Are you familiar with the genetic disorders of urolithiasis?

Can you recognize their characteristic kidney stones?

A quick guide to their diagnosis

Nutrition is a key factor in kidney stone development in the general population.[1]

But some kidney stones are the **result of inherited (genetic) metabolic disorders**, and their early identification is essential to help:[1,2]

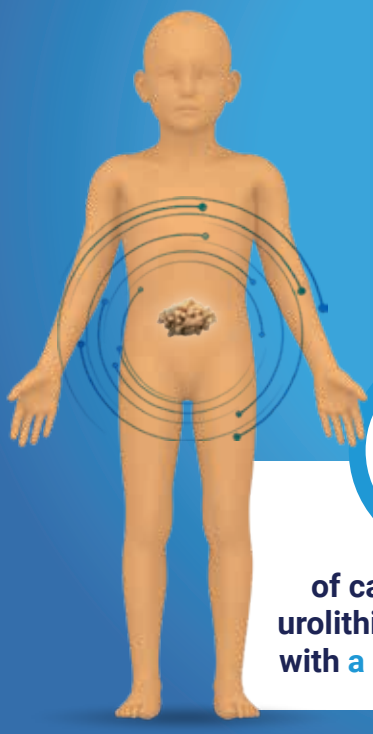
- Avoid the **recurrence** of stones
- Avoid the **development of chronic kidney disease**

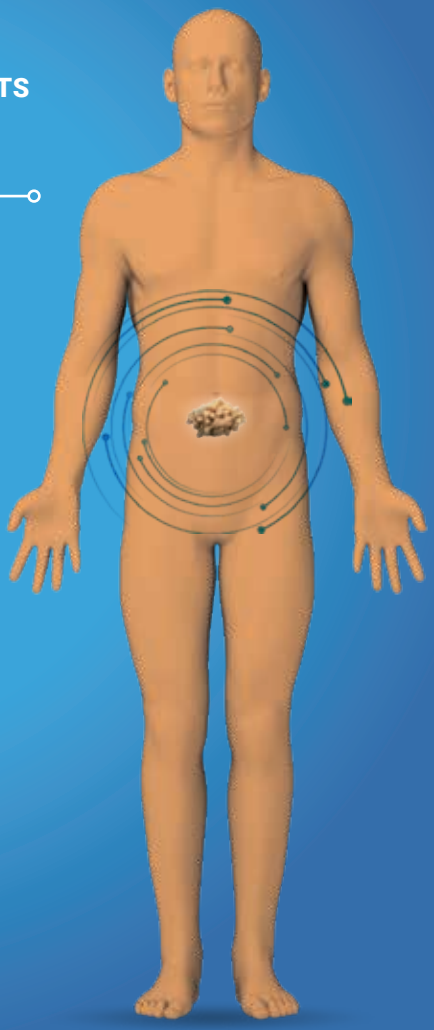
Early detection of these disorders is extremely important to allow patients to be offered **appropriate and specific treatment solutions** in a timely manner.[2]

ANY UNUSUAL CLINICAL PICTURE IN EVERY PATIENT WITH UROLITHIASIS WARRANTS ADDITIONAL INVESTIGATIONS

ANY KIDNEY STONE IN CHILDREN OR ADOLESCENTS OR RECURRENT KIDNEY STONES IN ADULTS[3]

- Multiple or bilateral stones
- Family history of urolithiasis
- Nephrocalcinosis
- Associated chronic renal failure
- Parental consanguinity





of cases of paediatric urolithiasis are associated with a metabolic disorder[4]

Information from Milliner et al. (2022)[3] is specific to patients with PH1.

An **examination of kidney stone composition** is **a key part of diagnosis.**[2]

Kidney stone analysis (crystal composition and morphological characteristics) helps the **diagnostic work-up of recurrent urolithiasis** and is sometimes in itself sufficient to diagnose a genetic disease.

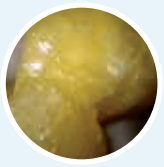
Metabolic evaluation should be considered if there is any **anomaly in the initial evaluation** or anything **unusual in the clinical picture** described on the first page.[2,3]

Certain types of kidney stones necessitate **referral to a local specialist in the metabolic evaluation of urolithiasis** (e.g. a nephrologist, endocrinologist or specialist urologist) for **early diagnosis** and guidance towards **genetic counselling.**[3]

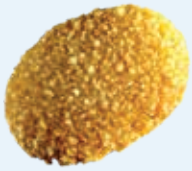
Of all the genetic disorders of urolithiasis, the following are the three most frequently encountered:[2,6]

CYSTINURIA[5]

Endoscopic view



Microscopic view



Cystine kidney stone, Va[8]

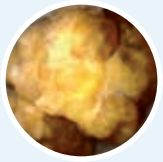
Vivid yellow colour, rough surface

Additional biological evaluation:

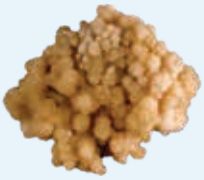
- Crystalluria
- Determination of urinary cystine
- Urinary amino acid chromatography showing massive excretion of the four dibasic amino acids

PRIMARY HYPEROXALURIA[3]

Endoscopic view



Microscopic view



Calcium oxalate monohydrate kidney stone, Ic[8]

Budding appearance

Additional biological evaluation:

- If renal function is preserved: determination of urinary oxalate over 24 h
- If renal function is greatly impaired: determination of plasma oxalate
- Confirmation by means of genetic testing

DISTAL TUBULAR RENAL ACIDOSIS (DTRA)[6,7]

Endoscopic view

Microscopic view

Calcium phosphate kidney stone, IVa2[8]

Glazed appearance with bumps and cracks

- In addition to the presence of an IVa2 stone, metabolic acidosis with inappropriate urinary pH or the presence of isolated hypocitraturia should suggest a diagnosis of DTRA
- In the case of hypocitraturia without acidosis, acidification testing can be proposed in nephrology

There are other even rarer genetic disorders of urolithiasis, such as:
APRT (adenine phosphoribosyltransferase) deficiency, xanthinuria or other purine base anomalies, Dent disease, or familial hypomagnesaemia with hypercalciuria.[2]

*All photos presented on this sheet were provided by **Dr Daudon** and **Dr Estrade**.*
*This sheet was produced in collaboration with **Dr Lemoine and Dr Abid**, nephrologist and urologist, respectively, at Lyon University Hospital.*

References:
1. Ferraro PM, et al. *Nutrients.* 2020;12(3):779; **2.** Edvardsson VO, et al. *Pediatr Nephrol.* 2013;28(10):1923–1942; **3.** Milliner DS, et al. Primary hyperoxaluria type 1. Available at https://www.ncbi.nlm.nih.gov/books/NBK1283/. Accessed January 2023; **4.** Copelovitch L. *Pediatr Clin North* Am. 2012;59(4):881–896; **5.** Leslie SW, et al. *Cystinuria.* 2022 Nov 28. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan–. PMID: 29262245; **6.** Dessombz A, et al. *J Urol.* 2015;193(5):1564–1569; **7.** Giglio S, et al. *J Nephrol.* 2021;34(6):2073–2083; **8.** Corrales M, et al. *Eur Urol Focus.* 2021;7(1):13–21.

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