

2000-2001 NEWSLETTERS

This information comes from a leaflet from the internet done by Hugh Markus. I have taken excerpt from it. Please go to there Website at for full details at:
<http://www.sghms.ac.uk/depts/cn/cad.html> (2001)

What causes CADASIL? We now know that CADASIL results from an abnormality in one very small part of the notch 3 gene. We think that the protein produced by the notch 3 genes, is responsible for communication between cells within the body, although much work is still required on this subject. As yet, we don't know why the abnormalities in the notch 3 gene in individuals with CADASIL, result in the disease. It is likely that it will take a number of years to fully understand the process. Although we don't fully understand the process, we do know that patients with CADASIL suffer from progressive damage within small blood vessels. This is likely to lead to both reduced blood flow and an inability of the blood vessels to regulate blood flow. Although abnormalities in blood vessels can be found throughout the body, they appear to be most severe in the brain, and only produce problems noticed by the person with CADASIL within the brain. We believe that the abnormalities within the brain result in reduced blood flow to certain parts of the brain.

What are the features of the disease? Almost all people with the disease will suffer from strokes. These most commonly first occur in the 30s or 40s although we are discovering that the disease can be very variable and in some people, no problems may occur until their 60s. The strokes are what we refer to as lacunar strokes (literally meaning a small lake or hole in the brain). Because they are small, they tend to be fairly mild and individuals often recover well. The most common type of stroke is weakness affecting one side of the body. If recurrent strokes occur, this can lead to some persistent disability, which is most usually weakness, or slurring of the speech. Migraine is another common feature of the disease. This most commonly starts in the 20s but the onset is variable. Quite frequently, this is what we call "complex" migraine. This means that in addition to the headache there are short-lived neurological symptoms, most commonly, some disturbance of vision.

Individuals with CADASIL can quite frequently suffer from anxiety or depression. Not surprisingly, depression is very frequent after any type of stroke and usually improves with time and treatment if necessary. However, occasionally, depression or anxiety may occur before any other symptoms of CADASIL. Rarely, seizures or epilepsy may occur as part of CADASIL, although this is present in less than one in twenty individuals with the disease. Over time, as the disease progresses, problems with memory may occur and if these become severe, they are likely to occur in the 50s or 60s. Recent studies show that the presentation of CADASIL is more variable than previously appreciated. While most sufferers experience the picture outlined above some individuals can remain stroke free until late there 60s or 70s . A small number of CADASIL sufferers may experience an encephalopathy illness characterized by a short period of impaired consciousness and neurological abnormalities that usually recovers after about 2 weeks.

Is there any treatment for CADASIL? There is no specific treatment for CADASIL available at the moment. In the long run, we hope that now that we know the underlying genetic abnormality, we will be able to discover exactly how this results in the blood vessel damage, and therefore design drugs to prevent this damage. However, this is likely to be a number of years away. Aspirin has been shown to reduce the risk of recurrent stroke by about a third, and most doctors would recommend that patients with CADASIL take a small dose of aspirin per day (75-300mg/day).. We feel that it's very important to prevent any other damage to the blood vessels. For this reason, it is important not to smoke, and that blood pressure and cholesterol are checked, and treated if abnormal. It is also advisable not to take the combined oral contraceptive pill.

If required during attacks of migraine, standard migraine painkillers can be taken. These include drugs such as migraleve. However, it is probably not advisable to take some of the newer anti-migraine drugs such as imigran, which act by reducing the blood flow to the brain.

Research at St. George's on CADASIL We are carrying out a study at St. George's to find out how common CADASIL is in the United Kingdom. This is funded by a grant from the National Health Service South Thames Region Research & Development. We regularly mail all neurologists and stroke doctors within the United Kingdom and follow up any cases, which they think could be CADASIL. By studying a large number of patients with CADASIL, we are hoping to answer many of the unresolved issues. These include things such as: why the disease can come on at different ages in different people, and why different people can suffer different types of disease. We are planning to see whether any treatments may delay the disease. Because CADASIL is a rare disease, and the disease progresses slowly, for such studies we need to have a method of accurately telling, as quickly as possible, whether any drug works. We have decided to do this using magnetic resonance scanning. We hope this will allow us to test whether drugs work over time period of about a year and we are currently developing the best imaging techniques. We will then look to see whether any particular drugs are likely to be beneficial in any individuals with CADASIL.

We may ask you whether you would be prepared to take part in these studies. If you are interested, we will explain the specific details of any individual study and it is always entirely up to you as to whether you take part. Before we plan any study, it is always approved by the local hospital ethics committee

How can I find out more information about CADASIL? Because CADASIL is a rare disease, and because much of the information on it is very new, it is quite difficult to find out information about CADASIL. As far as I know there are no books for the general public about CADASIL. There is an Internet site in the United States, which has been set up which is our Website OR Contact St. Georges Hospital **if you live in England**

www.sghms.ac.uk/depts/cn/cad.html

A little from Michelle's letter to let others know:

Hello, My name is Michelle my husband died from a biopsy on his brain.

