Different Types of Rickets in Children

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Outline

- Structure, growth and strength of a long bone
  - Mineralization: calcium and phosphate
  - Defective mineralisation: rickets vs osteomalacia
- Different types of rickets in children
  - Calcipenic and phosphopenic

Structure of a long bone

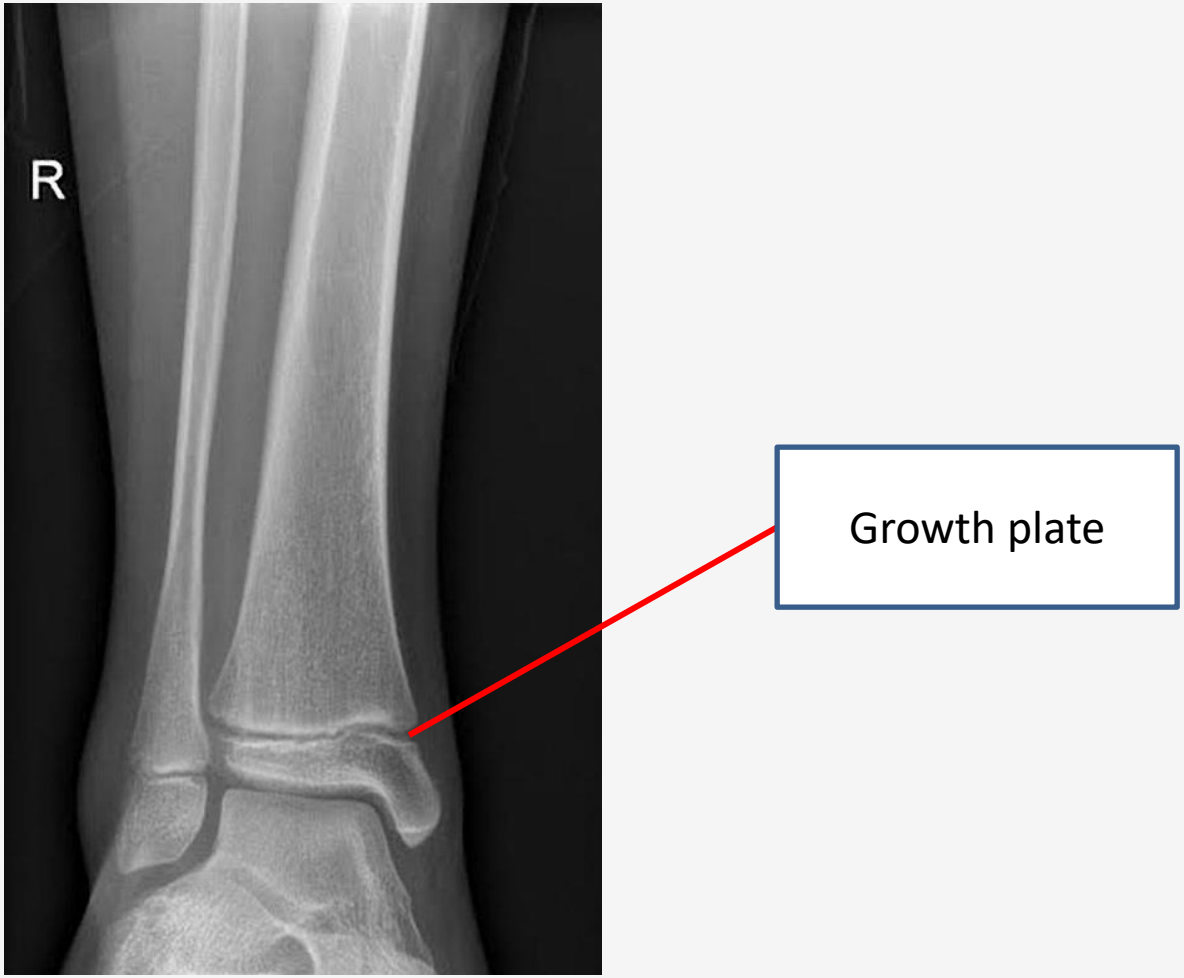
Diaphysis

Metaphysis

Physis

Epiphysis

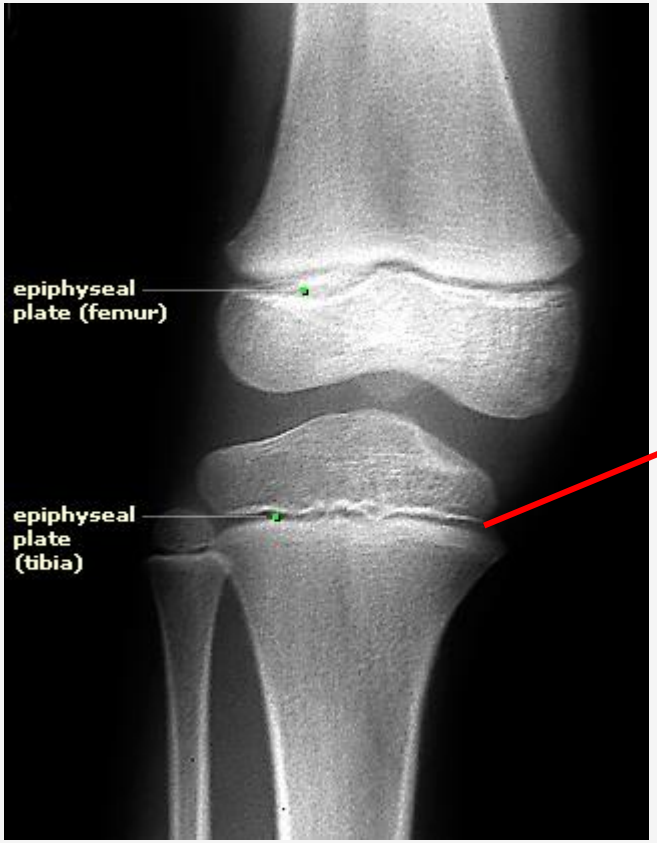
Structure of a long bone



Structure of a long bone

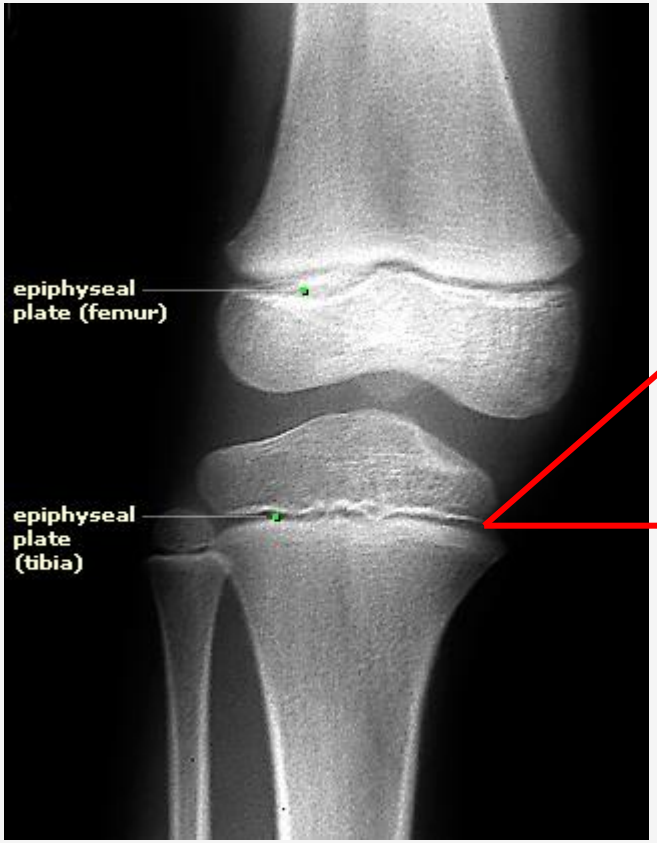
Area of rapidly dividing chondroblats

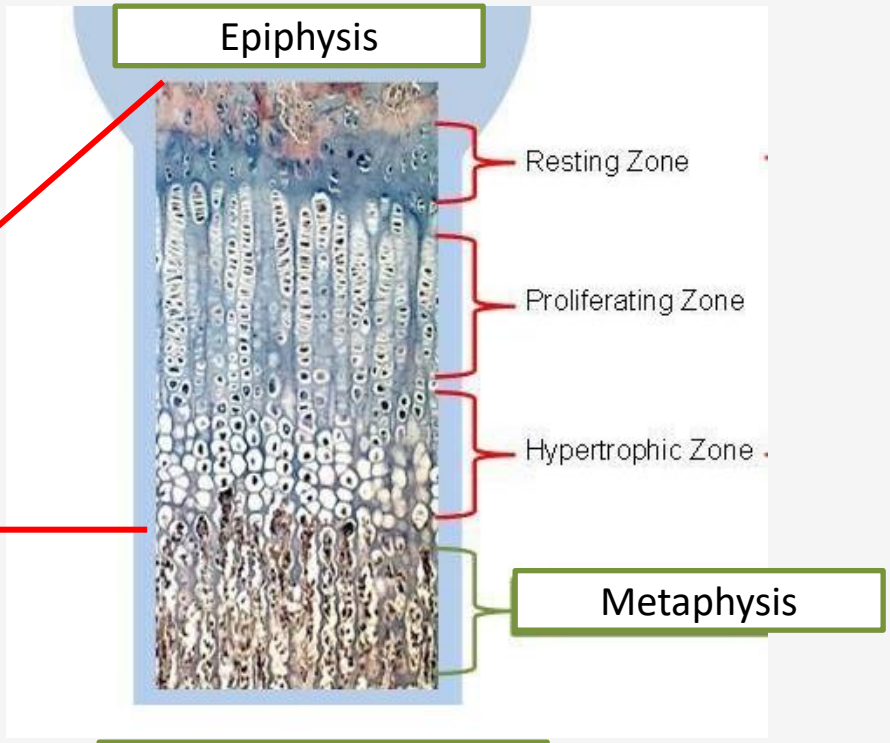
