Pediatric urolithiasis:

What may be the underlying diseases?

What is expected from imaging ?

What medical treatment?

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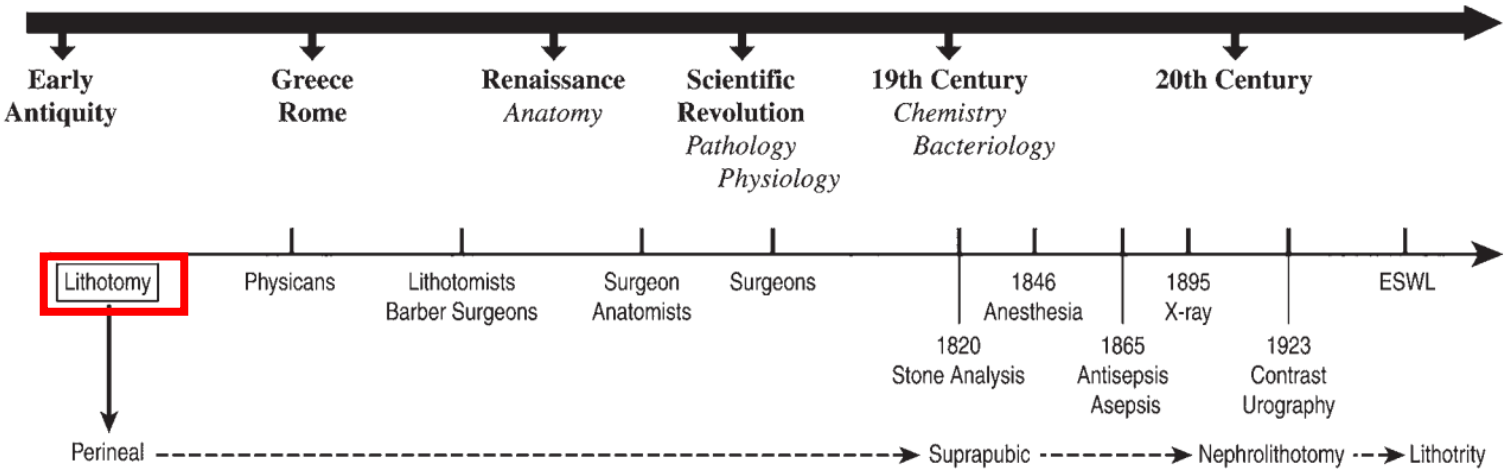
Inserm

LΦ2M

UROLITHIASIS AND HISTORY



- Asclépiade de Bythinie (-100 av JC) describes the surgical size
- Celsus (-25 av JC- 50 ap JC) : *De arte medica* 8 vol → codifies perineal size
- Avicenne, (980-1037) *Canon* → 12 paragraphs on lithiasis and its treatment
- A Paré. (1509-1590) *Œuvres complètes* (1575)

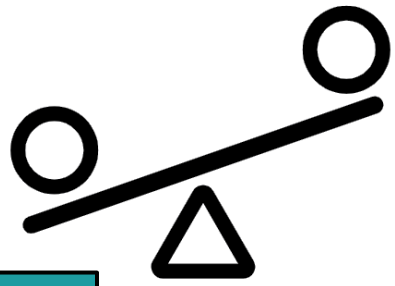
* The Montaigne's « gravelle » (1533-1592)
* Colbert's fatal urolithiasis (1619-1683)
* The defeat at Sedan and the death of Napoleon III

Jichlinski P. Revue médicale suisse, 2006
Androutsos G. Progrès en Urologie, 2004
Eknoyan G. Clinical Reviews in Bone and Mineral Metabolism, 2004

LITHIASIS FORMATION

- **Urine over-saturation: MULTIFACTORIAL**
  - Insufficient water intake
  - Urinary obstruction *(congenital uropathies)*
  - Excess of insoluble compound

Crystallization promoters



Crystallization inhibitors

- **Epidemiology**

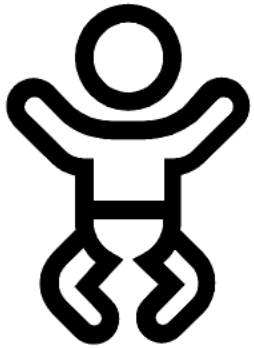
Life time risk	5-10%
In children	14-18 per 100,000
Incidence	+ 6-10% per year

Taylor EN, JAMA, 2005
Sas DJ, J Pediatr, 2010

CLINICAL FEATURES

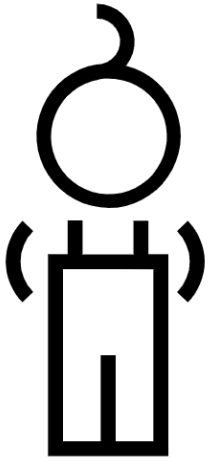
- **All ages are affected : NON-SPECIFIC**
  - Boys: 4.4 years
  - Girls: 7.3 years

Recurrent forms
Bilateral stones
Familial history
Consanguinity



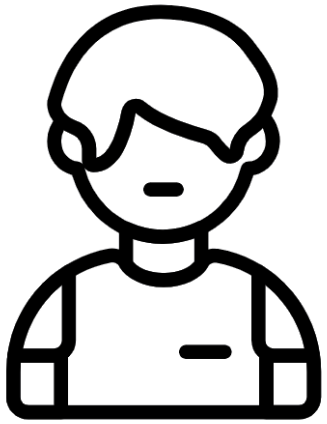
Below 2 years old

Incidentally discovered (29.9%)
Urinary tract infection (26.9%)



2-5 years old

Macroscopic hematuria (36.7%)



>10 years old

Flank pain (41.3%)
Hematuria (23.8%)

→ 10 % of lithiasis related to monogenic causes

Alpay, Pediatric Nephrol 2009

PATHOPHYSIOLOGY

- **Kidney stones**
  - Agglomerate of crystals bound
  - To an organic matrix

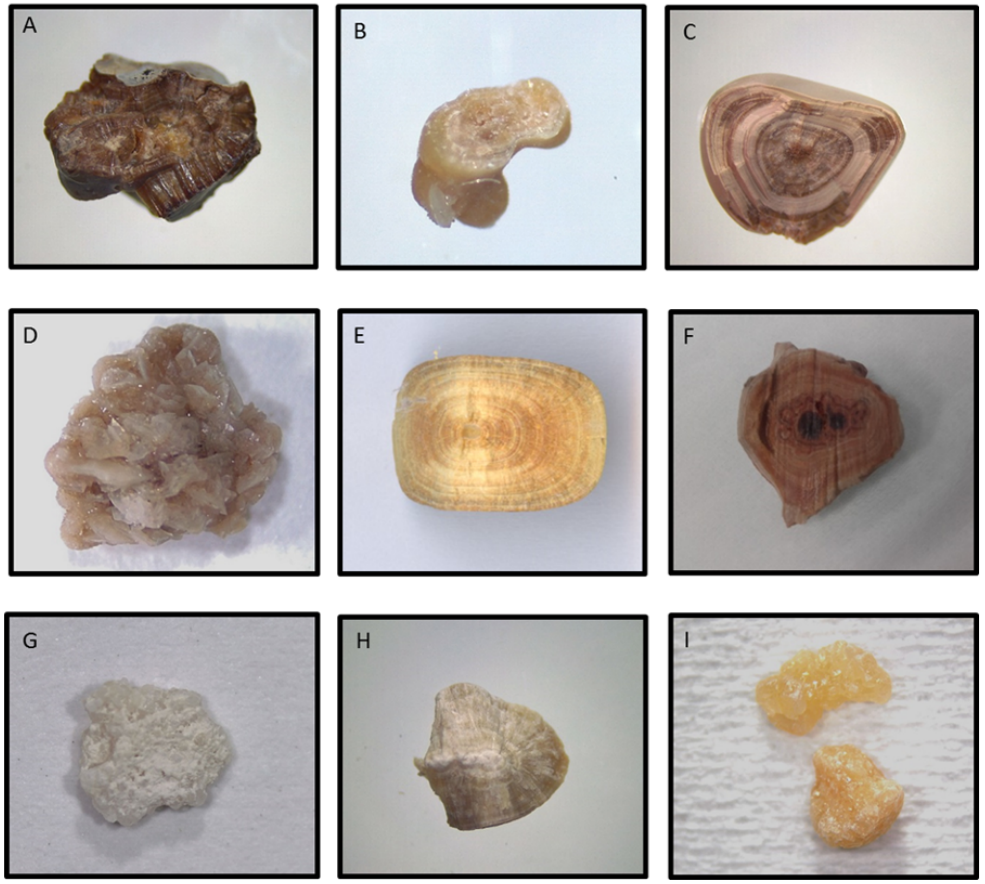
    - Nucleation: crystal nidus

- **Crystallization**
  - Promoters

    - Calcium, oxalate, phosphate
    - Uric acids, cystine, xanthine
    - Nutritional mistakes

