How is classic AS inherited?

It is inherited when someone who has an alteration or mutation in the COL4A5 gene passes it to his or her child. Alternatively, a child may have the genetic alteration as the result of a spontaneous mutation, which has not been inherited from either parent. About 15% of cases occur as the result of a new mutation.

MEN

Men only have one X chromosome, and this is passed to each of their daughters. Their sons inherit their Y chromosome. In other words:

- all the daughters of men with classic AS will inherit the altered gene
- none of their sons will be affected.

WOMEN

Women have two X-chromosomes, and they will only pass one of these to their child, be it a boy or a girl. In other words, there are four possible outcomes to each pregnancy that a "carrier" woman may have:

- a boy without the gene alteration
- a boy with the gene alteration
- a girl without the gene alteration
- a girl with the gene alteration.

Rarer (non-classic) forms of AS

Most families with AS have the classic X-linked type of AS, as described above. However, a few families have a different genetic pattern and genes other than COL4A5 cause the condition.

An autosomal recessive pattern

In this type, an affected person inherits two copies of a gene alteration, one from each parent. Both males and females can be affected equally, and their parents will all be carriers of a single copy of the gene mistake, which for them is harmless.

An autosomal dominant pattern

This type is very rare. Again, both men and women can be affected. Anyone inheriting just one copy of an altered gene will be affected .

For more information

If you need more advice about any aspect of Alport Syndrome, you are welcome to contact:

CLINICAL GENETICS DEPARTMENTS:

Northern Scotland (main base Aberdeen)
Tel: 01224 552120 / Fax: 01224 559390
(Aberdeenshire, Moray, Highland, Western & Northern Isles)

Tayside (main base Dundee)
Tel: 01382 632035 / Fax: 01382 496382
(Perth & Kinross, Angus, North East Fife)

South East Scotland (main base Edinburgh)
Tel:0131 537 1116 / Fax: 0131 537 1153
(Borders, Lothian, South West Fife)

West of Scotland (main base Glasgow)
Tel: 0141 354 9200 / Fax: 0141 232 7986
(Glasgow, Argyll & Bute, **AYRSHIRE**, Dumfries & Galloway, Stirling, Lanarkshire, Falkirk)

If you would like further information and the opportunity to talk to other parents you can contact:

www.kidney.org.uk/Medical-Info/alports/index.html

Seen in clinic by .....

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Alport Syndrome

A Patient Information Leaflet

What is Alport syndrome (AS)?

It is an inherited condition that causes kidney failure and hearing loss. The common form of AS (called classic Alport syndrome) is caused by an alteration in a particular gene that lies on the X chromosome.

What are genes & chromosomes?

Our genes are the unique set of instructions inside our bodies that make each of us individual. There are many thousands of different genes, each carrying a different instruction. As well as determining how we look, our genes control the way each cell or building block of the body works.

Genes lie on tiny structures called chromosomes, rather like beads threaded onto a string. Each chromosome contains thousands of genes.

Most of our body cells have 46 chromosomes, arranged in 23 pairs.

- We inherit one of each pair from our mother and the other of each pair from our father.
- 44 of these chromosomes are numbered in order of decreasing size, as 22 matching pairs.

The two remaining chromosomes are called the sex chromosomes, and they are given the letters X and Y rather than numbers.

- Females have two X chromosomes, one inherited from their mother and the other from their father.
- Males have one X chromosome (inherited from their mother) and a Y chromosome (inherited from their father).

The important gene in classic AS

The gene that is altered in classic AS is called the COL4A5gene. This gene can be altered in many different ways, all of which will cause classic AS.

Why is the COL4A5 gene important?

The **Instruction** that this particular gene gives is important in the formation of what is called the **glomerular basement membrane** (GBM). The GBM acts like a filter in our kidneys. It allows fluid containing some waste products from the body to move from our blood vessels to our urine. At the same time, it has to stop the blood cells and protein (both of which are essential to our bodies) from leaking out.

If there is an alteration (mistake) in the COL4A5 gene, the GBM becomes leaky, and fails to do its job properly as a filter.

In the eye and ear, similar basement membranes exist. These membranes are important for the shape of the lens in the eye, the retina at the back of the eye, and the structure of the inside of the ear.

Can both men and women have classic AS?

As they have two X chromosomes, women get two copies of the COL4A5 gene, one on each of their Xs. Therefore, even if one of those genes contains an alteration or mistake, they have a normal copy of the gene on their other X chromosome.

This normal copy usually seems to protect a woman who carries an altered gene from most of its effects. Some of these women do develop kidney problems, but this tends to be in later life.

Men, however, only get one X chromosome and therefore only have one copy of the COL4A5 gene. If that gene is an altered copy, then a man will develop full-blown classic AS, as there is no normal copy of the gene to act as a back-up.

What happens to a man who has classic AS?

He should be born a healthy baby. The first signs of the condition are very mild.

Nearly all boys who inherit classic AS have small amounts of blood in their urine by the age of 5 years. The blood may not be visible, and may only be detectable on a urine test. Eventually, as protein leaks out, the blood pressure rises and the kidneys fail, but the speed with which this happens varies from man to man. Some men need to have kidney dialysis in their teens or early twenties, but others do not need this until they are 30 to 40 years old. Many affected men have had a successful kidney transplantation.

Hearing loss becomes apparent during the school years. About 85% of boys have some degree of hearing loss by 15 years and many boys will need hearing aids by the time they are 25 years.

About one-third of all boys develop a particular change in the shape of their eye lenses which causes short sightedness.

What about women who have the COL4A5 gene alteration?

The majority of women who carry the gene alteration are only mildly affected and often do not know they have this alteration until they have a son who is diagnosed with classic AS. By the age of 20 years, all carrier women have a small amount of blood in their urine, but this is often only picked up on a urine test as it is usually not visible. About a third of all carrier women do develop high blood pressure and about a half have some hearing loss, although usually not as severe as the affected men. In addition, about 15% of carrier women do eventually develop kidney problems, and this may progress to kidney failure.