VITAMIN D, CALCIUM AND RICKETS

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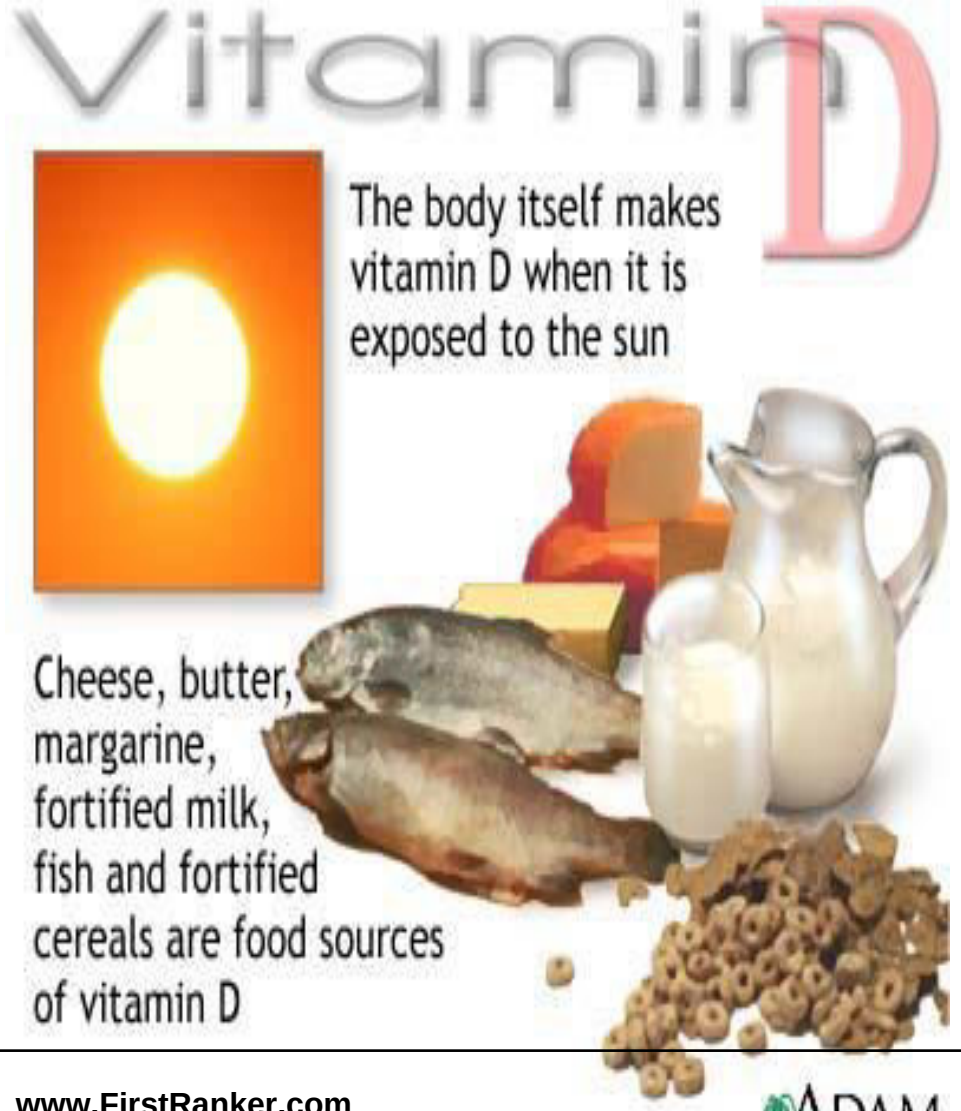
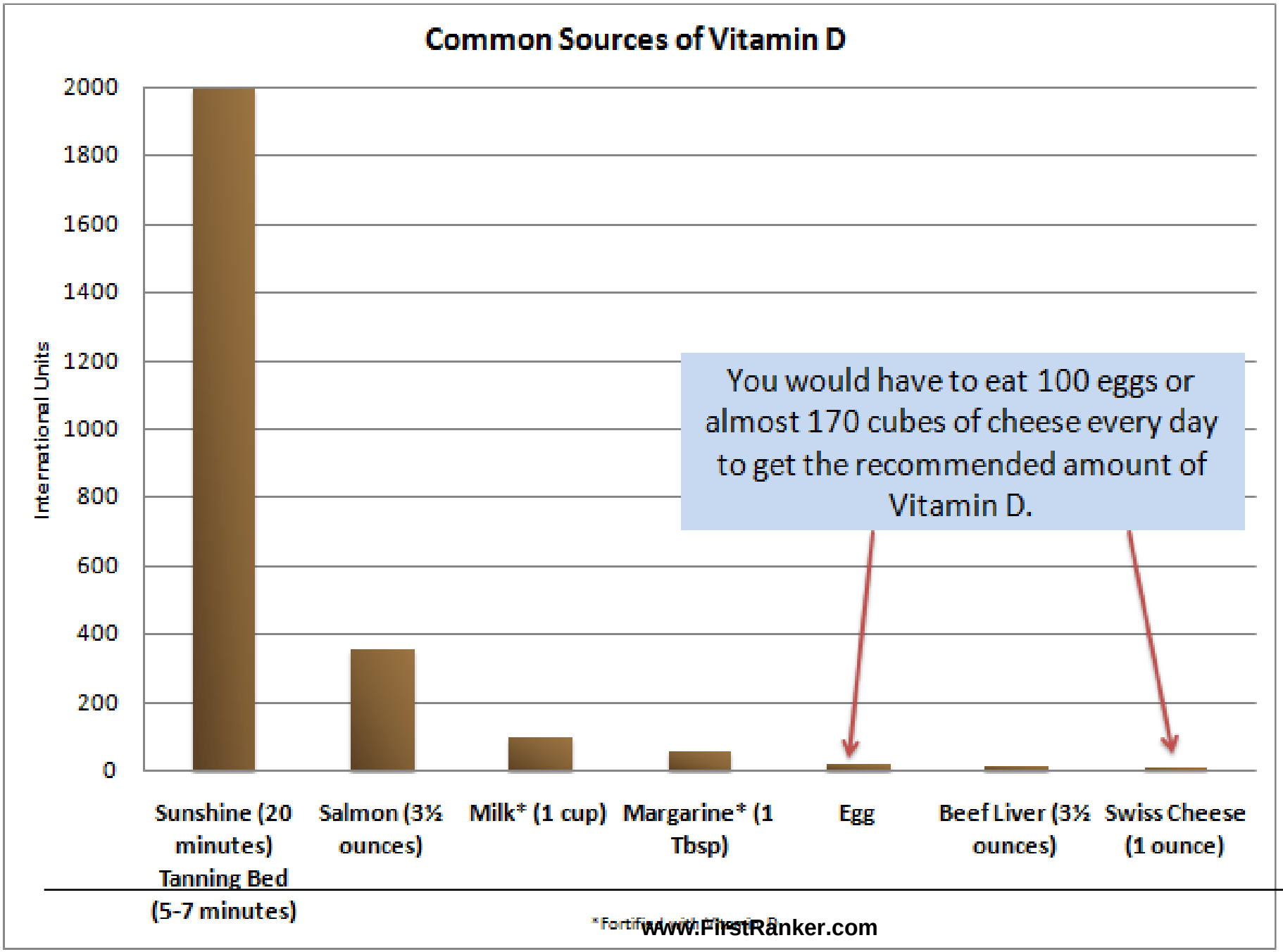
MIMS, Calicut

