What is CADASIL?

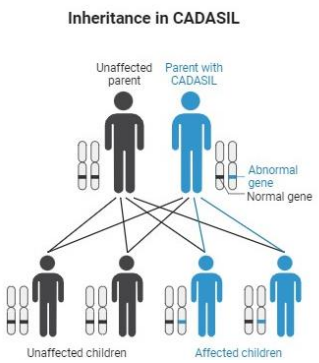
CADASIL is a rare, genetic form of small vessel disease. CADASIL stands for:

- **Cerebral** meaning related to the brain
- **Autosomal Dominant** meaning the type of inheritance, described below
- **Arteriopathy** meaning damage to blood vessels
- **Subcortical** meaning the internal part of the brain
- **Infarcts and Leukoencephalopathy** referring to strokes and other vascular brain injury in the deep brain

What is a genetic disease?

A genetic disease means that some, or all, of the risk of getting the disease is passed down from one's parents. This may be due to a combination of genes or, as in CADASIL, may be driven by a single gene. Only one of the two copies of this gene needs to be changed to cause disease. This is termed autosomal dominant, as the abnormal gene dominates over the normal gene.

Just because you have CADASIL does not necessarily mean you will pass this on to your children. There is a 50% chance they will inherit the copy of the gene.



What causes CADASIL?

CADASIL is caused by an abnormality in the NOTCH3 gene which is located on chromosome 19. This gene is involved in making a protein, also called NOTCH3, which is important for health of small blood vessels in the brain.

Exactly how the abnormality in the NOTCH3 gene causes CADASIL is still being researched. However, we know that patients with CADASIL have progressive damage to small blood vessels, particularly in the brain, and this leads to less blood flow and poorer regulation of blood flow.

How Does CADASIL present?

Strokes

Most people with CADASIL will have at least one stroke in their lifetime. These strokes are usually small, and individuals tend to recover well. In some cases, the stroke may be so small that the individual doesn't notice any changes, and this is only discovered by checking brain scans.

CADASIL strokes often arise early in the disease, in a patient's 30s-50s, but not everyone's CADASIL journey is the same.

Migraines

Migraines are present in approximately 1/3 of people with CADASIL and usually arise early in disease progression.

These are complex migraines, with headaches usually accompanied by 'aura' which involves visual changes, numbness of hands and/or feet and changes to speech.

The migraine frequency varies, however often family members will have similar experiences as each other.

Cognitive Impairment

Cognition is a term for mental processes, that is thinking, understanding, and remembering. During CADASIL, most patients will develop some level of cognitive impairment, which may progress to vascular dementia. Most patients who have cognitive impairment have difficulties with processing speed, attention, and focus.

This cognitive impairment is typically identified in the 40s and 50s; however, it tends to worsen with age and greater disease severity.

Mood Changes

Anxiety and depression are common after strokes. However, these features can also arise before any other CADASIL symptoms, in addition to hallucinations, delusions and changes to perception.

Seizures

Less commonly, individuals may experience seizures, or fits, which may be accompanied by confusion lasting up to a few days.

There's a possibility I have CADASIL, what happens now?

If you have a family history of CADASIL or you are starting to show some of the early symptoms, your doctor will run some tests to confirm if you have CADASIL. This will likely include:

Brain Scan

A brain scan, usually magnetic resonance imaging (MRI), shows the health of the deep areas of the brain and is useful for diagnosis and monitoring. MRI scans can show if you have had a bleed, if there is loss of neuronal connections or if there is a change to fluid drainage in the brain.

MRI scans use magnets, not radiation, to create images. They are generally safe, but some people find the experience claustrophobic or may be ineligible for other reasons.

Genetic Testing

A sample of blood can be tested to see if there is an abnormality in the *NOTCH3* gene, suggesting a patient may have CADASIL even if they have not yet developed any major symptoms.

If an individual has CADASIL, their family members may like to get tested. A decision to test for a genetic disorder is significant and can be confronting, so it is important that this decision is made with time, discussions with your doctor and with genetic counsellors who can explain any implications of having this test.

Skin biopsy

These days, skin biopsy is only performed when genetic testing is negative or inconclusive and diagnosis is uncertain. This process involves obtaining a small sample of skin to look at the blood vessels in the laboratory. This test can show whether there is an accumulation of material indicative of CADASIL.

What are the treatment options?

There are no specific treatments for CADASIL yet. Instead, individuals are treated for the symptoms of the disease. This will vary depending on individual needs but may include medications to help prevent stroke, treat depression or reduce the effects of migraine.

Since CADASIL affects the small blood vessels, individuals should maintain a healthy lifestyle to reduce additional risk to the vascular system. This includes not smoking, reducing sugar intake, exercise and drinking adequate quantities of water.

Where do I go for more information?

https://cheba.unsw.edu.au/research-projects/vascular-contributions-dementia-centre-research-excellence/auscadasil is a reliable source of information for patients and relatives. If you are worried about your risk of CADASIL, speak to your doctor or genetic counsellor.

AusCADASIL

This leaflet is designed to be a resource for family members, carers, or supporters of CADASIL.

The AusCADASIL study aims to study the progression and impact of CADASIL in an Australian cohort.

For more information about the study and details on participation see QR code or contact Dr Danit Saks:

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