My husband went in on April 6th and had his brain biopsy done as they did not know what he had only a white matter disease. After the surgery he had a seizure and was in intensive care for sixteen days. The day we left the hospital they took blood to test. It did come back positive after my husband died that he had CADASIL.

Two big things I have learned is this: think it over before allowing surgery on a disease-compromised brain. Then check out the hospital well. The post surgery room does not have working nurse call buttons. I was told the rooms had only one extra outlet (older portion of the hospital) and they decided to hook-up the televisions instead of the emergency buttons.

Thanks Michelle for letting other know.

CADASIL SUPPORT	
GROUP NEWSLETTER	
The unofficial CADASIL newsletter	Issue VII March 2001

CADASIL - Cerebral Autosomal dominant arteriopathy with sub cortical infarctions and Leukoencephalopathy Recently identified, CADASIL is a diffuse disease of small arteries predominating in the brain. It starts during mid adulthood and is characterized by recurrent ischemic events (transient or permanent), attacks of migraine with aura, severe mood disorders, sub cortical dementia and, at MRI, a white spread Leukoencephalopathy.

How did this newsletter began: February 1997, I looked up excessive white matter, anything from the results of MRI and CT scans. I went to Steve's Doctor and got copies of his files. I typed them out and copied them to a word-perfect file. I sent more than 300 E-mails out with my husbands' history and asked for help. I learned that sometimes you must be your own case manager to learn anything. I have hope for my husband and my family. I told my husband that each time I get on the computer and when I press the send button on an E-mail, that one day the hope is to find a cure for this nightmare. I developed a web site for CADASIL in hopes I could help others and find out more about this disease. Well, the response has been fantastic. This went from helping others to a support group link. No words could express the amount of thanks to everyone who has contributed to the web site and newsletters. Please remember "TOGETHER WE DO HAVE HOPE."

Please note this newsletter is long as the last newsletter was in September and I have tried to catch up on everything since then. Please read this newsletter at your own leisure and take one page at a time, as it can be very overwhelming. *TOGETHER WE DO HAVE HOPE – TESTS FOR CADASIL HERE IN THE USA AND CANADA.*

In the USA:

I have been contacted by the University of Pennsylvania Medical Center, Philadelphia,

PA 19104-4283, last week from David R. Lynch, M.D., PH. D. Dr. Lynch and his staff have developed a useful genetic blood test for CADASIL. Go to their web site at <http://www.med.upenn.edu/genetics/core-facs/gdl/staff.html>. Dr. Lynch is now in the process of having Steve's blood sent to PA for the final blood test to confirm CADASIL as in August of last year Steve had his blood sent to help with the test.

CANADA:

I was contacted by an person who asked not to say her name but in British Columbia, Canada the Molecule Diagnostic Lab, Department of Pathology Children and Women's Health Center Address: 4500 Oak, British Columbia v6H321 Canada has a genetic testing for CADASIL. Phone number 604-875-2852.

Resource on the web:

Great web site go to: <http://www.geneclinics.org/profiles/CADASIL> Click on Medline. Under search type in CADASIL. There are about 25 documentation related to CADASIL on this site.

Since the last Newsletter and Steve's progress:

The last newsletter was in September of last year. Hope everyone enjoyed the holidays and had a good New Year. Steve was unable to work from August 14th until January 2001. We nearly had to file disability and went through the first forms but he is now able to work full time. The company he works for have been wonderful and understanding, we are very lucky and fortunate. It has been a nightmare and I have not stopped worrying. Steve's gait was off, his migraine hurt so bad he seemed to be hard of hearing. I have noticed something, which I think does not help the progress of CADASIL, is stress. Stress seems to bring on an attack or a day later. I have had wonderful support from everyone including the e-mails. I have learned that planning is essential and we have the medical power of attorney and I have Steve's power of attorney now.

Steve suffers everyday with headache migraine and we keep going on. Life is so hard when you have CADASIL as it is not only a disease that effects the person but it is a family disease and we have to live with it. Someone wrote to me and said that each day she would hope that her husband would get out of bed and just try to go to work, (this was the same feeling I had) and then everything would be alright. We mourn each day as we see how CADASIL takes away a little of the person we love each day.

Steve has his sugar diabetics under control and in December 2000 we found out he has sticky blood, which means his blood clots easy. He is on blood thinners for this.

I had fallen (at 42 years old) in February and broke my wrist and was unable to get this newsletter out any earlier and I am sorry for such a delay.

