What is Primary Hyperoxaluria?

Primary hyperoxaluria (PH) is a family of severe, rare, genetic liver disorders. People with PH produce too much oxalate, a natural chemical in the body that is normally eliminated as waste through the kidneys.*

HYPER (Too Much) – **OXAL** (Oxalate) – **URIA** (In the Urine)

In patients with PH, the kidneys are unable to eliminate excess oxalate, which then accumulates in the kidneys and throughout the body.*

Three known types of PH*

Each results from a mutation in a specific gene that causes a decrease in the activity of a specific enzyme in the liver. Without these enzymes, glyoxylate is not properly broken down and is converted to oxalate.

PH1	PH2	PH3
AGXT **genetic mutation**	***GRHPR*** **genetic mutation**	***HOGA1*** **genetic mutation**
↓	↓	↓
AGT enzyme deficiency	**GR/HPR enzyme deficiency**	**HOGA enzyme deficiency**

Signs and Symptoms†‡

The three types of PH differ in severity and symptoms. Below is a list of potential signs and symptoms of all forms of PH. Patients with PH may not experience all of the symptoms listed below.

- Kidney stones
- Kidney damage
- End-stage renal disease and injury to other organs

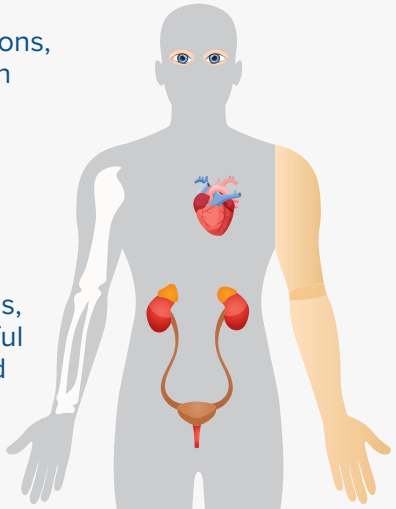
- Blood in the urine
- Urinary tract infections

- Retinal calcifications, resulting in vision problems

- Cardiac failure
- Arrhythmia

- Bone fractures

- Skin calcifications, resulting in painful skin nodules and necrosis



Prevalence of PH[§]

1-3 cases per **million** inhabitants

1 in **120,000** live births

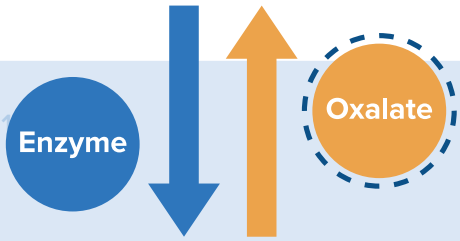
Estimated genetic prevalence for each type of PH:

PH1 – 1 in 151,887

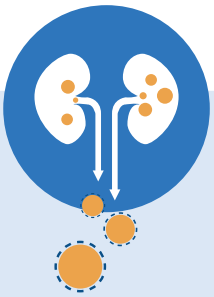
PH2 – 1 in 310,055

PH3 – 1 in 135,866

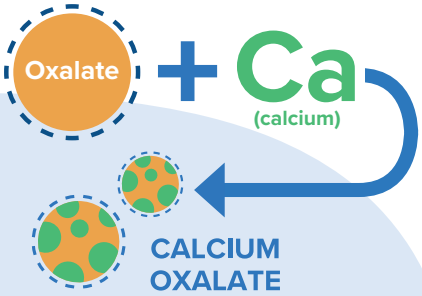
Progression of PH[‡]



1 Decreased enzyme activity results in overproduction of oxalate

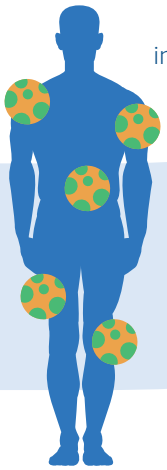


2 Kidneys filter excess oxalate resulting in abnormally high levels of oxalate in the urine



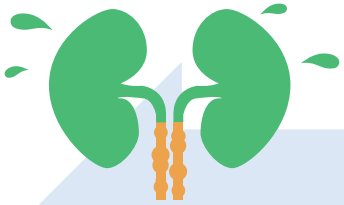
3 The main component of kidney and bladder stones

These deposits can damage the kidneys and other organs and lead to blood in the urine, urinary tract infections, kidney damage, and end stage renal disease



4 As kidney function decreases, oxalate levels in the blood rise, depositing oxalate in tissues throughout the body

5 Patients with decreased renal function may also experience oxalosis, which involves a build-up of oxalate in other organs, such as the bones, skin, heart, and retina, causing other complications



6 PH can result in end stage renal disease, a life-threatening condition that prevents the kidneys from filtering fluids and waste products from the body effectively

Note: PH can have varying levels of severity depending on the type

Current Treatment Options

There are **no specifically approved** therapies for people living with PH. All patients are treated as normal stone patients which does not address the underlying PH root cause. Patients with PH sometimes must undergo both liver and kidney transplants, which are major surgical procedures. They must then take immunosuppressant drugs for the rest of their lives.

References

*Oxalosis & Hyperoxaluria Foundation. Overview of hyperoxaluria. 2017. Available at: https://ohf.org/overview/. Accessed July 6, 2017.

†Mayo Clinic. Hyperoxaluria and oxalosis. 2018. Available at: https://www.mayoclinic.org/diseases-conditions/hyperoxaluria/symptoms-causes/syc-20352254. Accessed April 13, 2018.

‡NIH. Primary hyperoxaluria. 2018 Available at: https://ghr.nlm.nih.gov/condition/primary-hyperoxaluria#. Accessed April 13, 2018.

§Hopp, K, Cogal, A, Bergstralh, E, et al. Phenotype-genotype correlations and estimated carrier frequencies of primary hyperoxaluria. Journal of the American Society of Nephrology 2015; 26(10):2559-2570.