Structure of a long bone



Area of rapidly dividing chondroblats

Growth of a long bone



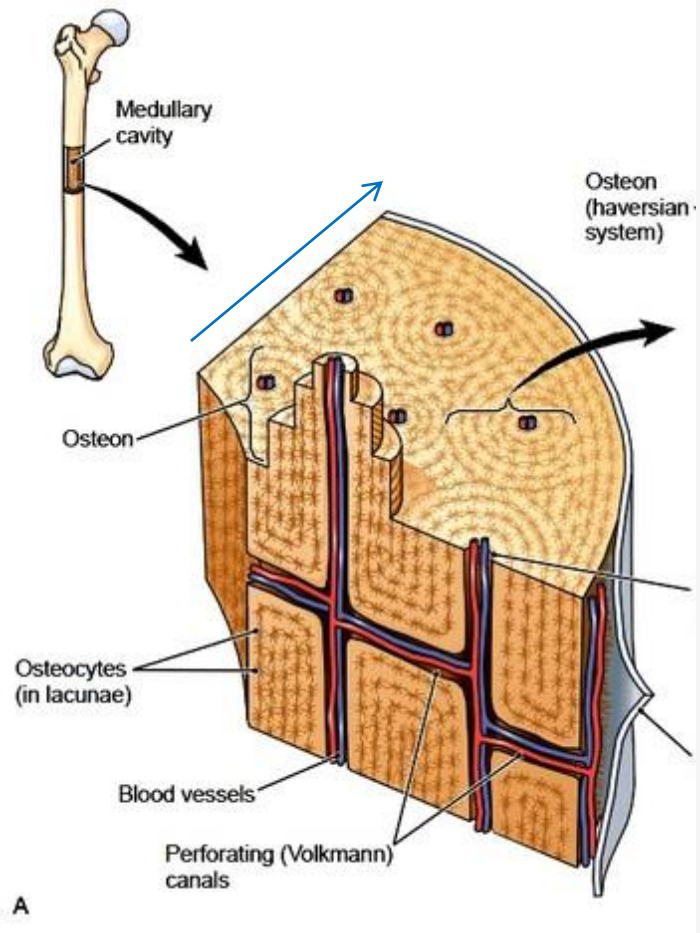


Mineralisation

Rickets

Deformities

Growth of a long bone



Bone pain
Easy fractures
Muscle weakness

Osteomalacia

Mineralisation

Strength of a long bone

Mineralization
(Calcium and phosphate)

