

RICKETS

MBCbB
August 2020

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Outline

- What is rickets
- Causes
- Clinical presentation
- Investigations
- Treatment
- Prevention

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Definition

- Rickets is a childhood disorder of growing bone.
- Defective mineralization results in amassing of osteoid beneath the growth plate leading to softness in the bone
- Low serum phosphate is fundamental to pathogenesis of rickets

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Calcipapenic Rickets

Vitamin D Related Rickets

- Vitamin D Deficiency
- Impaired Hepatic 25-hydroxylation
- Impaired Renal 1 α -hydroxylation of 25(OH)D
- End organ resistance to 1,25(OH)₂D

Rickets due to Dietary Calcium Deficiency

Raised PTH

Renal Phosphate Wastage

Hypophosphatemia

Impaired Apoptosis of Terminally Differentiated Chondrocytes in the Growth Plate

Mughal. Curr Osteoporos Rep. 2011;9(4):291-9

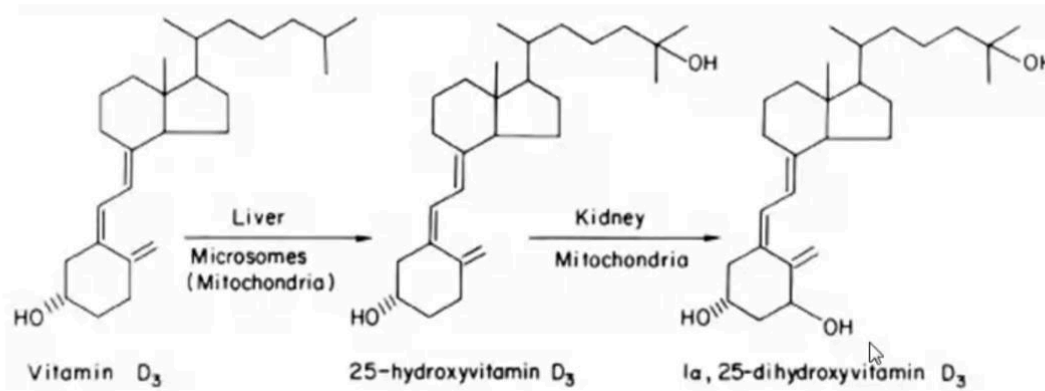
Phosphopapenic Rickets

Hypophosphataemic Rickets

- X-linked Dominant (PHEX gene mutation)
- Autosomal Dominant (FGF23 mutation)
- Autosomal Recessive Type 1 (DMP1 mutation)
- Autosomal Recessive Type 2 (ENPP1 mutation)
- With Hypercalciuria (SLC34A3 gene mutation)
- Associated with:
 - (a) McCune-Albright syndrome
 - (b) Tumour induced osteomalacia

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Vitamin D metabolism



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Nutritional rickets-lack of dietary Vit D, insufficient exposure to sunlight

7 dehydrocholesterol

Cholecalciferol (Vit D3)

Ergocalciferol

Chronic liver failure

25-OH vit D

Vitamin D dependent rickets type 1, Chronic Renal Failure

1-25 (OH)₂ D

Vit D dependent rickets type 2

Parathyroid glands

Decreased PTH production

Intestines

Increase absorption of calcium and phosphate
Decreased magnesium absorption

Bone

Release calcium and phosphate

Kidney

Auto-regulation of calcitriol production

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Other Conditions That Can Cause Rickets

- Medications
 - Antacids
 - Anticonvulsants
 - Corticosteroids
 - Loop diuretics
- Malignancy
- Prematurity
- Diseases of organs associated with vitamin D and calcium metabolism
 - Kidney disease
 - Liver and biliary tract disease
- Malabsorption syndromes
 - Celiac disease
 - Cystic fibrosis (rare)

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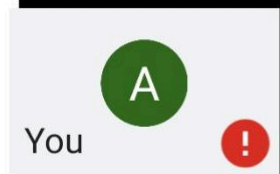
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Revision

- Role of Vitamin D and PTH in;
 - Calcium metabolism
 - Phosphorus metabolism
 - Magnesium metabolism



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History

- Gestational age, diet (breastfeeding vs formula) and degree of sunlight exposure
- Dietary specifics of vitamin D and calcium intake
- Growth concerns, milestones, recurrent infections
- Signs and symptoms of hypocalcemia:-Muscle cramps, numbness, paresthesias, tetany and seizures
- Family history:- short stature, orthopedic abnormalities, poor dentition, alopecia, parental consanguinity

