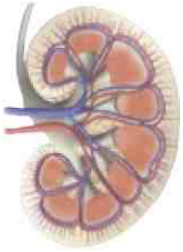
Alport Foundation of Australia



SUPPORT RESEARCH AWARENESS

"I've just been diagnosed with Alport Syndrome. Now what?"

You are not alone....

A guide for patients with Alport Syndrome

This document contains information for patients and families diagnosed with Alport Syndrome. It has been reviewed by the Medical Advisory Committee of the Alport Foundation of Australia.

Alport Syndrome is a rare condition with complex symptoms. Awareness about the disease, its inheritance and treatments, empowers patients to engage with doctors and caregivers in a meaningful way when making decisions regarding their treatment and care.

What is Alport Syndrome?

Alport Syndrome is a genetic kidney disease caused by mutations in the genes that produce collagen Type IV. It is considered rare because it is estimated to affect 1 in 5,000 people, although the prevalence is probably more than reported since the disease is often undiagnosed in women with mild symptoms. Collagen Type IV is an important component of the kidney filter or glomerulus. The collagen Type IV produced by an Alport Syndrome patient's mutated genes does not form correctly, which severely weakens the ability of the glomerulus to filter waste from the blood, causing symptoms such as blood and protein in the urine (haematuria), kidney failure, as well as hearing loss, abnormalities in the lens of the eye, and retinal spots or flecks.

Both men and women with Alport syndrome experience the clinical features of the disease, which vary in severity depending on the type of inheritance (X-linked, autosomal recessive and digenic, and autosomal dominant).

What is my treatment likely to involve?

While there is currently no known cure for Alport syndrome, there are a number of treatments available that can reduce the severity of your symptoms and improve your quality of life. The treatment plan that your nephrologist recommends will vary based on a number of factors, which may include the mode of inheritance that resulted in your condition, your current level of kidney function and your biological sex. However, as Alport syndrome is a progressive disease, you may have to consider dialysis or a transplant down the track. The aim of treatment is to delay the need for dialysis or kidney transplant as long as possible. If your symptoms are very mild, or you are a female with X-Linked Alport syndrome (see page 5 for details), you may be able to manage your condition indefinitely by taking medications and maintaining a healthy lifestyle.

Medications (Medicare funded)

Blood pressure medications, such as ACE inhibitors (ramipril, lisinopril, perindopril etc) and ARBs (angiotensin- blockers, such as telmisartan), may be prescribed to help you manage your blood pressure. Controlling your blood pressure will keep your kidneys functioning for as long as possible. ACEi and ARBs reduce the amount of scarring in the kidney and will also reduce your risk of cardiovascular disease.

SLGT2 inhibitors or flozins may also be prescribed. Taken with an ACEi or ARB, they provide an additional beneficial effect for Alport syndrome patients

Dialysis

Dialysis is treatment that removes waste products from your blood once your kidneys have stopped working. There are two types – haemodialysis, in which your blood is cleaned using an external machine, and peritoneal dialysis, in which a cleansing fluid called dialysate passes through a catheter tube into part of the abdomen known as the peritoneal cavity. The dialysate absorbs waste products from blood vessels in the lining of the abdomen. Then the fluid is drawn back out of the body and discarded. Dialysis can be performed at a hospital, a dialysis centre or at home, depending on your preference, and is covered by Medicare. The treatment is highly effective for kidney failure. Patients may choose the dialysis method that best suits their lifestyle.

Kidney Transplantation

A kidney transplant is the final step in treating any condition that will result in kidney failure. Your nephrologist will tell you if or when transplant will be necessary for you. Dialysis will be used to manage your condition until a donor organ is available. Your transplanted kidney may be the gift of a live donor, such as a family member or friend, or from a registered organ donor. A team of skilled health professionals will support you through this process. If successful, you should be able to cease dialysis.

Do I need to make changes to my lifestyle or diet to manage Alport Syndrome?

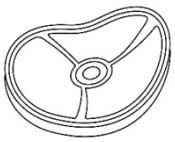
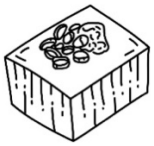
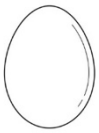
Taking medications as recommended by your doctor is vital. However, there are many ways that patients with Alport syndrome can help maintain healthy kidney function or slow down the rate of deterioration. Making healthy lifestyle choices, such as not smoking or vaping, reducing alcohol intake, exercising regularly, maintaining a healthy weight and reducing stress will help you to manage your Alport syndrome.

Your doctor may recommend you follow a diet that limits your consumption of certain nutrients, as your compromised kidney function limits your ability to remove high amounts of these nutrients from your bloodstream.

