AGXT & Primary Hyperoxaluria

What is primary hyperoxaluria?

- Primary hyperoxaluria is an inherited condition caused by changes in one of three genes – AGXT, GRHPR or HOGA1.
- These changes result in recurrent kidney and bladder stones. Depending on which gene has been affected, this can progress to kidney failure.
- Signs and symptoms of primary hyperoxaluria include blood in the urine, urinary tract infections and abdominal pain.

What is AGXT, and how do changes in AGXT affect the kidneys?

- The AGXT gene provides instructions for the production of enzymes which help remove harmful waste products from the body. These enzymes are produced in the liver.
- Normally, these enzymes break down waste products to less harmful forms before they are excreted by the kidney.
- When this gene is changed, waste products are not properly broken down, resulting in the build-up of a substance called oxalate in the kidneys. Oxalate combines with other substances to form kidney stones.
- These stones get stuck in the kidney and reduce its ability to function. Over time this may result in kidney failure.
- The extent to which the kidneys are affected and when failure occurs can vary, even among family members with similar changes in their AGXT gene.
- For around 1 in 4 individuals with this change in AGXT, the first symptoms can appear in infancy. They tend to present with kidney stones, failure to thrive, urinary tract infection and kidney failure.
- Symptoms such as abdominal pain, blood in the urine and urinary tract infection are associated with primary hyperoxaluria which begins in childhood.

Do these changes have effects on other parts of the body?

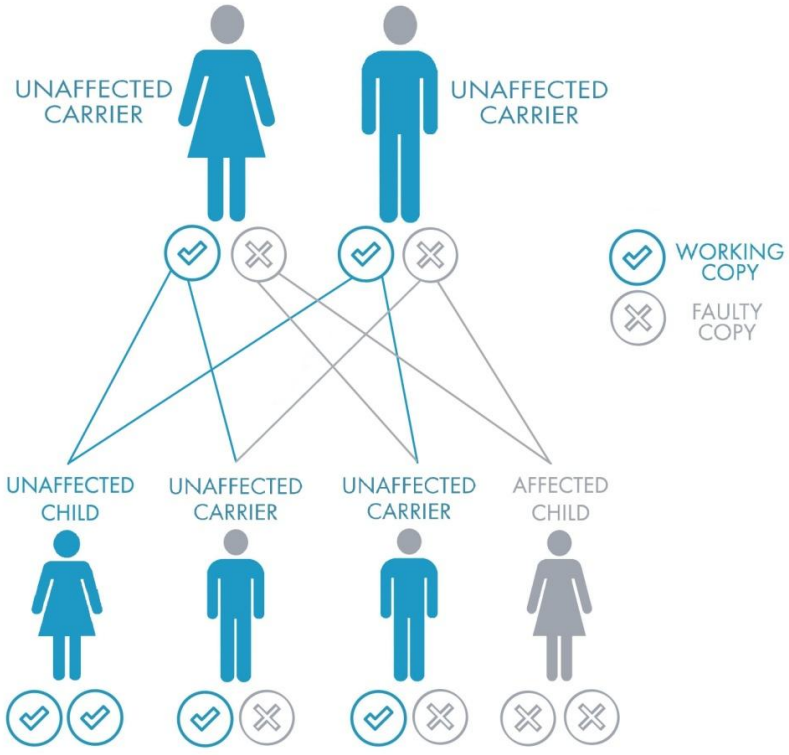
- Excess oxalate can also deposit in the heart, blood vessels, joints, bone and eyes and have a number of effects:
  - Disruption of electric signals in the heart.
  - Reduced blood circulation in the legs that can result in gangrene.
  - Joint pain and reduced mobility.
  - Impaired vision.
  - Dental problems such as tooth pain.
  - Bone pain, anaemia and an increased risk of bone fracture.

How is primary hyperoxaluria treated?

- Early treatment is vital as it can delay kidney failure and minimise effects outside of the kidney.
- Treatment focuses on reducing oxalate levels. This involves:
  - High fluid intake.
  - Orthophosphate, potassium citrate-citric acid and/or magnesium oxide.
- You may be prescribed pyridoxine, which in around 10 – 30% of individuals significantly reduces oxalate production. This can be continued indefinitely or until a transplant is performed.
- The cure for primary hyperoxaluria is liver transplantation – this replaces the dysfunctional enzymes and prevents oxalate overproduction.

How is this change passed down through a family?

- You have two copies of AGXT.
- To develop primary hyperoxaluria, two faulty copies of the AGXT gene must be inherited from each parent, one from each parent – they are “carriers” of the faulty gene and do not have the disease themselves.
- Each child of carrier parents has a 1 in 4 (25%) chance of inheriting the disease.
- If a child receives only one copy of a faulty gene, they themselves become carriers. They will not have primary hyperoxaluria but may pass on that faulty gene to their own offspring.



Should my family members be tested?

- Family members may be advised to undergo genetic testing, as early diagnosis / treatment can significantly improve outcomes. It is important that this is discussed with a genetic counsellor.