Mineralization
(Calcium and phosphate)

Strength of a long bone

Defective mineralization
(Osteomalacia)

Children

Defective mineralization
(Rickets)

Strength of a long bone

Defective mineralization
(Osteomalacia)

Adults

Hormonal control of mineralization (calcium and phosphate)

FGF-23
Vitamin D
Parathyroid hormone

Mineralization
(Calcium and phosphate)

7-Dehydrocolesterol

Sunlight

Vitamin D

Small intestine

25- hydroxylase

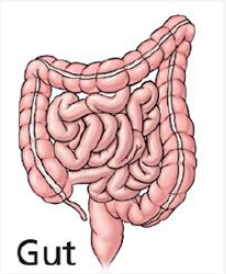
25- (OH) D

1ά - hydroxylase

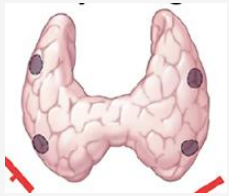
$1\alpha,25\text{-}(OH)_2$ D

Ca↑
PO4↑

Absorption of Calcium and phosphate



Na-Pi IIb

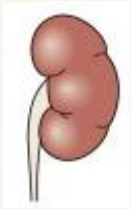


Parathyroid hormone

Releases calcium and phosphate into the blood stream

Ca↑
PO4↓

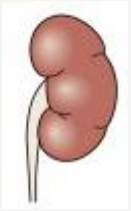
Inhibits phosphate reabsorption in the proximal tubule



Na-Pi IIa
Na-Pi IIc

FGF-23

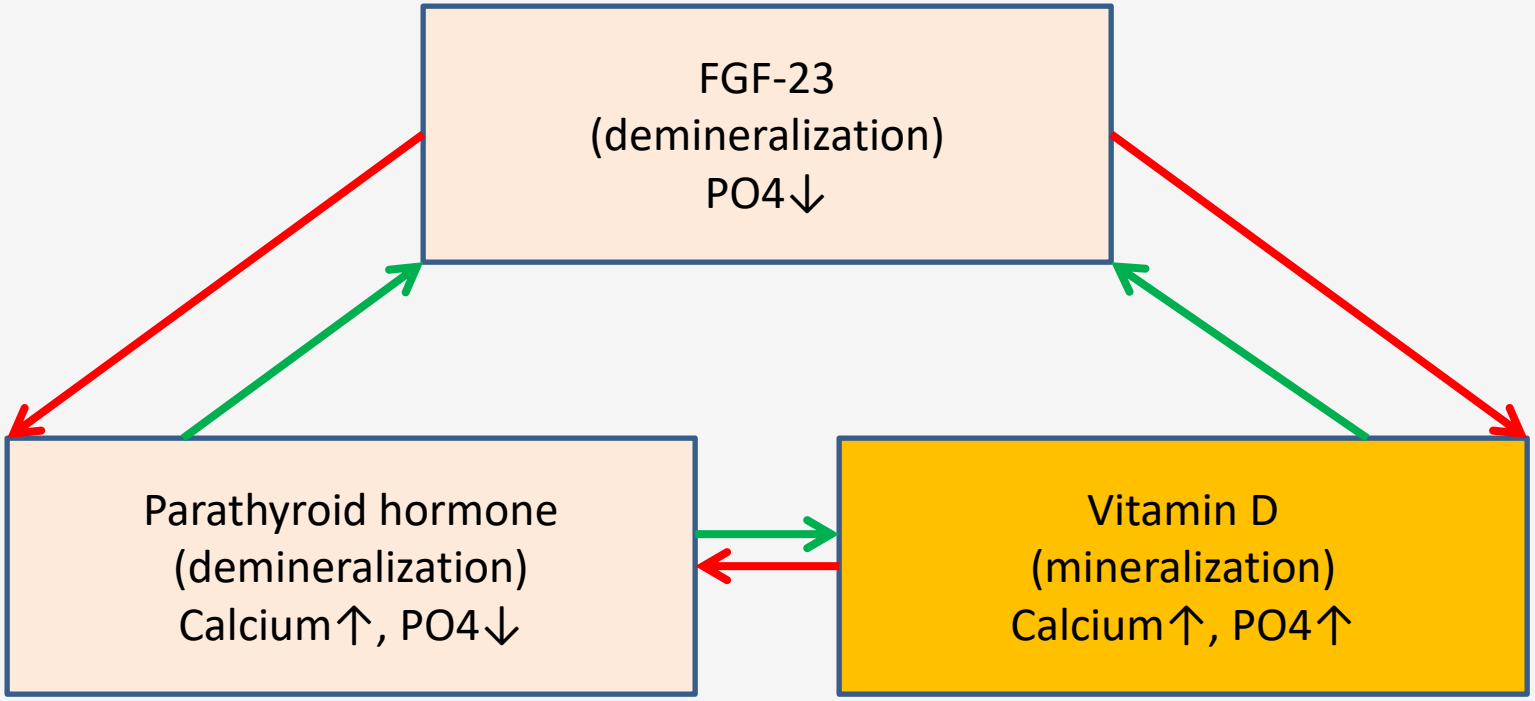
Inhibits phosphate reabsorption in the proximal tubule



