

## TESTING FOR CADASIL

### GENETIC TEST

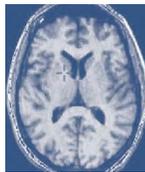
This test is the most popular to confirm CADASIL. It detects mutations in the NOTCH3 gene. Only a small amount of blood, which can be taken from a vein, is needed for this genetic test.

### SKIN BIOPSY

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). If these GOM are present, we can be almost certain that the individual does have CADASIL. However, the skin biopsy can be negative.

### A MRI Alone Cannot Confirm CADASIL

The magnetic resonance scan (MRI) is usually performed and shows characteristic appearances with abnormalities in the deeper parts of the brain or white matter, particularly in the temporal lobe poles. This can be repeated to determine whether the disease is progressing.



### A SPINAL TAP is not actually useful for diagnosis.

*It is important for you to know that there is nothing that you or your family did that caused you to inherit the CADASIL gene. We have no control over the genes we inherit, just as we have no control over the genes we pass on to our own children.*

### LEARN MORE



The information provided in the brochure is designed to complement, not replace, the relationship between a patient and his/her own physician.

## PROFESSIONALS

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## RESOURCES



CADASIL Together We Have Hope Non-Profit Organization was established on May 10, 2005 as a non-profit organization. We are devoted to promoting awareness, education, support, and research for patients, families, friends, and health care providers. We are dedicated to enhancing the established communication network among families as well as identifying sources of medical care and social services. We foster advocacy and open communication among all stakeholders as we work collaboratively to find a treatment or cure. 3605 Monument Drive, Round Rock, TX 78681 512-255-0209 or 1-877-519-HOPE [www.cadasilfoundation.org](http://www.cadasilfoundation.org)



CADASIL France Organization was established in 1999. Their mission is to provide support and information to patients and their families, as well as promoting clinical and medical research. CADASIL France works closely with CERVCO a reference center for CADASIL in Paris, France. [www.cadasil.com](http://www.cadasil.com)  
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## UNDERSTANDING CADASIL



**Cerebral - brain**  
**Autosomal**  
**Dominant – pattern of inheritance**  
**Arteriopathy – disorder of blood vessels**  
**Subcortical - below surface of brain**  
**Infarcts – type of small strokes**  
**Leukoencephalopathy - destruction of white matter**

**Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy** is a genetic disease affecting the small blood vessels of the brain. It leads to a poor irrigation of certain areas of the brain which causes symptoms that vary from person to person. CADASIL affects just as many men as women. This disease is caused by an anomaly (mutation) of one single gene, called Notch3, found on chromosome 19. This gene plays a part in the formation of the blood vessels and the way they work. Its mutation has an impact on the movement of blood inside the brain. So far, over 150 different mutations causing the disorder have been identified. NOTCH3 plays an important role during foetal 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. 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. The exchange of nutrients between blood and tissue is also disturbed. CADASIL typically affects small branches of long arteries penetrating deep into the white matter of the brain. 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). This is because many blood vessels supply the outermost layer of grey brain matter. Infarcts in this area are less likely to deprive the brain of oxygen and less damage results.

The current term Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy (CADASIL) was named in 1993. The disease was previously known as hereditary multi-infarct dementia. In the 1990s, it was shown to be caused by mutations in the NOTCH3 gene. The disease was possibly first described by the neurologist Van Bogaert in 1955.

## HEREDITARY

This is a hereditary familial disease. Its transmission is autosomal dominant, which means that a person already affected by the disease has a 50 percent chance of passing the abnormal gene on to his or her children. In a few known exceptional cases, the mutation of the Notch3 gene has occurred randomly ("de novo mutation"), without having been transmitted by one of the parents.

## SYMPTOMS

**MIGRAINE** like headaches are seen in approximately 40% of patients with CADASIL. Most often, the aura is visual and includes a fleeting visual disturbance that takes place prior to the onset of the headache. Migraine with aura can be the first sign of the disorder in about half of the cases. Severe migraine with aura may be difficult to distinguish from TIA's (transient attacks). Most CADASIL patients (85%) are affected by TIA's or minor strokes.

**TRANSIENT ISCHEMIC ATTACK (TIA)** is a reversible episode of oxygen depletion. The attacks are caused by the occlusion of a small artery leading to oxygen deficiency that can cause 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.

Patients who have suffered from a **MINOR STROKE** may experience speech difficulties, temporary episodes of memory loss or other cognitive problems sometimes occur.

**STROKE** is a term for brain hemorrhage and brain infarction. A stroke occurs when a blood vessel that carries oxygen and nutrients to the brain is either blocked by a clot or bursts (or ruptures). When that happens, part of the brain cannot get the blood (and oxygen) it needs, so it and brain cells die. After only a few minutes, the cells are irreparably damaged, a condition known as brain infarct. CADASIL is slowly progressive and around half of all individuals with the disease will suffer several TIAs or strokes. The average patient has two or three significant strokes during a lifetime, but the number of strokes can vary considerably.

In the vast majority of cases, patients affected patients will present with ischemic episodes, cognitive defects, migraine like headaches or psychiatric disturbances. The onset and severity of these symptoms is highly variable, even within families. Cognitive function worsens slowly over time, there is variability in the onset and severity of cognitive impairment. Patients demonstrate dementia in presence of severe loss of cognitive function. Seizures, although rare, has been observed in affected individuals. Other symptoms may include speech defects. The overall course of CADASIL is variable. Early onset of symptoms does not necessarily mean that the disorder will progress rapidly. 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 are not listed in this brochure.

## MEDICINES AND PROCEDURES TO AVOID

It is important to tell the doctors you have CADASIL so that certain treatments or tests can be avoided.

**\*Avoid Thrombolytics and Anticoagulant Treatments**, which aim at unblocking blood vessels as they increase the risk of a cerebral hemorrhage.

**\*Avoid Vasoconstricting Medicines (issued from rye ergot or from Triptan)** may increase the risk of cerebral infarction.

**\*Avoid Cerebral conventional angiographies (contrast agent within the arteries in the brain for examination of the cerebral vasculature)** should be avoided because of potential neurological complications (migraine with extended and severe aura)

**\*Using Anesthesia must be monitored** as it could cause abrupt changes in blood pressure.

Finally, you must tell the medical teams about current medications and the corresponding doses. This is a precaution so as to avoid the combinations of incompatible medication and any risk of overdose.

## LONG TERM MANAGEMENT

Supportive care is needed. At present, there is no treatment either to cure or to prevent the evolution of the disease. A healthy lifestyle and the treatment of individual symptoms as they appear can improve the quality of life of sufferers. Smoking is an established risk factor in this disease.

ClinicalTrials.gov is a listing of federally and privately supported clinical trials conducted in the U.S.A and around the world. The website is a searchable database, that provides patients, family members and the public with information about current and past clinical research studies on safe and effective medication and therapies.  
<https://clinicaltrials.gov/>