

# UncoveringPH

**Primary hyperoxaluria (PH) often appears similar to other kidney stone diseases.** Physiologically, PH is a family of ultra-rare genetic disorders that can lead to renal damage and chronic kidney disease (CKD).<sup>1-4</sup>



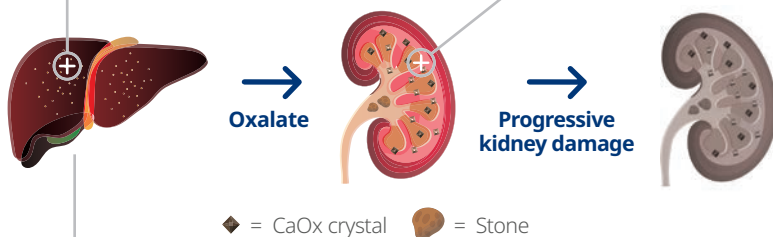
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Calcium oxalate (CaOx) crystals can cause nephrocalcinosis<sup>2</sup>

**In PH, toxic levels of oxalate produced by the liver lead to** recurrent kidney stones, nephrocalcinosis, progressive kidney deterioration, ESKD, and systemic tissue damage<sup>1</sup>

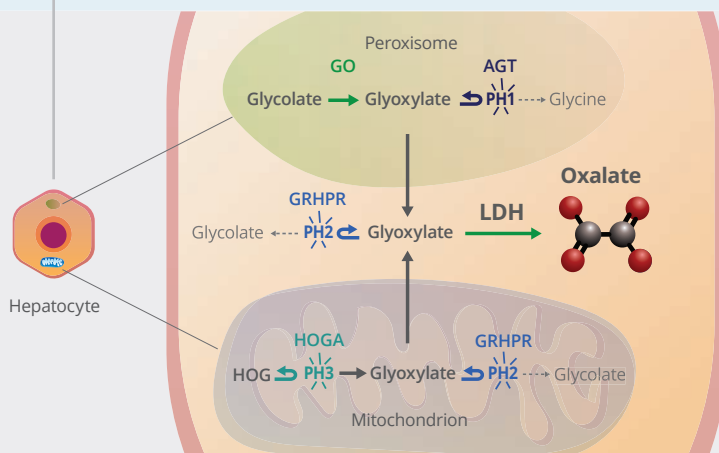
Genetic mutations cause liver enzyme deficiencies that result in a buildup of toxic levels of **oxalate**.<sup>1,2</sup>

Excess oxalate binds with calcium in the kidneys to form **CaOx crystals**, which in turn cause **kidney stones, nephrocalcinosis, and progressive kidney damage**.<sup>5</sup>



### Kidney Function Is Affected in All 3 PH Types<sup>6-11</sup>

- PH1**
  - 10% have ESKD by age 1 year
  - 57% have ESKD by age 40 years
- PH2**
  - >50% have CKD stage  $\geq 2$
  - 35% have ESKD by age 40 years
- PH3**
  - 22%-29% have CKD stage  $\geq 2$
  - 2 reports of ESKD



### Mechanism of Disease<sup>12</sup>

- AGT Enzyme Deficiency** → **PH1**
- GRHPR Enzyme Deficiency** → **PH2**
- HOGA Enzyme Deficiency** → **PH3**

Abbreviations: AGT=alanine-glyoxylate aminotransferase; GO=glycolate oxidase; GRHPR=glyoxylate reductase/hydroxyruvate reductase; HOG=4-hydroxy-2-oxoglutarate; HOGA=4-hydroxy-2-oxoglutarate aldolase; LDH=lactate dehydrogenase.

## PH Is Underdiagnosed

Based on a genetic study, it is estimated that **~8500 people in the United States have PH**, and **>80%** of individuals with PH may be undiagnosed.<sup>6,13</sup>



## One or a Combination of Symptoms Can Be Warning Signs of PH

The first warning sign may be a single kidney stone in children or recurrent stones in adults. Warning signs can include one or a combination of the following<sup>7,8,14-22</sup>:



**Family history**  
of kidney or bladder stones



**Recurrent stones in adults**



**Systemic oxalosis**



**Recurrent UTIs,**  
flank pain, hematuria



**CKD with no known etiology**



**Severe infantile form:**  
Failure to thrive, ESKD,  
severe retinal abnormalities



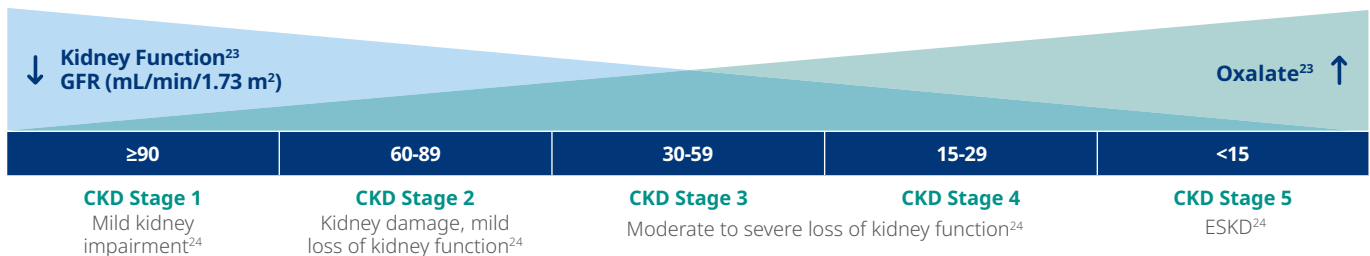
**Single kidney stone in a child**



**Nephrocalcinosis**



**ESKD**



**Oxalate accumulation can occur even in the absence of current symptoms<sup>23,25</sup>**

### Multiple Studies Show That Earlier Diagnosis Is Needed to Improve Patient Outcomes and Preserve Kidney Function\*



**>40% of patients with PH experience a significant delay in diagnosis<sup>26</sup>**

Patients experience ~3.5 years between first symptom presentation and diagnosis

**>25%** of patients are diagnosed at ESKD<sup>27</sup>

**>50%** of patients on dialysis are diagnosed after the start of dialysis<sup>28</sup>

**~5%** of patients are diagnosed after kidney transplant<sup>29</sup>

\*Each data point presented here is reported from a separate study.

### Delayed Diagnosis Affects Short- and Long-Term Outcomes in PH



**Preservation of Renal Function<sup>30</sup>**

Therapeutic delay is the only variable significantly associated with deterioration of kidney function in patients with PH1 (RR: 1.7/year)



**Kidney Graft Survival After Transplant<sup>29</sup>**

- **62%** survival when diagnosed after transplant
- **86%** when diagnosed before transplant

**Earlier diagnosis leading to aggressive supportive treatment can dramatically improve the prognosis and slow the progression to ESKD<sup>1,25</sup>**

Abbreviations: GFR=glomerular filtration rate; RR=relative risk; UTI=urinary tract infection.

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