Na-Pi IIa
Na-Pi IIc

Ca
PO4↓

Hormonal control of bone mineralization



Different types of rickets

- Bone mineralisation: deposition of calcium and phosphate
- Rickets: defective mineralisation
- Rickets: Calcipenic and phosphopenic

It is hard to differentiate between calcipenic and phosphopenic rickets by clinical features only.

Laboratory parameters of rickets

Parameters	Calcipenic rickets	Phosphopenic rickets
Calcium		
Phosphate		
ALP		
PTH		

Laboratory parameters of rickets

Parameters	Calcipenic rickets	Phosphopenic rickets
Calcium	↓	N
Phosphate		
ALP		
PTH		

Laboratory parameters of rickets

Parameters	Calcipenic rickets	Phosphopenic rickets
Calcium	↓	N
Phosphate	N	↓
ALP		
PTH		

Laboratory parameters of rickets

Parameters	Calcipenic rickets	Phosphopenic rickets
Calcium	↓	N
Phosphate	N	↓
ALP	↑↑	↑
PTH		

Laboratory parameters of rickets

Parameters	Calcipenic rickets	Phosphopenic rickets
Calcium	↓	N
Phosphate	N	↓
ALP	↑↑	↑
PTH	↑	N

Laboratory parameters of rickets

Parameters	Calcipenic rickets	Phosphopenic rickets
Calcium	↓ (or) N	N
Phosphate	N	↓
ALP	↑↑	↑
PTH	↑	N

Laboratory parameters of rickets

Parameters	Calcipenic rickets	Phosphopenic rickets
Calcium	↓ (or) N	N
Phosphate	N (or) ↓	↓
ALP	↑↑	↑
PTH	↑	N

Laboratory parameters of rickets

Parameters	Calcipenic rickets	Phosphopenic rickets
Calcium	↓ (or) N	N
Phosphate	N (or) ↓	↓
ALP	↑↑	↑
PTH	↑	N
25- (OH) D	↓	N

Calcipenic rickets

- Calcium deficiency
- Vitamin D deficiency

7-Dehydrocolesterol → Sunlight → Vitamin D ← Small intestine

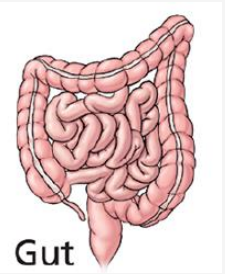
Vitamin D → 25- hydroxylase → 25- (OH) D

25- (OH) D → 1α - hydroxylase → 1α,25- $(OH)_2$ D

- Nutritional vit D deficiency
- 25- hydroxylase deficiency
- Chronic liver disease
- 1α- hydroxylase deficiency
- Chronic kidney disease
- Vit D receptor defect

