UncoveringPH

Recurring kidney stones in adults or a single kidney stone in children may be a sign of something more serious.

Primary hyperoxaluria (PH) often appears similar to other kidney stone diseases, but beneath the surface, you'll find a family of ultra-rare genetic disorders that can lead to renal damage and chronic kidney disease (CKD). As the disease progresses, it can lead to end-stage renal disease (ESRD), requiring dialysis and a dual liver-kidney transplant.[1-4]

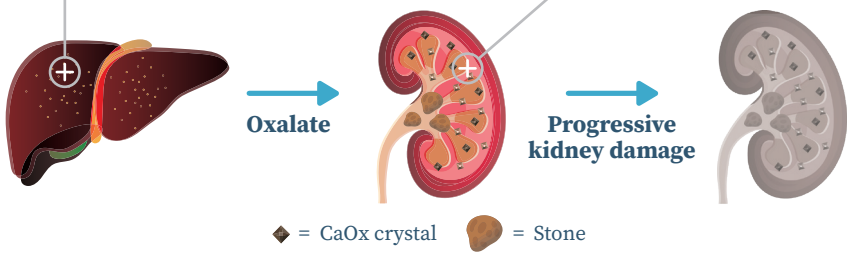
For more information, please visit **www.uncoveringph.com**

Calcium oxalate crystals accumulate, forming a kidney stone

In PH1, PH2, and PH3, Toxic Levels of Oxalate Accumulate in the Kidneys, Which Can Cause Kidney Stones, Kidney Damage,

Genetic mutations cause liver enzyme deficiencies that result in a buildup of toxic levels of **oxalate**[1,2]

Excess oxalate binds with calcium in the kidneys to form **calcium oxalate (CaOx) crystals**, which in turn cause **kidney stones**, **nephrocalcinosis**, and **progressive kidney damage**[5]



Kidney Function Is Affected in All 3 PH Types[6-11]

PH1
- 10% have ESRD by age 1 year
- 57% have ESRD by age 40 years

PH2
- >50% have CKD stage ≥2
- 35% have ESRD by age 40 years

PH3
- 22%-29% have CKD stage ≥2
- 2 reports of ESRD

Key Warning Signs and Symptoms of PH

Patients may have one or a combination of these warning signs[12-15]:

- **Multiple or recurrent kidney stones as an adult**
- **Single kidney stone in a child**
- **History of stones as a child, adolescent, or young adult**
- **A family history of kidney stones or PH**
- **Nephrocalcinosis**
- **CKD**
- **ESRD**
- **Systemic oxalosis**
- **Failure to thrive in infants**

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PH: A Hereditary Stone Disease That Causes Kidney Damage

Primary hyperoxaluria (PH) is a family of ultra-rare genetic disorders that results in toxic oxalate overproduction, kidney stones, and kidney damage. More than 70% of patients with PH require one or multiple stone removal procedures throughout their lives.[1,3,16]

PH1, PH2, and PH3 Often Have an Early Onset, but Symptom Timing Can Vary

Median Age at Symptom Onset[6,8,11,15,17]

PH1	PH2	PH3
3.9-5.2 years (Range: 0-66 years)	**3.2-7.4 years** (Range: 0.6-42 years)	**0.75-2.6 years** (Range: 0.1-48 years)

PH1, PH2, and PH3 Are Not Well Diagnosed

Based on a genetic study, it is estimated that **up to 8500 people in the United States have PH,** and **>80%** of individuals with PH may be undiagnosed[6,18]

>42% of diagnosed patients experience a significant delay in diagnosis[19]

>25% of patients with PH remain undiagnosed until reaching ESRD according to one study[20]

Earlier diagnosis, leading to aggressive supportive treatment, can improve prognosis and slow progression to ESRD[1,21]

Diagnosing PH1, PH2, and PH3

24-hour urine collection[22]

- One or two 24-hour urine collections (two preferred per American Urological Association guidelines)
  - Per guidelines, PH should be suspected when urinary oxalate excretion is:
    - >75 mg/day in adults without bowel disfunction[22]
    - >0.7 mmol/1.73 m^2/day[4]

— OR —

Plasma collection for patients with CKD stage ≥3b[1,13]

- Plasma oxalate >20 µmol/L is indicative of PH

Genetic testing for PH subtype[13]

- *AGXT* mutations: PH1
- *GRHPR* mutations: PH2
- *HOGA1* mutations: PH3

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