I encourage everyone to sign up on the egroups as even if you do not participate you can get some good information from others. When you post a message to the group it goes to

all the members of the CADASIL group. To sign up, simply go to:
<http://www.egroups.com/subscribe/CADASIL> for members already go to
<http://www.egroups.com/group/CADASIL>. This one line list did change web sites,
Thanks Dorene for letting us know. This is very helpful, wonderful and a little scary but
we do need this to support one another. Sometimes I feel guilty because I do not answer
the on line list because I sometimes just have to take two steps back to cope with
CADASIL. But I encourage everyone to sign up for the list as it is very helpful and
supportive.

United Leukodystrophy Foundation (ULF)

2304 Highland Drive * Sycamore, Illinois USA 60178 Phone: (800) 728-5483 FAX:
(815) 895-2432 the web site address is <http://www.ulf.org/>. If you would like more
information on ULF, you can contact them. They send newsletters out every quarter and
deal with all the Leukodystrophy diseases. The Leukodystrophies are genetically
determined progressive disorders that affect the brain, spinal cord and peripheral nerves.
The term Leukodystrophy derives from the Greek words "lueko" meaning white and
referring to the white matter of the nervous system. "Dystrophy" means imperfect growth
or development. If you know more, please let me know. Usually when CADASIL
patients are first evaluated the doctor's rule out M/S or another dystrophy as CADASIL is
still a new disease.

Others links:

If you want to link to others like us or want to be on the list for the support group contact
Billie. Please e-mail or mail me your e-mail or address.

Billie and Steve Duncan-Smith, CADASIL support group newsletter, 3605 Monument
Drive, Round Rock, TX 78681, 512-255-0209 home

You can contact other families who are also going through this nightmare. REMEMBER
YOU ARE NOT ALONE look at www.home.earthlink.net/~CADASIL/sup.htm for
others who are need support or going through this also.

Please let me know if I can publish your name and address and phone number on the web
site. I have never had a crank call since I established the web site and feel that it is a
benefit to publish this info. I respect your privacy and only want the best for everyone.

Other stories and e-mails (I believe instead of myself going on about Steve and how we
cope the e-mails I have received will help all us of understand CADASIL and how we all
cope with it)

Please remember this newsletter is to help others. I do not want to mislead anyone. I am
looking for HOPE, link to others with CADASIL, and find out as much about this disease
as possible and hopefully a cure one-day. I m not in the medical field or claim to be a
professional on CADASIL.

E-mail #1

My wife and two daughters have all been confirmed as having CADASIL. As you probably know, the disease (it is a disease) was first identified in 1993 as being due to a mutation in a small part of the Notch 3 gene on chromosome 19, which results in the wrong protein being made. As you explained G.O.M. (granular osmiophilic arterial) accumulates adjacent to the smooth muscle cells of arterioles causing progressive damage to the artery walls so that they are unable to regulate blood flow to certain parts of the brain.

You are probably also aware that the disease is present in the whole of the arterial system but only appears to cause damage in the brain, mainly in the white matter (the central nervous system). Diagnosis of CADASIL in the U.K. is made as follows. M.R.I. scanning which should reveal evidence of multiple small infarcts. A skin biopsy when a very small of skin is removed and examined under an electron microscope to see if there is evidence of G.O.M. and finally a blood sample is taken from which the DNA is extracted and submitted for genetic screening to see if the mutation is present.

My wife and daughters take one 75mg. aspirin each day, this is the only medication they are on and is shown to reduce the risk of recurrent strokes. In some instances where appropriate blood-clotting drugs are prescribed. In order to prevent further blood vessel damage it is advisable not to smoke and that blood pressure and cholesterol levels are checked and treated if necessary. Make sure any drugs you are taking do not contain any vaso constrictive agents, and avoid having an aneogram if possible. I am reliably informed that chelation therapy is unlikely to have any beneficial effect on CADASIL and this also applies to chemotherapy as any replacement cells will almost certainly be infected with the mutation. It is also unlikely that a headache attack precedes an infarct (which is painless). My wife has a permanent headache, which has varying degrees of severity but is not necessarily severe prior to her having a stroke. She has mini strokes at regular intervals, which are obviously causing progressive damage.

There are two research studies in progress in the U.K. trying to identify how common CADASIL is and also to try and find treatments to delay the progress of the disease. CADASIL is commonly overlooked due to its recent identification and the ignorance of its presence by the medical profession. There are probably less than 500 families diagnosed worldwide and approx. 50 in the U.K. CADASIL needs more publicity, all family doctors should be made aware of it. If many more cases can be diagnosed then maybe the pharmaceutical companies will get interested and contribute more to the research studies currently being undertaken.

I wish you well. Reg Pritchard.

