RENAL TUBULAR DEFECTS

CD POTGIETER

GAMARA

1. Renal tubule defects in Phosphate transport
2. Amino aciduria
3. Renal Glucosuria
4. Fanconi Syndrome
5. Nephrogenic Diabetes Insipidus
6. Renal Tubular Acidosis

Renal Tubule defects in Phosphate transport

- Main renal mechanism regulating phosphate excretion =
  1. Filtration
  2. Tubule reabsorption
     (Active, energy dependent)
- Proximal tubule: 60 - 70% absorbed.
- Henle descending and ascending: 10 - 15%
- Distal tubule: 5 - 10%
- Collecting tubule: 3 - 5%
- Parathyroid hormone (PTH)
  → phosphaturia
  Reason: Decrease in proximal tubule phosphate reabsorption
  (PTH inhibits phosphate reabsorption)
- Dietary phosphate intake - 2nd regulator of renal phosphate handling. Phosphate restriction → increase in renal phosphate reabsorption
  (within 3 days - urine is phosphate free)
- Vitamin D = antiphosphaturic (increase renal phosphate reabsorption)

Vitamin D - Resistant Rickets

- x linked dominant - Familial
- Rickets / osteomalacia
- Hypophosphatemia
- Decreased Renal reabsorption of phosphate
- Normal Serum Calcium
- Diminished calcium + phosphate gastro-intestinal absorption.
- Resistance to Vitamin D

Clinically

- Short stature
- Reduced growth rate
- */. Rickets in childhood
- Osteomalacia in adults.
- No muscle weakness / tetany or convulsions.
- Hypophosphatemia
- Dental abnormalities
- Facial and skull deformities
- Bone overgrowth at muscle insertion / Spinal cord compression.

Pathogenesis

Increased tubule sensitivity to normal PTH.
Decreased GIT Ca - absorption.
Proximal tubule phosphate reabsorption defect !!

Vitamin D - Dependent Rickets

(type I - Vit D ↓)

(type II - Vit D ↑)

Clinically

- Hypocalcaemia
- Hypophosphatemia
- Rickets - severe
- Response to large dosis of Vitamin D
- Phosphaturia

Defect: Impairment of renal tubule cell to hydroxylate 25 (OH) Vitamin D

Pseudohypoparathyroidism

Clinically:

- ✡ Hypocalcaemia
- ✡ Hyperphosphatemia
- ✡ Hyperparathyroidism
- ✡ PTH resistance - proximal tubule

Somatic:

- ✡ Short stature
- ✡ Round face
- ✡ Brachydactyly
- ✡ Impaired mentally

AMINOACIDURIA

- ☙ Excretion of abnormal amount of aminoacids in urine.
- ☙ Due to: Renal tubule transport defect

Amino Acid group and affected members	Disorder of transport
A. Monoamino, monocarboxylic amino acids	A. Hartnup disease
1. Methionine	1. Methionine malabsorption
2. Tryptophan	2. Blue diaper syndrome
3. Histidine	3. Histidinuria
B. Diamino amino acids	B. Cystinuria
1. Cystine	1. Isolated cystinuria
2. Lysine, arginine, ornithine	2. Dibasic aminoaciduria
3. Lysine	3. Lysinuria
C. Imino acids and glycine	C. Iminoglycinuria
1. Proline, hydroxyproline	1. None described
2. Glycine	2. ? Glycinuria
D. Dicarboxylic amino acids	D. Dicarboxylic aminoaciduria
E. Beta amino acids	E. None described

Renale Glucosuria

- Significant amounts of glucose in urine in the absence of hyperglycemia
- & Urinary glucose excretion in urine from 5 to 100gr / day
- & Glucosuria in all urine speciments including in urine after overnight fast.
- & Specific test in urine for glucose (exclude fructosuria / galactosuria)
- & Oral glucose tolerance test should be normal to exclude D.M.

Glucose - galactose malabsorption syndrome

Glucoglycinuria

Fanconi Syndrome

= Renal tubule transport defect (prox)

Results:
- ♌ Phosphaturia
- ♌ Aminoaciduria
- ♌ Glucosuria
- ♌ Sometimes losses of bicarbonate
  uric acid
  Potassium
  Calcium

Clinically:
- ♌ Osteomalacia / Rickets
- ♌ growth failure
- ♌ Chronic Acidosis
- ♌ Hypokalemia symptoms

- ♌ Commonest cause of Fanconi's in children = Cystinosis
- ♌ In adults = myeloma, Wilson's disease outdated, tetracycline, heavy metals, Vit D intoxication

Others - rarer: Lower syndrome glycogen storage disease, fructose intolerance, tyrosinosis, amyloidosis malignancy, familial and ideopathic.

Nephrogenic Diabetes Insipidus

fect:

- Renal tubular cell insensitivity to endogenous and exogenous antiduiretic hormone
- Inheritance: Sex-linked

Aquired:
* Hypercalcaemia
* Hypokalemia
* Drugs: Demecloeycline, Lithium
* Amyloidosis
* Sjögren syndrome
* Sickle cell disease

Clinically:
* Polyuria + Polydipsia
* Impairment of urine concentration ability
* Hypernatraemia
* Fever
* Nocturia
* Growth retardation
* Mental Retardation

Renal tubular Acidosis:

(RTA)

Features:
- Hypokalemia
- Hyperchloremic metabolic acidosis
- Urine that is less than maximally acidic (pH 5,4)

Distal RTA:
1. Primary - ideopathic
2. Secondary
   - Medullary cystic disease
   - Ehlers - Danlos syndrome
   - Hyperparathyroidism
   - Vitamin D intoxication
   - Glue sniffers
   - Amphotericin B
   - Renal Tx
   - Analgesics
   - SLE

Defects:
* Inability of distal nephron to establish a hydrogen ion Gradient between blood and tubule fluid regardless of the severity of the systemic acidosis
* With acid stimulus - urine pH remains > 5,4
* Reclamation of filtered HCO_3 is incomplete

* Loss of bicarbonate in urine accompanied by loss of cations, sodium and potassium.
* Loss of sodium - contraction extracellular volume and secondary hyperaldosteronism - further potassium wasting.
* ∴ Hypokalemia and hyperchloremic metabolic acidosis
* Hypercalciuria - renal stones
* Nephrocalcinosis
* Osteomalacia and bone pain.

Proximal RTA

proximal tubule is the primary site of bicarbonate reabsorption (85 - 90% reclamation)
Tm - HCO_3 saturated if s-HCO_3 more than 25 - 26 mM/L
Usually associated with multiple transport disorders eg: Fanconi syndrome
Tm - HCO_3 is reduced

atures:

Growth retardation
Bone lesions
Hypercalciuria
Nephrocalcinosis
Potassium waisting
Hypokalemia

Definition of Renal Tubular Acidosis

Def: Increased Cl- / Normal anionic gap metabolic acidosis.

ormal Acid loads buffered by:

1. PO_4 - major ionic component of titratable acid.
2. NH_3 to NH_4

Netto urine Acid Excretion:
Titratable acid + NH_4 - HCO_3

Fractional excretion of HCO_3 = Less than ± 5%
Glomerular filtration of HCO_3 per day = 4000mekw.
(Have to absorb ± everything)
mainly: proximal tubule

N.B. Blood pH less than 7,35 - urine pH should be less than 5,5

Test: 1 NH_4Cl 0,1gm/kg x 3 days measure urine pH (not in liver disease)
2. Fractional HCO_3 excretion more than 15% if P.HCO_3 20/more.