  - Inhibitors

    - Citrate, magnesium



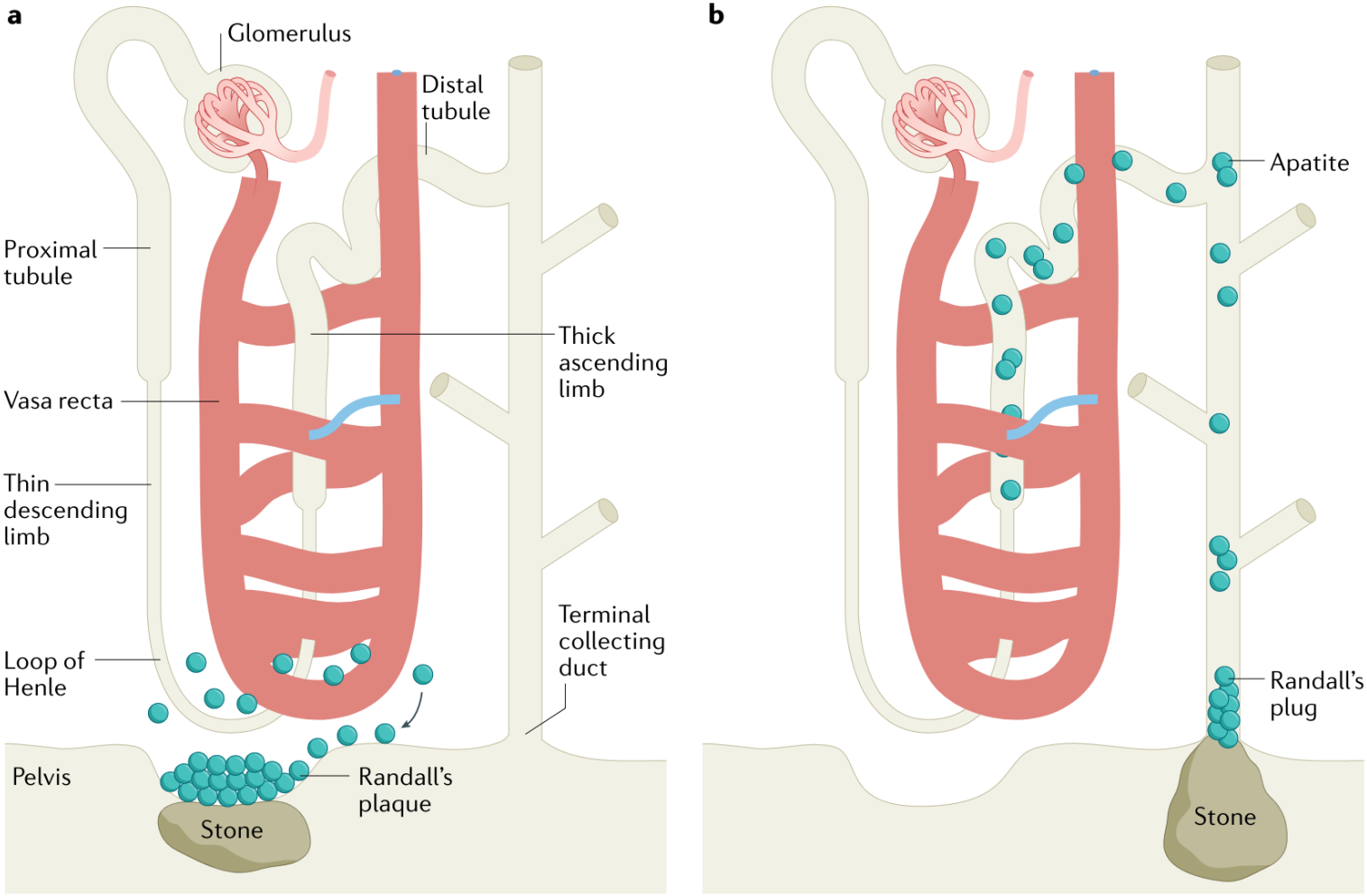
Bertholet-Thomas A., EMC 2020

- **2nd time: urinary retention**

→ **Pathophysiology remains mainly unknown …**

PATHOPHYSIOLOGY

- **Two hypotheses**



Randall's plaques

Tubular agglomeration

Singh P.,Nat Rev Nephrol. 2022

ETIOLOGIES IN CHILDREN

Genetic causes, but not only !

Table 2 Urinary metabolic abnormalities identified. Data are presented as total number of patients (N) and percentage of the population that underwent metabolic evaluation (70 patients). The total number exceeds 70 as some patients displayed more than one abnormality

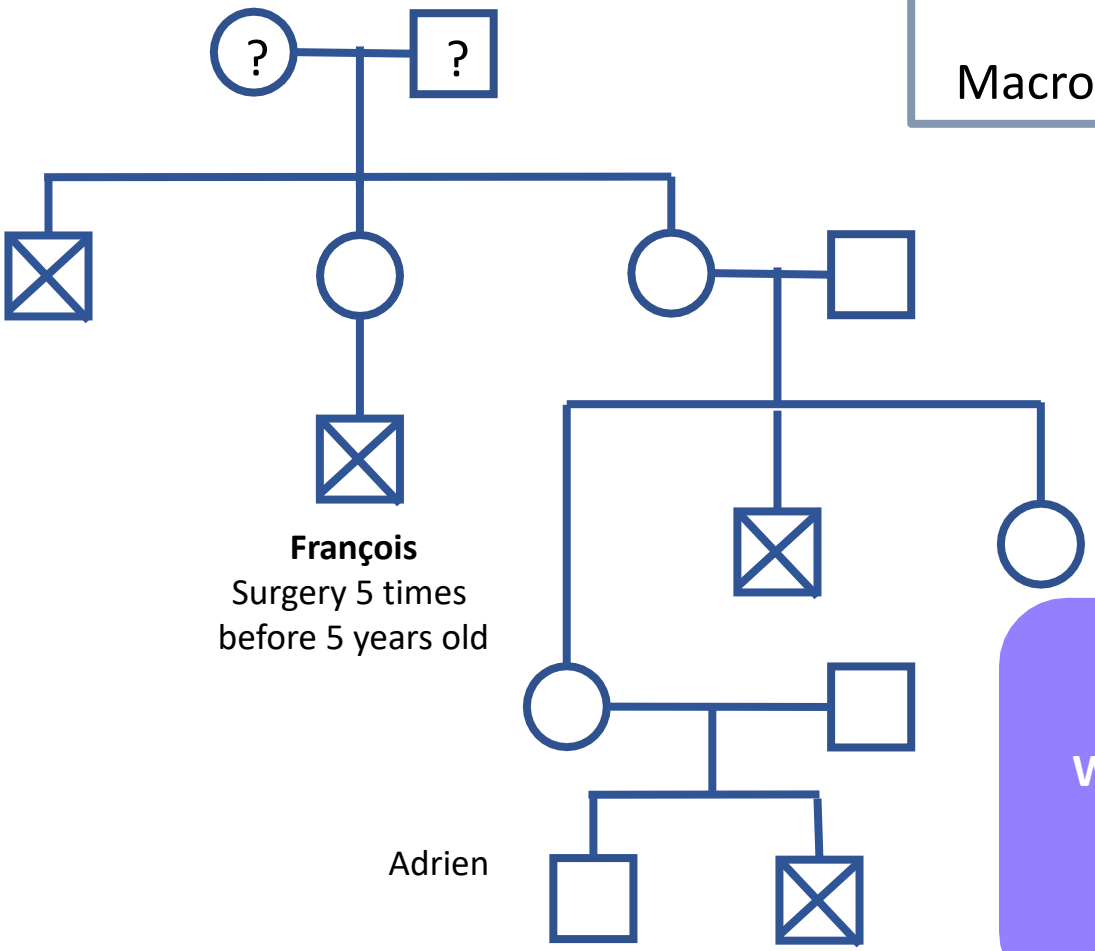
Metabolic abnormality	Patients N (% of the 70 patients evaluated)
Hypercalciuria	13 (19%)
Hyperoxaluria	10 (14%)
Hyperuricosuria	8 (11%)
Hyperphosphaturia	7 (10%)
Hypercystinuria	6 (9%)
Hypocitraturia	5 (7%)
No metabolic abnormality	35 (50%)

Rauturier C. Eur J Pediatr 2021

BACK TO A CLINICAL CASE

Colin

3 years old
Macroscopic hematuria



Urological abnormalities?
Medications ? Diet?
Infections conditions?
Intestinal malabsorption?
Obesity ?

What is the management ?
What is the treatment ?

WHAT IS THE MANAGEMENT ?

