COL4A5 & Alport Syndrome

What is Alport Syndrome?

- Alport Syndrome is an inherited condition involving kidney disease, hearing loss and eye abnormalities.
- It is a result of changes in forms of the COL4 or COL5 genes.
- The initial symptoms can vary depending on the nature of the change, but generally it is first noticed as recurrent episodes of blood in the urine.
- Over time, protein in the urine, high blood pressure and gradual loss of kidney function occurs until the kidneys fail. The age at which failure occurs depends on which gene has changed.

What is COL4A5, and how do changes in COL4A5 affect the kidneys?

- In the kidneys, COL4A5 produces proteins that form part of the filtration system to remove water and waste products from the blood.
- A change in this gene prevents the kidney from properly filtering the blood and allows blood and protein to pass into urine. This results in gradual scarring of the kidneys and eventually kidney failure.
    - With a COL4A5 change, kidney failure usually occurs between the ages of 16 and 35 years.

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

- COL4A5 is also an important part of inner ear structures. Changes in COL4A5 can lead to hearing loss, and this usually occurs during late childhood or early teen years.
- Changes in COL4A5 can also affect the eyes, causing misshapen lenses, eye pain and an abnormally coloured retina. However, these abnormalities do not usually lead to sight loss.
- Rarely, benign (non-cancerous) tumours called leiomyomas can develop.

How is Alport Syndrome treated?

- There is currently no cure for Alport Syndrome. Management mainly focuses on treating complications of kidney function loss.
- A kidney transplant is preferred over dialysis when kidney failure occurs. The disease does not develop again in the new kidney.

How is this change passed down through a family?

- Normally you have two copies of every gene – one from each parent. However, in the case of certain genes, only one copy is passed to males. COL45A is an example of such a gene.
- These genes are found on the X ‘sex chromosome’ – males have one X chromosome and one Y chromosome, while females have two X chromosomes.
    - Males only have one copy of COL4A5. If this copy is faulty, the syndrome will develop.
    - Females have two copies of COL4A5. If one copy is faulty, they will develop Alport Syndrome. However, as the other copy functions normally, the syndrome is generally a lot less severe and only a very small minority develop kidney failure.
- A faulty copy cannot be passed from an affected father to their son as the father only passes the unaffected Y chromosome to his son.

Should my family members be tested?

- Counselling and genetic testing are generally available to all family members at risk of having the disease.
- At-risk children may be monitored.
- If a living relative wishes to donate a kidney it is important for them to be tested.