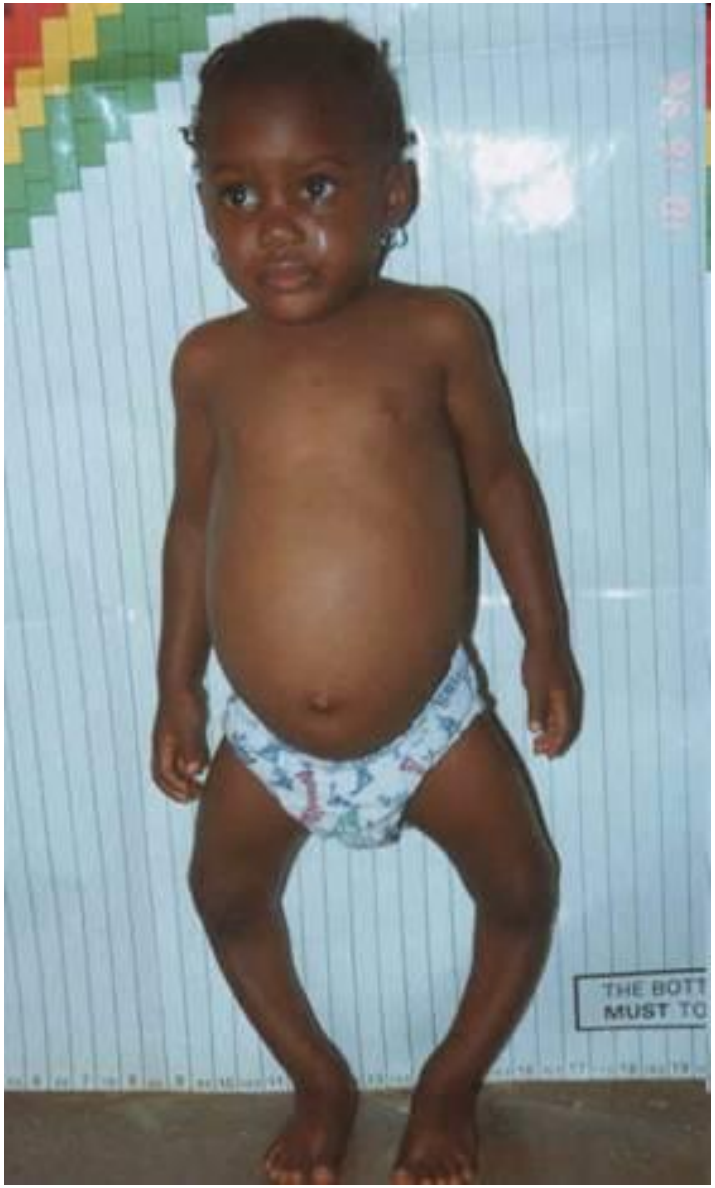
- Pelvis deformity, entrance is narrowed (add to cesarean section in females)
- Extremities- thickening wrist and ankles, tibia anterior convexity, bowlegs or knock knees legs.
- Deformities of the spine, pelvis and legs result in reduced stature, rachitic dwarfism.
- Delayed motor development (head holding, sitting, standing, walking).



