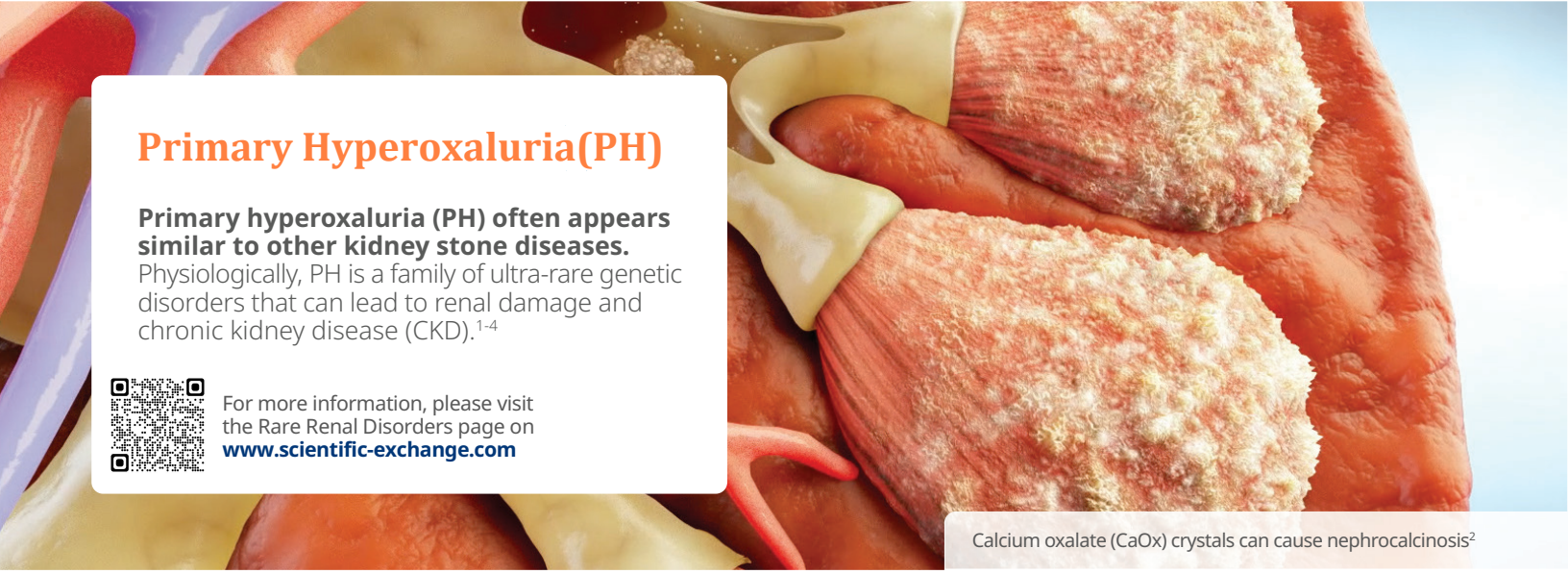
Primary Hyperoxaluria(PH)

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).[1-4]

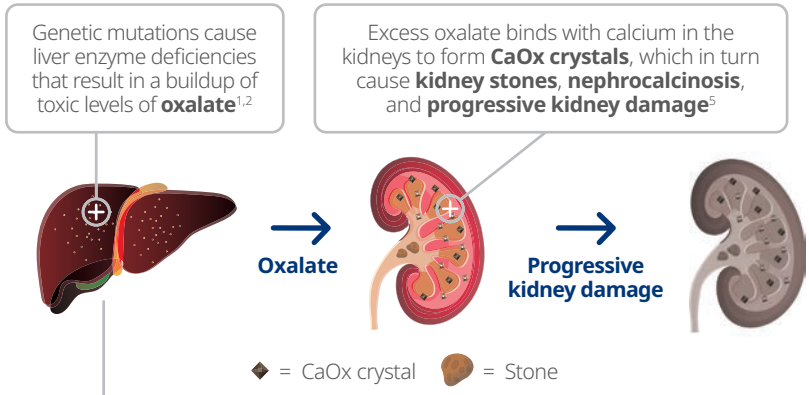
For more information, please visit the Rare Renal Disorders page on **www.scientific-exchange.com**



Calcium oxalate (CaOx) crystals can cause nephrocalcinosis[2]

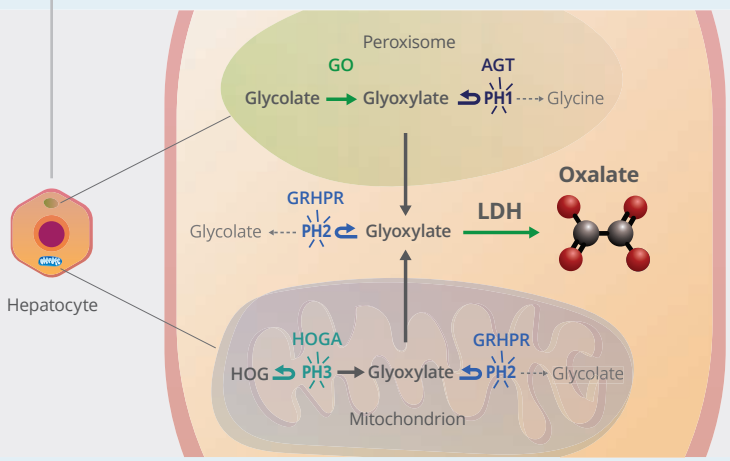
In PH, toxic levels of oxalate produced by the liver lead to

recurrent kidney stones, nephrocalcinosis, progressive kidney deterioration, ESKD, and systemic tissue damage[1]



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

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



Mechanism of Disease[12]

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

Abbreviations: AGT=alanine-glyoxylate aminotransferase; GO=glycolate oxidase; GRHPR=glyoxylate reductase/hydropyruvate 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[6,13]

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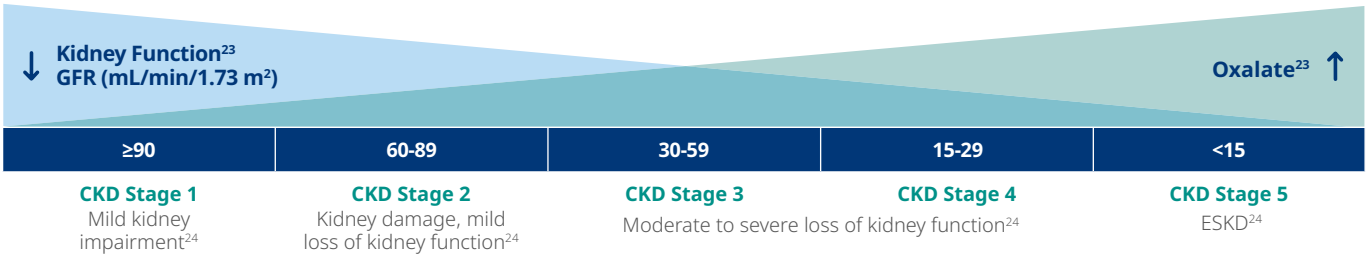
One or a Combination of Symptoms Can Be Warning Signs of PH

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[7,8,14-22]:

- **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[23,25]

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[26]

Patients experience ~3.5 years between first symptom presentation and diagnosis

>25%	of patients are diagnosed at ESKD[27]
>50%	of patients on dialysis are diagnosed after the start of dialysis[28]
~5%	of patients are diagnosed after kidney transplant[29]

*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[30]

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[29]

- **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[1,25]

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

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