Primary hyperoxaluria type 1 (PH1): an underdiagnosed disease[1]

BEHIND THE STONE

When should PH1 be suspected?

PH1 is a **rare, progressive, inherited, and potentially life-threatening disease** that leads to **a build-up of calcium oxalate** in the **kidneys**. Over time, these oxalate deposits can cause a **progressive decline in the glomerular filtration rate** and develop into end-stage kidney disease (ESKD) and systemic oxalosis.[2,3]

Recognizing the warning signs and various evaluations can allow for **prompt diagnosis**, which may help **manage symptoms**, including mitigating kidney damage.[1-3]

PATIENTS AFFECTED BY PH1 MAY PRESENT WITH ONE OR MORE OF THE FOLLOWING CLINICAL MANIFESTATIONS[2-4]*:

PH1 can present at any age. Kidney stone formation is the sign that most often leads to a diagnosis, though not all patients with PH1 may be stone formers.[4-7]

- **Recurrent and/or unusual† kidney stones in adults**
- **Kidney stone in a child**
- **Nephrocalcinosis**
- **Failure to thrive (infants and children)**
- **Progressive kidney function decline**
- **Family history of kidney stones**

Systemic oxalosis may lead to the following[8]:

- **Bone disorders**
- **Cutaneous and vascular manifestations**
- **Cardiac manifestations**
- **Ophthalmologic manifestations**
- **Neurologic manifestations**

*These are not the only manifestations of PH1. Patients may not experience all of these symptoms or may not experience them at the same time.
†Including multiple, bilateral, and/or large stones.

Up to 50% of adults are diagnosed following progression to ESKD.[2]

If PH1 is suspected, further investigation can help identify prospective patients

The American Urological Association (AUA) recommends a **full metabolic evaluation** if there is a clinical manifestation suggestive of PH1. **24-hour urine testing** is recommended for patients with preserved function. For patients who cannot complete 24-hour urine testing, spot urine oxalate:creatinine tests may be done. **Plasma oxalate** measurements can be used for patients with impaired kidney function.[2,5,9]

Certain types of kidney stones necessitate **referral to a local specialist in the metabolic evaluation of kidney stones** (eg, a nephrologist or specialist urologist) for **prompt diagnosis**.[1,2]

The AUA recommends genetic testing, which can identify gene mutations to help confirm a PH1 diagnosis in adult patients with elevated urinary oxalate excretion (regardless of kidney function) and to identify its type, which is of both **diagnostic and prognostic importance**. The identification of a mutation in the ***AGXT* gene** will direct the **diagnosis toward PH1**.[3,9‡]

The Rare Kidney Stone Consortium recommends **genetic testing for family members of anyone with a PH1 diagnosis**, especially siblings.[10]

‡After excluding bowel dysfunction.

Visit AboutPH1.com to learn more

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

What to do if primary hyperoxaluria type 1 (PH1) is suspected

In patients with preserved kidney function

PERFORM A 24-HOUR URINE TEST[2,9,11]*

- Normal UOx level (all ages): <45 mg (<0.50 mmol)/1.73 m^2/24 hours[12]
- Spot testing can be used when 24-hour urine test is not possible[5]

If 24-hour UOx is high (>75 mg [0.83 mmol])[†‡]

In PH1, UOx levels are often >2 times higher than the upper limit of normal[13]

In patients with impaired kidney function

EVALUATE PLASMA OXALATE (POx)[2,5,15]

- Normal POx level: 2.0 µmol/L[14§]

If POx is high

Substantially elevated levels are typical when eGFR <30 mL/min/1.73 m^2. Levels >50 µmol/L are suggestive of PH1[1]

Search for genetic variants responsible for primary hyperoxaluria[1]

Identification of variants in the *AGXT* gene[¶]

Confirmation of diagnosis of PH1

Cr, creatinine; eGFR, estimated glomerular filtration rate.

*Values of UOx are laboratory- and method-dependent.
[†]Or spot UOx:Cr > age-dependent normal range.[5]
[‡]In adult patients without bowel dysfunction.[9]
[§]Reference values have not been established for patients <21 years old or >81 years of age.[14]
[¶]Identification of variants in the GRHPR or HOGA1 genes confirm a diagnosis of PH2 or PH3, respectively.

AlnylamAct®

One option for genetic testing when you suspect PH1 is the Alnylam Act® program: Third-party genetic testing and counseling for patients who may have PH1.

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 uses 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

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