It is fat soluble vitamin and Hormone.
Essential for bone growth and Calcium absorption

- **Sources:**
- Sunlight
- Human milk(30-40 IU/L)
  (Requirement in infants:200 IU/D)
- Fish liver oil
- Fatty fish
- Egg yolk
- Fortified foods- formula and milk
  (400 IU/L)



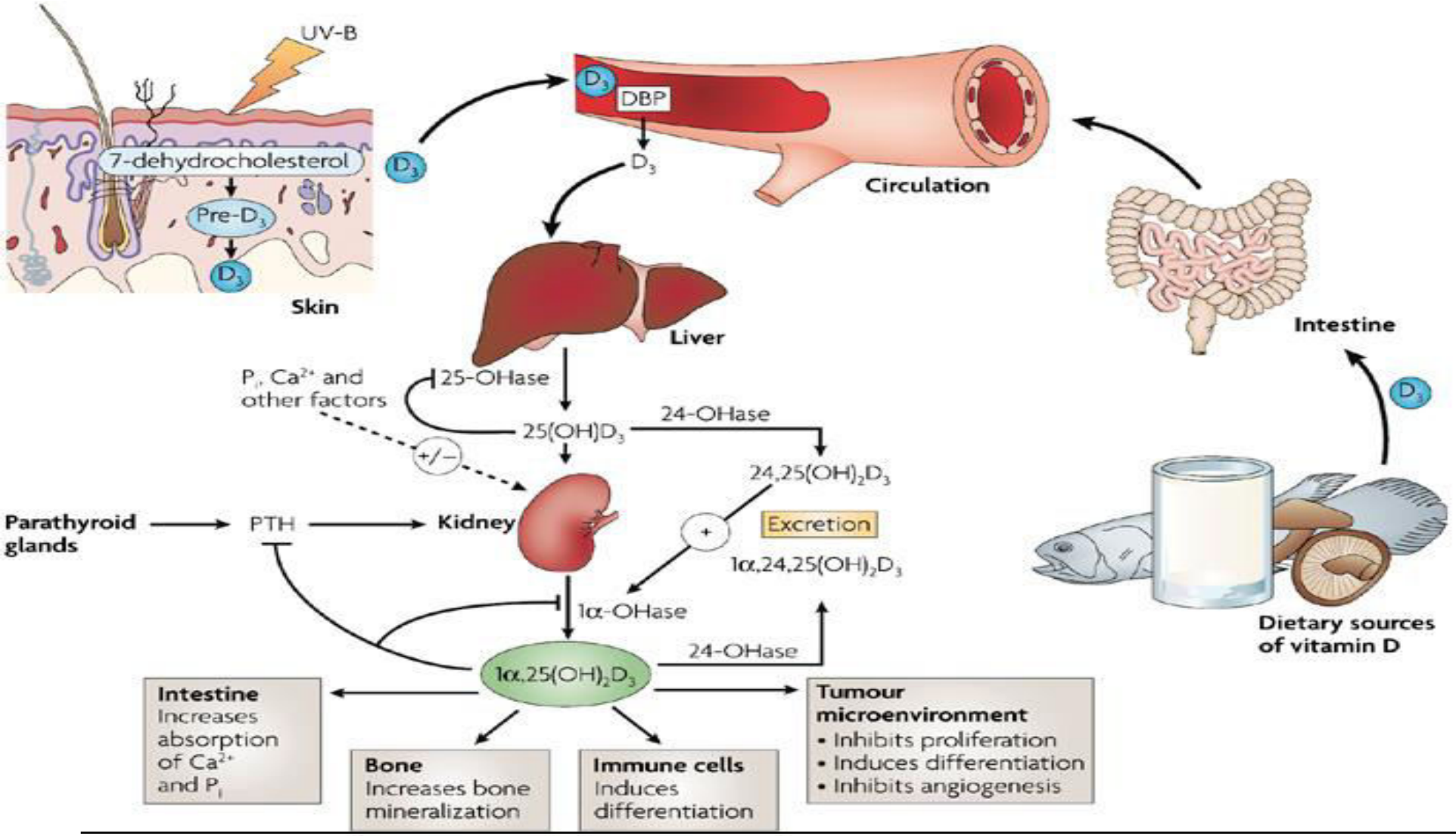


Requirements :

- Infants→200IU/D((Infants daily exposed to sunlight for 15-20 min.to prevent Rickets))

- Children→400 IU/D
- Breast feed infants must receive vit.D supplementations.