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Examination

- Hypotonia, Short stature
- Skeletal abnormalities- bow legs, knock knees, windswept deformity, rickets rosary, frontal bossing, kyphosis, scoliosis, lordosis, pectus excavatum, pectus carinatum, Harrison's sulcus, skull bossing, craniotabes, wide anterior fontanelle,
- Delayed dentition, dental caries,
- Tetany – may be latent- Chvostek's, Trousseau's,

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Investigations

- Bone chemistry
 - Calcium, phosphorus, Alkaline phosphatase, magnesium
 - U/E/Cs
- Vitamin D levels, PTH levels
- Urinary excretion of phosphorus, calcium
- X-ray left wrist (or the knees)

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Bone Biochem interpretation

Type	Calcium	Phosphorus	Alkaline phosphatase	PTH	25 (OH)D	1,25 (OH) ₂ D
Calcipenic rickets						
Vitamin D deficiency	↓ or N	Y or N	↑ or ↑ ↑	↑	↓	Variable
Vitamin D-dependent rickets type I	↓	Y or N	↑ ↑	↑	N	↓
Vitamin D-dependent rickets type II	↓	Y or N	↑ ↑	↑	N	N or ↑
Phosphenic rickets						
Nutritional phosphate deficiency	↑ or N	↓	↑ or ↑↑	Y or N	N	↑
X-linked hypophosphatemic rickets	N	↓	↑	N or ↑ slightly	N	N or ↓
Autosomal dominant hypophosphatemic rickets	N	↓	↑	N	N	↓
Autosomal recessive hypophosphatemic rickets	N	↓	↑	N	N	↓
Hereditary hypophosphatemic rickets with hypercalciuria	N	↓	↑	N or ↓	N	↑

Rahul Chanchlani et al; An Overview of Rickets in Children.; Kidney Int Rep (2020) 5, 980–990; <https://doi.org/10.1016/j.ekir.2020.03.025>

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Biochemical stages of Vit D Deficiency rickets

Stage 1:

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

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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 ALP.
- Raised Ca tubular re-absorption and decrease phosphate tubular re-absorption. Phosphates are lost in the urine, Ph alkaline.
- X-ray findings: Osteoporosis and metaphis-epiphesial changes.

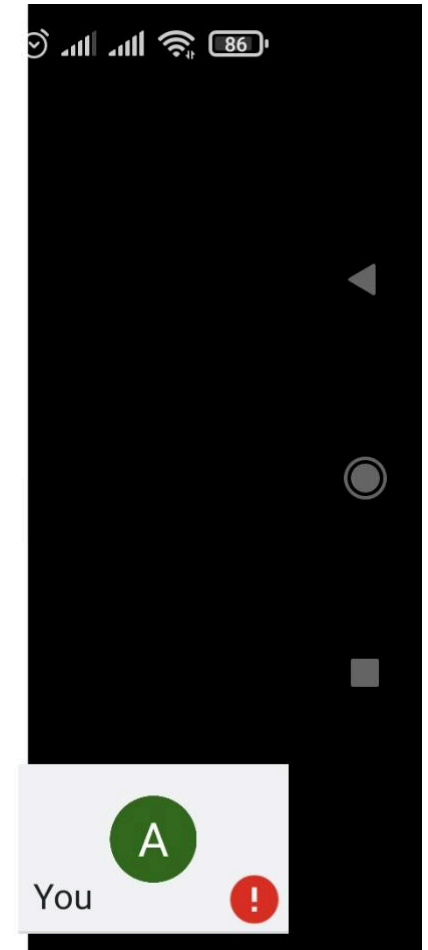
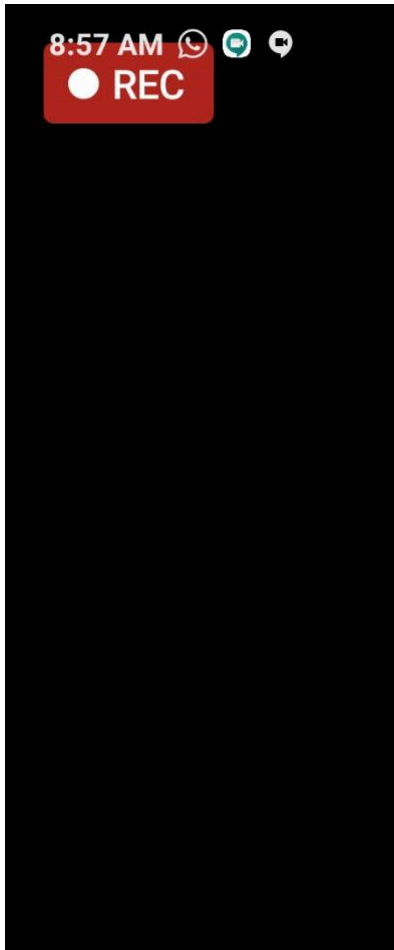
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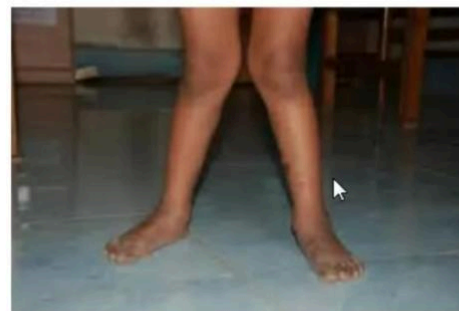
Biochemical stages of rickets

