# Hereditary angiopathy with nephropathy, aneurysms, and muscle cramps syndrome

## Description

Hereditary angiopathy with nephropathy, aneurysms, and muscle cramps (HANAC) syndrome is part of a group of conditions called the *COL4A1*-related disorders. The conditions in this group have a range of signs and symptoms that involve fragile blood vessels. HANAC syndrome is characterized by angiopathy, which is a disorder of the blood vessels. In people with HANAC syndrome, angiopathy affects several parts of the body. The blood vessels as well as thin sheet-like structures called basement membranes that separate and support cells are weakened and more susceptible to breakage.

People with HANAC syndrome develop kidney disease (nephropathy). Fragile or damaged blood vessels or basement membranes in the kidneys can lead to blood in the urine (hematuria). Cysts can also form in one or both kidneys, and the cysts may grow larger over time.

Compared to other *COL4A1*-related disorders, the brain is only mildly affected in HANAC syndrome. People with this condition may have a bulge in one or multiple blood vessels in the brain (intracranial aneurysms). These aneurysms have the potential to burst, causing bleeding within the brain (hemorrhagic stroke). However, in people with HANAC syndrome, these aneurysms typically do not burst. About half of people with this condition also have leukoencephalopathy, which is a change in a type of brain tissue called white matter that can be seen with magnetic resonance imaging (MRI).

Muscle cramps experienced by most people with HANAC syndrome typically begin in early childhood. Any muscle may be affected, and cramps usually last from a few seconds to a few minutes, although in some cases they can last for several hours. Muscle cramps can be spontaneous or triggered by exercise.

Individuals with HANAC syndrome also experience a variety of eye problems. All individuals with this condition have arteries that twist and turn abnormally within the light-sensitive tissue at the back of the eyes (arterial retinal tortuosity). This blood vessel abnormality can cause episodes of bleeding within the eyes following any minor trauma to the eyes, leading to temporary vision loss. Other eye problems associated with HANAC syndrome include a clouding of the lens of the eye (cataract) and an abnormality called Axenfeld-Rieger anomaly. Axenfeld-Rieger anomaly is associated with various other eye abnormalities, including underdevelopment and eventual tearing

of the colored part of the eye (iris), and a pupil that is not in the center of the eye.

Rarely, affected individuals will have a condition called Raynaud phenomenon in which the blood vessels in the fingers and toes temporarily narrow, restricting blood flow to the fingertips and the ends of the toes. As a result, the skin around the affected area may turn white or blue for a brief period of time and the area may tingle or throb. Raynaud phenomenon is typically triggered by changes in temperature and usually causes no long term damage.

## Frequency

HANAC syndrome is a rare condition, although the exact prevalence is unknown. At least six affected families have been described in the scientific literature.

## Causes

Mutations in the *COL4A1* gene cause HANAC syndrome. The *COL4A1* gene provides instructions for making one component of a protein called type IV collagen. Type IV collagen molecules attach to each other to form complex protein networks. These protein networks are the main component of basement membranes, which are thin sheet-like structures that separate and support cells in many tissues. Type IV collagen networks play an important role in the basement membranes in virtually all tissues throughout the body, particularly the basement membranes surrounding the body's blood vessels (vasculature).

The *COL4A1* gene mutations that cause HANAC syndrome result in the production of a protein that disrupts the structure of type IV collagen. As a result, type IV collagen molecules cannot attach to each other to form the protein networks in basement membranes. Basement membranes without these networks are unstable, leading to weakening of the tissues that they surround. In people with HANAC syndrome, the vasculature and other tissues within the kidneys, brain, muscles, eyes, and throughout the body weaken.

Learn more about the gene associated with Hereditary angiopathy with nephropathy, aneurysms, and muscle cramps syndrome

- COL4A1

## Inheritance

This condition is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder.

## Other Names for This Condition

- Autosomal dominant familial hematuria, retinal arteriolar tortuosity, contractures
- HANAC

- HANAC syndrome
- Hereditary angiopathy with nephropathy, aneurysm, and muscle cramps syndrome

## Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Autosomal dominant familial hematuria-retinal arteriolar tortuosity-contractures syndrome (https://www.ncbi.nlm.nih.gov/gtr/conditions/C2673195/)

Genetic and Rare Diseases Information Center

- HANAC syndrome (https://rarediseases.info.nih.gov/diseases/10889/index)

Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD) (https://rarediseases.org/)

Catalog of Genes and Diseases from OMIM

- ANGIOPATHY, HEREDITARY, WITH NEPHROPATHY, ANEURYSMS, AND MUSCLE CRAMPS; HANAC (https://omim.org/entry/611773)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28hanac%5BTIAB%5D%29+OR+%28hanac+syndrome%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D)

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**Last updated September 1, 2011**