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CARRIER SCREEN

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.[1] 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.[2] 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.[2] Deficiency in type IV collagen can also lead to abnormalities of the inner ear and eye.[1,2]

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:[1,3]

- 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.[3]

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.[1] One of these genes, *COL4A3*, can be inherited in an autosomal recessive or autosomal dominant manner.[1,3,4] 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.[1] 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.[5]

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?

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

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