IDENTIFICATION
high-risk factors

Clinical factors in recurrent stone formers can help identify metabolic stone diseases[1]

HYPOTHETICAL PATIENT PROFILE:
Mark
Male | Age 44 | Caucasian | BMI 32 kg/m^2
A recurrent stone former with declining kidney function, family history of stone formation, and nephrocalcinosis

This case study is hypothetical and is not representative of all patients with PH1.

This information is provided for educational purposes only and is not intended to replace the independent medical judgment of any healthcare professional. For U.S. HCPs only

PATIENT TIMELINE: First 5 weeks

STONE EVENT & STONE MANAGEMENT

PRESENTING SYMPTOMS
Severe, sharp pain in the right flank[2]

SCREENING EVALUATION
Medical history[1,3]**:** Second stone event; first one occurred 3 years ago (age 41)

Family history[1,3]**:** Younger brother has experienced 3 stone events (at ages 29, 33, and 35)

Dietary history[1]**:** No nutritional factors associated with stone formation; normal fluid intake

Serum chemistry[1]**:**
- Stage 3a CKD

Spot urine analysis[1,4]**:**
- Normal pH
- Hematuria
- Negative cultures

CKD = chronic kidney disease

DIAGNOSTIC IMAGING
CT scan[1,5]**:**
- 10-mm stone at the right ureteropelvic junction
- Evidence of bilateral nephrocalcinosis[1]

STONE REMOVAL[5]
- URS, laser lithotripsy, and stone manipulation performed
- Stone fragments collected for composition analysis

NEPHROLOGIST CONSULTATION
Urologist sets up a consultation with a nephrologist based on findings of compromised kidney function and nephrocalcinosis

CT= computed tomography
URS=ureteroscopy
All CT scan images provided by Dr David Schulsinger.

2 weeks after the procedure

FOLLOW-UP VISIT WITH UROLOGIST

FOLLOW-UP EVALUATION
Serum chemistry:
- CKD Stage 3b, indicating a decline in kidney function when compared to the last visit

STONE ANALYSIS[1,3]
Stone composition:
100% calcium oxalate monohydrate

DIAGNOSTIC STEPS[1,7]
- Urologist suspects an underlying metabolic disorder; instructs the patient to collect two 24-hour urine samples for metabolic workup
- Results to be reviewed by nephrologist

3 weeks later

FOLLOW-UP VISIT WITH NEPHROLOGIST

24-HOUR URINE TEST RESULTS[1]
- Nephrologist orders and reviews the 24-hour urine test results

ANALYTE	PATIENT VALUE	REFERENCE RANGE*
Volume	3.1 L/day	0.5-4L/day
Oxalate	**120 mg/day (1.33 mmol/day)**	20-40 mg/day (0.22-0.44 mmol/day)
Calcium	180 mg/day (4.51 mmol/day)	male <250 mg/day (<6.25 mmol/day), female <200 mg/day (<5 mmol/day

*Reference ranges assay-dependent and intended to provide a guide for clinicians

- Nephrologist suspects primary hyperoxaluria; orders genetic testing

1 month later

DIAGNOSIS OF UNDERLYING CAUSE OF STONE FORMATION

GENETIC TESTING RESULT[6]
Nephrologist identifies AGXT mutations and confirms a diagnosis of primary hyperoxaluria type 1 (PH1)

FAMILY SCREENING[8]
A month later, the nephrologist confirms via family screening that the patient's brother (with the history of stone events) also has PH1

IDENTIFICATION — 3 TAKEAWAYS FROM GUIDELINES ON MEDICAL MANAGEMENT OF KIDNEY STONES, INCLUDING THOSE FROM THE AMERICAN UROLOGICAL ASSOCIATION (AUA):

- **Screening for family history of stones can lead to earlier diagnosis and management of genetic stone diseases[9]**
- **Imaging can help detect nephrocalcinosis, which may indicate an underlying metabolic disorder[1]**
- **Determining stone composition can help distinguish underlying metabolic or genetic conditions[1]**

ACTIONS THAT MAY IMPACT THE DIAGNOSTIC JOURNEY OF A STONE FORMER

IDENTIFICATION of high-risk factors

TESTING according to the guidelines on medical management of kidney stones, including those from the American Urological Association (AUA)

CONSULTING with a nephrologist when warranted

24-hour urine testing in high-risk, recurrent, and interested first-time stone formers, as recommended by guidelines, including those from the AUA, can help identify metabolic stone disease.[1] Consider ordering or referring your patients for genetic testing when you suspect an inherited stone disease such as PH1.[10,11]

ONE OPTION FOR TESTING WHEN YOU SUSPECT PH1 IS THE ALNYLAM ACT® PROGRAM:
Third-party genetic screening and counseling for patients who may have PH1 at no charge to patients.

AlnylamAct

The Alnylam Act® program was created to provide access to genetic testing and counseling to patients as a way to help people make more informed decisions about their health
- While Alnylam provides financial support for this program, tests and services are performed by independent third parties
- Healthcare professionals must confirm that patients meet certain criteria to use the program
- Alnylam receives de-identified patient data from this program, but at no time does Alnylam receive patient-identifiable information. Alnylam may use healthcare professional contact information for research purposes
- Both genetic testing and genetic counseling are available in the US and Canada
- Healthcare professionals or patients who use this program have no obligation to recommend, purchase, order, prescribe, promote, administer, use, or support any Alnylam product
- No patients, healthcare professionals, or payers, including government payers, are billed for this program

FOR MORE INFORMATION, VISIT ALNYLAMACT.COM AND ABOUTPH1.COM

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References:
1. Pearle MS, Goldfarb DS, Assimos DG, et al. *J Urol.* 2014;192(2):316-324. **2.** Brisbane W, Bailey MR, Sorensen MD. *Nat Rev Urol.* 2016;13(11):654-662. **3.** Goldstein R, Goldfarb DS. *Urol Nurs.* 2017;37(2):81-102. **4.** Williams JC Jr, Gamboro G, Rodgers A, et al. *Urolithiasis.* 2021;49(1):11-16. **5.** Assimos D, Krambeck A, Miller NL, et al. *J Urol.* 2016;195(4):1161-1169. **6.** Cochat P, Hulton SA, Acquaviva C, et al. *Nephrol Dial Transplant.* 2012;27(5):1729-1736. **7.** Ennis JL, Asplin JR. *Int J Surg.* 2016;36(Pt D):633-637. **8.** Millner DS, Harris PC, Sas DJ, et al. Updated November 30, 2017. Accessed June 9, 2022. https://www.ncbi.nlm.nih.gov/books/NBK1283/ **9.** Ferraro PM, D'Addessi A, Gambaro G. *Nephrol Dial Transplant.* 2013;28(4):811-820. **10.** Hoppe B. *Nat Rev Nephrol.* 2012;8(8):467-475. **11.** Cochat P, Rumsby G. *N Engl J Med.* 2013;369(7):649-658.

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