

June 2007

CADASIL

Newsletter - June 2007

CADASIL support group www.cadasil.org.uk

Special points of interest:

- Information about some new research projects
- Three peaks fundraising for CADASIL
- Raising awareness

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Our first newsletter

Welcome to our first newsletter for CADASIL patients and their families.

Our intention is to provide information and any news about CADASIL.

It's always difficult knowing what to put in newsletters, but if there is something you would like to see in future issues—please let us know.

Many CADASIL people feel quite alone with this illness. But there are others out there, more than you might think.

There is also a website, www.cadasil.org.uk which has further information.

We are in the early stages of setting up a support group in the UK, but there are other support groups in other countries which have been running for some time.

For example, in the America, the CADASIL foundation has been set up by Billie Duncan-Smith and they have a website at www.cadasildoundation.org.

Snowdon



Mount Snowdon—one of the mountains in the 3 peaks challenge—see fundraising article.

France also has a group — which can be found at www.cadasil.com

CADASIL Research

We know that there is currently no cure or effective treatment for CADASIL, but there is ongoing research into understanding this genetic disease. This newsletter contains details of some of the research into CADASIL.

Given the aging of the UK population, and the increasing number of patients with Alzheimer, there is also a lot of money going into research into that area, which may prove beneficial to

CADASIL patients.

Research Update—Manchester University

A post-graduate research project is due to start in September 2007 for CADASIL.

This project is designed to clarify the Notch3 function in VSMCs and then to investigate the molecular mechanism that leads to CADASIL pathology.

Hopefully this will lead to insights into how

the genetic fault in CADASIL patients affects small arteries and how this affects disease progression.

Being able to influence the progression of the disease is possibly the most important thing CADASIL patients need, apart from an actual cure.

Research Update- Cleveland Clinic Foundation (USA)

Shu Liu is part way through a project on CADASIL which is due for completion early in 2008:

"In this study, we are particularly interested in understanding the potential interactions of Notch3 with two other genes"

This project is funded by the American heart foundation. This recognises the fact that many CADASIL patients have heart problems associated with this disease.

"Being able to influence the progression of the disease is possibly the most important thing CADASIL patients need, apart from an actual cure."

Other research in the UK

- Dr Muir at Glasgow University has been researching blood pressure in relation to CADASIL. This project has now completed and we look forward to seeing the research results.
- Prof Kalaria at Newcastle University is working on the pathogenesis of CADASIL, particularly how mutations in the NOTCH3 gene cause blood vessel wall degeneration."

We need more research into CADASIL as the amount of funding is currently far too low. It is generally recognised that CADASIL is under-diagnosed in the UK.

CADASIL is unusual in that researchers have successfully pinned the illnesses down to a single defect in a gene. We would have thought that this makes it an ideal candidate for attempts at gene therapy compared with illnesses caused by multi-gene faults.

Please consider writing to your local MP to try and get a reasonable level of funding into research. Due to the long-term nature of CADASIL, patients will need a significant amount of health care, so there are sound financial reasons for trying to find a treatment for CADASIL.

CADASIL management—Prof RN Kalaria

CADASIL and current strategy on management

Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) is the most common form of hereditary small vessel disease of the brain. Recent work from several groups including ours at the Institute for Ageing and Health suggest that there are now more than 600 families worldwide with CADASIL. It appears that nearly 1 in 2 of CADASIL sufferers will have migraine attacks with aura. The long-term prognosis for disability and death is worse for men than women. Smoking and raised systolic blood pressure worsen outcome. Therefore, it is wise to control factors that will increase or put a patient at risk for cardiovascular disease or increase blood pressure. Smoking should be stopped and if hypertension persists it can be lowered by taking appropriate blood pressure medication. The regular use of statins (cholesterol lowering drugs) is not a bad idea if CADASIL patients have high risk factors for vascular disease or high cholesterol. However, under no circumstances are use of anticoagulants and thrombolytic agents advocated. Until further advances are realised use of low doses of aspirin seems best at present. Coated aspirin also has the advantage of being associated with the least number of complications. The dose of aspirin most currently evaluated in therapeutic trials is between 75 mg to 325mg per day.

Some patients with CADASIL will suffer seizures or depression. Epileptic seizures and depressive illness can be treated with conventional prescription drugs. However, it should be noted that some agents such as triptans (e.g. sumatriptan, rizatriptan) for migraine may increase risk of stroke. Measures that increase vascular perfusion such as use of oral L-arginine, a nitric oxide substrate which promotes vasodilation could be beneficial. Patients with MELAS (for mitochondrial myopathy, encephalopathy, lactic acidosis and stroke), a progressive neurodegenerative disorder, administered L-arginine intravenously at the acute phase or orally at the initial phase significantly improved all stroke-like symptoms.¹ Furthermore, two years of supplementation with oral L-arginine significantly improved blood vessel (endothelial) dysfunction for treating stroke-like episodes in MELAS. Certain nuts and meat are rich in L-arginine, which can also be obtained from health food stores. In addition to medication, physical and supportive measures including practical aid, emotional support, speech and occupational therapy and counselling should be encouraged where appropriate for affected individuals and their families.