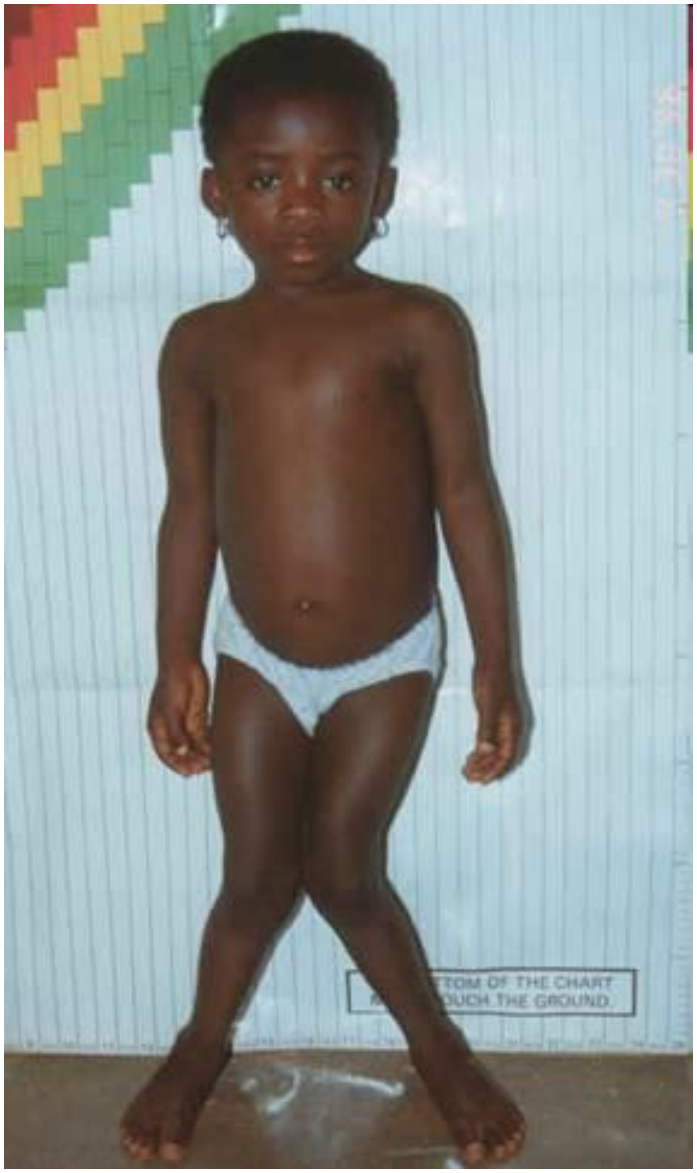
**Thickening of the wrists**

**Deformation of the legs**





“O”- shaped legs



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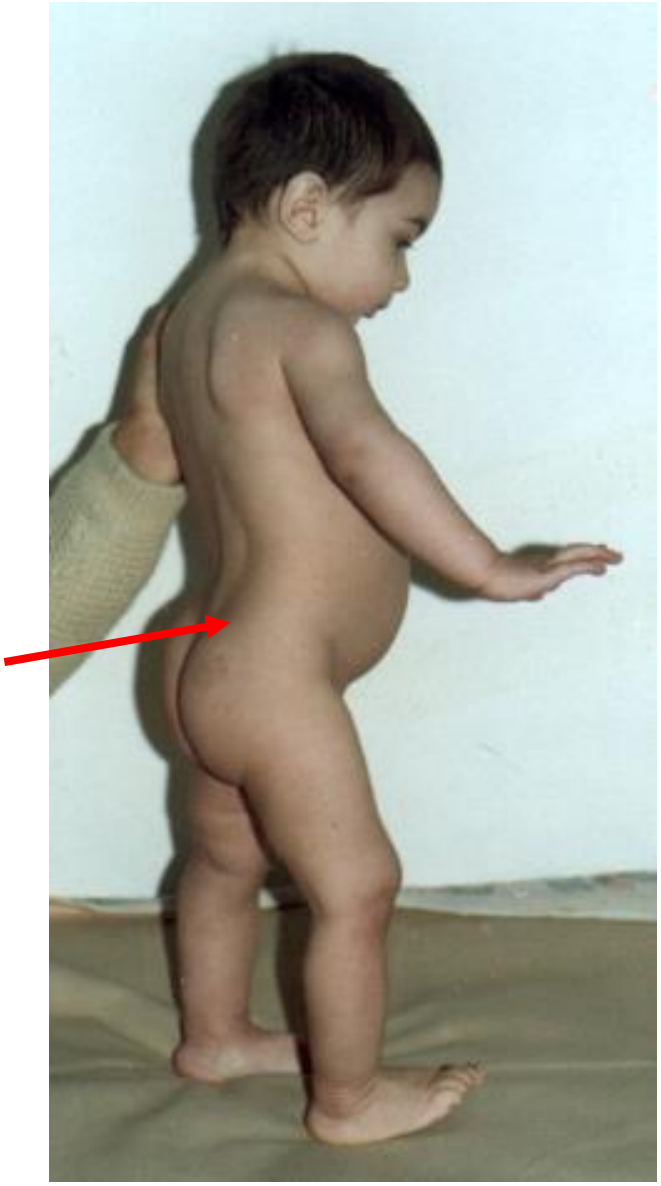
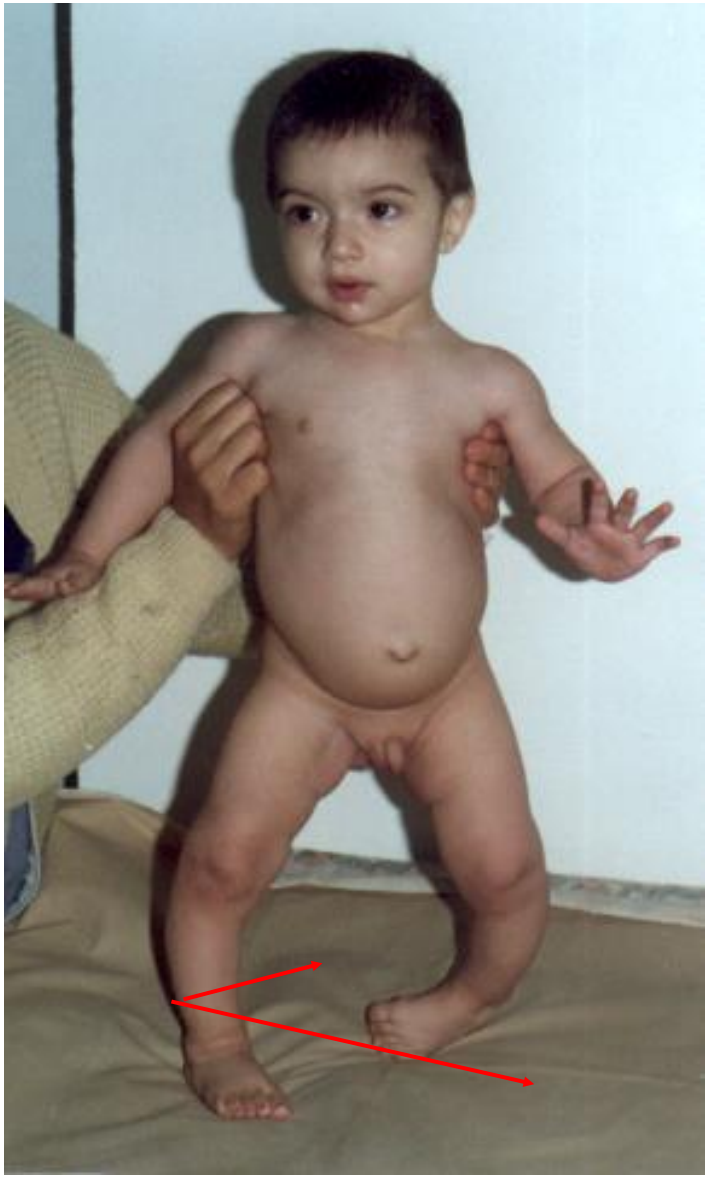