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Email # 2

My husband has CADASIL. His first known stroke was over 8 yr. ago. It was only the last 3 yr. that he has had TIA's on a steady recurring basis. He had been on aspirin since

his first stroke but it didn't stop them. Often after a TIA he would develop a terrible headache. I think the worse being last week when the symptoms were migraine like. As he only whispers and it is hard to understand him I didn't realize until he was blinking his eyes in the emergency room at hospital last Tues. He was released from hospital Friday after the CT Scan showed he had suffered another stroke and there were signs of others since last summers CT Scan. He had thrown up that morning and the Doctor agreed that it was probably from the migraine. So it seems the headaches are progressively getting worse. I keep coping with the changes. This support group has helped. Marie

E-mail # 3

I am new to this so bear with me. My name is Marcelle. I am 42, just newly diagnosed with CADASIL through DNA testing. My brother Piche (Marie's husband) was diagnosed a year and a half ago...and you are all aware of where he is at in the process. (I assume) My husband and I have already had medical power of attorney set up... but I was unable to get long-term care insurance. I can keep my term life insurance policy in effect, but that is not worth nearly enough. I am still working and still healthy. The neurologist at Children's in Denver has suggested I go to see another neurologist who can do an MRI (and then also make sense of it. Am working on it but the process is slow. The reason for the MRI is to get some of benchmark starting point of where we are. Although I suspect that I am not as bright (cognitively speaking) as I once was, there are many who would tell me that we all lose a bit as we age, and I don't know if what I am feeling/knowing is part of the normal aging process or part of the CADASIL process. My husband & I reside in Colorado; I am Canadian by birth and worked there until I was 36. We have no plans to move back to Canada, so I don't think I will be able to access any disability from Canada when the time comes. We will be visiting our Financial Planner in the next two weeks to see if there is anything else we can organize. I am trying to plan ahead as much as possible while I can and to be as realistic as possible. We have a son who is just 18 and although he knows about this, he has no symptoms and I do not feel he is anywhere near ready to be tested.

E-mail # 4

I don't know whether or not it is a symptom of CADASIL, but I, too, have ear problems. My right ear will pound real loud at times (quite frequently) and the noise will make me feel like I'm going crazy. My left ear will be very painful way deep down and go into an extremely painful headache. This does not happen all the time, but when it happens it will last for a few days, go away, and come back again maybe a week later. Otherwise, I seem to be doing pretty well for having had this disease for at least 14 years now (my first stroke was in 1987 at the age of 35). I basically have the fatigue problem, headaches, dizziness, problems with eating for past year or so (no appetite really~~food just doesn't seem to taste as good as it used to). Just this past year, 2 of my aunts and an uncle (in there 70s) have had strokes and are in nursing homes. Don't know yet if they may have CADASIL. Everyone in the family seems to be scared of being checked for it, my

brothers included. My headaches are more of a sudden, sharp pain type~~don't really know if they're classified as migraines or not. Otherwise, they're usually dull, longer lasting headaches. My back seems to be getting worse (had surgery on that in '96) and I'm afraid of having any more surgery. After my right knee replacement, things just don't feel any better. In fact, after extensive checking and x-rays after the surgery (after my complaints to the doctor of a shattering type of pain where the artificial joint was put in) he concluded that due to the disease, I felt pain where I really shouldn't be experiencing pain. Now, my left knee needs replacing and I guess I'll just have to suffer with the pain, as I feel if I have it done, I'll probably be wheelchair bound.

My memory is still about as sharp as ever (it's always been unusually good), although I do tend to forget things at the moment more than usual. During the time of 1987 through about 1997, I had multiple small strokes. Now, as far as I can tell, they seem to have stopped. My last MRI in 2000 showed no change from the first MRI in '96. I'm thankful for that!

I don't mean to go on about myself, but if it will give someone some hope that not everyone goes downhill fast, that is the purpose of my telling you about my symptoms.

No one should give up hope! My mother started having her strokes in 1988 (major stroke) at the age of 68. She had several other strokes, which left her unable to speak, eat, and communicate in any way. or walk. She was basically in a hospital bed all the time at the nursing home and basically almost vegetative and being fed through a tube in her stomach. The past few months now, at almost 81 years old, she is trying to talk, has tried to get out of wheelchair, nods her head and says yes, is more alert, and shows recognition of people now. The nursing home is starting therapy now, and says when asked things like picking out either a red, black, or white piece of paper, she always chooses correctly. So, there is hope, and I believe that what is happening with my mom is a miracle. Hope some of this helps someone out there. God Bless, Dorene

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E-mail # 5

hello. me too have ear trouble. I'm getting deafer in my right ear, then the left is ok so far. That is strange because I had my stroke on the left side. So Billie and Steve, Keep going on. There is always people worst then us. At least we have hope to find a cure one-day. So may God bless you all and keep the faith that one day, we will all be change.
Daniel C

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E-mail # 6

Hi from us here in Vancouver. I have read with interest that CADASIL presents its self-different in all people. My husband comes from a family of nine children and all have

been told they have the gene, but in that family unit there are various degrees ,if I can call it that , that the condition develops His older sister has hardly any signs of it and she is 64. To be honest she shows no sign of it at all, and then there is his brother who does have a lot of problems, if I've learned anything in all of this it is to take one day at a time and that is easier said than done . Some days I can do it and other days forget it, but all of you have helped so keep up the information.