- **Imaging**
  - Ultrasound examination: first choice modality // follow-up

→ Imaging urolithiasis, complications and interventional. **Magdalena Wozniak**

- **Biologic assessment : first episode // spaced from episode**
  - Urine analyses
    - Creatinine
    - Ionogram, pH u
    - Calcium, phosphate
    - Oxalate
    - Amino acids
    - Uric acid, Xanthine
    - Cystine
    - Beta2 microglobulin

    → Calculation of fractional excretion
  - Serum chemistry
    - Creatinine, Urea
    - Ionogram
    - Calcium, phosphate
    - Uric acid
    - pH, bicarbonate
    - PTH
    - 25-OH-D

    +/- 1.25OH-D
    +/- genetic analysis
  - Stone analysis
    - Morpho-constitutional analysis

    → Fourier Transform Infrared Spectrometry

    - Dietetic assesment

    +/- Dynamic tests

AFTER MORPHO-CONSTITUTIONAL ANALYSIS

- **Main components of stones**

- French tertiary center (2013-2017) N=111children
- Median age 7.5 (3.1–10.5) years

▫ Calcium oxalate

- Weddellite 31%
- Wewellite 21%

▫ Calcium phosphate

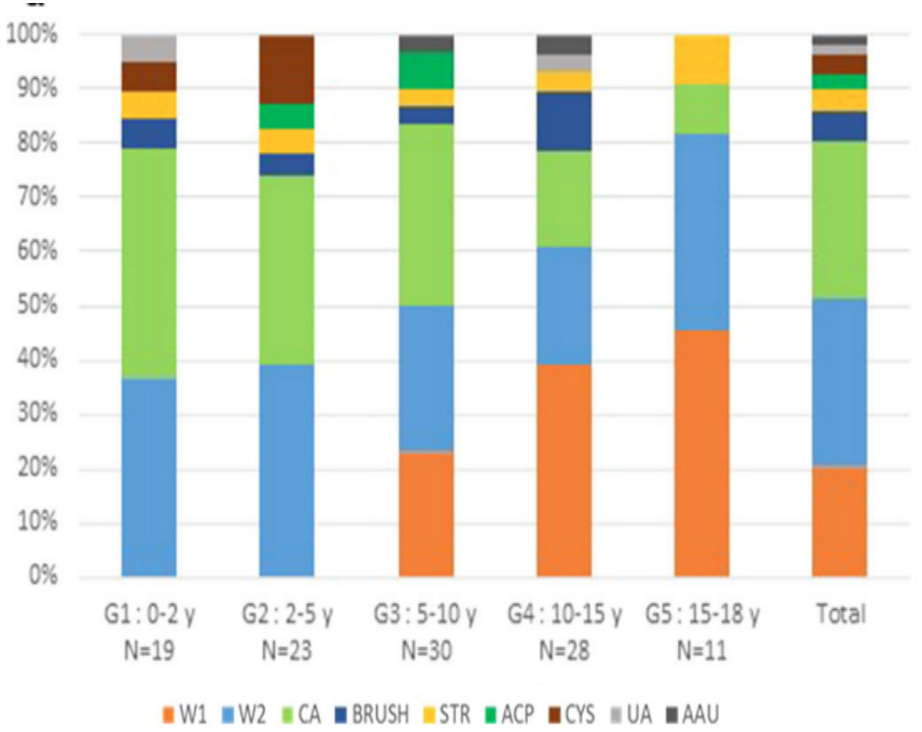
- Carbapatite 29%
- Brushite 5%
- Amorphous 3%

▫ Struvite 5%

▫ Cystine 4%

▫ Uric acid 2%

▫ Ammonium acid 2%



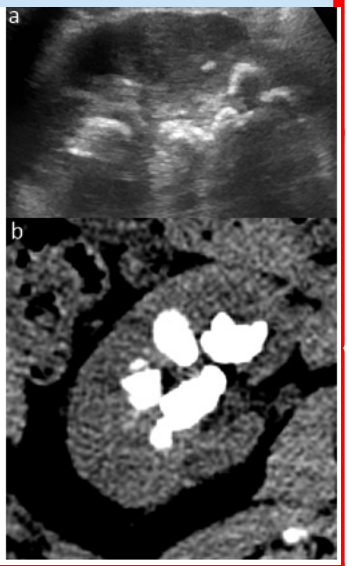
Rauturier C. Eur J Pediatr 2021

- **An etiology is found in 30-80%**

- Urolithiasis associated with urinary infection 22%
- Metabolic abnormalities with infectious stones 65%

SECONDARY UROLITHIASIS

Secondary urolithiasis	Etiologies	Stones contents	Imaging fundings
With hypercalciuria	Dietary factors - High intakes of sodium - Rich animal proteins diet - High fructose intake	Calcium oxalate	Radiopaque urolithiasis
With hyperoxaluria	Increasing intestinal oxalate absorption - Short bowel syndrome // Crohn disease - Bariatric surgery - Exocrine pancreatic insufficiency - Low calcium diet	Calcium oxalate	Radiop
Infections	Bacteria with urease activity - Proteus Mirabilis - Klebseilla Pneumoniae - Pseudomonas - Staphylococcus (Aureus or Pneumonia)	Struvite or Carbapatite	Coral
Iatrogenic	Loop diuretics Vitamin D Vitamin C	Carbapatite	Radiopaque urolithiasis
Congenital Abnormalities of Kidney and Urinary Tract	- Ureteropelvic Junction (UPJ) Obstruction - Neurogenic bladder - - Horseshoe Kidney - Obstructive Renal Dysplasia - …	Struvite or Carbapatite	Infectious stones Bladder stones



MONOGENIC UROLITHIASIS

Monogenic Causes	Etiologies	Stones contents	Imaging fundings
With hypercalciuria	Primary hyperparathyroidism	Calcium oxalate	Radiopaque urolithiasis Nephrocalcinosis
	- Variants in 24 hydroxylase gene - Variants renal phosphate transporter NPT2a - Variants renal phosphate transporter NPT2c	Calcium oxalate	Radiopaque urolithiasis Nephrocalcinosis Prenatal hyperechogenic kidneys
	Tubular disorders - Renal Fanconi syndrom - Dent's disease - Lowe disease - Fanconi Bickel Syndrome - Type I-II-IV-V Bartter syndrome	Calcium oxalate	Radiopaque urolithiasis Nephrocalcinosis
Cystinuria	- Type 1 - Type 2	Cystine	Radiopaque lithiasis Antenatal hyperechoic colon
Distal renal tubular acidosis	Genetic abnormality: 80% of cases	Calcium phosphate	Radiopaque lithiasis Nephrocalcinosis Cysts
Hyperoxaluria	- Type 1 - Type 2 - Type 3	Calcium oxalate	Radiopaque lithiasis Nephrocalcinosis
Purine metabolism disorders	- Hypoxanthine-Guanine phospho-ribosyltransferase deficiency - PhosphoRibosylpyrophosphate Synthetase hyperactivity - - Hereditary Xanthinuria	Uric	Radiolucent lithiasis

MONOGENIC UROLITHIASIS AND HYPERCALCIURIA

Table 1 Genetic defects associated with some monogenic forms of hypercalciuria

Disease[a]	Mode of inheritance[b]	Gene[c]	Human chromosomal location	Reference
Idiopathic hypercalciuria				
	A-d	SAC	1q23.3-q24	[35]
	A-d	VDR	12q12-q14	[30]
	A-d	?	9q33.2-q34.2	[31]
ADHH	A-d	CASR	3q21.1	[40]
Hypercalcemia with hypercalciuria	A-d	CASR	3q21.1	[38]
Bartter syndromes				
Type I	A-r	SLC12A1/NKCC2	15q15-q21.1	[90]
Type II	A-r	KCNJ1/ROMK	11q24	[91]
Type III[d]	A-r	CLCNKB	1q36	[92]
Type IV[d]	A-r	BSND	1q31	[93]
Type V	A-d	CASR	3q21.1	[48]
Type VI[e]	X-r	CLCN5	Xp11.22	[50]
Dent's disease	X-r	CLCN5	Xp11.22	[52]
Lowe's syndrome	X-r	OCRL1	Xq25	[60]
HHRH	A-r	NPT2c/SLC34A3	9q34	[69]
Nephrolithiasis, osteoporosis and hypophosphatemia	A-d	NPT2a/SLC34A1	5q35	[64]
Familial hypomagnesemia with hypercalciuria and nephrocalcinosis	A-r	PCLN1/CLDN16	3q28	[73]
Familial hypomagnesemia with hypercalciuria and nephrocalcinosis with ocular abnormalities	A-r	CLDN19	1p34.2	[77]
dRTA	A-d	SLC4A1/kAE1	17q21.31	[81]
dRTA with sensorineural deafness	A-r	ATP6B1/ATP6V1B1	2p13	[85]
dRTA with preserved hearing	A-r	ATP6N1B/ATP6V0A4	7q34	[88]