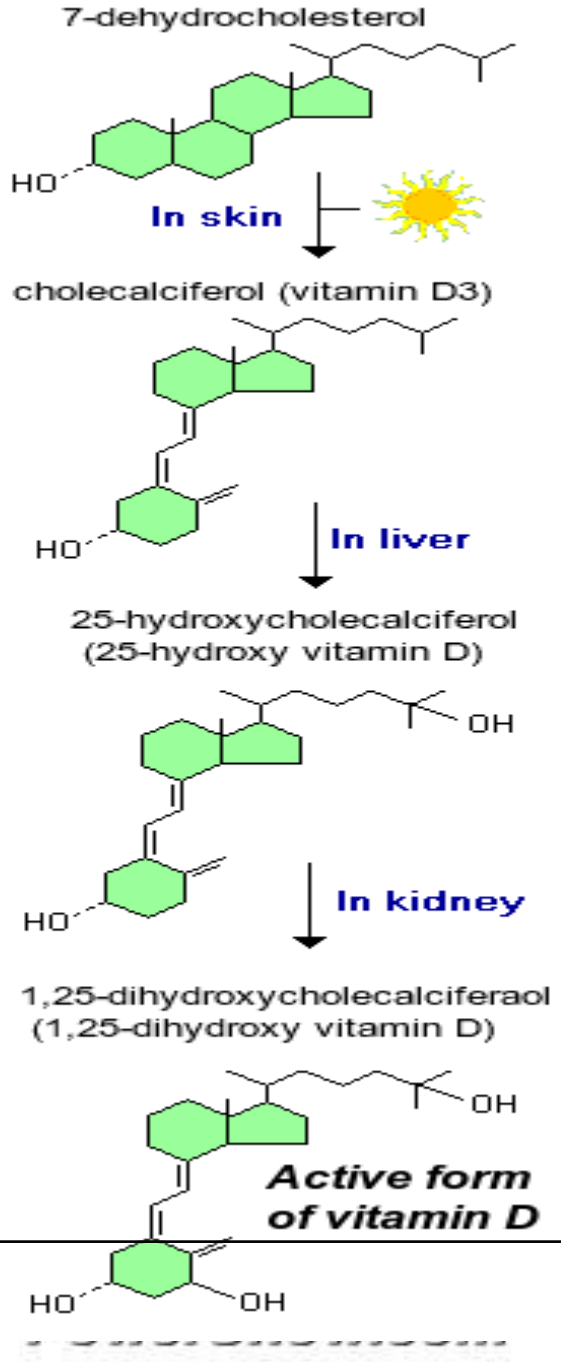
Absorption and metabolism



Nature Reviews | Cancer

Absorption and metabolism

- ✓ **Maximum absorption in Duodenum by Active transport.**
- ✓ **Enterocyte--- >Chylomicron---------> Liver-----> Hydroxylated--> secreted in Alpha2 globulin-----> which is carrier for of vit. D**



RICKETS:

- Disease of growing bones ,occurs in children only before the fusion of epiphyses, and due to unmineralised matrix at the growth plates.
- Inadequate mineralization →Thick G.Plate
- Bones become soft.

Causes of Rickets

•VITAMIN D DISORDERS

•Nutritional Vitamin D deficiency
•Congenital Vitamin D deficiency
•Secondary Vitamin D deficiency
- Malabsorption
- Increased degradation
- Decreased Liver 25-hydroxylase

•Vitamin D dependent ricket Type 1
•Vitamin D dependent ricket Type 2
•Chronic Renal Failure

•PHOSPHORUS DEFICIENCY

•Inadequate intake
- Premature infants
- Aluminium containing antacids

•CALCIUM DEFICIENCY

•Low intake
- Diet
- Premature Infant

•Malabsorption
Primary Disease
Dietary inhibitors of calcium absorption

RENAL LOSSES

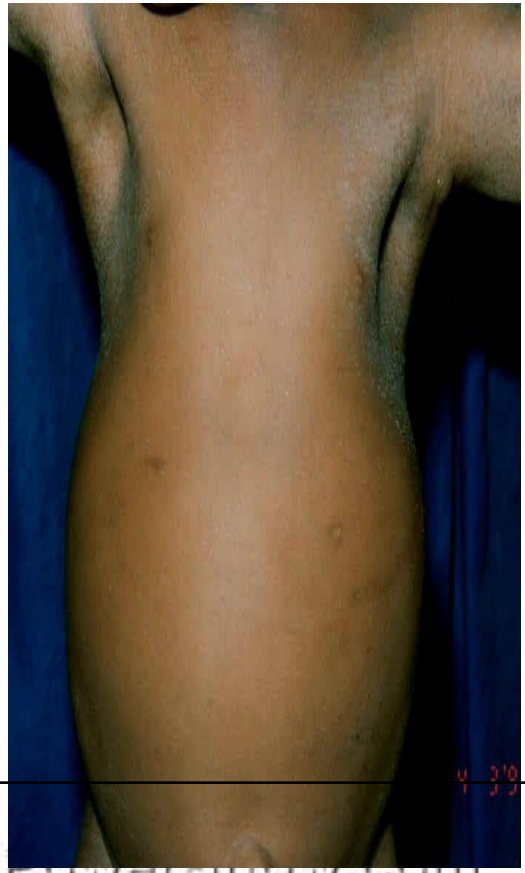
•X- linked hypophosphatemic ricket
•AD hypophosphatemic ricket
•Hereditary hypophosphatemic ricket with hypercalcuria
•Overproduction of phosphatonin
- Tumors induced rickets
- Mccunealbright syndrome
- Epidermal nevus syndrome
- Neurofibromatosis

