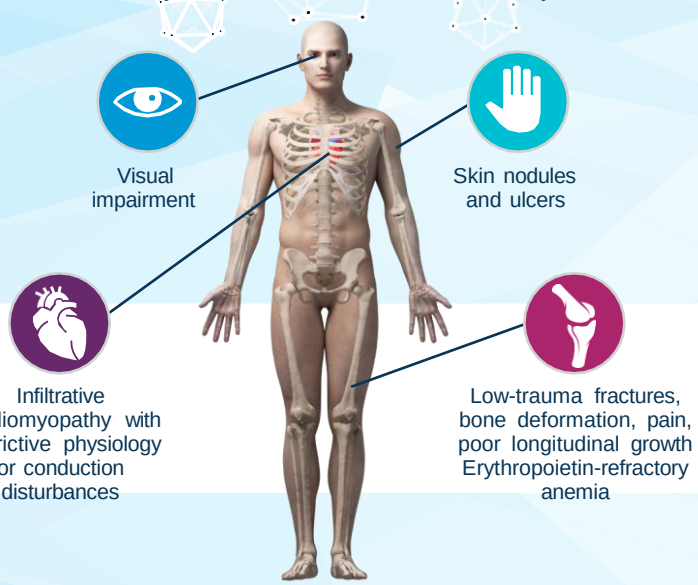
Diagnosis of PH1 with CKD, or in the Dialysis Setting

Intended for US healthcare professionals only

As PH1 progresses, systemic manifestations develop as oxalate deposition occurs due to decline in kidney function[1,2]

As eGFR declines, **oxalate clearance is reduced**, leading to an **increase in POx** until the **supersaturation point is reached** and systemic oxalate deposition occurs.[1,2] Systemic manifestations of PH1 may include:[2]



The above figure does not include all possible systemic manifestations of PH1[2]

Current Literature Recommends that Oxalate and Genetic Testing can be Informative for PH1 Diagnosis[3]

Kidney insufficiency/failure
- High serum creatinine with CaOx stones
- CaOx tissue deposits
- Nephrocalcinosis

→ **UOx and/or POx testing**
UOx >0.50 mmol/1.73 m²/24 hours and/or POx >20 µmol/L

Secondary cause identified?
- Malabsorption
- Gastrointestinal disease
- Very high oxalate, low-calcium diet
- Premature infant

Yes → **Evaluate and treat accordingly**

No → **Genetic testing**
Homozygosity or compound heterozygosity for known variants of *AGXT, GRHPR, or HOGA1*

No → **Liver biopsy** for AGT and GRHPR enzyme activities

Yes →
- *AGXT* variants → **PH1** (*AGT* activity ↓)
- *GRHPR* variants → **PH2** (*GRHPR* activity ↓)
- *HOGA1* variants → **PH3**

Normal AGT and GRHPR activity → **Oxalate disorder of undetermined type**

Key Points

- Patients with a declining eGFR may present with systemic manifestations of PH1 due to systemic oxalate deposition[2]
- In patients with kidney insufficiency/failure, UOx, POx and genetic testing are crucial to help confirm the diagnosis of PH1.[3] Diagnosis is based on clinical judgment

AG(X)T, alanine-glyoxylate aminotransferase; CaOx, calcium oxalate; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; GRHPR, glyoxylate reductase/hydroxypyruvate reductase; HOGA, 4-hydroxy-2-oxoglutarate aldolase; PH1, primary hyperoxaluria type 1; PH2, primary hyperoxaluria type 2; PH3, primary hyperoxaluria type 3; POx, plasma oxalate; UOx, urinary oxalate.

1. Cochat P et al. *Nephrol Dial Transplant* 2012:27;1729–1736; 2. Sas DJ et al. *Urolithiasis* 2019;47:79–89; 3. Edvardsson VO et al. *Pediatr Nephrol* 2013;28:1923–1942.

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