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E-mail # 7

Hello, I am a 48-year-old male. I started with CADASIL when my wife started noticing my memory was malfunctioning. There were times when I forgot to be at our house when I was supposed to, to watch my 14-year-old mentally handicapped daughter. By the way, I don't know if her condition is related to CADASIL or not. Do you know anything about this topic? She took me to the doctors and after pleading with the doctor that something was wrong with me, He refereed me to a neurologist who suspected CADASIL and referred me to a neurologist at Yale who then diagnosed me with CADASIL through a skin biopsy. This was in June 1999, shortly afterwards in March 2000 I had a stroke, from which I recovered to near normality and now . I am waiting for my next battle with CADASIL. As of the time of writing my story, January 18, 2001. Bruce

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E-mail # 8

I JUST WANTED TO TELL YOU I HAVE HAD HEADACHES FOR SEVERAL MONTHS NON-STOP. I WENT TO A NEW NEUROLOGIST THE BEGINNING OF THIS WEEK AND HE PRESCRIBE A NEW MEDICINE. IT IS CALLED ZANAFLEX FOR MY MIGRAINES AND IT IS WORKING . I'VE HAD SOME HEADACHES WHICH I TAKE TYLENOL FOR AND BELIEVE ME I FEEL 100 % BETTER. I JUST WANTED TO PASS THIS INFO ON IN CASE ANYONE ELSE CAN TRY IT. I HOPE STEVE IS DOING BETTER BECAUSE THIS DISEASE IS QUITE PAINFUL. I HAD A STIMULATOR IMPLANTED IN MY BACK TO HELP THE LEG PAIN AND IT ALSO IS WORKING GOOD FOR ME

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E-mail # 9

My daddy is 59 years old. He has been diagnosed with CADASIL. We have struggled for answers since 1991 when he became depressed, incoherent. His physician diagnosed depression and prescribed Prozac, which he took briefly and then "returned to normal". We did not have any problems from 1991 until 1997. Physician well except for "mini-strokes" and "white matter" diagnosed all in 1997. Since that time, there have been so many behaviors, symptoms and changes that did not add up. Our neurologist told us to live with it...there was nothing we could do. We initiated a trip to Research Hospital in

Gainesville, FL and found out 10/4/00 that Daddy has CADASIL. I am 28 and my sister is 31...there are three grandchildren. My sister and I have not told my parents that this horrible disease is genetic, and we probably never will. I was told to give him 2000 units of Vitamin E daily and 100 mg of Zoloft. He has problems swallowing, speaking and shuffles when he walks. He has never had migraines or headaches. He is not in any pain at present. We have very little family medical history. We have traced the disease to my Daddy's mother whose father was placed in the State Hospital (early 1900's). Daddy's mother was in a car wreck at age 56 and stayed in the hospital for @ 4 months. She was a vibrant, active and very out going lady from the stories I have heard. Especially so when she was hospitalized for those 4 months. However, the story goes that she was told by the hospital that she was not going to get to go home b/c her leg had not healed. According to the history, she simply died shortly thereafter. No symptoms, no mini-strokes, no personality changes at age 56---Could this mean that if you are healthy you may not develop the disease? Also, does the disease weaken with every generation? Sorry to ramble and bombard you w/ so many questions. It sounds as if my Daddy has it pretty good as he has no pain at all like your husband Steve. Thank you for this web site and your dedication. Please send information if you have any. --HOLLY

E-mail #10

My wife, age 67, is in a terminal mode with CADASIL. I will take the time to write her history and send it to you later. There is research being carried out at Michigan University - the doctors there say the expect to have a therapeutic resolution in a few years, long before anyone comes up with a genetic fix. One treatment tried on my wife was to take down her immune system with chemo to see if the system would come back with an unmutated gene. The first treatment given over three months didn't work and of course as the condition progresses, you don't recapture mental capability.

A second treatment in March 1999 was more concentrated, a single thrust. Since then my wife who is heavily impaired and under Hospice care at home, does not appear to have suffered any further progression of the condition to date. She is in no pain, can still recall early events in our married life, is unable to talk or swallow and is confined to bed and totally dependant on my ministrations. I love her dearly and do my best to keep her comfortable. Some members of our family are exhibiting migraines and MRI's are displaying early symptoms.