Stechmann Pediatr Nephrol 2009

PEDIATRIC RANGE

- **Hypercalciuria: CaU/24hours : difficult +++**
  - Normal — 4mg/kg/day
  - Adults — >0.1 mmol/kg/day
  - Child — >0.15mmol/kg/day

- **Calciuria/creatininuria ratio (mmol/mmol)**

<1yr		<2.0
1-3 yrs		<1.5
3-5 yrs		<1.0
5-10 yrs	<0.8	
>10 yrs		<0.6

- **Cristallization : CaU/L > 3.8 mmol/L**

Matos, Journal of Pediatrics, 1997
Bacchetta J. Calcif Tissue Int. 2021

PEDIATRIC RANGE

Age group (years)	Girls			Boys			Boys and girls	
	Central 95% reference interval	Upper limit 90% confidence interval	Number of samples	Central 95% reference interval	Upper limit 90% confidence interval	Number of samples	Central 95% reference interval	Upper limit 90% confidence interval
Calcium (mg/mg)								
7–9	0.01–0.46	0.34–0.78	148	0.01–0.43	0.37–0.60	178	0.01–0.43	0.37–0.53
10–12	0.01–0.31	0.28–0.40	154	0.01–0.30	0.27–0.32	177	0.01–0.30	0.28–0.32
13–15	0.01–0.31	0.27–0.36	165	0.01–0.29	0.25–0.31	180	0.01–0.30	0.28–0.31
16,17	0.02–0.27	0.23–0.33	136	0.01–0.26	0.24–0.34	123	0.01–0.27	0.24–0.31
Phosphorus (mg/mg)								
7–9	0.15–1.44	1.26–1.63	147	0.17–1.68	1.43–2.08	179	0.173–1.88	1.54–2.14
10–12	0.14–1.32	1.15–1.46	153	0.14–1.23	1.10–1.35	176	0.145–1.28	1.16–1.34
13–15	0.08–0.93	0.87–1.04	164	0.10–1.13	1.00–1.48	177	0.100–1.03	0.94–1.15
16,17	0.06–0.85	0.75–1.00	133	0.07–0.87	0.75–1.23	123	0.069–0.86	0.78–0.94
Total protein (mg/mg)								
7–9	0.07–0.30	0.26–0.34	140	0.06–0.22	0.19–0.30	180	0.06–0.28	0.25–0.30
10–12	0.06–0.34	0.27–0.43	151	0.06–0.22	0.17–0.28	172	0.06–0.28	0.24–0.33
13–15	0.03–0.31	0.23–0.39	162	0.04–0.26	0.20–0.38	173	0.04–0.29	0.23–0.37
16,17	0.04–0.31	0.21–0.35	134	0.03–0.19	0.11–0.28	120	0.03–0.27	0.20–0.32

1 mg/dL = 0.25 mmol/L calcium

1 mg/dL = 88.4 µmol/L creatinine

Slev, Pediatr Nephrol 2010

MONOGENIC UROLITHIASIS

Monogenic Causes	Etiologies	Stones contents	Imaging fundings
With hypercalciuria	Primary hyperparathyroidism	Calcium oxalate	Radiopaque urolithiasis Nephrocalcinosis
	- Variants in 24 hydroxylase gene - Variants renal phosphate transporter NPT2a - Variants renal phosphate transporter NPT2c	Calcium oxalate	Radiopaque urolithiasis Nephrocalcinosis Prenatal hyperechogenic kidneys
	Tubular disorders	Calcium	Radiopaque urolithiasis
	- Renal Fanconi syndrom - **Dent's disease** - Lowe disease - Fanconi Bickel Syndrome - **Type I-II-IV-V Bartter syndrome**	oxalate	Nephrocalcinosis

DENT'S DISEASE

- **X-linked recessive**
  - Type 1: CLCN5 (50-60%), Type 2: OCRL (15%)

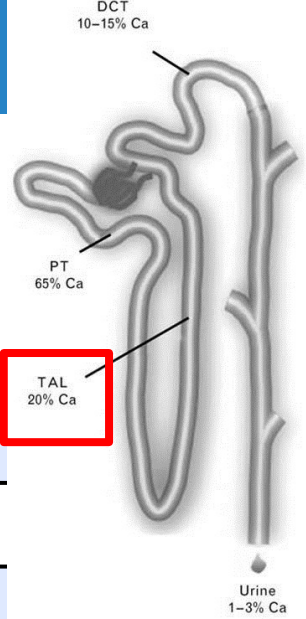
Table 4. Phenotype of Male Patients with Dent Disease 1 in the Literature and in Our Cohort

	Large published cohorts			Global literature analysis	This study		
Phenotype	Europe and North America[a]	Japan [Sekine et al., 2014]	Bökenkamp et al. (2009) (include literature data)	57 articles (n = 377)	Patients with clinical diagnosis of Dent disease (n = 103)	Patients with screening after diagnosis in a relative (n = 14)	Total (n = 117)
Age at diagnosis (years)				9 (0.2–67)[b] (n = 311)	7 (0.1-55)[b,c] (n = 89)	5.5 (0.2-32)[b] (n = 14)	7 (0.1–55)[b] (n = 103)
LMW proteinuria	100%	100%	(212/212) 100%	(365/365) 100%	(99/99) 100%	11/12	(110/111) 99%
Hypercalciuria	95%	89%	(180/200) 90%	(287/359) 80%	(89/95) 94%	6/11	(87/99) 88%
Nephrocalcinosis	74%	76%	(137/182) 75%	(156/282) 55%[d]	(59/91) 65%	3/11	(62/102) 61%
Aminoaciduria	76%	–	(31/75) 41%	(45/93) 48%	(23/34) 67%	1/5	(24/39) 61%
Renal insufficiency	64%	42%	(60/203) 30%	(92/347) 26.5%	(52/97) 53%	0/13	(52/110) 47%
Hypophosphatemia of renal origin	50%	–	(35/156) 22%	(72/200) 36%	(39/65) 60%	2/11	(41/76) 54%
Hypokalemia of renal origin	35%	–	(10/67) 15%	(22/60) 37%	(33/75) 44%	1/11	(34/86) 39%
Lithiasis	49%	–	ND	(41/235) 17%[d]	(27/81) 33%	3/10	(30/91) 33%
Rickets	30%	33%	ND	(53/247) 21%	(14/81) 17%	0/12	(14/93) 15%
Metabolic acidosis	–	–	(2/68) 3%	(6/66) 9%	(9/60) 15%	0/8	(9/68) 13%
Glycosuria	54%	–	(18/108) 17%	(27/105) 26%	(27/62) 43%	1/8	(28/70) 40%

[a]Adapted from Scheinman (2009).
[b]Median (minimum–maximum).
[c]For nine probands, the precise age was not available but the proximal tubulopathy was diagnosed in childhood.
[d]72 additional cases were described as nephrocalcinosis or nephrolithiasis. Including these case, the value for nephrocalcinosis/nephrolithiasis is 232/354 (65.5%).