Lordosis of vertebral column lumbar part



“O”-shaped deformation of the legs

# Changes of osseous system in rickets

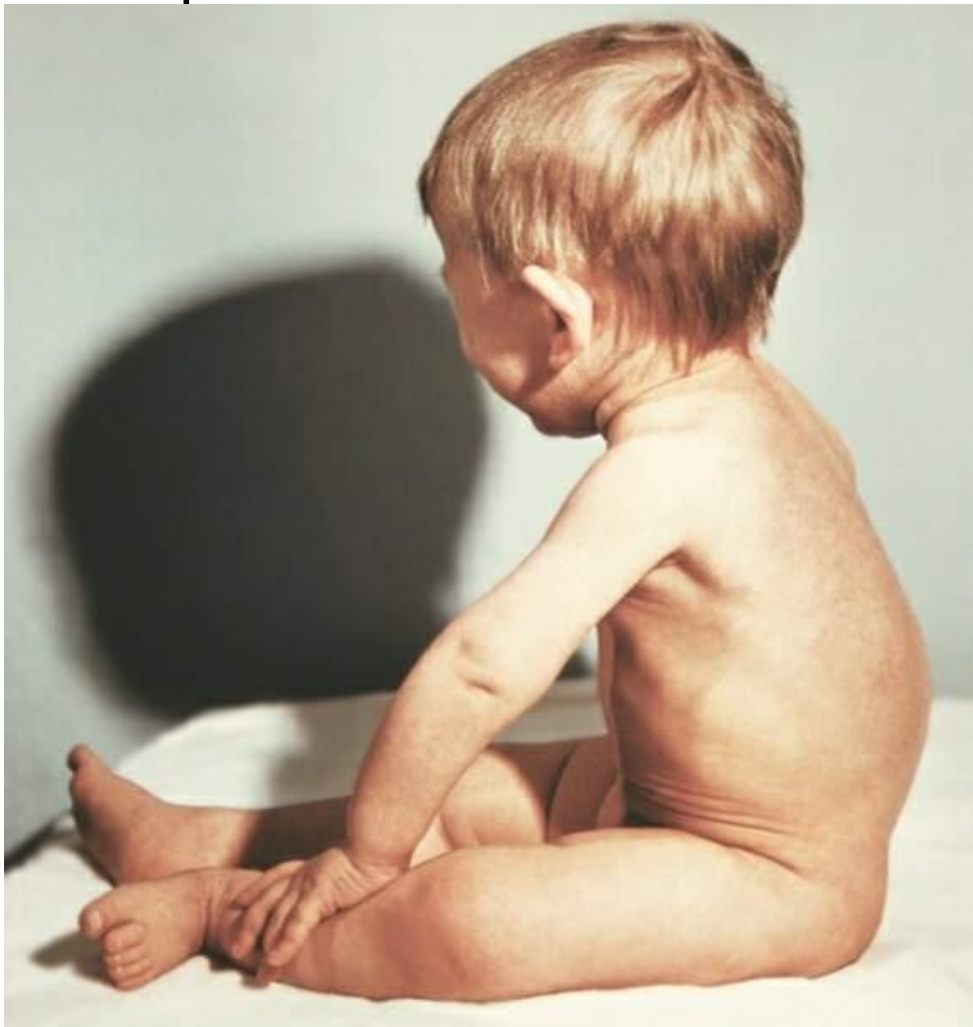
## Deformation of vertebral column

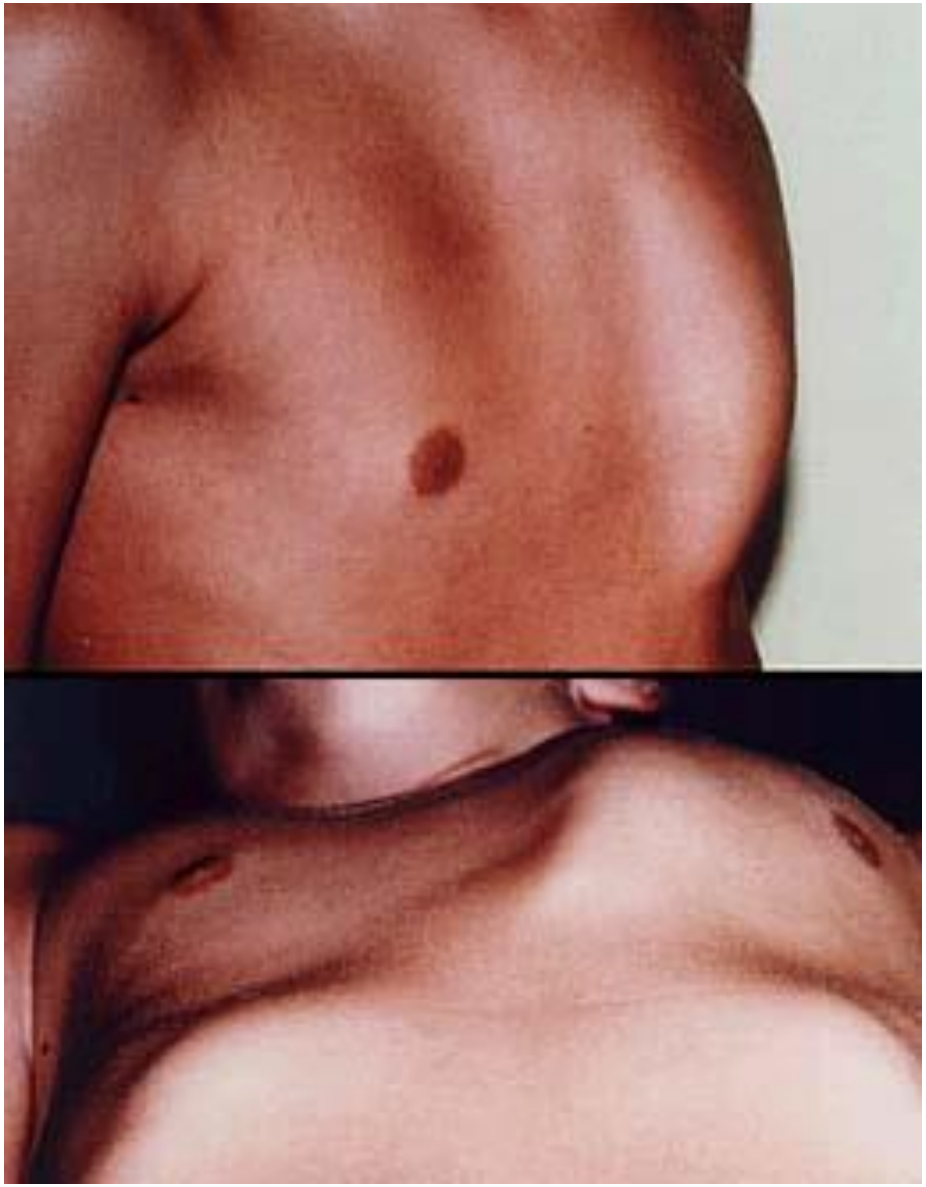
Kyphosis in the lower part of thoracic vertebrae. Kyphosis or lordosis in lumbar part. Scoliosis in thoracic part.