It seems to me that a good course of prophylaxis is to keep clear of stress, (a major cause of migraine onset) have a clean diet and at the first signs of a headache assume the brain arteries are inflamed and go in heavily for strong anti inflammatory medication and blood thinners to prevent the brain from being deprived of blood flow. An aspirin per day and lots of vitamin E could also help deter an onset.

I feel confident we will see a solid therapeutic prophylactic approach in the next few years. I am not a doctor but have been close to this for twelve years and for most of that time the doctors did not have any idea of what was happening let alone how to treat it.

I also believe CADASIL is far more prevalent than I care to think about and is frequently misdiagnosed.

More later. Keep the faith

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E-mail #11

Hello, I found your web site just now and decided to contact you for ??????? My lovely 41-year-old daughter was given this diagnosis about 2 hours ago and guess we are in state of shock. The docs have been toying with MS but one doc held out and said no. So this is where we are. =====

E-mail #12

my family is finding a history of CADASIL now. In short the problem was discovered in my uncle first. He had lots and lots of "mini strokes" they led to short-term blindness, temporary paralysis and dementia similar to Alzheimer's. As of now he is in his 60's and is being cared for in a nursing home. He is not sure who any one is most of the time but seems generally happy. No anger or short temper at all. I don't remember him ever having migraines but I am not sure. Since the onset of his problems my other uncle has been diagnosed with CADASIL as well and it is expected that my grandfather, 2 of his brothers, and several of his cousins all died from CADASIL! Now I have 2 uncles with it and just yesterday my cousin was diagnosed. He is currently in the hospital and recovering from the blindness. I don't have a lot of info on the situation at this time but I will be communicating with my family to get further info. In my family it has been all men who have the disease. there were 4 children on that side of the family. 2 have CADASIL 1 died at age 37 from heart disease (my father) and the other, female is in her early 40's and seems to have no problems with CADASIL but has had some mental illness and has been on medication for it for some time. I'm not sure if that would be related or relevant. She may have migraines but I can't remember. She may well have CADASIL to. I'm thankful for your web site info. My family is having a very hard time finding info on this disease so this is helping. I will ask and get more info and email you again. If you have any info other than what is in your web site feel free to email me back. Also my grandma said that the disease was first discovered in France. A family there had 11 members with CADASIL, 3 of which were women. My one uncle with CADASIL, Wayne, who was diagnosed first is not well off, in a nursing home and suffers constant strokes and other problems. But his temperament is very well. He is a happy guy who has no clue what is going on most days. As if he has Alzheimer's. My uncle Howard is not as bad, has only had a few strokes and just the beginning of the trouble Wayne has had but he has always been a terrible rotten mean person and is very much worse now. You can

hardly bear to be around him he is so mean and grouchy and awful!! Again, not sure if its a symptom or not but just info from my situation. I am a 30-year-old female and I have not started a family yet and am seriously considering not! My grandma says don't worry about it and go on with life because you cant do anything about it but I don't know if I want to put my children through what my cousins are going through nor do I want to pass it on to them. I already have cancer, heart disease and stroke in my family tree, now this! Not something I want to pass on. Let me know what the chances are of passing this to your children as I know it is hereditary.

E-mail #13

I want to thank you for the tremendous research you undertook to compile the questions and answers on CADASIL.

I just returned from seeing my neurologist to get the results of an MRI of my head and an MR angeogram. He informed me that the results suggest that I have CADASIL. Both of my parents died of strokes and my brother has had a series of strokes, the first of which was 10 years ago when he was 45; all of which makes him think that CADASIL could explain what recent tests have shown. I have been having headaches for the past 4-5 months, which prompted a CT scan in July 2000.

The CT scan report noted "there is a subtle area of hypo density seen within the sub cortical white matter of the right anterior frontal lobe". In 1995 I started having two disturbing problems: a) memory problems and difficulty concentration; b) I had developed a tremor which prevented me from writing or holding things without trembling. (The tremor is still with me, and is often worse; fortunately, I am able to type, and the tremor does not affect my typing.) To explore these problems, the neurologist at that time ordered and MRI angeogram, which has served as a baseline to compare the MRI and MR angeogram that was carried out in October 2000. In the earlier test, the report noted signs of atrophy in the white matter. The latest report shows a significant deterioration and damage to the white matter and indications of lack of blood circulation in the area. I have not history or diabetes, high blood pressure or high cholesterol and I do not smoke. However, my doctor says that the extent of the damage is similar to someone with years of diabetes, high blood pressure, high cholesterol and a heavy smoker. Therefore, considering my family history and the results of the latest MRI compared with the earlier one, he has made a preliminary diagnosis of CADASIL.