Stage 3.

- Severe deficiency of vit.D for a long duration
- Laboratory reports:
 - Hypocalcemia
 - hypophosphatemia,
 - Elevated serum levels of ALP and PTH
- Radiological changes more expressive.



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Skeletal
abnormalities

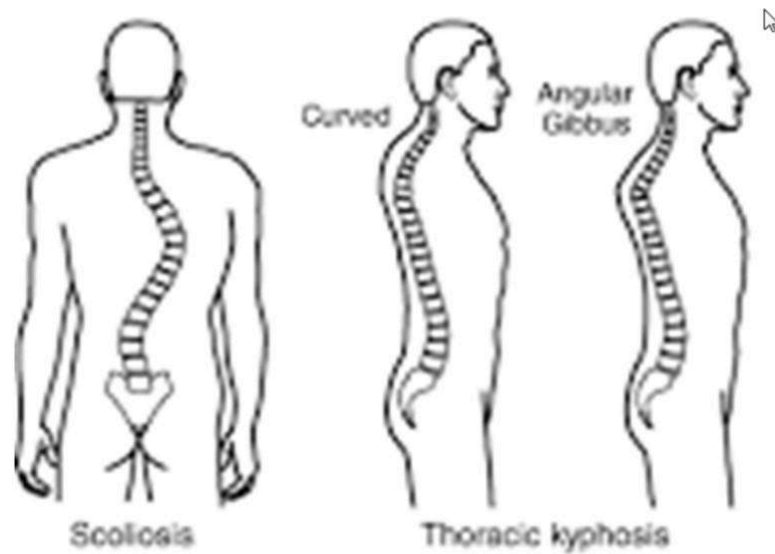


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Skeletal abnormalities- kyphosis and scoliosis



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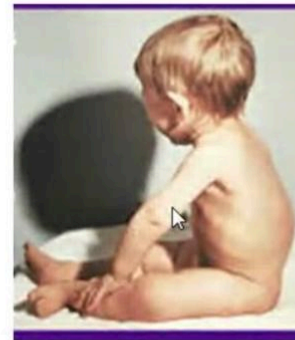
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Skeletal abnormalities



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Radiological features



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Treatment

Vitamin D Deficiency rickets

- Vitamin D
 - Daily, weekly or every 3 months
 - Stoss therapy- one large dose – may repeat in 3 months
 - 1-6 months
 - 6 months -12 years
 - 12-18 years
 - Supplement for a year thereafter 400 units daily
- Calcium supplementation in early stages
 - 40 mg/kg/day
 - Calcium levels at 2 weeks of Rx
- Orthopaedic procedures for deformities

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Treatment

VDDR Type I

- Physiological doses of calcitriol ($1,25(\text{OH})_2\text{D}$) or alphacalcidol (1-OH D)

VDDR Type II

- Pharmacological doses of calcitriol or alphacalcidol and Oral calcium
- Long-term treatment calcium infusions (especially patients with alopecia)

