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
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). 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 (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.

REFERENCES
CERVO, Paris, France
Genetics Home Reference, U.S.A.
National Board of Health & Welfare, Sweden
National Institute of Health, U.S.A.
University of Newcastle, England

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

Cadusil Together We Have Hope Nonprofit Organization
CTWHH is devoted to promoting awareness, providing education and support to patients and families affected by the disease, as well as advocating for greater research. CTWHH continues to work collegially with various CADASIL organizations, doctors, researchers, and groups to ensure the channels of communication are kept open among all stakeholders to find a treatment or cure. Our Scientific Advisory Committee is comprised of CADASIL specialists from America, Canada, France, and the United Kingdom. We are a 501(c)(3) nonprofit and donations are tax deductible. We have no paid staff, no membership, and depend solely on donations. www.cadasilfoundation.org
512-255-0209 or 1-877-519-HOPE

Cadusil France is a nonprofit organization devoted to informing, comforting, and supporting individuals concerned with the CADASIL genetic rare disease and their families. 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 e-mail: info@cadasil.com

The United Leukodystrophy Foundation (ULF) The ULF is dedicated to helping children and adults who have Leukodystrophy and assisting the family members, professionals, and support services that serve them. www.ulf.org e-mail: office@ulf.org
You are not Alone!
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, was shown to be caused by mutations in the NOTCH3 gene. The disease was possibly first described by the neurologist Van Bogaert in 1955.

**HEREDITY**

CADASIL 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. *Please remember 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.* 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 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 headaches may be difficult to distinguish from TIA’s (*transient ischemic attacks*). TIAs or minor strokes affect most CADASIL patients (85 per cent). *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 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, 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 destructed. 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 CADASIL patient has two or three significant strokes during a lifetime, but the variation is considerable. In the vast majority of cases, patients affected with CADASIL will present with ischemic episodes, cognitive defects, migraine, or psychiatric disturbances. The onset and severity of these symptoms is highly variable, even within families. In CADASIL, 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.

**LONG TERM MANAGEMENT**

Unfortunately at this time there are no interventions that can effectively prevent the course of CADASIL or its clinical manifestations. Certain signs and symptoms can be treated, as they appear - headaches, migraines, dementia, etc. Supportive care is needed.

**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 and Vasocostricting Medicines (issued from rye ergot or from Triptan) may increase the risk of cerebral infarction.

* 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.

**RESEARCH STUDIES**

Further research of CADASIL or studies are crucial to providing a treatment or cure for better quality of life. Keep abreast of the latest research projects by searching the worldwide web or go to www.cadasilfoundation.org, www.cervo.fr/pathologies/cadasil1.html, or www.ulf.org. "LEARNING MORE ABOUT CADASIL"

Go to our website at www.cadasilfoundation.org

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

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