

## TESTING

**MRI:** A magnetic resonance scan (MRI) is usually performed and shows characteristic appearances with abnormalities in the deeper parts of the brain or white matter. This is a safe scan that involves no radiation but some people find it rather claustrophobic. This scan may be repeated to determine whether the disease is progressing. **A MRI Scan cannot diagnose CADASIL alone.**

**Blood Tests:** Detects mutations in the Notch3 gene. Only a small amount of blood, which can be taken from a vein is needed for this genetic tests. There are over 100 mutations known.

**Skin Biopsy:** CADASIL results in characteristic changes in the blood vessels. A very small skin biopsy is easily performed under local anesthetic. It is important this is processed in a special way allowing it to be looked at under high magnification using an electron microscope. Under this magnification, one can frequently see abnormal collections of material, which we call GOM (granular osmiophilic material) as shown by the arrows in the figures. If these GOM are present we can be almost certain that the individual does have CADASIL. However, the skin biopsy can be normal.

SPINAL TAP **DOES NOT** DIAGNOSE CADASIL. CADASIL DOES NOT INVOLVE THE SPINAL CORD OR OPTIC NERVE AS IN M.S.

## 50% HEREDITARY

CADASIL is passed as a dominant mutation and offspring have a 50% chance of developing the disease. All mutation carriers develop some form of the illness (complete penetrance) though the timing and severity and symptoms may vary in family members with the same mutation. Women with CADASIL live longer than men on average. So there are other genetic and environmental factors, yet to be identified, that modulate gene expression. A de novo mutations (A de novo mutation is a new mutation) can rarely occur in exceptional isolated cases without a prior family mutation.

## VISIT OUR WEBSITE

Our website index includes newsletters, professional healthcare page, fact sheets, emergency plans, confirmed cases from all around the world, understanding genetics, news articles, symptoms, testing sites, website links and much more.  
[www.cadasilfoundation.org](http://www.cadasilfoundation.org)

## SIGN OUR REGISTRY

We are the only known site that holds the most comprehensive registry of affected individuals and families with CADASIL. Every number counts..... If you or someone in your family has CADASIL, please sign our registry with complete accurate information and make your numbers known. If you provide us with your mailing address during registration we will be glad to mail you a welcome information packet. All information provided to us is kept strictly confidential! We do not require membership to join the foundation.

## JOIN THE DISCUSSION GROUP

You are invited to sign up for the Forum. The e-mail Discussion Group Lists allows people to communicate on their own time concerning CADASIL issues. We will periodically send out announcements about key information via the Discussion Group List. To join the announcements and discussion group you simply send us an e-mail with a brief introduction of yourself to:  
[discuss-on@cadasilfoundation.org](mailto:discuss-on@cadasilfoundation.org).

## HISTORY OF THE FOUNDATION

In 1997, a website was developed for CADASIL in hopes of assisting others with CADASIL and a central location was created on the website for information. On May 10, 2005 CADASIL Together We Have Hope was recognized by the I.R.S. as a 501 (c)(3) Charitable Organization. Donations to CADASIL Together We Have Hope are tax deductible. We do not have any paid staff. If you would like to volunteer or make a donation you can e-mail us at [info@cadasilfoundation.org](mailto:info@cadasilfoundation.org).

# Understanding

**C** - Cerebral  
**A** - Autosomal  
**D** - Dominant  
**A** - Arteriopathy with  
**S** - Sub-cortical  
**I** - Infarcts and  
**L** - Leukoencephalopathy

**What is CADASIL?**



**How is it diagnosed?**

**What are the symptoms?**

**CADASIL TOGETHER WE  
HAVE HOPE**

[www.cadasilfoundation.org](http://www.cadasilfoundation.org)  
**e-mail: [info@cadasilfoundation.org](mailto:info@cadasilfoundation.org)**

**OUR MISSION:** We are devoted in promoting awareness, support and research for this rare genetic disease for CADASIL patients, families, friends and healthcare providers. Creating a communication network among families and identifying sources of medical care and social services.

**You are welcome to copy this brochure and pass this on to your doctors, friends and family. Its intent is to help others who might have CADASIL or inform medical staff about CADASIL.**

## WHAT DOES THE NAME CADASIL MEAN

Cerebral is relating to the brain or cerebrum.

**Autosomal** - inheritance means that the gene is located on one of the autosomes (chromosome pairs 1 through 22). This means that males and females are equally affected.

**Dominant** means that only one gene is necessary to have the trait. When a parent has a dominant trait, there is a 50 percent chance that any child they have will also inherit the trait.

**Subcortical**—the portion of the brain immediately below the cerebral cortex.

**Infarcts**—An area of tissue that undergoes necrosis as a result of obstruction of local blood supply, as by a thrombus or embolus.