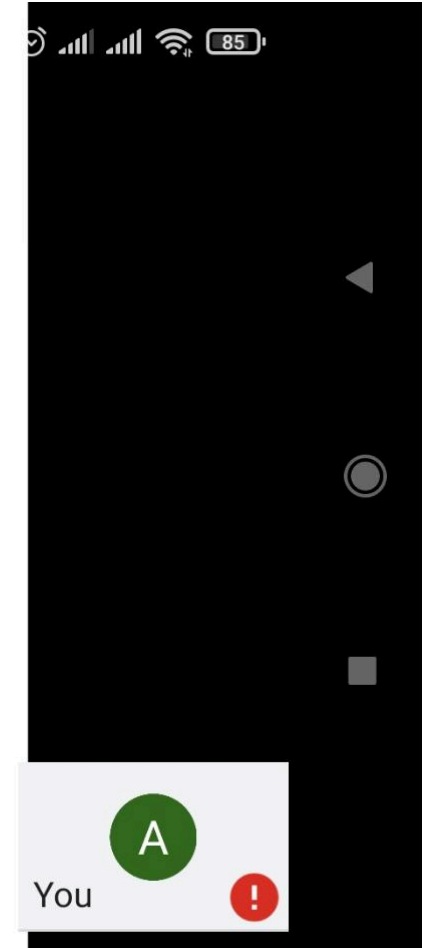
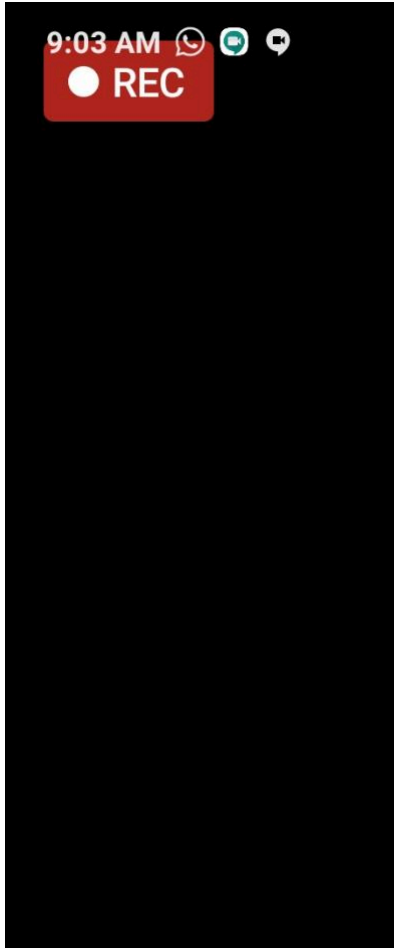
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Follow-up

- Monitor
 - ✓ Improvement in symptoms (~ 2weeks)
 - ✓ ↓ in serum PTH & alkaline phosphatase
 - ✓ ↑ in serum phosphate, calcium & 25(OH)vitamin D
 - ✓ Radiological healing (~ 3 months)
 - ✓ Improvement of bow legs or knock-knees (~ 2 years)
- If healing not achieved then reassess, and may retreat



Prevention

- Supplement mothers during pregnancy and lactation
 - Calcium
 - Vitamin D
- Adequate sunshine
- Calcium containing diet
- Supplement Vitamin D for those at risk
 - Preterm infants
 - Inadequate sunshine
 - Dark skinned living out of the tropics