•Fanconi syndrome
•Dent Disease

Clinical Features of Rickets:

GENERAL

- **Failure To Thrive**
- **Listlessness**
- **Protruding Abdomen, UMBILICAL HERNIA due to** hypotonia of abdominal wall muscles
- **Muscle Weakness (specially proximal)**
- **Fractures**



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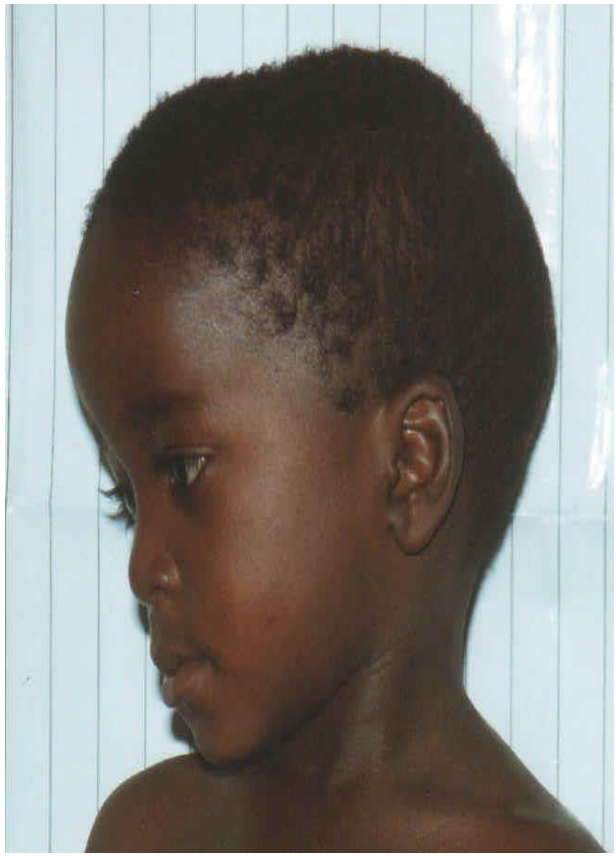
HEAD



- **CRANIOTABES:** softening of cranial bones
- **Frontal Bossing**
- **Delayed Fontanelle Closure**
- **Delayed Dentition, early numerous caries,enamel hypoplasia - mostly deciduous teeth are concerned**
- **Craniosynostosis**

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Chest:

1.RACHITICROSARY: Widening of costochondral junction

2.Harrison Groove : pulling of softened ribs by the diaphragm during inspiration, Muscle traction on the softened rib cage.