**Leukoencephalopathy** - the destruction of the myelin sheaths that cover nerve fibers. These sheaths, composed of lipoprotein layers, promote the transmission of a neural impulse along an axon

## WHAT IS CADASIL?

CADASIL is a hereditary disease affecting small and medium-sized arteries, predominantly in the brain. Progressive blood vessel damage reduces the blood flow and causes oxygen deficiency and subsequent tissue death (infarction). The symptoms of brain infarct, commonly referred to stroke like symptoms, migraines with or without aura, speech problems, and cognitive impairment and depression. The disease is caused by a mutation (a defect) in *NOTCH3*, a gene located on chromosome 19. So far, over 130 different mutations causing the disorder have been identified. *NOTCH3* plays an important role during fetal development as it regulates the formation of different kinds of tissues, for example smooth muscle in the arteriolar wall. The function of the gene later in life is still unknown. CADASIL symptoms result from changes in the arteriolar wall. Cells in the smooth muscle layer of the arteriolar walls gradually degenerate, and are replaced by connective tissue. As a consequence the arteries thicken and become more rigid, resulting in decreased blood flow and ischemia. CADASIL typically affects small branches of long arteries penetrating deep into the white matter of the

The long arteries have few branches and the obstruction of a branch causes restricted blood flow and oxygen deficiency. As a consequence, small lacunar infarcts (diameter less than 20mm) develop in the white matter and in deep parts of the grey matter (the basal ganglia). Infarctions deep in the brain are often more serious than blood vessel infarctions in the cerebral cortex. This is because many blood vessels supply the outermost layer of grey brain matter with blood. Infarcts in this area are less likely to deprive the brain of oxygen and less damage results. Ref: <http://www.sos.se/smkh/2006-110-10/2006-110-10.htm#Avsnitt1>

## WHAT ARE THE SYMPTOMS

The symptoms differ from patient to patient. In CADASIL patients can experience **migraines** with or without aura. Aura can mean signs and symptoms that a headache is coming on. The aura is sometimes severe, involving symptoms such as arm and/or leg weakness, visual disturbances, slurred speech and aphasia. Anxiety, sleeping problems, loss of appetite, fatigue and other signs of depression occur.

A **TIA** is a reversible episode of oxygen depletion. The attacks are caused by blood clots that dissolve before oxygen deficiency has caused permanent brain damage. The symptoms are similar to stroke, but are relieved within a few hours. The most common symptom of **minor stroke** is mild paresis or numbness in the arm or leg on one side of the body. The condition usually improves within a few days. People who have suffered from a minor stroke may experience speech difficulties, particularly if they are fatigued. Temporary episodes of memory loss or other cognitive problems sometimes occur.

**Stroke** is a term for brain hemorrhage and brain infarction. If a brain artery is blocked, for instance by a blood clot, the flow of oxygen-saturated blood to a large number of nerve cells is obstructed. After only a few minutes, the cells are irreparably damaged, a condition known as brain infarct. CADASIL patients can have two or three strokes during a lifetime, but the variation is considerable. Some people are never affected by stroke, others have as many as 10. Motor function remains relatively in

-tact for several years. The ability to take initiatives, make plans and solve problems is slowly weakened. Memory loss usually does not occur until a late stage of the disease. **Dementia** is a slowly progressive condition. In CADASIL, the dementia is of a frontal subcortical type, meaning that the deep parts of the frontal lobe are particularly affected. Episodic memory (memory of events) remains fairly well preserved in this type of dementia, but the ability to recall facts and concepts is impaired. Symptoms and the degree of disability vary a great deal, even among people in the same family. The reason why some individuals develop a more severe form of the disease is still unknown. **People with CADASIL manage their daily lives for a long time despite having suffered several strokes, concentration problems may arise, and the ability to think clearly declines.** Please note: other symptoms may occur which were not listed in this brochure.

**LONG TERM MANAGEMENT** CADASIL has no known treatment so far or no cure. CADASIL tends to progress slowly. However, many aspects of CADASIL can be treated effectively by treating the symptoms with medicines, etc. Asymptomatic CADASIL patient should have a low dosage of aspirin and a patient with a history of TIA's or stroke could be given a higher dose of aspirin per day. It is recommended to take coated aspirin between 75 mg to 325 mg..

## IT IS RECOMMENDED NOT TO TAKE:

Warfarin (coumadin), TPA, Thrombolytic and anticoagulant treatments, Arteriography, Vasoconstricting medicines (issued from rye ergot or from Triproptan) and products aimed at unblocking blood vessels or dissolve blood clots as they increase the risk of a hemorrhage or have a risk of bleeding in the brain. Triptans to treat migraines should also be avoided because the increase of the risk of stroke. The contraceptive pill is also a risk factor. If possible, women should stop using the pill or, if necessary, switch preparation having a lower estrogen content (estrogen content less than 50 mg). (<http://www.memorydisorder.org>)