**Pelvic bones:**

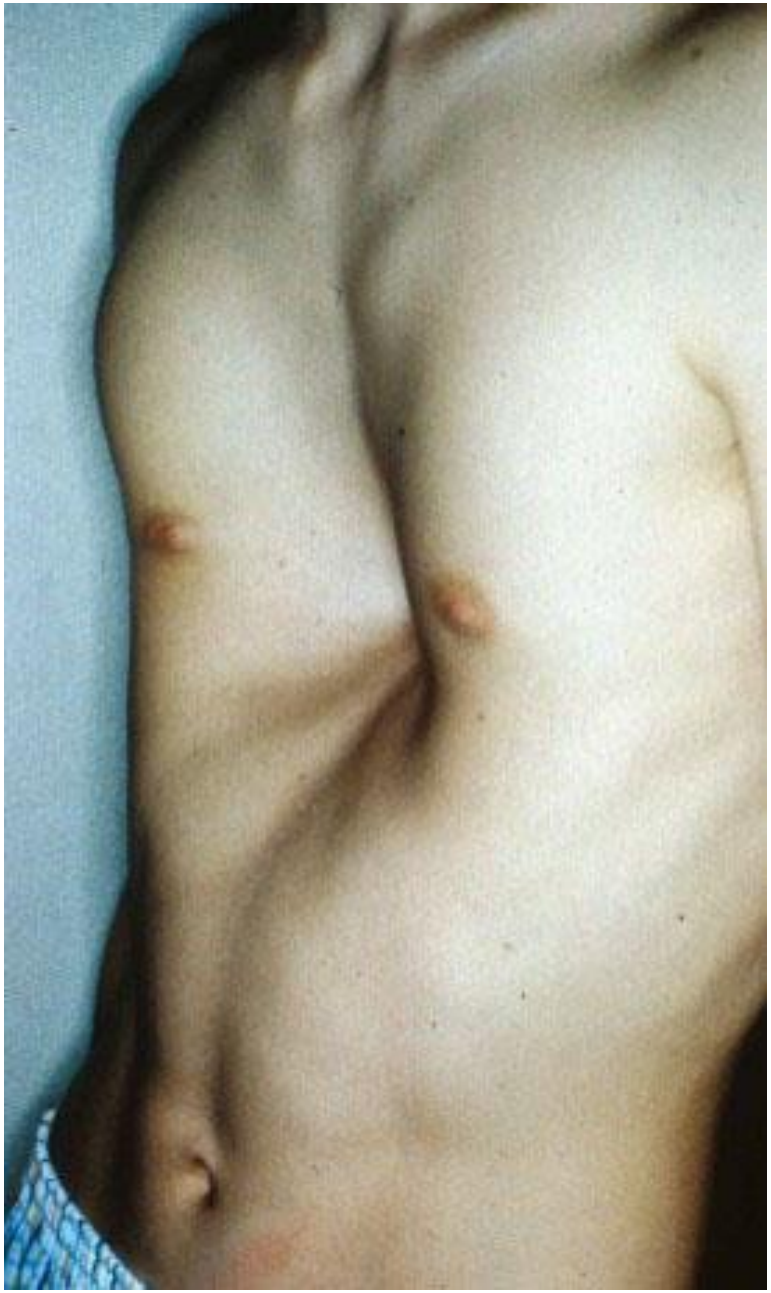
-flat pelvis,

-narrowing of pelvic cavity





Chest deformities



# LABORATORY DATA

1. Serum calcium level (N=2.2-2.6mmol/l). At the level <2.0mmol/l convulsions sets in.
2. Phosphorus normal (1.5-1.8mmol/l). Normal ratio of Ca : P= 2:1; in rickets become 3:1; 4:1.
3. Serum 25(OH)D3 (N=28+2.1ng/ml); and 1,25(OH)2D3(N=0.035+0.003ng/ml)
4. Serum alkaline phosphatase is elevated >500mmol/l.
5. Thyrocalcitonin can be appreciated (N=23.6+3.3pM/l)

Serum parathyroid hormone (N=598+5.0pM/l)

In urine: Aminoaciduria >1.0mg/kg/day

- Urinary excretion of 3’5’ cyclic AMP
- Decreased calcium excretion (N=50-150mg/24h)

# Radiological findings

Only in difficult diagnostic cases.

1. X-ray of the wrist: concave (cupping) ends of ulna and radius in contrast to normally sharply, large rachitic metaphysis and a widened epiphyseal plate.
2. Osteoporosis of clavicle, costal bones, humerus.
3. Greenstick fractures.
4. Thinning of the cortex, diaphysis and the cranial bones.

# EVOLUTION

The evolution is slow with spontaneous healing at the age of 2-3 years.

If vitamin D are administered the normal bony structure is restored in 2-3mo.

Severe chest, spine and pelvis deformities may permanent  persist.

# DIFFERENTIAL DIAGNOSIS

1. Vitamin D-dependent rickets type I and type II
2. Malabsorption disorders.
3. Hereditary Fanconi syndrome- multiple defects of proximal renal tubules, familial X-linked hypophosphatemia, renal tubular acidosis, osteogenesis imperfecta

# Vitamin D-resistant rickets

- Type I called 1-alpha hydroxylase gene deficiency, result in inability to hydroxylate calcidiol in 1,25(OH)D3 (calcitriol)
- Clinical and biochemical evidence of rickets starting in infancy, identified as unique form of vitamin D resistant rickets
- Calcitriol therapy 1-2mcg/day until healed bone, maintain dose varies 0,25-1mcg/day

# Vitamin D-resistant rickets

- Type 2 vitamin D-dependent rickets, hereditary autosomal-recessive disorder, with end-organ resistance to calcitriol
- Rickets develop in first 2yr, peculiar syndrome is alopecia, marker of severity
- Additional ectodermal anomalies: multiple milia, epidermal cysts, oligodontia
- Treatment: Calcitriol 2mcg/day, calcium1g/day, increased gradually to restore normal biochemical parameters

# X-linked familial hypophosphatemia

- Autosomal recessive bone disease with tubular phosphorus reabsorption defect and reduced synthesis 1,25(OH)2D3
- Clinical manifestation of waddling gait, bowing legs, coxa vara, genu varus, genu valgum, short stature, enamel defects
- X-ray cupping of distal and proximal metaphysis of arm and legs

# Treatment of familial hypophosphatemia

- Infants intake of sodium phosphate 0.5-1.0 g/24h, older children 1-4g/24h+vitamin D2 2000/kg/24h or 1,25(OH)2 D3 20-50ng/kg/24h
- Treatment used since patients become

# Osteogenesis imperfecta

- Four genetic syndromes account in osteogenesis imperfecta: type I and IV autosomal dominant; type II and III autosomal recesive
- Clinical manifestation are common in all types: bone fragility, fractures, deformity of long bones and spine, short stature
- Calcium and calcitonin therapy increase skeletal mass and decrease fractures

# Fanconi syndrome

- Rickets associated with multiple defects of the proximal renal tubule; de Toni-Debre-Fanconi syndrome, genetic disorder of metabolism or primary idiopathic
- Dysfunction in proximal tubule membrane with lost of bicarbonate, aminoaciduria, glycosuria, phosphateuria resulting in metabolic acidosis, hypophosphatemia, impaired conversion of vitamin D=>rickets

# PROPHYLAXIS IN RICKETS

Specific antenatal prophylactic dose administration : 500-1000IU/day of vitamin D3 solution at the 28-th week of pregnancy. The total dose administered is 135000-180000IU. In term infants prophylactic intake of vitamin D2 700IU/d started at 10 days of age during the first 2 years of life; in premature the dose may increase to 1000IU/day.

# PROPHILAXIS IN RICKETS

WHO recommendation for rickets prophilaxis in a children coming from unfavorable conditions and who have difficult access to hospitals is 200000IU vitamin D2 i/muscular,

On the 7day, 2, 4, 6 month- total dose 800000IU. In case of the necessary prolongation 700IU/day till 24mo are given.

# SPECIFIC TREATMENT IN RICHETS

The treatment is with vitamin D3 depending on the grade.

In grade I- 2000-4000IU/day for 4-6weeks, totally 120000-180000IU.

In grade II- 4000-6000IU/day for 4-6 weeks, totally 180000-230000IU.

In grade III- 8000-12000IU/day for 6-8 weeks, totally 400000-700000IU.

# SPECIFIC TREATMENT IN RICHETS

- Along with vitamin D, calcium is also administered (40 mg/kg/day for a term baby,
- 80 mg/kg/day for a premature baby); also indicate vitamin B&C preparations.
- From the 7-th day of the treatment massage can be started.
- Intramuscular administration of 1% ATP solution in case of myopathy 1ml/day is preferred.

# RICKETS COMPLICATIONS

1. Rickets tetany in result of low concentration of serum calcium (<2mmol/l), failure of the PTH compensation and muscular irritability occur.
2. Hypervitaminosis D occur after high oral dosing, extensive skin exposure to sunlight.

# Clinical manifestation

1. Manifest tetany:

- Spontaneous spasm: flexion at the elbow, extension of 2-5-th digits, extension and adduction of the thumb.
- Painful extension and adduction in the tibia tarsal joint.
- Rarely contractures in the eyelids and lips muscles.
- Laryngeal or bronchial spasm, manifesting as sudden dyspnea, apnea or cyanosis.