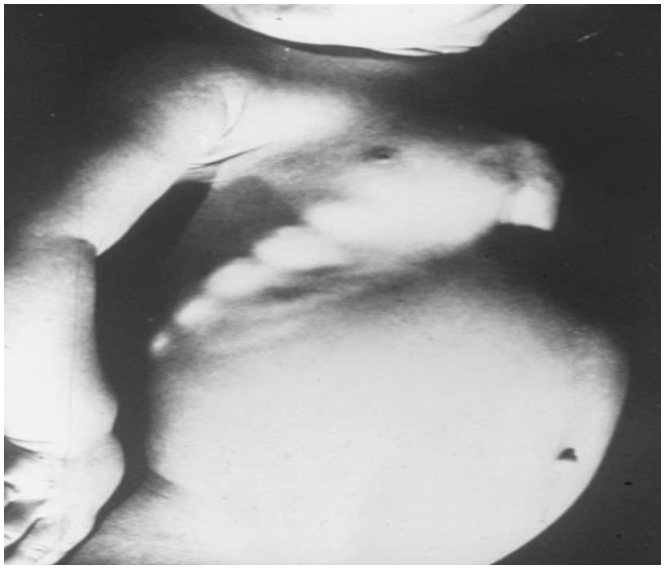
3.Pectus carinatum

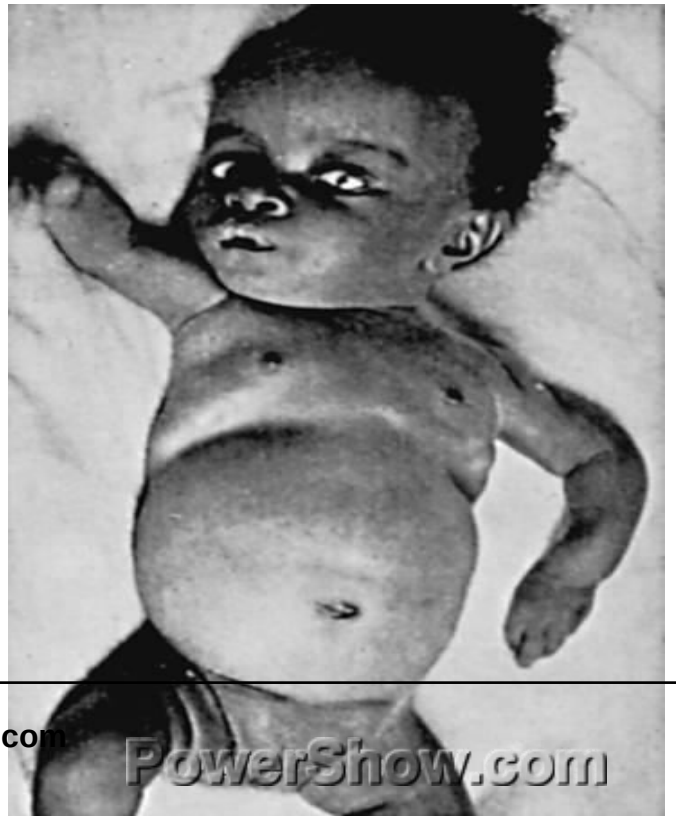
5.Thoracic asymmetry

6.Widening of thoracic bone

7.Respiratory Infections

8. Atelectasis impairment of air movement





BACK

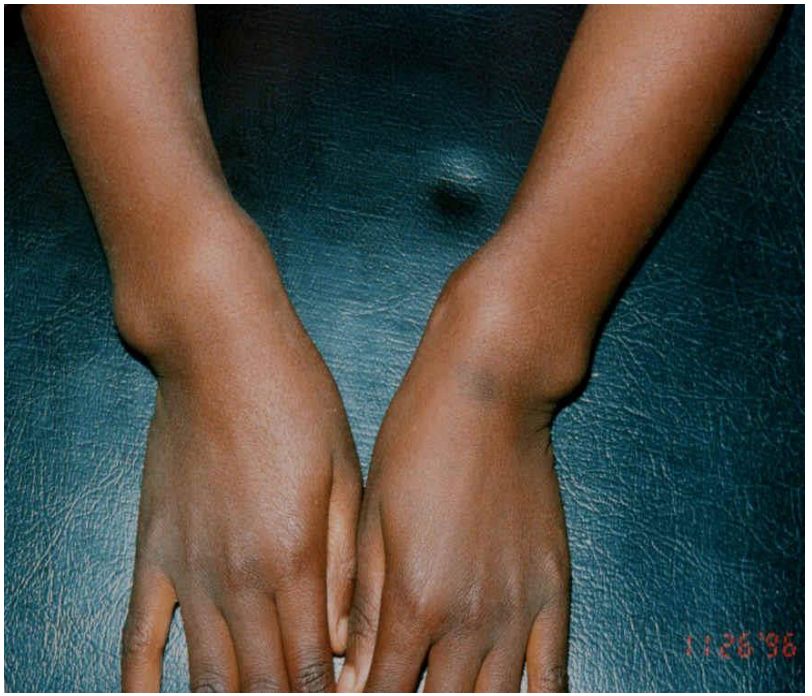
in severe long standing rickets Deformities of spine and pelvis are very unusual today- described

