**CAN YOU BELIEVE TWO**

**CADASIL STUDIES ARE HAPPENING NOW!**

We are proud to announce we are working with Dr. Swati Sathe of New York University and Dr. Viera Saly MD, MSc, FRCP (C), Neurologist Victoria General Hospital, Victoria B.C. with Vancouver Island Health Authority Research ON TWO SEPARATE CADASIL Studies. Please go page# 2 to participate in these studies today.

A note from Billie—CADASIL (Conference 2010)

I look back and think I was in a dream the weekend of July 30 - July 31, 2010. It has been 13 years since I began working to get a conference on CADASIL together. Thank you to the attending 100+ participants from Canada and the United States and also to the ULF for being the main host of the conference. This was an opportunity to visit with doctors, ask questions, and get to know them. It was also a heartwarming experience to meet many patients and their families who the foundation aided with support or guidance in obtaining a diagnosis. I heard many individuals comment on how rewarding it was to meet others diagnosed with CADASIL. The patients and their families felt this was the highlight of the conference for them and was well worth the money to attend. For those who could not attend the conference, it was broadcast over the internet as a webcast. The family conference DVD is available (go to page 8 of this newsletter to order the DVD).

CADASIL TWHH runs solely on donations, with no paid staff. The donations are for outreach and awareness efforts; education around the world; as well as for costs related to production and distribution of newsletters, educational brochures, and other CADASIL informational items. Additionally, donations are used to reduce conference costs. **Without your support, the foundation would not exist as funds are not obtained from any other means. Thank you so much for your continued support as Together We Have Hope.** I was honored to be invited to serve on the United Leukodystrophy Foundation (ULF) Board of Directors. By accepting this invitation, I am the first foundation director to ever serve on their board. The ULF will expect donations for CADASIL research by mailing the donation directly to them, since they have the ability to fund research grants for CADASIL and mirror the guidelines of the National Institute of Health. The French Team has asked if they could link the CADASIL TWHH website to their website and vice-versa. CADASIL TWHH and the ULF will work collaboratively on joint projects but will maintain separate foundation entities to continue the mission of each individual foundation.
CADASIL RESEARCH/STUDY BY NEW YORK UNIVERSITY SCHOOL OF MEDICINE

Dr. Swati Sathe is on our scientific advisory committee and is the Principal Investigator of this critical study. She presented at the first ever 2010 CADASIL Symposium and Family Conference. She is dedicated with the NYU team and is working hard on the study to help everyone with CADASIL.

The purpose of this study is to better understand the early symptoms of CADASIL so the medical profession may learn to diagnose CADASIL early and may help them in developing awareness and guidelines for appropriate diagnosis and management of CADASIL.

As you are aware, CADASIL is often misdiagnosed due to lack of awareness of this condition among healthcare providers and because the disease can closely mimic other neurological conditions. People with CADASIL struggle to find a doctor who has knowledge about this condition. The responses and questionnaire are very valuable.

NYU School of Medicine may contact some candidates for a more detailed telephone interview. Together We Have Hope endorses this study and the more participants NYU School of Medicine has will make this important study a success for CADASIL patients and the professional community.

NYU has a full time staff member, e-mail him at Edward.Nunziato@nyumc.org or call Edward at New York University at 212-263-5912 to participate. NYU will mail a questionnaire for you or your caregiver to complete and mail back to them with a stamped return addressed envelope.

For more information with this study, please to the National Institute of Health website at: http://clinicaltrials.gov/ct2/show/NCT01114815

This study is currently recruiting participants but will be closing soon.

CADASIL SURVEY/STUDY BY VANCOUVER ISLAND HEALTH AND VICTORIA GENERAL HOSPITAL, CANADA

Dr. Viera Saly MD, MSc, FRCP(C), Neurologist Victoria General Hospital, Victoria B.C. is working with Vancouver Island Health Authority Research soon after she attended the CADASIL Symposium. The goal of the survey is to examine if your diet makes a difference. The strength of this type of study is in the number of participants.

