

## **CADASIL: Clinical Q&A**

### **Why are some people well with CADASIL until their seventies whereas others present with symptoms much earlier?**

The severity of CADASIL can vary widely within families. For example, within one family one member may have strokes in their forties or fifties whilst another may still be well when they are seventy. We do not fully understand why this is the case. Our research has shown that common risk factors such as smoking and high blood pressure make stroke occur earlier in patients with CADASIL, but this does not fully account for the differences within families. Other unknown factors also contribute. There is some evidence that genes other than the NOTCH3 gene may alter the severity of the disease and we are carrying out research trying to identify which these genes are.

### **How do I distinguish between a migraine attack and a TIA/mini stroke?**

Migraine attacks are usually accompanied by headache, a feeling of sickness, and often intolerance of bright light. In CADASIL migraine attacks are also usually accompanied by an aura. The aura can be visual (often bright or coloured lights), sensory (often a feeling of tingling), speech (often the inability to find words), confusion, and loss of power in an arm or leg.

Sometimes it can be difficult to distinguish an aura which can occur without headache, from a mini stroke. In a mini stroke in CADASIL the most common symptoms are loss of power down one side of the body, or loss of sensation down one side of the body. The abnormality tends to on at the same time in both the arm and leg. Visual symptoms and inability to find the right words do not occur in CADASIL stroke.

Sometimes loss of power and an abnormal sensation can be difficult to differentiate between TIA and migraine, but a helpful pointer is that the symptoms in migraine often occur in one part of the body (for example, the face) and then spread gradually to other parts (for example, the arm), whereas in stroke they all come on at the same time. Also migraine symptoms are often positive (e.g. a tingling) whereas in stroke symptoms are usually negative (e.g. an inability to feel).

### **Is one's gait affected in CADASIL as it progresses?**

Gait can be affected in CADASIL. If a CADASIL patient has a stroke then they can have a limp secondary to weakness. However, gait can occasionally be affected without a stroke in a syndrome called gait apraxia. This is where disruption of connections within the white matter in the brain alters the ability to coordinate one's walking. This can result in an unsteady and wide based gait or sometimes an abnormal gait due to small steps.

### **Should antiplatelet agents such as Aspirin be prescribed in CADASIL?**

Drugs such as Aspirin reduce the risk of recurrent stroke in people who have already had common stroke. We don't know whether they have a similar effect in CADASIL. Our policy is usually to recommend Aspirin or a similar antiplatelet drug called Clopidogrel (Plavix) in CADASIL patients who have suffered a stroke, or who are over age forty. However the evidence for this is not strong.

We would advise patients not to take both Aspirin and Clopidogrel because this combination is associated with an increased risk of bleeding into the brain in people with diseases of the small blood vessels in the brain. Similarly, we would advise against taking Warfarin or one

of the new oral anticoagulant drugs unless there is a good reason for it (such as atrial fibrillation).

### **Should statins be prescribed in CADASIL?**

Statins have been shown to reduce the risk of recurrent stroke in people with common stroke. The evidence that they work in stroke caused by disease of the small blood vessels in the brain is much less strong. There is no evidence to show whether they do, or don't, help in CADASIL. Because of their benefit in common stroke we tend to recommend taking statins in CADASIL if the cholesterol is elevated although the evidence for this is not strong.

### **What lifestyle changes can help with CADASIL?**

Because it has been shown that common cardiovascular risk factors such as smoking and high blood pressure worsen CADASIL we would recommend that a healthy lifestyle is adopted which reduces cardiovascular lifestyle factors. This includes maintaining a normal weight, having a healthy heart friendly diet (details of such a diet can be found on websites such as the British Heart Foundation), not smoking, and avoiding excessive alcohol.

Regular exercise reduces blood pressure and has also been shown to reduce the risk of common stroke. There is increasing evidence that regular exercise also protects the brain from cognitive decline and dementia and therefore we would strongly recommend this.

### **Are there any supplements that have been shown to help with CADASIL symptoms such as co-enzyme Q10, omega-3, L-arginine or B vitamins?**

There is no evidence that any of these supplements help in CADASIL. It was suggested that L-arginine might improve CADASIL and this could possibly increase the blood flow to the brain in people with CADASIL. However there is no evidence from clinical trials that this improves the outcome.

In people who have very elevated homocysteine levels we sometimes recommend reducing these with B vitamins and folic acid.

### **What happens after a diagnosis; should I have periodic reviews? If so, how frequently?**

This is up to you and patient preferences vary. If people with a CADASIL diagnosis remain well we often review them, and this can be by telemedicine, on a yearly basis. If they are having problems we would review them more frequently. However, some people who have had a CADASIL gene diagnosis but remain well prefer not to be seen and to just get on with their life. This is an equally reasonable option. If this is the case it is important that you occasionally have your blood pressure checked by your GP and continue to practice a healthy lifestyle.

### **In what way is CADASIL dementia different from Alzheimer's disease?**

CADASIL can cause cognitive problems and dementia by damaging the white matter in the brain through which pathways run connecting different regions of the brain. It therefore causes what we call a "disconnection syndrome" in which complex networks in the brain are disrupted. This tends to produce symptoms such as slowing of brain processes, and also difficulty in planning or multi-tasking. Sometimes attention is also affected. Memory problems can occur but are not such a prominent early feature of the disease.

In contrast, Alzheimer's disease affects the cortex (outer surface) of the brain and tends to produce prominent memory and orientation problems earlier in the disease.

### **Can CADASIL affect Libido?**

Many diseases including CADASIL can affect libido when the disease becomes severe. Libido can also be greatly affected by psychological consequences of disease such as anxiety and depression. Therefore if you suffer from this symptom it is worth asking your doctor because if it is due to anxiety or depression treating this can improve libido.

### **Can CADASIL cause problems in children?**

Occasionally children with CADASIL can develop migraine, but migraine is common in children and young adults anyway. Other than this CADASIL does not produce problems in children.

### **Can CADASIL alter personality?**

Sometimes the cognitive problems in CADASIL can result in an apparent alteration in personality. It can make the sufferer lose motivation and interest in their previous activities; this is called apathy. Sometimes they can make the sufferer appear less tolerant and become angry more easily. These symptoms can be distressing for both the CADASIL patient and their family. Similar symptoms can also be produced by depression and therefore it is important to ask your doctor if they could be due to depression because this can respond to treatment.