- **Scoliosis**
- **Kyphosis**
- **Lordosis**

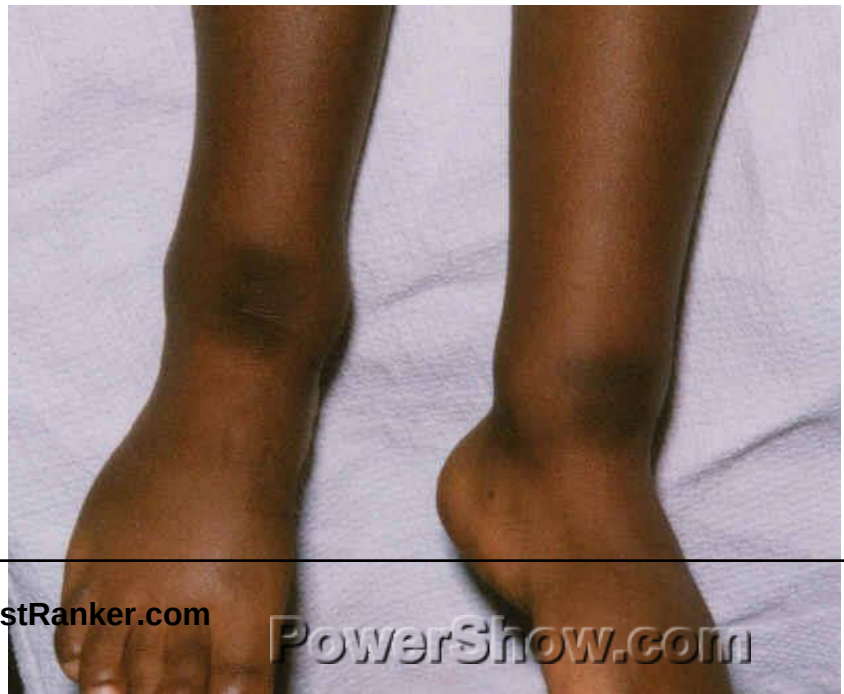
EXTREMITIES

- **Enlargement of wrists and ankles**

  Growth plate widening



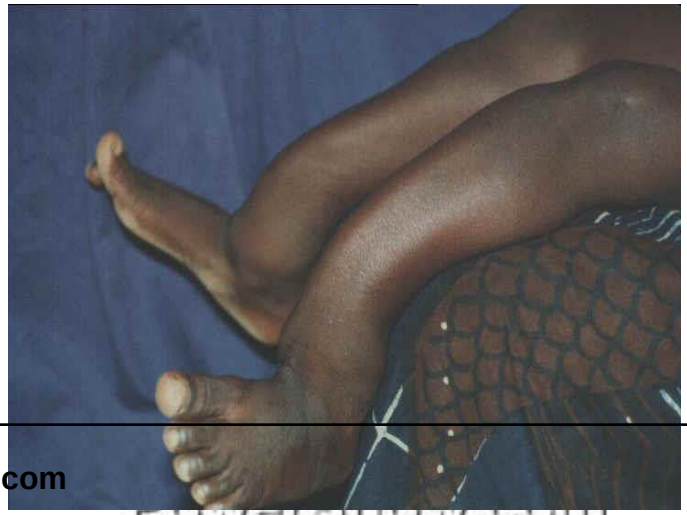
- **Valgus or varus deformities**



WINDSWEPT DEFORMITY

combination of varus deformity of 1 leg with valgus deformity of other leg

Anterior bowing of tibia and femur



- Coxa Vara
- Leg pain

HYPOCALCEMIC SYMPTOMS

- **Tetany**
- **Seizures**
- **Stridor due to laryngeal spasm**

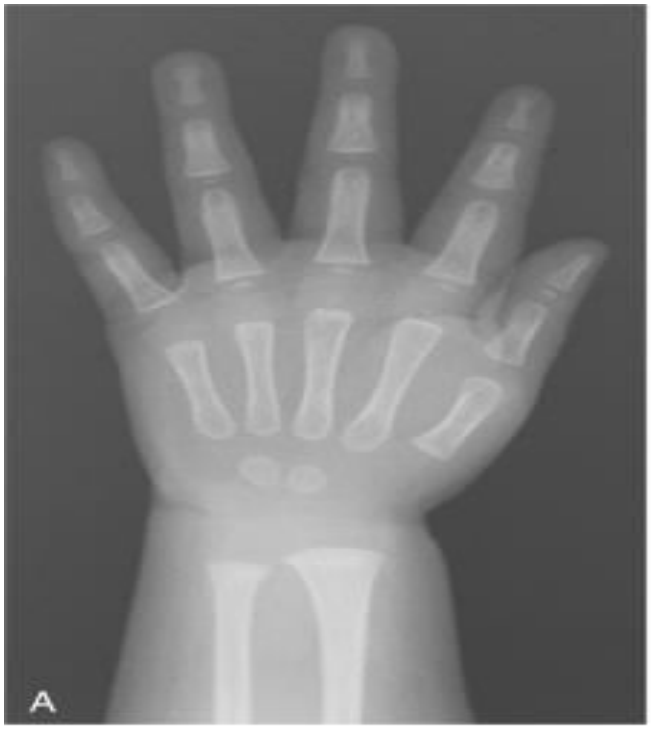
INVESTIGATIONS

RADIOLOGY

- **Changes are most easily visualized on PA view of wrist- although characteristic racitic changes are seen at other growth plates**
- **Alterations of the epiphyseal regions of the long bones- *most characteristic***
- **Accumulation of uncalcified cartilage**

Widening of the radiolucent space between end of bone shafts (metaphyseal lines) and epiphysis

Edge of metaphysis loses its sharp border
FRAYING
Edge of metaphysis changes from convex or flat surface to a more concave surface
CUPPING (most easily seen at distal ends of radius, ulna and fibula)
Widening of Metaphyseal end of bone **SPLAYING**
Metaphyseal lines spread laterally forming **CORTICAL SPURS**
Widening of distal ends of metaphysis (A-Normal, B-Rickets)



Other Radiological Findings:

- Changes of diaphysis – appear a few weeks later
- Coarse trabeculation
- generalized rarefaction
- Cortical thinning
- Subperiosteal erosion

Approach to Rickets:

- Diet history- vit-D deficiency.
- Cutaneous sun exposure: culture ,clothing etc.
- Maternal risk factors for vit-D
- Child is on anticonvulsant, Al-containing antacids
- Malabsorption: GI symptoms ,liver disease
- Fat Malabsorption: Look for ADEK defi.
- Renal disease: CRF, Polyuria -Fanconi syn.
- Family h/o short strature ,bone disease, unexplained death of sibling →cystinosis → M.C.C. Fanconi syn.
- Alopecia → Vit-D dep. Type-2 rickets

VITAMIN- D DEFICIENCY

ETIOLOGY

VITAMIN D DEFICIENCY is MC cause of Rickets Worldwide.

- **Most commonly occur in infancy due to poor intake and inadequate cutaneous synthesis**
- **Formula fed infants- receive adequate vit D even without cutaneous synthesis**
- **Breast fed infants rely on cutaneous synthesis or vitamin D supplements**

Cutaneous synthesis is limited due to:

- ✓ **Ineffectiveness of winter sun**
- ✓ **Avoidance of sunlight**
- ✓ **Decreased cutaneous synthesis due to increased skin pigmentation**

LABORATORY FINDINGS

- **Hypocalcemia** – variable finding due to action of ↑PTH
- **Hypophosphatamia** - due to PTH induced renal loss of phosphate and decreased intestinal absorption
- **1,25D level-N,↑,↓**- secondary to up regulation of renal 1 α hydroxylase due to hypophosphatemia and hyperparathyroidism
- Some patients have **Metabolic acidosis** secondary to PTH induced renal bicarbonate wasting
- **Generalized aminoaciduria**

MANAGEMENT OF VITAMIN D DEFICIENCY

1)Should receive Vitamin D and adequate nutritional intake of calcium and phosphorus

2)STROSS THERAPY- **3-6 Lakh IU** of Vitamin D oral/IM as **2-4 doses** over **1 day**

0R

3)Daily High dose Vitamin D **2000-5000 IU/day** over **4-6 weeks**

4)Hypocalcemia correction**: 100 mg/kg**

- Good prognosis

PREVENTION OF VITAMIN D DEFICIENCY

Universal administration of a daily multivitamin containing 200-400 IU of Vitamin D to children who are breast feed.

For older children, the diet should be reviewed to ensure that there is a source of Vitamin D

CONGENITAL VITAMIN D DEFICIENCY

- Occur when there is severe maternal vitamin D deficiency during pregnancy

Risk factors-

- Poor dietary intake of Vitamin D
- Lack of adequate sun exposure
- Closely spaced pregnancies

Clinical Features

- Symptomatic hypocalcemia
- IUGR
- Decreased bone ossification + classic rachitic changes

Treatment

- Vitamin D supplementation
- Adequate intake of calcium and phosphorus
- Use of prenatal vitamin D

SECENDARY VITAMIN D DEFICIENNCY

ETIOLOGY

- **Liver and GI diseases incl.**

1. **Cholestatic Liver Disease**
2. **defect in bile acid metabolism**
3. **cystic fibrosis and other causes of pancreatic dysfunction**