**Latent tetany**: The symptoms are not evident, but they can be performed.

Chvostek sign- percussion on the facial nerve leading to contraction of the superior lip, nasal wings, hemi or bilateral facial muscle contraction.

Trousseau sign- blood pressure cuff around the mid arm induce carp spasm.

Erb sign- <5mA galvanic current induced the nerve impulses.

The diagnosis of rickets tetany is based on the clinical manifestation of rickets, low levels of serum calcium, phosphorus, PTH; high serum alkaline phosphatase.

# TREATMENT

- 1-2% of calcium chloride in milk- 4-6g/day for the first 2 days; after that
- 1-3g/day continued for1-2wk. Calcium chloride in more concentrated may cause gastric ulceration. Calcium lactate may be added to milk in 10-12g/d for 10 days.
- Oxygen inhalation is indicated in convulsive seizures. Started treatment with vitamin D
- 5000-10000IU/d for 6-8weeks, continued calcium intake. When the rickets is healed, the dose of vitamin D decrease to the usual prophylactic one.

# HYPERVITAMINOSIS D

- Symptoms develop in hypersensitivity to vitamin D children or after1-3mo of high doses intakes of vitamin D; they include hypotonia, anorexia, vomiting, irritability, constipation, polydipsia, polyuria, sleep disorder, dehydration. High serum level of acetone, nitrogen
- Ca>2.9mmol/l are found. Increase calcium concentration in urine may provoke incontinence, renal damage and calcification.

# Treatment

- Preventing calcium rich food, cheese and cow's milk
- Intake mashed fruits and vegetables, juices, hydrating fluids- Ringer solution, water.
- Vitamin A, B, E according to age. In severe intoxication administration of Phenobarbital for 2-3 weeks or prednisone 1mg/kg 5-7 days reduces the calcium absorption and increases the calcium excretion. In the case of acidosis 4% sodium hydrocarbonate 5ml/kg is given.

# Rickets Can be Prevent!

# *Skeleton and its functions*

- gives the form and support to the body
- represents the storage of easy mobilizing calcium (97%)
- Some elements of skeleton protect the body from external and internal forces.
- The bones offer the attaching surfaces for muscles and represents the movement levers.
- The dynamic agent of locomotion is represented by skeletal muscle.

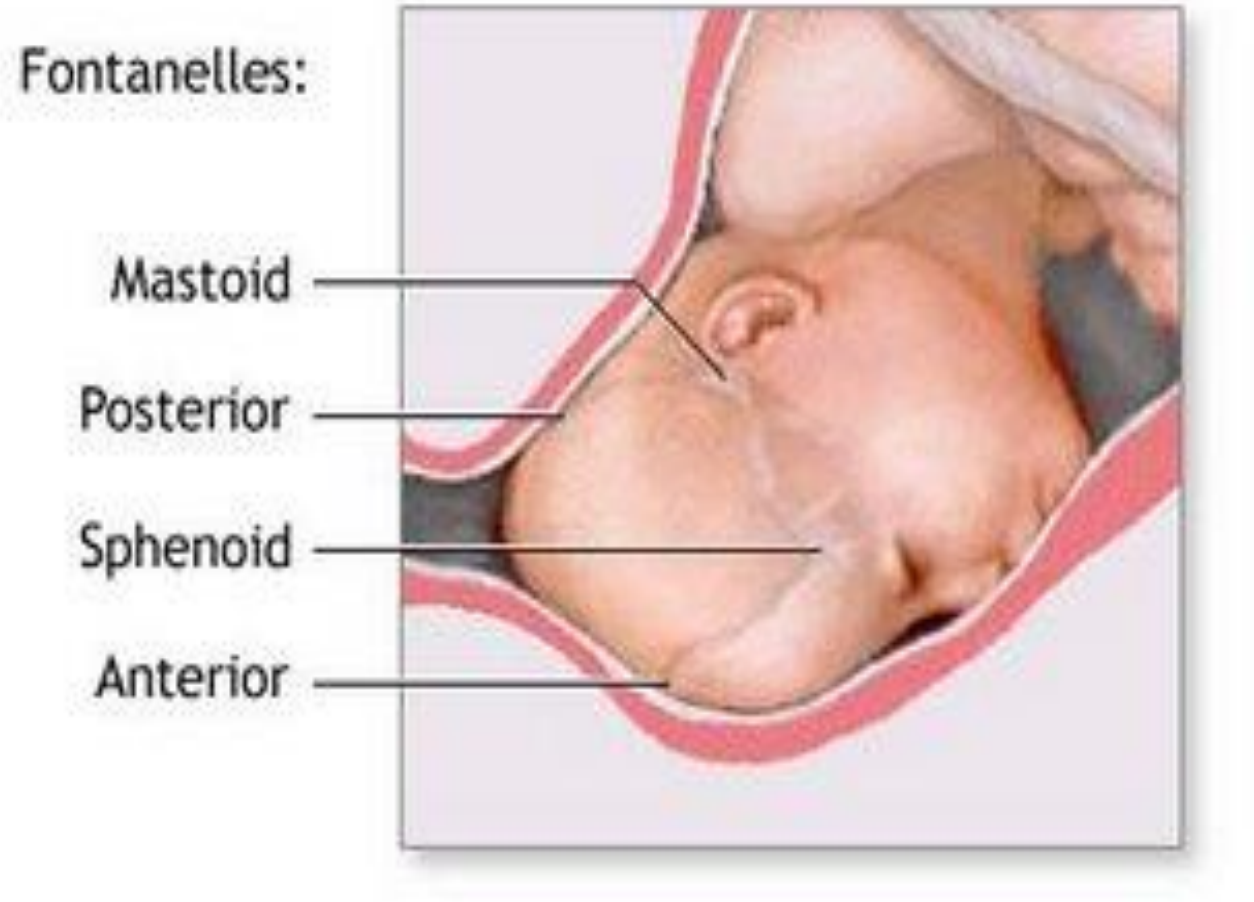
# Function of bone tissue

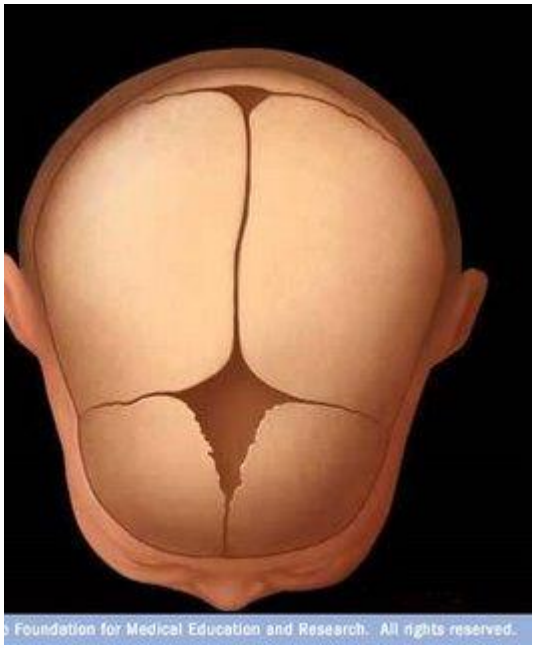
- **Protection**
- **Shape**
- **Blood production**
- **Mineral storage**
- **Fat Storage**
- **Movement**
- **Acid-base balance**
- **Detoxification**
- **Sound transduction**