He has referred me to a stroke specialist to run a series of tests to try to confirm this. I see him in a month. I have a few questions and I wonder if you could share your thoughts. (I appreciate that you are not a medical practitioner, so I am not asking you for medical advice....only your experience based on someone who has been so intimately involved with the disease.

E-mail #14

Dear CADASIL newsgroup's members and readers, I am a French person who feels very much involved in the CADASIL disease's cause. This illness was discovered in my family. Many relatives took part in the medical research, which was launched in France more than 15 years ago and led to the identification of the genetic disorder at the origin of it, in 1993. My grandmother died of it, as several of her brothers and sisters, and the genetic disease has unfortunately spread among the following generations. In France, about 100 families have been identified having cases of CADASIL in their genealogical tree. This means that many people suffer from it, or are afraid of seeing their health situation worsen, or are afraid of transmitting it to their children, or are afraid of having got the genetic abnormality from their parents, or live with persons suffering from it and strive to give them medical and moral support, and so on... You live in different countries, but the same feelings arise in the messages you exchange through the newsgroup. There are no boundaries in our concerns with CADASIL... It is quite necessary to find understanding and solidarity when such a rare illness invades your life, but, with an exterior view, I find very few hopeful or scientific proven messages in your newsgroup. Do you have some associations for sharing your feelings, exchanging advice for caring of ill people and getting medical information ? In France, some scientists work on this illness, but each of us or our doctors cannot individually contact them to get information, whereas an association can be very helpful for these researchers to have a way of conveying information and for us, as a group, to get real and positive reasons for knowledge and hope. Here, in France, we founded an association (ACF France : Artériopathies Cérébrales Familiales France, which means : familial cerebral arteriopathies, France). One of our main objectives is exchanging information with the French research team and communicating it to our members, but also to medical medias, neurologists, hospital teams, etc. In that purpose, we are preparing a Website (we will give you its address; it will be firstly in French, but we plan to translate it in English later), we will prepare a newsletter, get some contacts with medias, and give support to families... Our association has already 90 members and has also subscribed to another French association, dealing with rare genetic diseases. Our first annual meeting will be held in the coming weeks and it will be followed by a medical conference. Together, we will be stronger ! There's a French Website where you can find some extracts of medical articles on CADASIL, in English. Its address is www.infobiogen.fr/services/orphanet Choose "search the orphaned database", then "disease", enter CADASIL and select [search], click then on the CADASIL name and a list of more than one hundred articles is displayed, you can click on their names for getting options like displaying abstracts. I hope we can help you in knowing better the CADASIL illness and having information on the prospects for medical research. Yours sincerely, Chantal

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E-mail 15

My husband has also been diagnosed with this disease. He has been struggling with strokes since the age of 43 and is now 45 and is also suffering from dementia. I am at the

point where I don't think he can live at home any longer. The MDs can give me no time frame. This is the most difficult disease as people tend to shy away from you and your problems. I have two boys 11 and 15 and I don't want the day to come where their dad doesn't know whom they are. My husbands MDs Neurological Clinic in Amherst, New York. He also has two other cases. We have been to the Cleveland Clinic where he was seen and tested who has helped to determine his disease. I am especially scared for my two boys as this disease is hereditary and I don't know which side of my husband's family it comes from. Gary's brother has severe progressive multiple sclerosis. My children know that my husband will forget all and pass.

E-mail 16

My mother has just been diagnosed with CADASIL, after a stroke at the age of 54. We now believe that it runs through her father's side. He died from a blood clot @ the age of 64. Both my mothers' sisters display symptoms. One with stroke, the other severe migraines. The doctors have been unable to give us any information, all that I know (which is very little) has been from the web. I would love receive your newsletters and perhaps chat with you about this further.

E-mail 17

My husband is looking at going on disability now in January. He is unable to focus at work and the headaches are severe each day. he is 47. We had an interesting thing happen, however. Nile's muscle biopsy was positive but his DNA was negative. Our Dr here at the University of Utah, which is a research, based hospital and our neuro knows of the French studies. . . so they redid Nile's biopsy this past week and sent it and vials of blood to France for study. This gives us hope. But, I too still have children at home, will now be the sole breadwinner, he does have disability insurance that will help to pay bills. But it really came up on me. I'm sure that's how you felt also. I just thought if he gets up and goes to work everything there must be fine.