- **Celiac disease**
- **Crohn's disease**
- **Intestinal Lymphangiectasia**
- **Intestinal resection**
- **Medications- anticonvulsants (**phenobarbitone, phenytoin , isoniazid, rifampicin)

TREATMENT

Vitamin D deficiency due to malabsorption - high dose of Vitamin D

25-D- 25-50 µg/day or 5-7 µg/kg/day

↓

superior to D3

dose adjusted based on serum 25-D

or

1,25-D better absorbed in presence of fat malabsorption

or

PARENTERAL VIT. D

VITAMIN D DEPENDENT RICKET TYPE 1

- AR
- Mutation in the *gene encoding renal 1α hydroxylase*
- Present during first 2 yr of life
- Can have any of the classical features of rickets incl. symptomatic hypocalcaemia
- Normal level 25-D, low 1,25-D

TREATMENT

- Long term treatment with **1,25-D(calcitriol)**

initial dose **0.25-2 µg/day-->**lower doses used once ricket has healed

- Adequate intake of calcium

(Dose of calcitriol is adjusted to maintain a low normal serum ca, normal serum P, high normal serum PTH)

Low normal Ca. and high normal PTH avoids excessive dose of calcitriol (causes hypercalcuria, nephrocalcinosis)

→Monitoring: periodic assessment of urinary calcium excretion

Target <4mg/kg/day

VITAMIN D DEPENDENT RICKET TYPE 2

- AR
- Mutation in the *gene encoding the vitamin D receptor* prevention of normal physiologic response to 1,25 D
- Level of 1,25-D extremely elevated
- 50-70% have Alopecia (tend to be associated with more severe form of the disease)
- Epidermal cysts- less common

TREATMENT

Some patients specially those without alopecia responds to **extremely high dose of vitamin D2, 25-D or 1,25-D** (due to partially functional vitamin d receptor)

↓

All pts should be given a ***3-6 months*** trial of high dose Vitamin D and oral calcium

↓

initial dose of **1,25-D** 2µg/day(some require 50-60 µg/day)

Calcium 1000-3000mg/day

Pts not responding to high dose Vitamin D – **long term I V calcium**, with possible transition to very high dose oral calcium supplement

CHRONIC RENAL FAILURE

- Decreased activity of 1 α hydroxylase in the kidney
- Decreased renal excretion of phosphate

  hyperphosphatemia
- Direct effect of CRF on growth hormone axis

FTT and growth retardation may be accentuated

TREATMENT

- **Calcitriol(1,25 vit-D)** (act without 1 α hydroxylase)
- **Normalization of serum phosphorus level by**
- Dietary phosphorus restriction
- Oral phosphate binders
- Correction of chronic metabolic alkalosis by **alkali**

CALCIUM DEFICIENCY

- Early weaning(breast milk and formula are excellent source of calcium)
- Diet with low calcium content(<200 mg/day)
- Diet with high phytate, oxalate, phosphate(due to reliance on green leafy vegetables decreased absorption of dietary calcium)
- Children with unconventional diet (children with milk allergy)
- Transition from formula or breast milk to juice, soda, calcium poor soy milk without alternative source of dietary calcium
- I V nutrition without adequate calcium
- Calcium malabsorption- celiac disease, intestinal abetalipoproteinemia, small bowel resection

TABLE 6. Calcium Content of Foods

FOOD	AMOUNT	CALCIUM (MG)
Dairy products		
Milk, liquid*	1 c	300
Milk, powdered*	1 c	60
Cheese, natural or processed*	1 oz	200
Cottage cheese*	1/4 c	60
Yogurt*	1 c	300
Ice cream*	1/2 c	110
Cream cheese*	1 tbsp	10
Meat and other protein sources		
Meat, poultry, fish*	3 oz	10 to 20
Canned fish with bones*	3 oz	250
Egg*	1 egg	30
Cooked dried beans	1/2 c	70
Nuts and seeds	2 tbsp	20 to 40
Peanut butter	2 tbsp	20
Bread, cereal, pasta		
Bread	1 slice	25
Biscuits	1 roll	25
Corn tortilla	1 tortilla	60
Cooked and dry cereals	1 serving	15
Noodles, macaroni	1/2 c	15
Vegetables and fruits		
Vegetables, average	1/2 c	20 to 40
Green, leafy vegetables, average	1/2 c	100
Fruits, average	1/2 c	20 to 40
Calcium-fortified orange juice	1/2 c	160

**Not included in vegan diets.*

Adapted from Ellyn RD. **Child of Mine: Feeding with Love and Good Sense.** *Palo Alto, Calif: Bull Publishing Co; 1986.*

CLINICAL MANIFESTATION

- Classical s/s of rickets
- Presentation may occur during infancy/childhood although some cases are diagnosed at teen age
- Occur later than nutritional vitamin D deficiency

DIAGNOSIS

- ↑alkaline phosphatase, PTH, 1,25-D
- calcium ↓ or normal
- ↓ urinary calcium
- ↓ serum P level(renal wasting from secondary hyperparathyroidism)

TREATMENT

- **Adequate calcium- as dietary supplement**

  350-1000 mg/day **of elemental calcium**

- **Vitamin D supplementation- if there is concurrent vit. D def.**

PREVENTION

1.Discouraging early cessation of breast feeding

2.Increasing dietary sources of calcium

PHOSPHORUS DEFICIENCY

INADEQUATE INTAKE

- **Decreased P absorption-**
  - celiac disease
  - Cystic fibrosis
  - Cholestatic liver disease
- **Isolated P malabsorption - long term use of P containing antacids**

X LINKED HYPOPHOSPHATEMIC RICKETS

- ***Most common*** **genetic disorder causing ricket due to hypophosphatemia**

- **Defective gene is on x- chromosome, but female carriers are affected (x linked dominant)**