# Anatomophysiological peculiarities of osseous (bone) tissue in children

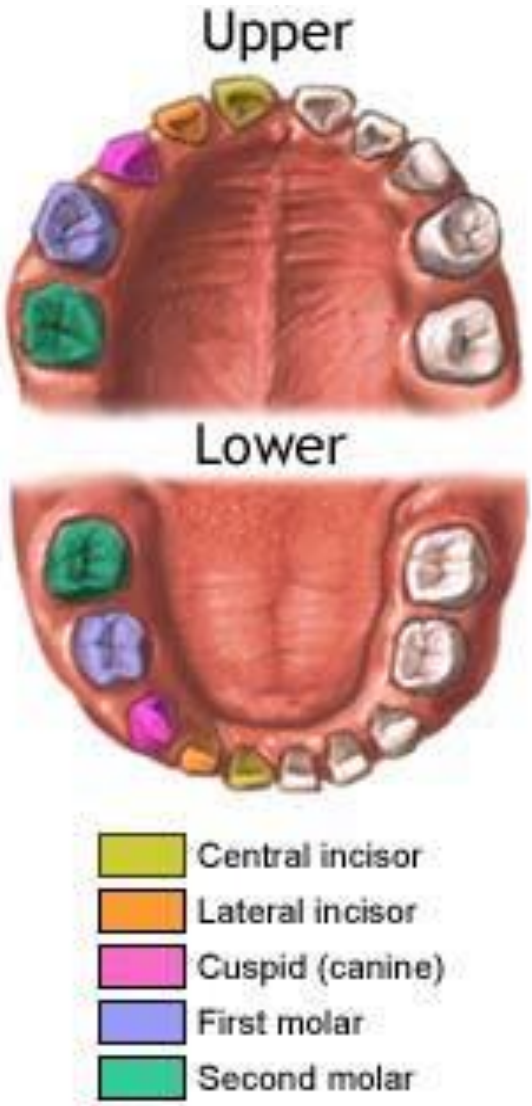
- **The energy of growth and bone regeneration is high**
- **Higher content of water and lesser percentage of solid constituents**
- **Comparatively greater softness and resilience to pressure bending, and a lesser tendency to fractures**
- **Fibrous structure of bone in children (greater extent in the fetus) and laminar structure in the adult**
- **Greater vascularisation of children's bones**
- **Periosteum is thick, with a particularly well-defined internal layer**
- **Presence growing zone of cartilage in long bones**