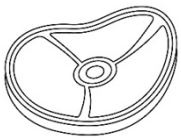
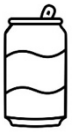
The Three P's

The "Three P's" are the three main nutrients that renal patients need to monitor. It is important to understand that you *must not* cut out these nutrients from your diet entirely – you just need to ensure that your kidneys can handle the amount of each nutrient that you are consuming. The three key nutrients are protein, phosphate and potassium.

Protein: Your body needs protein to build muscle and repair damage to your tissues. However, eating too much protein as an Alport patient can cause protein waste to build up in your blood, and your kidneys won't be able to remove the waste effectively. Protein is found at its highest concentration in animal products like meat, fish, and eggs, but can also be found in plant-based alternatives like tofu.

Phosphate: Phosphate is an essential mineral for bone maintenance. However, if you have impaired kidney function, an excess of phosphate can accumulate in your blood and may leach calcium out of your bones. Foods that are high in phosphate include dairy, meat and soft drinks - particularly cola.

Potassium: This mineral is needed to maintain your body's electrolyte balance, and helps your heart and muscles to function properly. A build-up of potassium in your bloodstream due to impaired kidney function can cause irregular heartbeat, muscle weakness and, in some cases, heart attacks. High levels of potassium can be found in fresh fruits and vegetables such as bananas, avocados, and spinach.



The amounts of the Three P's that you can safely eat will vary based on whether you are currently on dialysis. You should seek the advice of an Accredited Practising Dietitian, who will be able to create an eating plan that is best for you and your kidneys.

You can use this website to find a dietitian near you - https://member.dietitiansaustralia.org.au/Portal/Portal/Search-Directories/Find-a-Dietitian.aspx

Kidney Health Australia recommend that patients with eGFR <30 mL/min/1.73m^2 should have a nutrition assessment by an Accredited Practising Dietitian.

Kidney Health Australia: CKD Management in Primary Care handbook

Will other members of my family be affected by Alport Syndrome?

Alport Syndrome is a genetic (hereditary) condition, so other members of your family may also have inherited a faulty collagen Type IV. Therefore, it is advised that all members of your family consider undergoing genetic counselling and testing to diagnose Alport Syndrome. This is free with Medicare if ordered by a kidney specialist.

Alport Syndrome has different modes of inheritance which affect different genes that code for collagen, namely *COL4A3, COL4A4 and COL4A5*. Having genetic testing will enable you to determine the gene mutation type and the mode of inheritance which resulted in your own diagnosis. This, in turn, will inform you and your family members of the risk of inheriting the disease, identify other family members who may have already inherited the mutation, and enable you to consider various family planning options, such as Pre-Implantation Genetic Testing (PGT), to prevent the genetic condition in future generations.

X-Linked Alport Syndrome (XLAS)

This is the most common mode of inheritance for Alport Syndrome, impacting an estimated 85% of all patients. It is also the most severe form of Alport syndrome typically with haematuria, kidney failure, hearing loss, lens abnormalities and retinal flecks. In this mode of inheritance, the mutant collagen IV gene (*COL4A5*) is carried on the X chromosome, which is one of the two sex chromosomes. Affected males and females have inherited a single copy of a mutation in *COL4A5*.

Men will only inherit the mutation from their mother, while females may inherit the mutation from either parent affected by Alport syndrome.

Men with X-linked disease will pass the mutation to *all* daughters, but *none* of their sons are affected. Their affected daughters will have haematuria, and possibly hearing loss and kidney failure

Boys and men with X-linked disease are more likely to develop kidney disease, hearing loss and the eye abnormalities. Affected men usually develop kidney failure between the ages of 15 and 50.

Women with X-linked disease have a 50% chance of passing the affected X chromosome to her daughters *or* sons.

Although generally the clinical features are less severe in women than men, women with X-linked inheritance are no longer thought to be only ‘carriers’ of the disease, since 20-30% develop renal failure by age 60 and often hearing loss by middle age. Twice as many women are affected as men, and half of their sons and half of their daughters inherit the gene mutation and thus are affected.

Men and women with Alport syndrome are advised to consult with relevant health professionals regarding the risk of their children inheriting the X chromosome carrying the mutated collagen IV gene, and consider family planning options, such as PGT (see page 6).

Autosomal Recessive Alport Syndrome (ARAS)

Autosomal Recessive (ARAS) is significantly less common than XLAS, occurring in fewer than one in 40,000 normal individuals. The mutant collagen IV gene *(COL4A3 or COL4A4)* is carried on an autosome, that is, a numbered chromosome (not one of the sex chromosomes, X and Y). We inherit 2 copies of each numbered autosome, one from each parent.

In ARAS, both parents have one copy of the mutant Alport gene and one normal gene. A copy of the mutated gene must be inherited from *both* parents for the offspring to develop Alport syndrome. Generally, one in 4 children will inherit the mutated collagen IV gene from both parents.