¹ Koga Y, Akita Y, Nishioka J et al. L-arginine improves the symptoms of strokelike episodes in MELAS. *Neurology*. 2005;64:710-712

*Contributed by Prof RN Kalaria
Institute for Ageing and Health
Newcastle General Hospital*

Fundraising—Three Peaks challenge

Three adventurous souls are embarking on the three peaks challenge in June 2007.

The challenge involves climbing three mountains in 3 days.

The three fundraisers have been in hard training for the past months.

We will let you know how they get on.....

Part of the funds for this challenge will be donated to CADASIL research.



Scafell Pike

Fundraising - Drumalane support trust

THE year 2004 will always be fresh in the memories of Margaret Ruddy and her family from Drumalane Park.(Belfast) It was then that she was first told that her devoted husband and father Gerry was diagnosed with Cadasil. This was traumatic news as little or nothing was known about the illness at the time and the information they were given failed to enlighten them.

Gerry's family decided to do some research of their own into the causes of the illness and as a result came across The Cadasil Research and Support Trust which was set up by fellow sufferer, 75-year-old Jack Shields from Newcastle upon Tyne. This proved a major asset to the family's lack of knowledge and gave them much needed comfort and support. The main aims of

the Trust are to increase awareness of Cadasil to provide information and support to sufferers and their families, to co-ordinate research into positive treatment and a possible cure and to develop a treatment centre for sufferers. They also are trying to get the medical establishment to do more research into the illness.

In order to continue with this work they will need adequate funding. With this in mind the Ruddy family organised a fundraising event . This turned out to be a bigger success than was ever imagined.

*'This turned out to be a bigger success than ever imagined..'
The Drumalane fundraising event.*

Fundraising and donations

If you know of any other fundraising events, please let us know so that we can include them in future newsletters.

For donations, it is probably best to donate to the hospitals involved in CADASIL research—i.e. those departments which Dr Muir (Glasgow) and Prof Markus (London) are responsible for.

Raising Awareness of CADASIL

A member of the support group from Sheffield recently contacted the stroke association to try and raise awareness. An extract of this thought provoking letter is included here. It might be worth other CADASIL people contacting the stroke association as well.

Dear Ms Warburton

CADASIL – an Article for Stroke News?

I enjoy reading Stroke News because it is always interesting and topical. However, as far as I am aware, there has never been an article about CADASIL, a vascular disease which, I am sure, would be of interest and concern to many of your readers.

CADASIL is an acronym and stands for Cerebral Autosomal Dominant Arteriopathy with Sub cortical Infarcts and Leucoencephalopathy. The disease usually presents itself with multiple small strokes but migraine is also a prominent feature. Individuals also suffer from anxiety and depression. Many sufferers (like me) are incorrectly diagnosed initially with Multiple Sclerosis because many of the symptoms are the same.

CADASIL usually presents itself in early middle age and progresses slowly, but recurrent strokes can lead to persistent disability, and, eventually, vascular dementia. The strokes

are lacunar strokes. Unfortunately, very few Consultant Neurologists know much about this disease and hardly any GPs have even heard of it. Thus sufferers are either diagnosed incorrectly, late in the progress of the disease, or perhaps not at all. To date, there is only very limited treatment centred around lowering blood pressure and cholesterol levels.

Sadly, this disease is genetic. It is a disease of families, not just individuals. Each child of a sufferer has a 50:50 chance of inheriting the faulty Notch 3 gene. There are about 200 families in Great Britain with CADASIL, and it is found in many other countries too. For example, doctors in the USA and in Germany are researching it. I think it is about time the medical world paid some serious attention to researching possible methods of treatment and an eventual cure for this tragic disease. Any publicity your publication could give sufferers would be very welcome.

So would you consider publishing an article on this disease?

‘Many sufferers (like me) are incorrectly diagnosed initially with Multiple Sclerosis because many of the symptoms are the same.’

Raising Awareness—what else can we do?

- We are trying to get links added to websites and discussion forums.
- It might be worth contacting your local MP to ask about funding for CADASIL research.
- Consider writing (anonymously if required) to your local newspapers to highlight some of the problems you have found in dealing with authorities.
- Please let us know of any other suggestions!

CADASIL support group *www.cadasil.org.uk*

We are people trying to help others with CADASIL.

There is more strength in numbers, please join us. You do not have to make any commitment.

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CADASIL needs a cure

WE ARE ON THE WEB
WWW.CADASIL.ORG.UK

In the next issue (Autumn 2007).....

- *Hopefully an update from the CADASIL update session at the VasCog 2007 conference (www.vas-cog.org/vas-cog2007) in San Antonio...*
- Update on the three peaks challenge fundraiser.
- \$2 Million Research funding in USA
- CADASIL wallet information card
- Letters page (contributions appreciated)

In memory of my Mother

My mother died of CADASIL nearly a year ago. She had been ill for many years, but it was only in the final year or so that she became bedridden.

One of the things I will always remember is the way she used to smile when we used to visit. Even though so many awful things had happened to her, she always managed that beaming smile.

During the final days of her life, my Father agreed to the very difficult request to donate her brain to CADASIL research.

We had not discussed this before those final days and so it was very hard to ask my Father at such a sad time.

We arranged for the tissue donation to be done through the institute of Ageing and health at Newcastle.

My thanks to the people at the institute for the way in which they dealt with such a delicate issue.

I like to think that perhaps the donation might help others with CADASIL in the future. I know that is what she would have wanted.

Keep smiling mum, wherever you are...