# Fontanelles



# Deciduous (milk) teeth

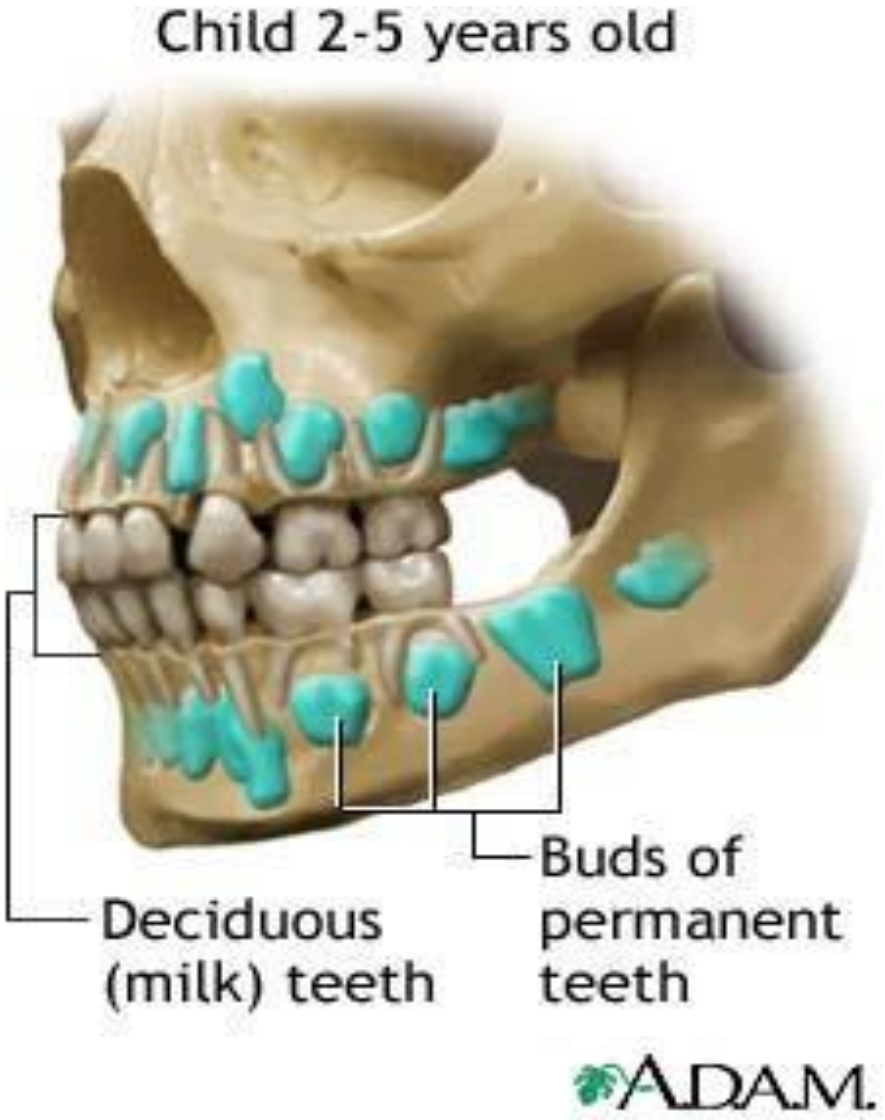



X=n-4

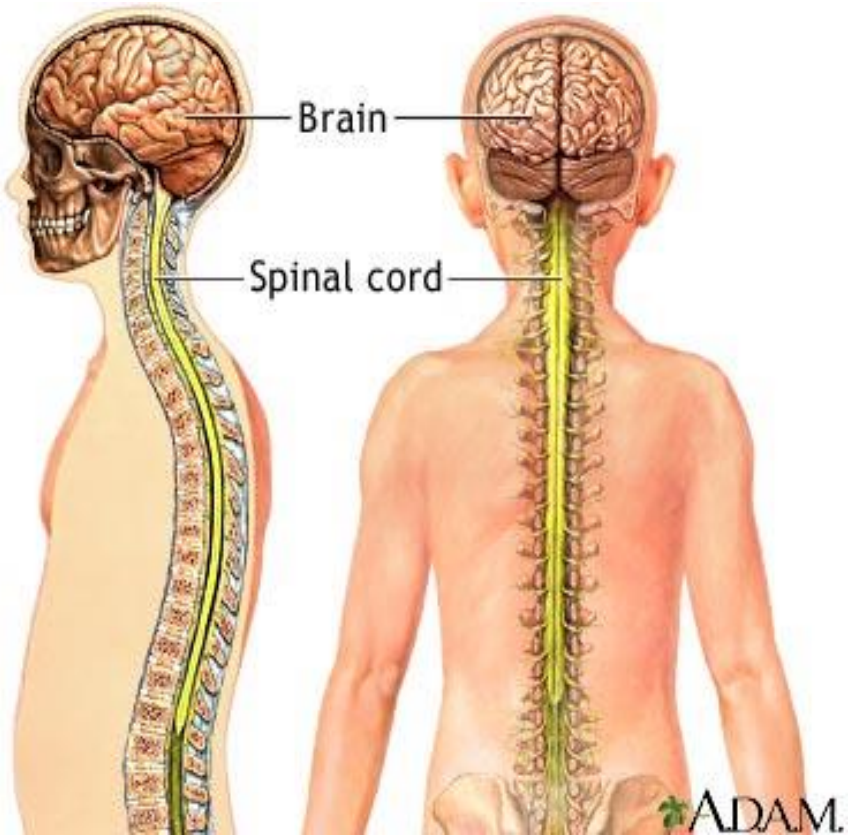
| UPPER | ERUPTS BY | LOWER | ERUPTS BY |
|---|---|---|---|
| Central incisor | 8-10 Mo | Central incisor | 6-9 Mo |
| Lateral incisor | 8-10 Mo | Lateral incisor | 15-21 Mo |
| Canine (Cuspid) | 16-20 Mo | Canine (Cuspid) | 15-21 Mo |
| First molar | 15-21 Mo | First molar | 15-21 Mo |
| Second molar | 20-24 Mo | Second molar | 20-24 Mo |