Treatment

1α,25- $(OH)_2$ D → Absorption of Calcium and phosphate → Deposition of Calcium and phosphate



Na-Pi IIb

Dehydrocolesterol

Sunlight

Vitamin D
Cholecalciferol

Small intestine

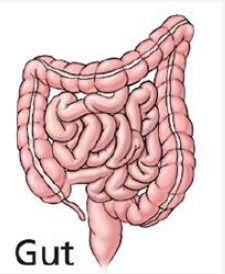
25- hydroxylase

25- (OH) D

1α - hydroxylase

$1\alpha,25\text{-}(OH)_2\ D$

Absorption of Calcium and phosphate



Deposition of Calcium and phosphate

Na-Pi IIb

- Nutritional vit D deficiency
- Chronic liver disease

Vitamin D
(Cholecalciferol)

Dehydrocolesterol

Sunlight

Vitamin D

Small intestine

25- hydroxylase

25- (OH) D

1ą - hydroxylase

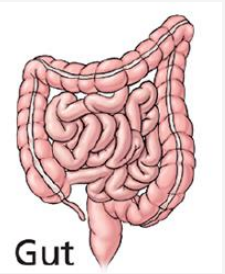
1ą,25- $(OH)_2$ D

- 1ą - hydroxylase deficiency
- Chronic kidney disease

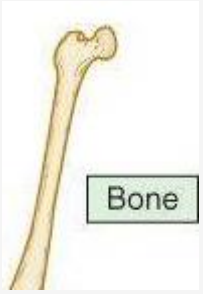
1ą- (OH) D

1ą,25- $(OH)_2$ D

Absorption of Calcium and phosphate



Deposition of Calcium and phosphate



Na-Pi IIb

Dehydrocolesterol

Sunlight

Vitamin D

Small intestine

25- hydroxylase

25- (OH) D

Vit D receptor defect

1α,25- $(OH)_2$ D

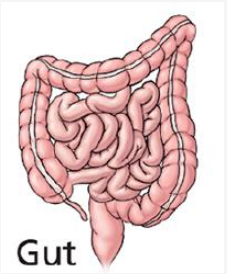
Calcium

Phosphate

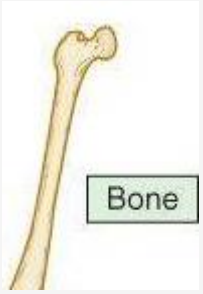
1α - hydroxylase

1α,25- $(OH)_2$ D

Absorption of Calcium and phosphate



Deposition of Calcium and phosphate



Na-Pi IIb

Phosphopenic rickets

- Nutritional deficiency
- Defective renal tubular reabsorption of phosphate

1. Tubular reabsorption of phosphate (TRP)
2. Maximal tubular reabsorption of phosphate per GFR (TmP/GFR)

Phosphopenic rickets

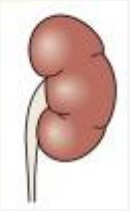
- Nutritional deficiency (high TmP/GFR)
- Defective renal tubular reabsorption of phosphate (low TmP/GFR)

Defective renal tubular reabsorption of phosphate

- Defective reabsorption of multiple solutes
  - Phosphate, glucose, amino acids, proteins, uric acid, potassium, metabolic acidosis (Fanconi syndrome)
- Isolated phosphate reabsorption defect
  - (Hypophosphataemic rickets)