Mansour-Hendili, Hum Mut 2015

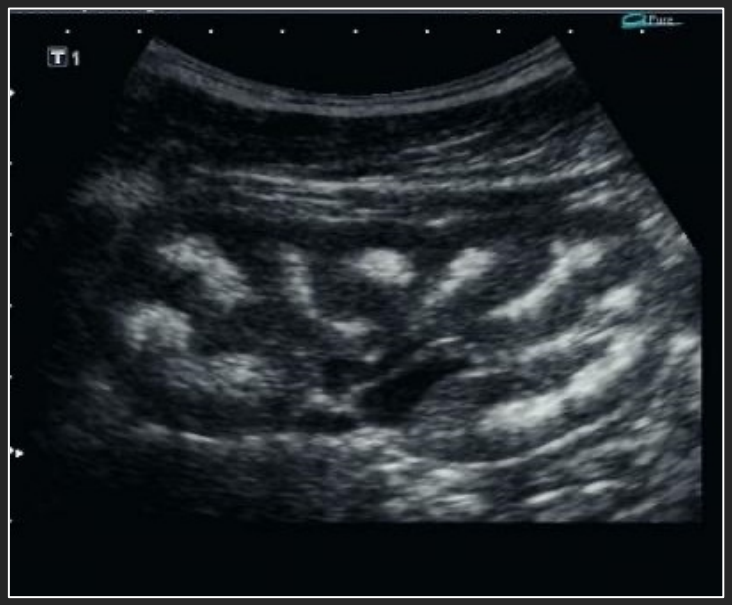
BARTTER SYNDROME



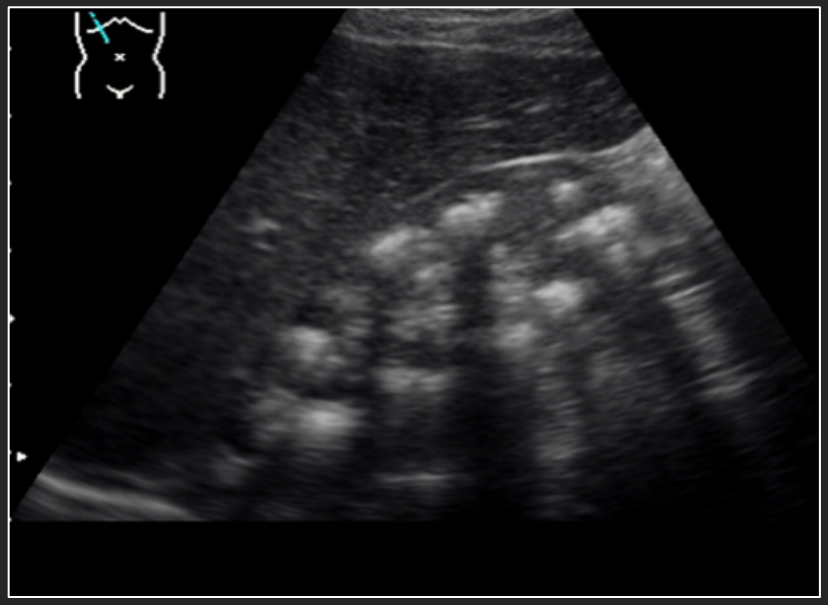
- **Different types**
  - Type 1: NKCC2 (neonatal); Type 2: ROMK (neonatal)

Characteristic	Type 1	Type 2	Type 3	Type 4a/b	Type 5
Age at onset	prenatally	prenatally	0 -5 years	prenatally	prenatally
Polyhydramnios	severe	severe	absent/mild	severe	very severe
Gestational age	32 (29-34)	33 (31-35)	37 (36-41)	31 (28-35)	29 (21-37)
Leading symptoms	polyuria hypochloremia alkalosis hypokalemia	polyuria hypochloremia alkalosis neonatal hyperkalemia	hypokalemia hypochloremia alkalosis failure to thrieve	polyuria hypochloremia alkalosis hypokalemia	polyuria hypochloremia alkalosis hypokalemia
Calcium excretion	high	high	variable	variable	high
Nephrocalcinosis	very frequent	very frequent	rare, mild	rare, mild	rare, mild
Plasma Cl/Na ratio	normal	normal	decreased	decreased	increased
Other findings			low magnesium	deafness risk for CKD ESKD	large for gestational age transient disease

ANTENATAL BARTTER SYNDROME



KCNJ1



NKCC2

Konrad M. ERKNet Webinar, 2021

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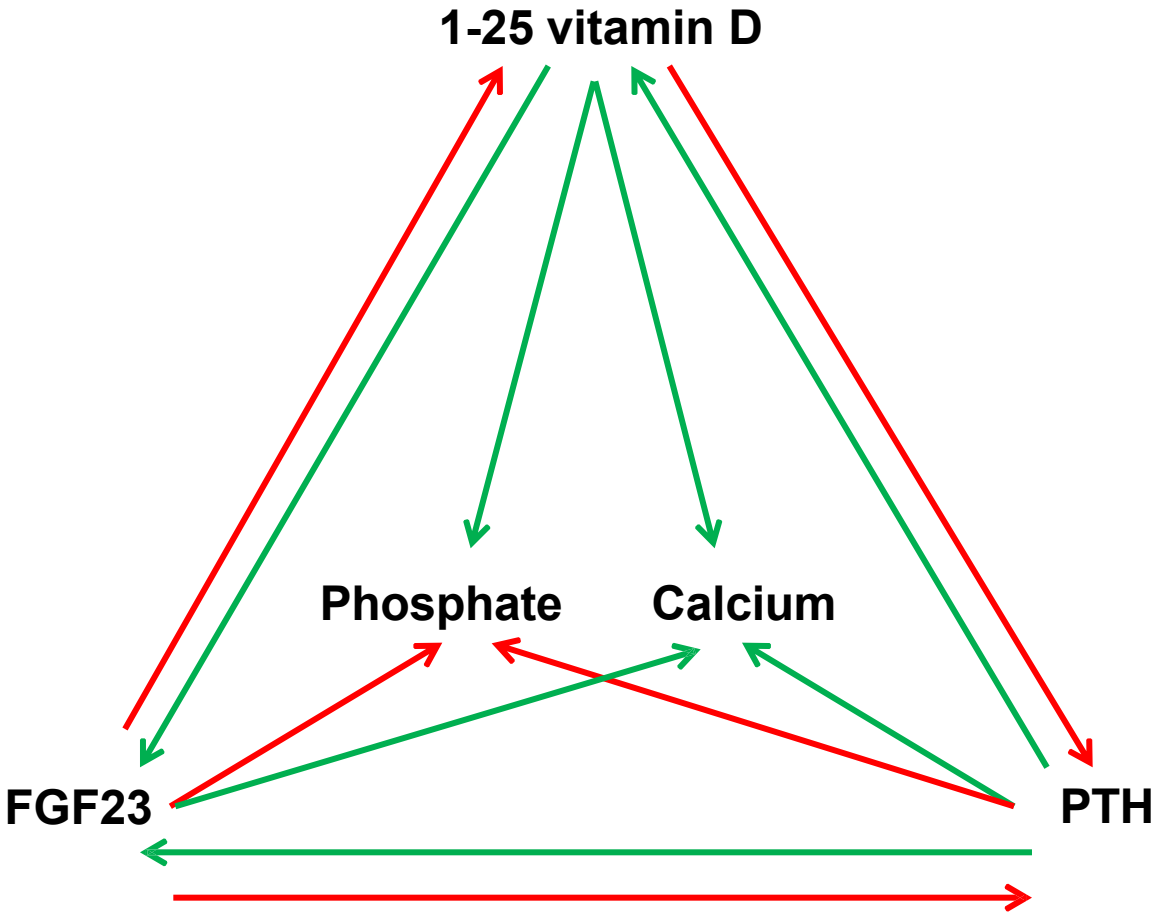
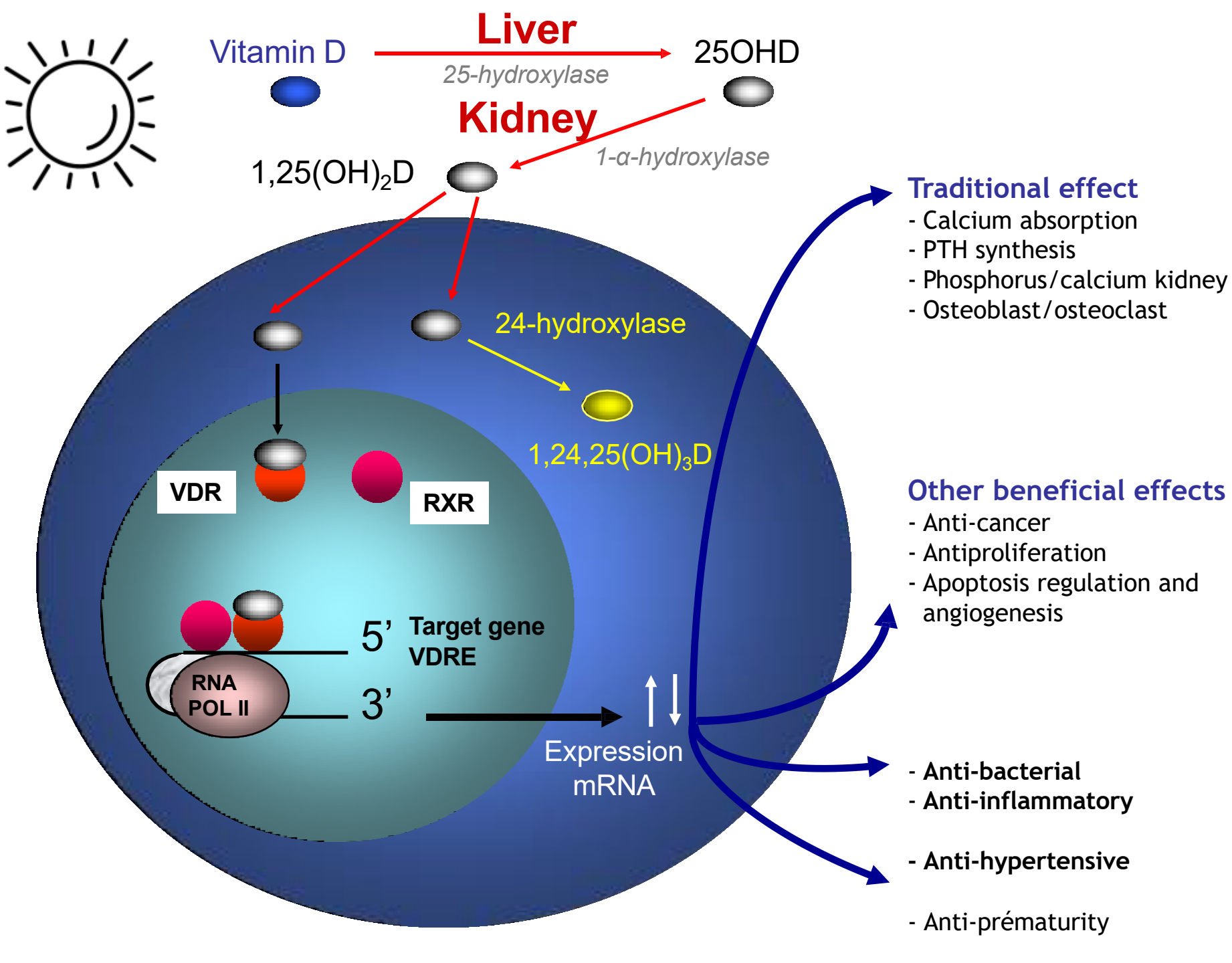
PHOSPHOCALCIC METABOLISM