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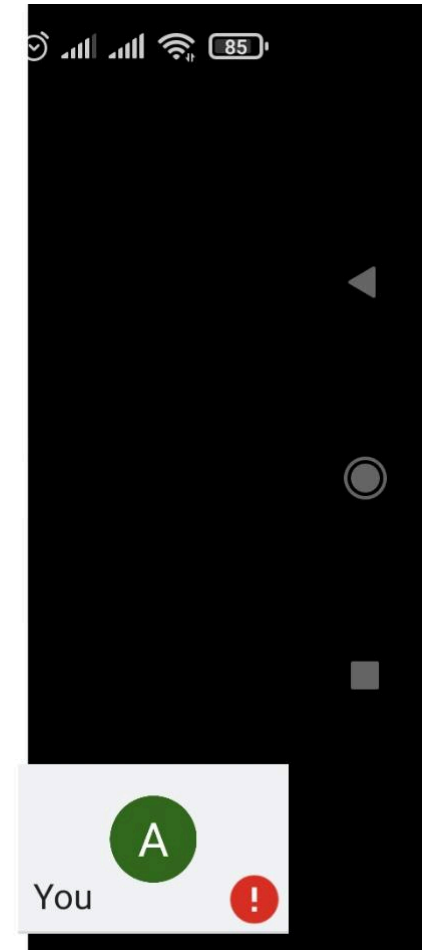
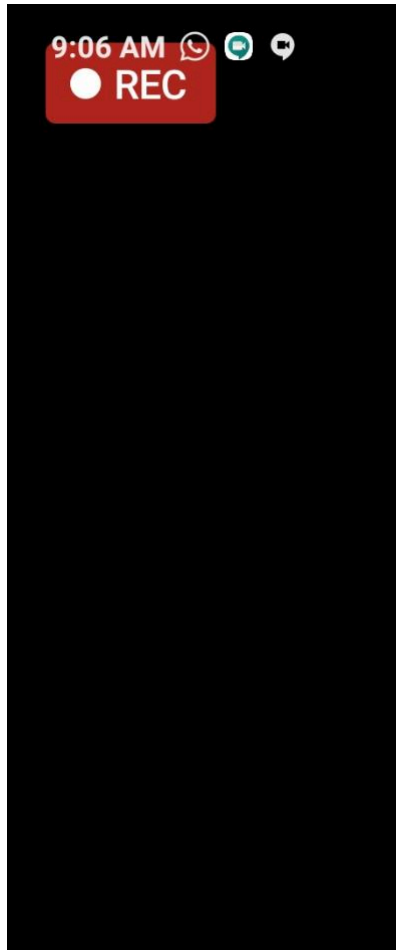
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Sunshine

UVR from the sun is less available

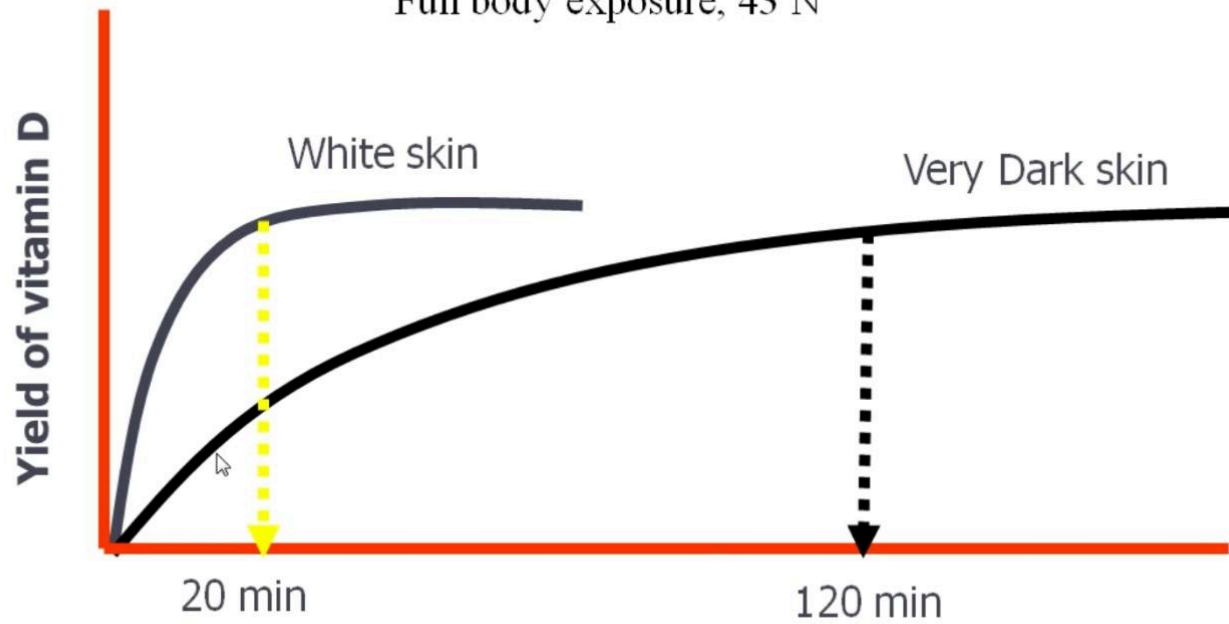
- Blocked by air pollution
- Tendency to wear clothes eg religious dressing
- Cities with high buildings
- Children kept indoors
- Sunscreens to prevent skin cancer
- Geographical regions with little sunlight
- Time of day- less early morning and late afternoon



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Effect of UVB exposure time and skin color on Vitamin D production

Full body exposure, 43 N



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