FGF-23

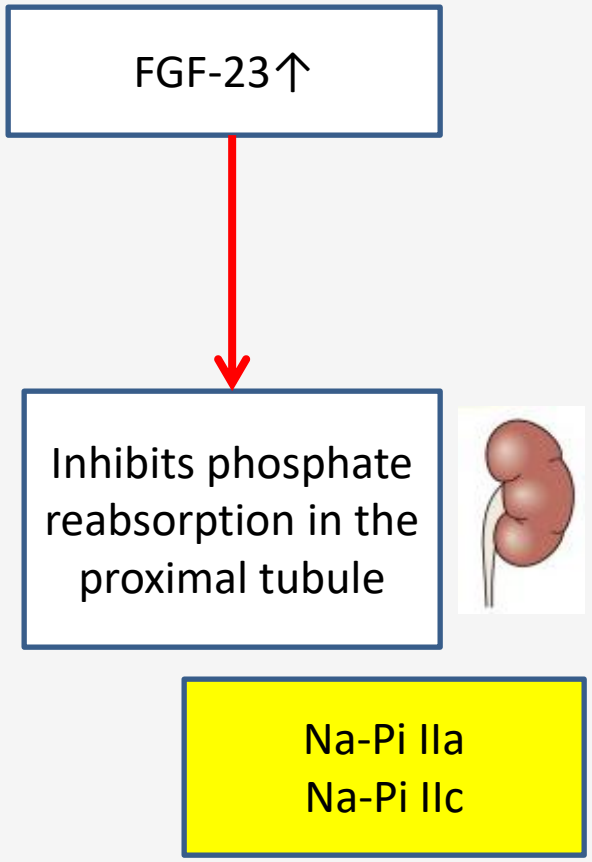
Inhibits phosphate reabsorption in the proximal tubule



Na-Pi IIa
Na-Pi IIc

Hypophosphataemic rickets

- X-linked dominant
- Autosomal dominant
- Autosomal recessive
- Hereditary hypophosphataemic rickets with hypercalciuria (HHRH)



Hypophosphataemic rickets

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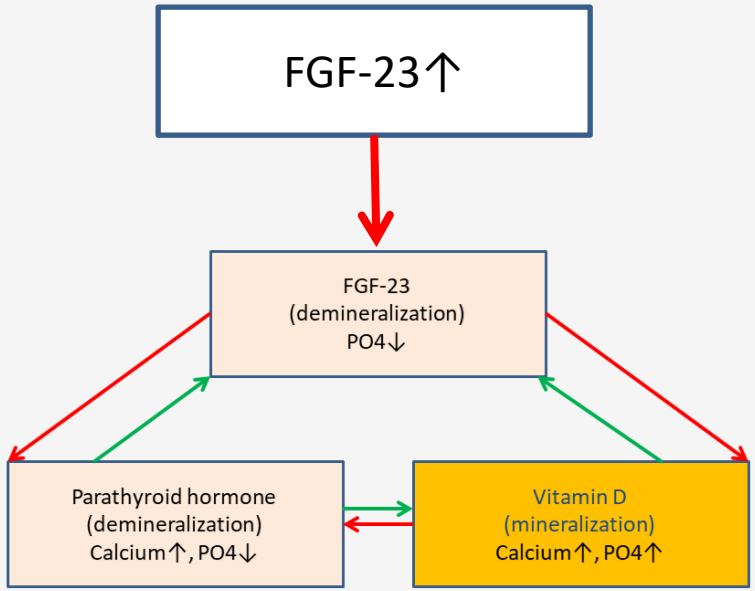


Low Vit-D levels
Low calcium
High PTH

Mimic calcipenic rickets.

Treatent

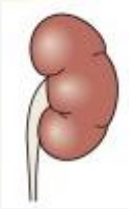
burosumab

Hypophosphataemic rickets

Hereditary hypophosphataemic rickets with hypercalciuria (HHRH)

FGF-23 normal
Vit- D normal

defective phosphate reabsorption in the proximal tubule



Hypercalcaemia
Hypercalciuria
Nephrocalcinosis

Na-Pi IIa
Na-Pi IIc

Treatent

Summary

- Rickets: defective mineralisation at the growth plate
- Rickets: calcipenic and phosphopenic rickets

Summary

Calcipenic rickets

- Calcium deficiency
- Vitamin D deficiency
  - Nutritional vit D deficiency
  - Chronic liver disease
  - 1α - hydroxylase deficiency
  - Chronic kidney disease
  - Vit D receptor defect

Phoshopenic rickets

- Nutritional deficiency
- Defective renal tubular reabsorption of phosphate
  - Fanconi syndrome
  - Isolated phosphate reabsorption defects

THANK YOU VERY MUCH