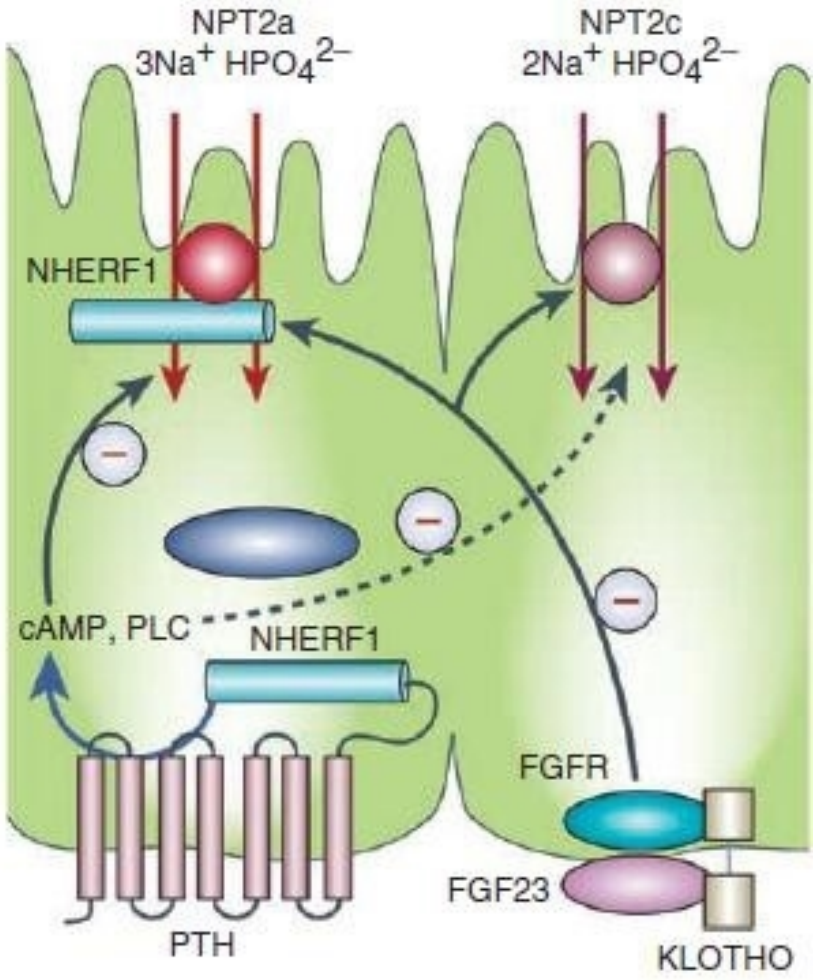
Stimulating effect / Inhibitory effect

Adapted from Bacchetta. EMC 2015


Vitamin D
Liver
25-hydroxylase
25OHD
Kidney
1-α-hydroxylase
1,25(OH)2D
24-hydroxylase
1,24,25(OH)3D
VDR
RXR
5'
Target gene
VDRE
3'
RNA
POL II
Expression
mRNA
Traditional effect
- Calcium absorption
- PTH synthesis
- Phosphorus/calcium kidney
- Osteoblast/osteoclast
Other beneficial effects
- Anti-cancer
- Antiproliferation
- Apoptosis regulation and angiogenesis
- Anti-bacterial
- Anti-inflammatory
- Anti-hypertensive
- Anti-prématurity

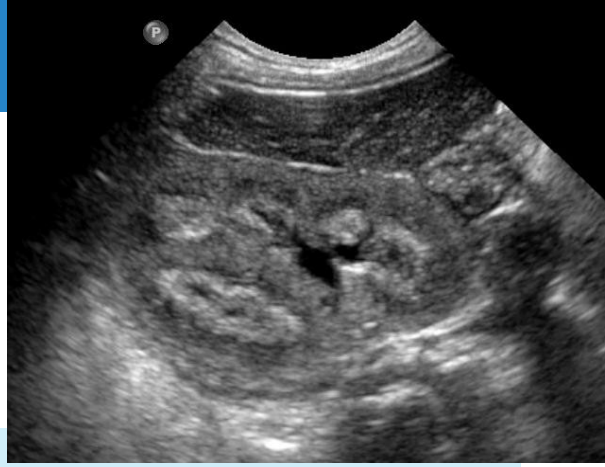
RENAL PHOSPHATE METABOLISM

- **Phosphate reabsorption**
  - Proximal tubule: 100%
  - Npt2a (SLC34A1) // Npt2c (SLC34A3)



Prie, Kidney Int 2009
Prie, N Eng J Med 2002

HYPERSENSITIVY TO VITAMIN D



- ***CYP24A1*, *SLC34A1* and *SLC34A3* mutations**
  - Clinical features

Radio-opaque lithiasis
Nephrocalcinosis
Growth delay

  - Biological results

Hypercalcemia
Low PTH; innapropriatly high 1.25OH vitamin D
Genetic test

n=	Number of patients with biallelic variations		Number of patients with heterozygous variations			Patients without mutation
	CYP24A1 25	*SLC34A3* 9	*CYP24A1* 3	*SLC34A3* 5	*SLC34A1* 1	142
serum calcium (mmol/L)	**2.95 ± 0.11** (25)	**2.43 ± 0.10** (3)	2.94 ± 0.52 (9)	2.50 ± 0.04	2.97	2.88 ± 0.48 (132)
serum phosphate (mmol/L)	1.11 ± 0.08 (21)	1.14 ± 0.12 (3)	1.49 ± 0.18 (7)	1.30 ± 0.11 (5)	1.7	1.65 ± 0.04 (116)
serum phosphate (SD)	**-1.0 ± 0.4** (21)	**-2.3 ± 1.2** (3)	-1.0 ± 0.5 (7)	-1.0 ± 0.3 (5)	-1.3	-0.8 ± 0.1 (116)
serum PTH (pg/mL)	**6.8 ± 0.8** (25)	**8.0 ± 0.6** (3)	**8.4 ± 1.8** (8)	**16.1 ± 1.4** (5)	5	9.3 ± 0.5 (134)
25-OH-D (nmol/L)	**114.3 ± 11.5** (22)	**52.3 ± 8.8** (3)	91.6 ± 27.6 (9)	85.6 ± 28 (5)	130	88.7 ± 6 (122)
1,25-$(OH)_2$D (pmol/L)	195.3 ± 22.6 (21)	234.1 ± 24.6 (3)	202.4 ± 43.2 (9)	243.2 ± 76.8 (3)	188	256.2 ± 15.2 (97)

In bold, statistically significant differences.
mean ± standard error of mean (number of values).

Schlingmann, Konrad NEJM 2011; Molin Frontiers in Paediatrics 2021

MONOGENIC UROLITHIASIS

Monogenic Causes	Etiologies	Stones contents	Imaging fundings
With hypercalciuria	Primary hyperparathyroidism	Calcium oxalate	Radiopaque urolithiasis Nephrocalcinosis
	- Variants in 24 hydroxylase gene - Variants renal phosphate transporter NPT2a - Variants renal phosphate transporter NPT2c	Calcium oxalate	Radiopaque urolithiasis Nephrocalcinosis Prenatal hyperechogenic kidneys
	Tubular disorders - Renal Fanconi syndrom - Dent's disease - Lowe disease - Fanconi Bickel Syndrome - Type I-II-IV-V Bartter syndrome	Calcium oxalate	Radiopaque urolithiasis Nephrocalcinosis

PRIMARY HYPERPARATHYROIDISM

- **Etiologies**

Table 1. Hereditary States of Hyperparathyroidism.