E-mail 18

I was shocked to finally find a link on the Internet regarding this terrible, scary disease! about 12 years ago, my mother was misdiagnosed as having brain cancer, then corrected to what was known as Binswangers then finally a group of neurologists got together and with my fathers assistance, and of course all 4 of their children and many, many different doctors analyzing my mom, they discovered CADASIL! Not that I'm happy with the outcome, just happy with a diagnosis. well, this past April, my father passed away and 9 mo. previous, my family (husband and 2 kids) moved into my childhood home with parents so that I can help my father take care of my mother. I am now sole caretaker of my mom, and wouldn't have it any other day, my mom turned 64 in Sept. 00. She is a

vivacious, hot headed, strong willed Irish woman who is trapped inside this CADASIL world. She also suffered a major stroke the spring of 1996, which took her speech, and her right side of her body. She is totally dependant, and between me and my 14 yr. old and my 4 yr. old she communicates the best with us!! We have come to read her quite well! she is very expressive with her eyes! I am so glad I've had this chance to connect with someone else dealing with this debilitating progressive disease. Please, please keep in touch with me. I will soon forward our local Neuro. team for they are in contact with research teams!! sincerely, Laura

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Notes about Binswangers disease similar to CADASIL.

E-mail A – I'm stretching the imagination here but here is my question. My dad was diagnosed by a skin biopsy w/ no definite confirmed family history. His symptoms are more like Binswangers disease than CADASIL. Just wondering if it is possible that he could have been misdiagnosed? Anyone have any thoughts? We have an appt to see a new neurologist this month (1st contact w/ one since diagnosis in Oct) and I'm trying to weed out some of my many questions for him!

BINSWANGERS DISEASE is characterized by damage in the deep white matter of the brain (is this the same as excessive white matter?), loss of memory and cognition, and mood changes. Patients usually show signs of abnormal blood pressure, stroke, blood abnormalities, disease of the large blood vessels in the neck, and disease of the heart valves. Other prominent features of the disease include urinary incontinence, difficulty walking, shaking similar to that seen in Parkinson's disease, and depression. Thank Holly

E-mail B – Binswangers disease is closely related to CADASIL from what I've been told by my doctor. I had an aunt (on my mom's side) who was diagnosed with Binswangers disease and died about 7-8 years ago. Several others in my family on my mom's side have been diagnosed with the CADASIL including cousins, my mom, my brother, and me. My aunt deteriorated rather quickly with strokes and dementia. I could not get a lot of information about her though since I live in Michigan and she lived in Denver CO. I have tried to get more info, but no response. What they said about her was that "her brain turned to flour". So, in my family, CADASIL and Binswangers Disease run in it.

Hope this helps.

E-mail C – I'm not the resident expert, but I think you've asked a valid question, especially since there is no solid family connection. Did you go to the site at <http://www.geneclinics.org/profiles/CADASIL/details.html> ? Under the section "Differential Diagnosis" it does list Binswangers. The features you list for Binswangers - such as difficulty walking, incontinence, shaking, and depression are also shared with CADASIL. My answer is not complete... I believe there is a Doctor who tunes in occasionally and perhaps she can answer your question more correctly. I only responded so that you would know that we are out here and we care. Good luck with your search for

a better answer. Marcelle

E-mail D – CADASIL he feels causes a built up in the small blood vessels similar to cholesterol and that if we can determine what this substance is then we will be able to treat it like we do cholesterol." FYI: When I went to the Mayo Clinic in '96 and was originally diagnosed with CADASIL, the doctor said that high homocysteine levels were prevalent in all my family members that have CADASIL. He seemed to think that the 2, that is CADASIL and high homocysteine, were relative to each other. Have any of you ever had your homocysteine levels checked? It has something to do with the cholesterol and other harmful things in the blood. I, too, have high homocysteine levels and take high dosages (5-mg. daily) of folic acid to help that. Also, Vitamins B6 and B12 are also recommended. I do not take the vitamins. Other than headaches and "swimming head" feelings, I seem to maintain the same level year after year. I have stopped having the TIAs and think normally (other than a little short-term memory problems) and am still intellectually in good shape. High homocysteine is also responsible for coronary artery disease, as I read in an article in PARADE magazine last week. Also, on TV last night there was a show about stress in women. They stated that women with high stress levels seem to have high homocysteine levels in their blood. So, maybe when we were talking at one time about stress bringing on the CADASIL syndrome perhaps we were on to something? Dorene

E-mail E - We have had some discussions with our neurologist re. Binswangers. My wife's father passed away several years ago and, at the time, was diagnosed with Binswangers. Now Ellen and two of her three siblings have CADASIL. According to our doctor, Binswangers is always characterized by high blood pressure, that is the symptom that most commonly distinguishes its diagnosis from CADASIL. Otherwise the symptoms are very similar.

This newsletter goes out to people in America, England, Scotland, Sweden, France, Chile and Australia. If you know of anyone who is interested in this newsletter, please photocopy it, and pass it on. Also, contact me so we can add their name on the email lists or mailing address..

Please e-mail you updates on your progress with CADASIL. Also, if you would like to tell your story (we can leave out your names) please send this to me. It seems to help to tell others. This is how I cope with my husband's illness. When I do these newsletters I sit at the computer and sometimes cry but it does seem to help the stress.