PATHOPHYSIOLOGY

- Defective gene is called **PHEX** because it is a **PH**osphate regulating gene with homology to **E**ndopeptidases on the **x**-chromosome

↓

Product of this gene appears to have either a direct or an indirect role in inactivating a phosphatonin (inhi. Ph. absorption) – FGF23 may be the target phosphatonin

↓ ↓

Absence of PHEX **decreased degradation of phosphatonin**

1.increased phosphate excretion

2. decreased production of 1,23-D

CLINICAL FEATURES

1-Abnormalities of lower extremities and poor growth are dominant feature

2-Delayed dentition

3-Tooth abscess

4-Hypophosphatemia

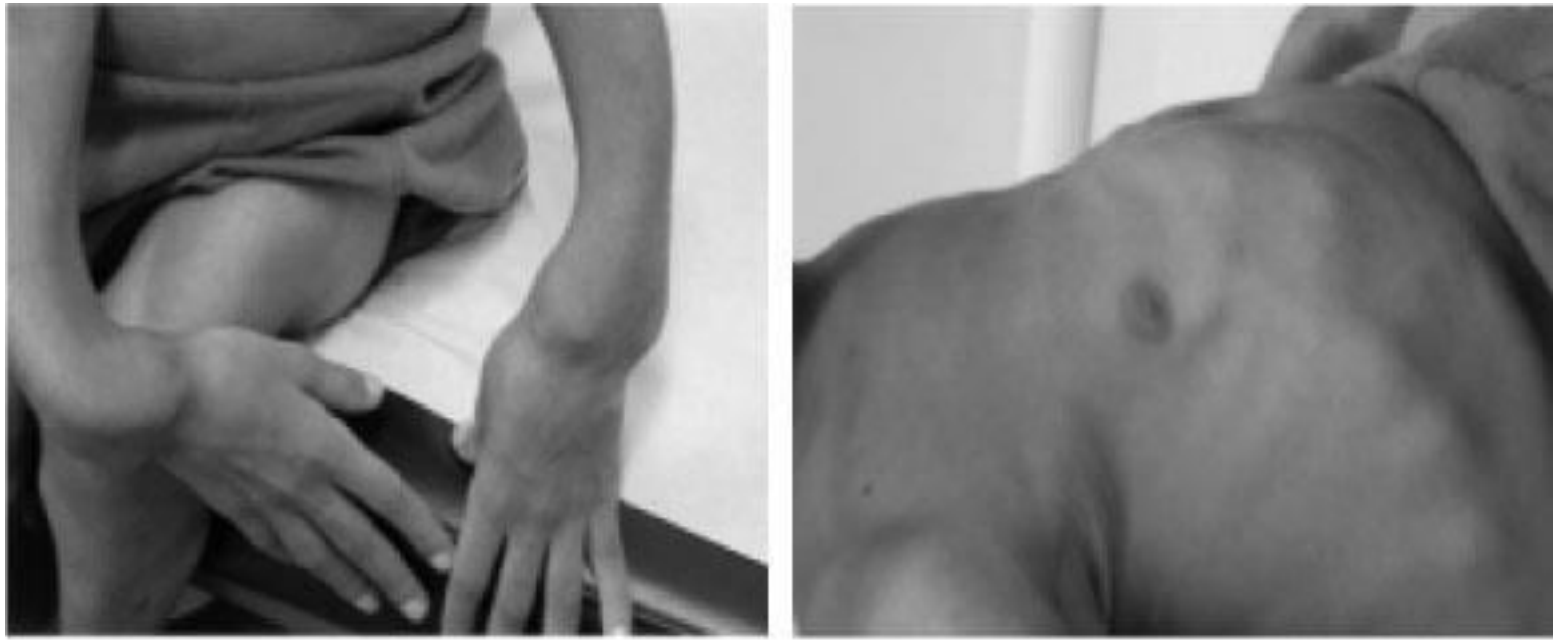


Figure 1. Child with hypophosphatemic rickets, presenting multiple bone deformities and recurrent fractures.

LABORATORY FINDINGS

- High renal excretion of phosphate
- Hypophosphatemia
- Increased alkaline phosphatase
- Normal PTH and serum calcium

TREATMENT

A combination of **Oral Phosphorus and 1,25-D**

Phosphorus- 1-3 gm of elemental P divided into 4-5 doses

Calcitrol - 30-70 ng /kg/day in 2 div. doses

AUTOSOMAL DOMINANT HYPOPHOSPHATEMIC RICKETS

- Less common than XLH
- Variable age of onset
- Mutation in the gene encoding FGF-23

↓

Degradation of FGF-23 by proteases is prevented

↓

Increased phosphatonin level(phosphatonin decreases renal tubular reabsorption of phosphate)

Hypophosphatemia ↓

Inhibition of 1 α hydroxylase in kidney ↓ decreased ,25D synthesis

LABORATORY FINDINGS

Hypophosphatemia

↑alkaline phosphatase

↓ or inappropriately normal 1,25D level

TREATMENT

Similar to XLH

HEREDITARY HYPOPHOSPHATEMIC RICKETS WITH HYPERCALCURIA

- **Primary problem- renal phosphate leak**

↓

hypophosphatemia

↓

stimulation of production of 1,25D

↓

high level of 1,25 D increases intestinal absorption of calcium

↓

PTH suppression ——→ **hypercalcuria**

CLINICAL MANIFESTATIONS

Dominant symptoms are

- rachitic leg abnormalities
- Muscle weakness
- Bone pain

Patients may have short stature with a disproportionate decrease in length of lower extreamity.

LABORATORY FINDINGS

Hypophosphatemia

Renal phosphate wasting

↑serum alkaline phosphatase

↑1,25D level

TREATMENT

Oral phosphate replacement

1-2.5gm of elemental phosphorus in 5 divided oral doses

THANKS!!!

ANY???

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