Disorder	Responsible Gene	Pathogenic Mechanism	Associated Clinical Features
MEN type 1*	*MEN1, CDKN1B*	Loss-of-function mutation	Pituitary and gastroenteropancreatic tumors; less frequently, adrenal tumor, facial angiofibroma, collagenoma, and lipoma
MEN type 2A	*RET*	Gain-of-function mutation	Medullary thyroid cancer, pheochromocytoma, cutaneous lichen amyloidosis
Hyperparathyroidism–jaw tumor syndrome	*CDC73* (formerly known as *HRPT2*)	Loss-of-function mutation	Fibromas in the mandible or maxilla, renal and uterine tumors, increased rate of parathyroid carcinomas (15–20%)
Familial hypocalciuric hypercalcemia	*CASR*	Loss-of-function mutation	Rare pancreatitis, relative hypocalciuria (24-hr urinary calcium:creatinine ratio, <0.01)
Neonatal severe primary hyperparathyroidism	*CASR*	Loss-of-function mutation	Life-threatening condition with marked hypercalcemia, hypotonia, and respiratory distress
Familial isolated hyperparathyroidism	*MEN1, CDC73, CASR, CDKN1B*	Loss-of-function mutation	Lack of the specific features of the other syndromic forms

* Multiple endocrine neoplasia (MEN) type 1, a syndrome associated with a *CDKNB1* gene mutation, is also referred to as MEN type 4.[11]

- **Clinical features**
  - Hypercalcemia; hypercalciuria
  - Radiopaque urolithiasis; nephrocalcinosis

MONOGENIC UROLITHIASIS

Monogenic Causes	Etiologies	Stones contents	Imaging fundings
Cystinuria	- Type 1 - Type 2	Cystine	Radiopaque lithiasis Antenatal hyperechoic colon
Distal renal tubular acidosis	Genetic abnormality: 80% of cases	Calcium phosphate	Radiopaque lithiasis Nephrocalcinosis Cysts
Hyperoxaluria	- Type 1 - Type 2 - Type 3	Calcium oxalate	Radiopaque lithiasis Nephrocalcinosis
Purine metabolism disorders	- Hypoxanthine-Guanine phospho-ribosyltransferase deficiency - PhosphoRibosylpyrophosphate Synthetase hyperactivity - - Hereditary Xanthinuria	Uric	Radiolucent lithiasis

CYSTINURIA

- **Epidemiology**
  - Prevalence 1/7000
  - Children urolithiasis 8-10%
  - Most prevalent hereditary stone disease
- **Abnormal transport of dibasic aminoacids**
  - Cystine, ornithine, lysine, arginine
- **Cystine stones**
  - Very poorly soluble // Increasing with pH
  - Early, bilateral, multiple, recurrent
  - Sometimes coralliform, weakly radiopaque

Figure 1 : calcul de cystine pure

Girls	12 years old
Boys	15 years old
CKD progression	5-17%

- **Antenatal diagnosis: hyperechoic colon**

Andreassen KH, Urolithiasis 2016

CYSTINURIA

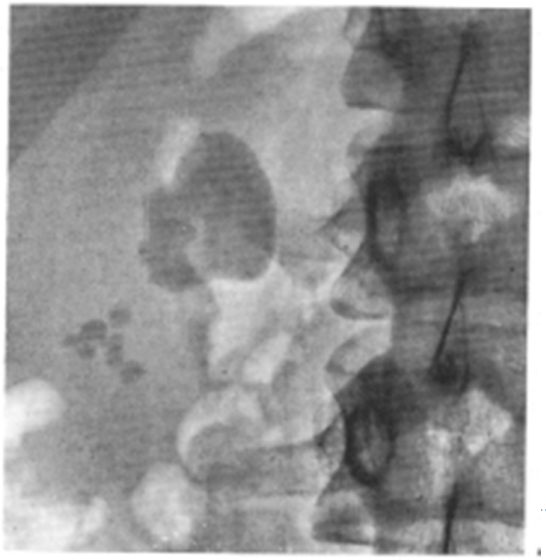
KUB X Ray

Small stones can be translucent opacity

< vertebral bones

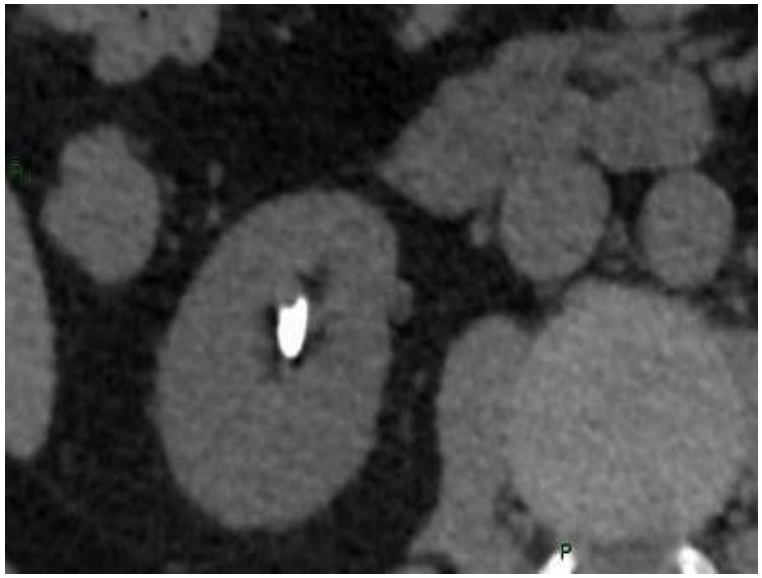
Smooth aspect

Often staghorn calculi



Low dose CT KUB

600-700 HU



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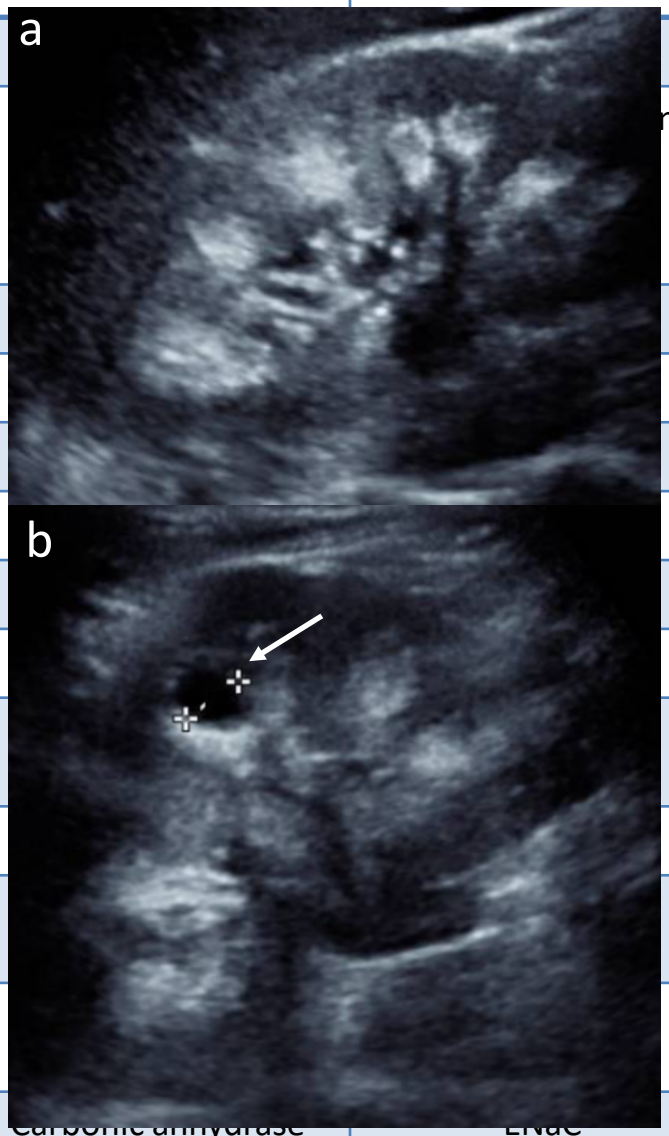
DISTAL TUBULAR ACIDOSIS

		Distal		
Type	2	1		
Pathophysiology	Impaired reabsorption of bicarbonates	Impaired excretion of the physiologic acid load		
U anionic gap	-	+		
HCO3 (mmol/L)	12-20	Variable, < 10		
pHu	Variable, < 5.5	> 5.5		
U Ca	N	↑		
U citrate	N	↓		
U NH4	N	↓		
Excretion HCO3 after HCO3 load	> 10-15%	< 5%		
Nephrocalcinosis	-	YES		
Other tubular signs	YES	-		
Associated signs	Variable (eye, DDTDF)	Deafness, bone		
Genes	NBC1 (SLC4A4), AR	AE, ATP6V0A4	II	ENaC



