

Alport's syndrome

What is Alport's syndrome?

Alport's syndrome is a relatively uncommon genetic disease that causes progressive kidney damage. The disease affects the tiny blood vessels of the kidney (the glomeruli), causing a gradual but persistent process of destruction that reduces their capacity to filter waste from the blood, leading to kidney failure in many cases.

Alport's syndrome affects about 2 in 10,000 people. It is usually much more severe in men than women. Males with Alport's syndrome inevitably develop kidney failure, but kidney failure in females is unusual. The age at which boys with Alport's syndrome develop kidney failure varies from family to family. It may occur as early as 15–20 years of age, but in some families, kidney failure does not develop until the men are 40–50 years of age.

How is Alport's inherited?

The genetics of the syndrome are quite complicated. The gene for the disease is located on the X chromosome, which is one of the chromosomes that determines a person's sex. Women have two X chromosomes, men have an X and a Y chromosome. About 15–20 percent of those with Alport's syndrome do not have a family history of the disease. In these cases, Alport's occurs as a result of a new mutation in the gene that determines the presence of the condition. If this is the case, the affected person will be the first member of the family to develop the disease.

Females are generally less affected because they have two X chromosomes – the one normal X chromosome limits the effect of

the one with the Alport's gene. In women, the disorder is usually mild, with minimal or no symptoms. However, since men only have one X chromosome, there is no normal gene to counteract the effects of the Alport gene.

Consequently, males are usually more severely affected. A father cannot pass the gene on to his son, but will transmit one abnormal X chromosome to his daughters. A mother who carries the gene can give the gene to her sons or daughters. A woman may transmit the gene to her offspring without exhibiting any symptoms of Alport's syndrome herself. Any daughters of people with Alport's will have Alport's syndrome but will usually be asymptomatic. Each son of a woman who is an Alport's carrier has a 1 in 2 risk of having the disease.

Can Alport's be prevented?

As Alport's is an inherited condition. People who have the condition can pass it on to any children they may have. As such, couples with a family history of Alport's Syndrome may wish to discuss their situation with a doctor or genetic counsellor to determine any potential risks when starting a family.

What are the signs and symptoms of Alport's?

The most common signs and symptoms of Alport's Syndrome are:

Blood in the urine: The major symptom exhibited by most people with Alport's Syndrome is the presence of blood in the urine (haematuria). This is present almost all the time. This symptom is seen from infancy in males with Alport's, whereas it may not be present at all in females with the condition.

Protein in the urine: As people with Alport's enter their teenage and young adulthood years, protein may be detected in the urine. This is usually the first sign that kidney function is beginning to deteriorate. Loss of large amounts of protein in the urine may result in fluid retention and subsequent swelling of the extremities (ankles, wrists) and eye area.

Kidney disease: With increasing age, boys with Alport's Syndrome will develop signs and symptoms typical of kidney failure, including high blood pressure, swelling, decreased appetite and fatigue. These symptoms relate to the progressive destruction of the kidney filters (glomeruli) and reflect the body's increasing inability to rid the body of waste and excess water.

Eventually, kidney failure will occur, however it is impossible to predict exactly when this will happen. In general, it often develops between adolescence and the age of forty. Kidney failure in females with Alport's does tend to occur later than males, but this is not absolute. When the kidneys fail, dialysis or transplantation will be necessary to survive.

Deafness: Alport's Syndrome is often associated with progressive loss of hearing, and may be a clue to diagnosis. Not everyone with Alport's will suffer from deafness, but those who do generally develop it at a young age (the loss is usually detectable by age 8-10). Loss of hearing in girls with Alport's Syndrome tends to be milder than in boys, rarely requiring the use of hearing aids. Hearing impairment appears to worsen roughly in step with increasing renal impairment.

Eye defects: Although uncommon, defects of the eye may occur in some individuals with Alport's Syndrome. Generally, these defects will involve either an abnormally shaped lens of the eye (anterior lenticonus) or poor function of the retina in the back of the eye. This results in a reduction in the clarity or sharpness of vision.

How is Alport's diagnosed?

Unless a history of the condition occurring in other family members is known, it can often be difficult to diagnose Alport's Syndrome. The symptoms of Alport's are similar to those of other kidney diseases, and absolute diagnosis is only confirmed by microscopic examination of a sample of kidney tissue.

To examine the kidney microscopically, a small piece of kidney tissue is removed in a procedure known as a biopsy.

Under a microscope the sample is examined, looking for changes to the structure of the glomeruli that are seen only in people with Alport's Syndrome.

How is Alport's treated?

As Alport's is a genetic condition, there is currently no treatment that can halt or reverse its progress. The primary goal of treatment is to control the progress of the disease through monitoring health and treating symptoms.

Treatment focuses on a number of areas:

Blood pressure: Strict control of blood pressure is important. Prolonged high blood pressure will have a detrimental effect on kidney function, hastening the disease process toward kidney failure. A medication specific to the control of blood pressure is used to delay or prevent the development of kidney failure.

Hearing: Hearing loss in most males will be gradual, and hearing aids may be helpful to some degree. Those with Alport's should protect their hearing when in noisy environments. Loss of hearing is likely to be permanent, so education and counselling to cope with this change and acquire new communication skills may be useful.

Vision: Lenticulus can lead to severe visual impairment, and if this occurs, intraocular lens implantation or repair of the anterior lenticulus are suitable treatment options. Surgical repair of cataracts may also be necessary.

Dialysis and transplantation: Researchers are currently investigating new approaches to treatment for Alport's syndrome which attempt to preserve kidney function in people with chronic kidney failure. Ultimately, chronic renal failure progresses to end-stage renal disease, requiring dialysis or transplantation.

Alport's does not recur in kidneys that have been transplanted. The genetics of the disease mean that if living related transplantation is being considered, care should be taken when selecting the potential donor.

What is the outlook for Alport syndrome?

Researchers have identified that Alport's syndrome is caused by a mutation in the gene for collagen. The three mutations that are present in the gene cause defects in the glomeruli (the kidney filters), reducing their capacity to filter blood effectively. Identification of this gene means that further investigation into the way the gene works can take place, and future gene therapy for this condition becomes a possibility.

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