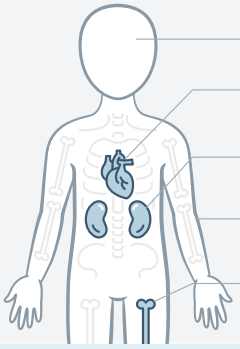
Primary hyperoxaluria (PH), a kidney stone disease that starts in the liver and can lead to systemic damage[1,2]

PH is a family of ultra-rare genetic disorders in which excess levels of **oxalate** produced by the liver lead to[1,2]:

- **Recurrent kidney stones (CaOx crystals)**
- **Nephrocalcinosis**
- **Chronic kidney disease**

Progressive kidney damage can result in **end-stage kidney disease** and **systemic oxalate deposition**, which can be life-threatening.[1]

Systemic Oxalate Deposition in PH Causes[1,3,4]



- Retinopathy
- Cardiomyopathy, conduction disturbances
- Kidney stones, nephrocalcinosis, CKD
- Skin ulcers, nodules
- Bone fractures, bone deformation, inhibited bone growth, anemia, severe pain

Warning Signs of PH[5-11]

(one or a combination of)

The first warning sign may be a single kidney stone in children or recurrent stones in adults.

- **Family history** of kidney or bladder stones
- **Recurrent stones in adults**
- **Single kidney stone in a child**
- **CKD with no known etiology**
- **Nephrocalcinosis**
- **Systemic oxalosis**
- **Severe infantile form:** Failure to thrive, ESKD, severe retinal abnormalities
- **ESKD**

↓ **Kidney Function[12] eGFR (mL/min/1.73 m²)** — **Oxalate[12]** ↑

≥90	60-89	30-59	15-29	<15
CKD Stage 1 Mild kidney impairment[13]	**CKD Stage 2** Kidney damage, mild loss of kidney function[13]	**CKD Stage 3**	**CKD Stage 4**	**CKD Stage 5** ESKD[13]
		Moderate to severe loss of kidney function[13]		

Oxalate accumulation can occur even in the absence of current symptoms[12,14]

For more information, visit the **Rare Renal Disorders page on scientific-exchange.com**

Abbreviations: BSA=body surface area; CaOx=calcium oxalate; CKD=chronic kidney disease; COD=calcium oxalate dihydrate; COM=calcium oxalate monohydrate; eGFR=estimated glomerular filtration rate; ESKD=end-stage kidney disease; ESWL=extracorporeal shock wave lithotripsy; HOG=4-hydroxy-2-oxoglutarate; PCNL=percutaneous nephrolithotomy; Pox=plasma oxalate; RNAi=ribonucleic acid interference; siRNA=small interfering ribonucleic acid; Uox=urinary oxalate; URS=ureteroscopy.

For full list of references, please scan the QR code

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Please note that this content is not meant to provide diagnosis or treatment recommendations.
The best diagnosis strategy and management options are to be determined by the patient's physician.

PH Diagnosis

Diagnostic Workup

Or

Refer to a Nephrologist for Diagnosis
Visit **OHF.org** for Resources and for Guidance

Urine Collection (eGFR >30 mL/min/1.73 m²)[15]:

24-hour collection (preferred)[15,16]
Elevated Uox on at least 2 assessments:

- >0.83 mmol/24 h/1.73 m² or >75 mg/24 h

Spot urine[15]
Oxalate: creatinine ratio > normal for age

Plasma Collection (eGFR <30 mL/min/1.73 m²)[1,15]:

Pox >50 µmol/L

Stone Analysis[17-19]:

- **PH1:** >95% COM (whewellite)
- **PH2:** Typically >80% COM
- **PH3:** Composed of COM and COD, with 24% to 100% COM

Urinary Metabolites (Nonconfirmatory)[1,4,15]:

- Elevated glycolate → **PH1**
- Elevated L-glycerate → **PH2**
- Elevated DHG → **PH3**

Rule Out Secondary Causes[5,15]:

- Enteric causes (eg, chronic pancreatitis, cystic fibrosis, inflammatory bowel syndrome, bariatric surgery)
- Very high-oxalate, low-calcium diet
- Premature infant

Genetic Testing[5,15]:

AGXT mutation →	**PH1**
GRHPR mutation →	**PH2**
HOGA1 mutation →	**PH3**

Urine and genetic testing can be done simultaneously or sequentially.

PH Management

Current Available Management Options

Or

Refer to Nephrology for Management
Visit **OHF.org** for Resources and for Guidance

CaOx Crystal Inhibition[15]:

Hyperhydration

- Adults: 3.5 L to 4 L daily
- Children: 2 L to 3 L/m² BSA daily
- Infants: gastrostomy tube

CaOx crystallization inhibitors

- Potassium citrate (preserved renal function patients)

Kidney Stone Management[15]:

PCNL or URS instead of ESWL

Oxalate Reduction:

Pyridoxine (vitamin B6) in responsive patients with PH1[15]

- Test for responsiveness[15]
- B6-responsive *AGXT* mutations: Gly170Arg, Phe152Ile, Ile244Thr[11,20,21]

RNAi/siRNA therapy for patients with PH1[15]

Advanced CKD (eGFR <30 mL/min/1.73 m²)[15]:

Dialysis
For CKD stage 4 to 5, high Pox, systemic oxalosis

Organ transplant

- **PH1**, eGFR <30 mL/min/1.73 m², B6-unresponsive, no access to RNAi → **liver-kidney transplant**
- **PH1**, CKD stage 5, B6-responsive → **kidney transplant**
- **PH2**, eGFR <30 mL/min/1.73 m² → **liver transplant**

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