Courtoisy J. Bacchetta

MONOGENIC UROLITHIASIS

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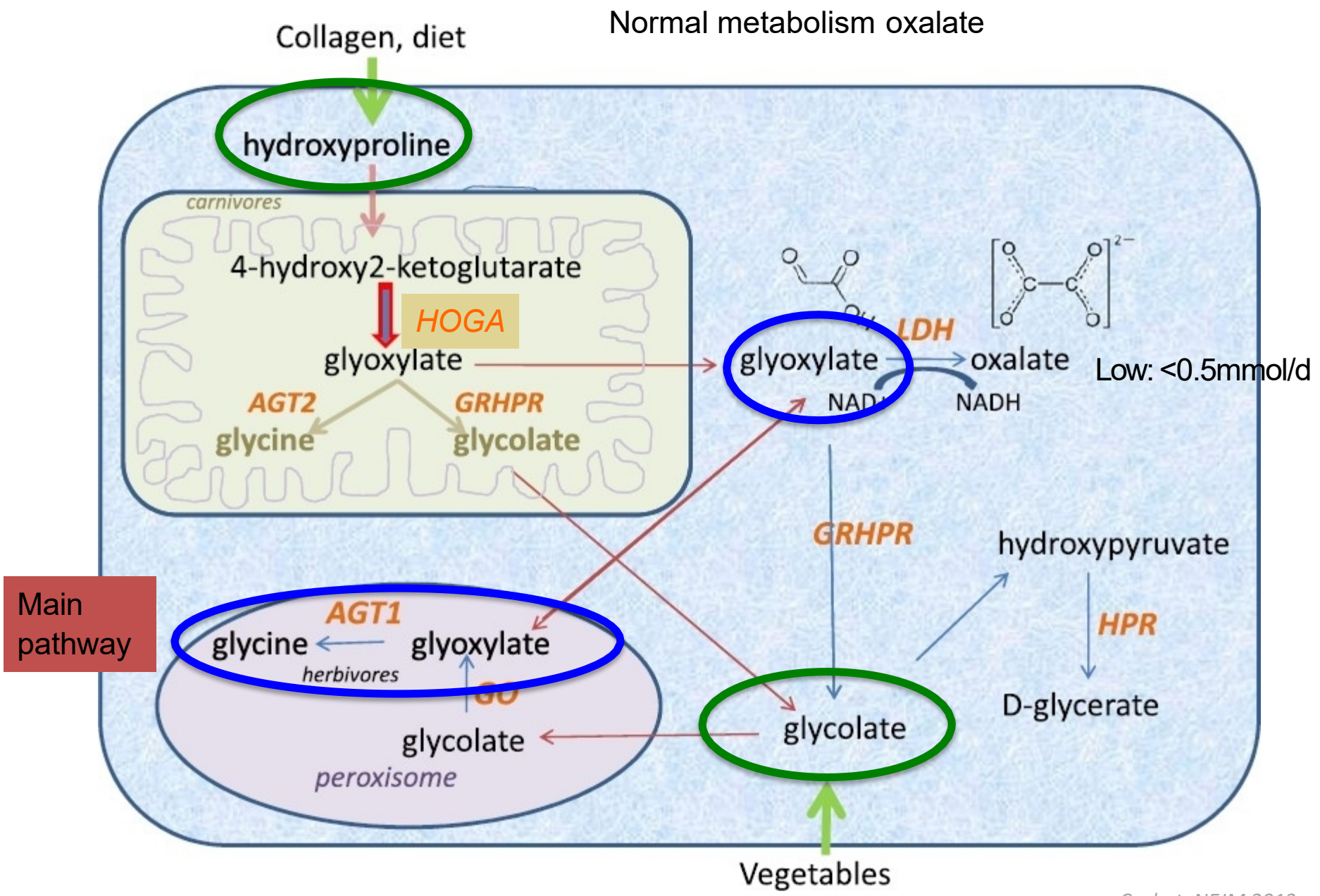
PHYSIOPATHOLOGY OF HYPEROXALURIA



Cochat, NEJM 2013

HYPEROXALURIA

Table 2. Features and Treatment of the Inherited Primary Hyperoxalurias.

Feature	Type 1	Type 2	Type 3
Chromosomal location	2q37.3	9p13.2	10q24.2
Age at onset	All ages, although mostly in childhood	All ages	All ages
Presentation	Calcium oxalate renal stones, nephrocalcinosis, renal failure	Calcium oxalate renal stones	Calcium oxalate renal stones
Treatment			
Supportive treatment	Hydration, citrate, pyridoxine	Hydration, citrate	Hydration, citrate
Transplantation	Liver and kidney	Kidney	Not required — no reported cases of renal failure to date

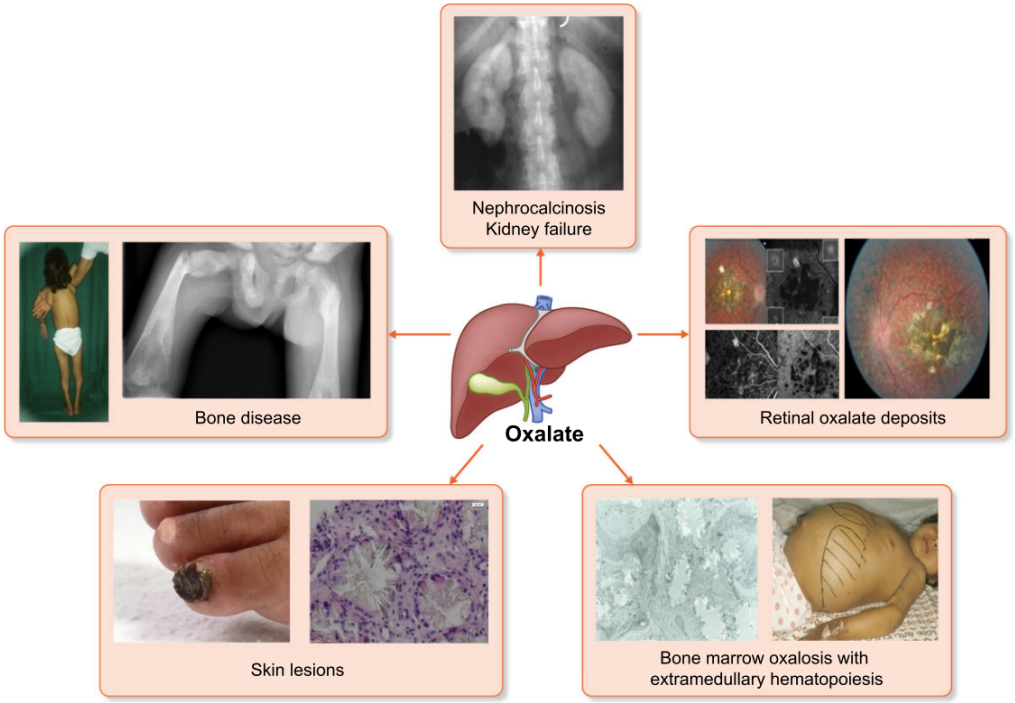
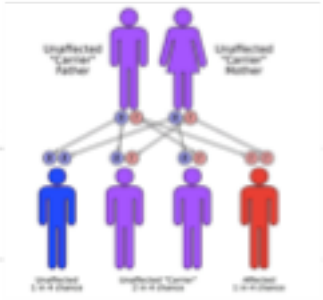


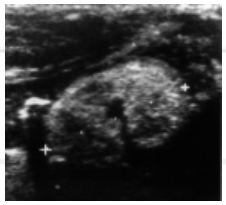
FIGURE 1: Manifestations of systemic oxalosis.

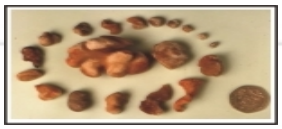
- **Recent therapeutic treatment**
  - RNA inhibitors

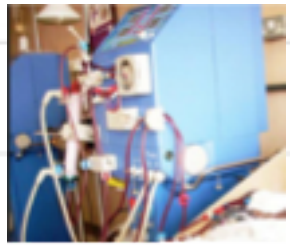
Cochat, NEJM 2013
Ben-Shalom E., Clin Kidney J 2022

SYMPTOMS AT TIME OF DIAGNOSIS









Oxaleurope database, ERKNet webinar 2021

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GENERAL TREATMENT

- **Forced increase in fluid intake and dietary measures**
  - Dietary salt restriction
  - No dietary calcium restriction
  - Normal protein intake
- **Pharmacologic treatment**

  Alkaline citrates
  Magnesium
  Phosphate supplementation
- **+/- Specific treatment**
- **+/- Surgical management**

  → New trends in pediatric urosurgery. **Alice Faure**

CONCLUSION

- **Mostly secondary urolithiasis**
- **Specificities of management**
  - Cystinuria
  - Primary hyperoxaluria …
  - Risk of CKD
- **Biological assessment**
  - Even in case of uropathy
  - First episode

THANK YOU FOR YOUR ATTENTION

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