# Permanent teeth

X= 4n-20



# The physiological curvatures of spinal (or vertebral) column

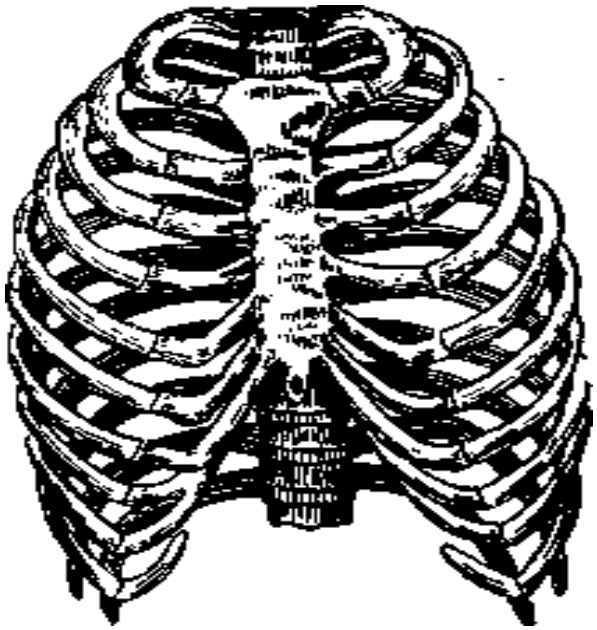


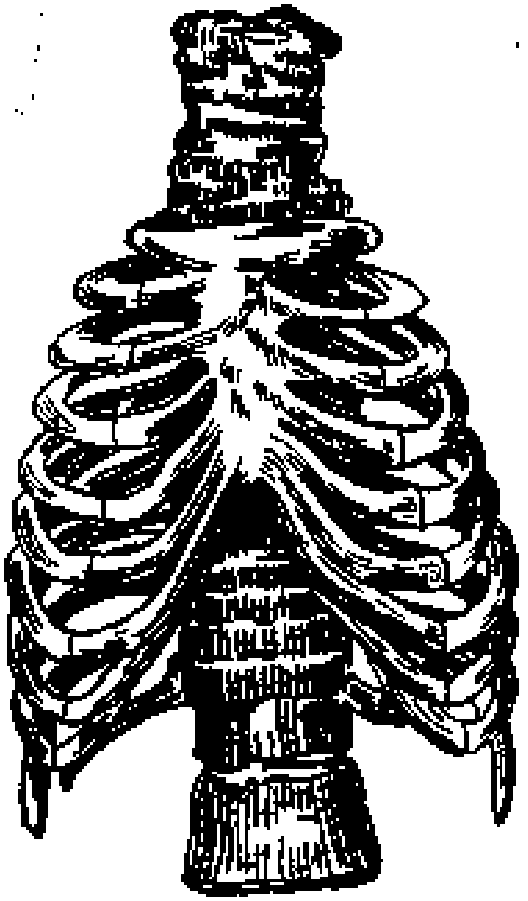

cervical lordosis

thoracic kyphosis

lumbar lordosis

# Chests of children and adults





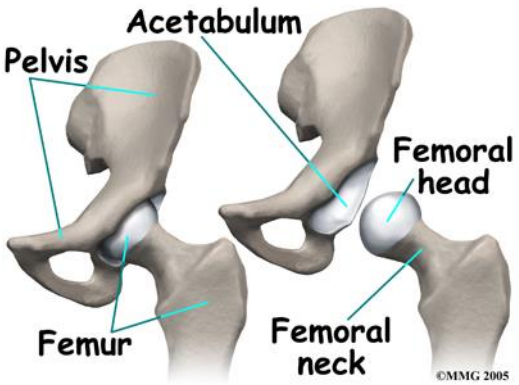
# Paraclinical methods of investigation

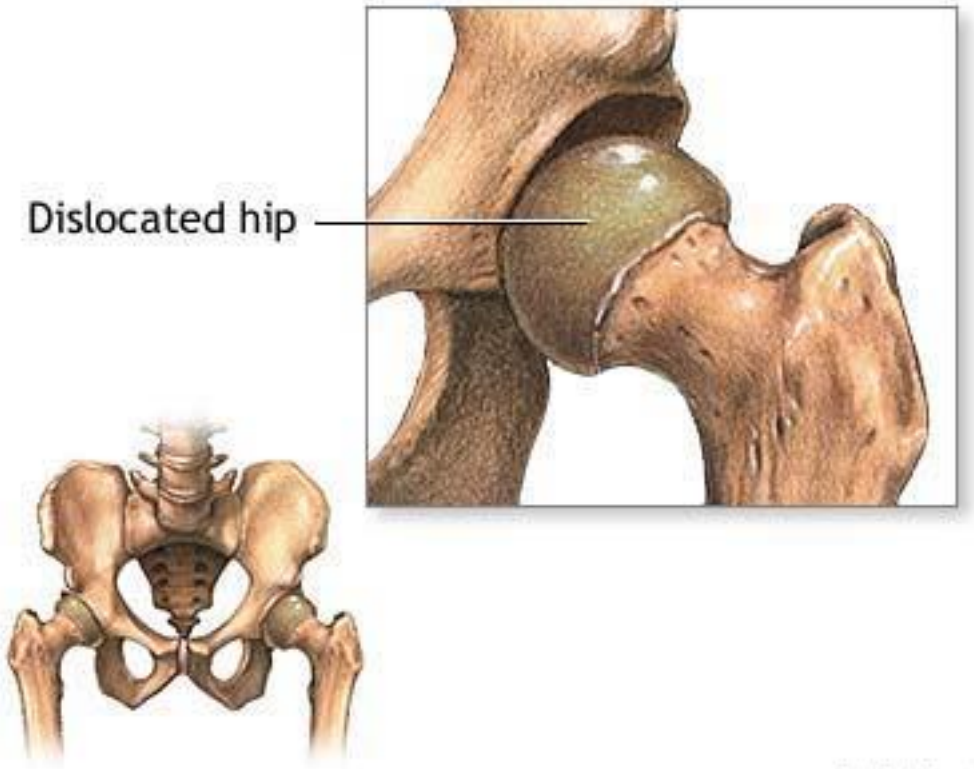
- Laboratory Tests
- X-ray Evaluations
- Arthrogram
- Computed Tomography

# Congenital dysplasia of the hip –

is the hypoplasia of an acetabulum, reduction its depth

and inadequate size of the femoral head



# Clinical sings of Congenital dysplasia of the hip:

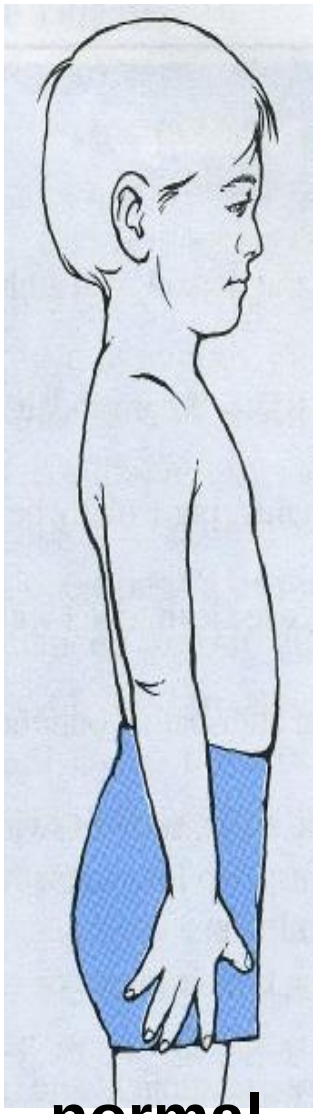
- Asymmetry of thigh skin folds
- Shortness of one of the extremities
- Knee joints are situated at different levels
- The level of abduction of the leg less than 600

- Ortalani's symptom – a click of

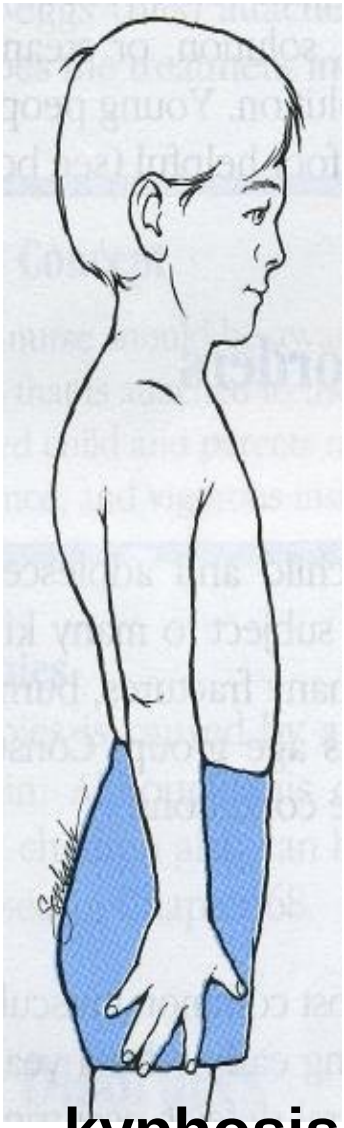
entrance will be felt as femoral head slips into the acetabulum (when the thigh is gradually adducted)

- Late sign – "goose" gait (limping at walking)

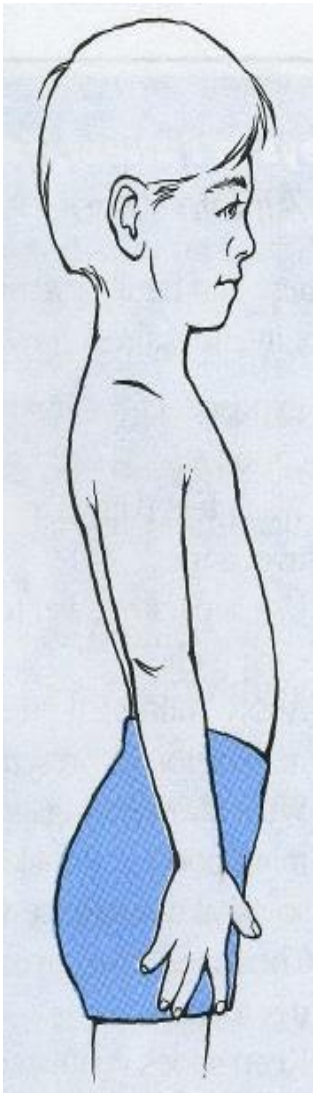
# Semeiology of spinal cord affections



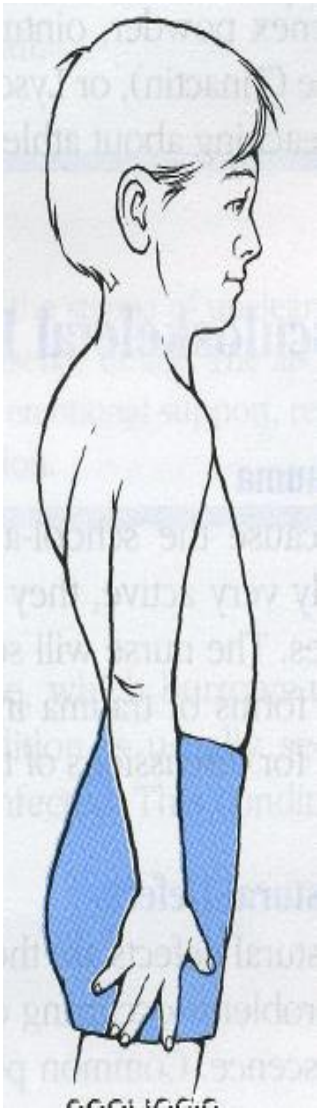
normal



kyphosis



lordosis



scoliosis