Alport syndrome, COL4A3-related

What is Alport syndrome, COL4A3-related?

Alport syndrome, COL4A3-related, is an inherited disorder characterized by kidney disease, hearing loss, and eye abnormalities. Individuals with Alport syndrome, COL4A3-related, have a defect in the type IV collagen protein, which plays an important role in forming the complex protein networks that make up a large portion of the basement membranes that separate and support cells. When there is a deficiency in type IV collagen, other types of collagen may accumulate in the basement membranes of the kidneys, leading to kidney failure. Deficiency in type IV collagen can also lead to abnormalities of the inner ear and eye.

What are the symptoms of Alport syndrome, COL4A3-related, and what treatment is available?

Alport syndrome, COL4A3-related, is a disease with variable severity and age of onset. Symptoms may include:

- Progressive loss of kidney function
- Hematuria (blood in urine)
- Proteinuria (protein in urine)
- End-stage renal disease
- Sensorineural hearing loss, usually developing in late childhood or early adolescence
- Anterior lenticonus (misshapen lenses in the eye)
- Abnormal coloration of the retina

There is no cure for Alport syndrome. Treatment is supportive and may include medications, surgery for cataracts, and kidney transplant for end-stage renal disease.

How is Alport syndrome, COL4A3-related, inherited?

Alport syndrome is a disease that may be inherited in an X-linked, autosomal recessive, or autosomal dominant manner and can be caused by mutations in at least three different genes. One of these genes, COL4A3, can be inherited in an autosomal recessive or autosomal dominant manner. In autosomal recessive inheritance, an individual who inherits one copy of a COL4A3 gene mutation is a carrier. Carriers are not usually affected with Alport syndrome; however, some carriers may be at increased risk of developing a less severe condition called thin basement membrane neuropathy. An individual who inherits two COL4A3 mutations, one from each parent, is expected to be affected with Alport syndrome.

If both members of a couple are carriers of mutations in the same gene, the risk for an affected child is 25% in each pregnancy; therefore, it is especially important that the reproductive partner of a carrier be offered testing.

Who is at risk for Alport syndrome, COL4A3-related?

Alport syndrome, COL4A3-related, can occur in individuals of all races and ethnicities. The carrier frequency in the Ashkenazi Jewish population is estimated to be 1 in 183. Having a relative who is a carrier or who is affected can increase an individual’s risk to be a carrier. Consultation with a genetics health professional may be helpful in determining carrier risk and appropriate testing.

What does a positive test result mean?

If a gene mutation is identified, an individual should speak to a physician or genetics health professional about the implications of the result and appropriate testing for the reproductive partner and at-risk family members.

What does a negative test result mean?
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A negative result reduces, but does not eliminate, the possibility that an individual carries a gene mutation. The likelihood of being a carrier is also influenced by family history, medical symptoms, and other relevant test results.

Where can I get more information?

National Kidney Foundation: https://www.kidney.org/atoz/content/alport
Alport Syndrome Foundation: http://alportsyndrome.org/
National Organization for Rare Disorders: http://rarediseases.org/rare-diseases/alport-syndrome/

References