If only one copy of the mutated gene is inherited (one in two chance), the normal gene from the other parent will override the effects of the mutated gene. The individual is considered to be a 'carrier' of a single mutant collagen IV gene.

If a normal gene is inherited from both parents (one in four chance), the individual will not be affected by Alport syndrome.

Autosomal Dominant Alport Syndrome (ADAS)

Autosomal Dominant (ADAS) is the third mode of inheritance in which haematuria is usually the only clinical feature, and most individuals do not develop kidney failure, hearing loss or eye abnormalities.

In ADAS, the mutated gene is dominant. If *one* copy of the dominant mutated gene is inherited, the individual will develop Alport syndrome. In this instance the mutated gene will override the 'unaffected' gene. Males and females are affected equally, and can both transmit the disorder with each child having a 50% chance of inheriting the mutated collagen Type IV gene.

Pre-Implantation Genetic Testing (PGT)

Pre-Implantation Genetic Testing is a type of IVF in which people with a diagnosed genetic condition can request their IVF embryos be tested for a known disease-causing gene before implantation. Affected embryos are excluded from the rest of the IVF process, eliminating the risk of passing on the disease to the next generation.

To learn more about the process of PGT, you can read this article by Dr Alison Blatt: https://alport.org.au/genetic-diagnosis/

Are there any other complications of Alport syndrome that I should know about?

Collagen Type IV is an important component of the kidney filter or glomerulus, as well as the cochlea of the ear, the lens and retina of the eye. Thus, the pathogenic variants (mutations) associated with Alport syndrome can potentially impact hearing and eyesight as well as kidney function.

Problems with the eyes and ears tend to develop or worsen as kidney function deteriorates. If you notice any changes to your hearing or blurred vision, you should consult an ophthalmologist or audiologist. These specialists will be able to suggest possible treatments or devices to mitigate your symptoms, such as minor surgery (lens replacement) to correct vision issues, and hearing aids to minimise hearing loss.

Find an ophthalmologist: https://ranzco.edu/home/patients/find-an-ophthalmologist/

Find an audiologist:
https://audiology.asn.au/ccms.r?pageid=10217&TenID=AUDA

Where can I find more information and support?

We understand that being diagnosed with any genetic disease can be extremely stressful and overwhelming. There are a number of different resources and communities listed below that you can turn to for support and guidance.

ALPORT
FOUNDATION OF AUSTRALIA

Alport Foundation Community

Join the Alport Foundation Community to be connected with other patients and families, and to receive updates about research progress and the foundation's activities.
Website:
https://alport.org.au

You can register for community membership with this online form:
https://alport.org.au/community-membership/

Stay informed:
: https://www.facebook.com/AlportFoundationOfAustralia

KIDGEN

KIDGEN is a collaborative formed in 2017 to improve care outcomes for genetic kidney disease (GKD). KIDGEN is focused on providing a diagnosis to as many people with genetic kidney disease as possible in Australia, through cutting-edge research. Visit the KIDGEN patient page for participating clinics around Australia and links to information regarding genomic sequencing.

KIDGEN website: https://www.kidgen.org

BEAT CKD

Better Evidence and Translation – Chronic Kidney Disease (BEAT-CKD) began as a collaborative research network aiming to improve the lives of people living with chronic kidney disease. Their aim is to generate high-quality research evidence to help patients, health professionals, and policy makers make informed decisions about healthcare.

BEAT CKD website: https://beatckd.org

AGSA

The Association of Genetic Support of Australasia facilitates support for those affected directly or indirectly by genetic condition throughout Australasia.
AGSA is a network of people who are affected by genetic conditions, either directly or indirectly. They have built up a contact register with over 850 genetic conditions plus 250 rare chromosome abnormalities.

Visit the AGSA website or email them at info@agsa-geneticsupport.org.au

Centre for Genetics Education

The Centre for Genetics Education provides current and relevant genetics information, enabling health professionals to improve treatment outcomes for individuals and family members affected by genetic conditions. The Centre is a division of the NSW Health Education& Training Institute (HETI), and is based at St Leonards, NSW. The Centre's research and educational activities aim to bring genetics information to the widest audience possible.

https://www.genetics.edu.au

About the Alport Foundation of Australia

You are not alone....

In 2007 we became aware of the need for an Australian support group for patients and families affected by Alport Syndrome, a genetic kidney disease. In August 2008 the Alport Foundation of Australia, a non-profit organisation, was formed.

Our goal is to raise awareness about Alport Syndrome, offer support to patients and families, and fund vital Australian research. We reach out across Australia through our website, social media, and brochures distributed hospitals and treatment centres.

We hope a greater number of people with Alport Syndrome will become aware of their condition years sooner than they might otherwise have been. This will not only give those people the opportunity to take health promotion steps to slow down their decline, but will also give them access to information on any emerging preventative treatments, under the guidance of our board which includes several eminent and highly qualified Australian clinicians and researchers.

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