The Notch 3 mutation does not completely determine the course of CADASIL. There are likely many genetic and/or environmental factors which influence each individual patient’s reaction to the disease. We know that some lifestyle habits are detrimental (smoking, untreated hypertension), but we do not know if dietary habits can alter the course. A Mediterranean diet was found to be protective against stroke and Alzheimer’s dementia and perhaps it is also protective in CADASIL.

Go to the website now to complete the survey: http://fluidsurveys.com/s/cadasilsurvey/.

The survey has 33 short, mostly yes/no questions; it is completely anonymous and takes only 5-10 minutes. We trust that if you chose to take the survey, your answers will be, to the best of your knowledge, accurate and sincere. Your participation in the study is entirely voluntary. You may withdraw at any time by closing the web-page.

We are not asking you to give us your name or your e-mail address. EVERYTHING IS CONFIDENTIAL. No-one will be able to determine your identity or whether you completed the questions.

Questions or concerns, please contact Dr. Viera Saly MD, MSc, FRCP(C), Neurologist, Victoria General Hospital or contact us at 512-255-0209.
WEBSITE FORUM, TWITTER AND FACEBOOK

Through these three support communities, the foundation will keep you informed of any important announcements and information. The website support forum is strictly confidential concerning your name and info and will be still be available if you feel you do not want to use Facebook or Twitter due to personal reasons. This is your choice.

You can go to http://www.facebook.com/#!/pages/Cadasil-Together-We-Have-Hope-Non-Profit-Organization/190494710963967 or search CADASIL Together We Have Hope Non-Profit Organization, make sure you use the Non-Profit Organization site.

Please remember, with the Forum, Facebook and Twitter is the world wide web, and CADASIL Together We Have Hope is not responsible for what others post, but we have faith that everyone will share openly, warmly and often, while always respecting the privacy and emotions of the rest of the CADASIL Family.

There are other support groups like Yahoo Groups, Facebook, MDJunction, etc. Thank you for everyone by getting the word out about CADASIL.

GENETICS

THE LAW EQUAL OPPORTUNITY ACT has added: Title II of the Genetic Information Nondiscrimination Act of 2008 protects applicants and employees from discrimination based on genetic information in hiring, promotion, discharge, pay, fringe benefits, job training, classification, referral, and other aspects of employment. GINA also restricts employers’ acquisition of genetic information and strictly limits disclosure of genetic information. Genetic information includes information about genetic tests of applicants, employees, or their family members; the manifestation of diseases or disorders in family members (family medical history); and requests for or receipt of genetic services by applicants, employees, or their family members. http://www.dol.gov/ofccp/regs/compliance/posters/pdf/eeopost.pdf

CADASIL BROCHURES

Brochures have been updated by the medical profession. We have mailed these brochures to over 180 Multiple Sclerosis Centers to raise awareness. The Leukodystrophy Foundation (ULF) will have their scientific advisory board professionals distribute these to all the neurologist conference, meeting, etc around the world. The goal of the foundation is to have these brochures printed and distributed to the medical professional and doctors offices. Please if you have any ideas, contact us.

MULTIPLE SCLEROSIS CAMPAIGN

Over 180 Multiple Sclerosis Professionals were contacted to raise awareness with CADASIL. As you may be aware, CADASIL is often misdiagnosed due to lack of awareness of this condition among health care providers and because the disease can closely mimic MS. This campaign stared in October. Sara (who has CADASIL) had volunteered to assist with the campaign and worked diligently with the foundation by providing the name and addresses of the MS clinics. We also enclosed the foundations brochure to educate the doctors. In the letter we had asked the clinics to e-mail the foundation or register online, The results of the campaign was not very successful, we never had a MS doctor or clinic acknowledged the information we sent. Please keep checking back on the MS Campaign as we will not stop raising awareness among the MS communities. Since the conference, we have started to track new patients, if they were diagnosed first with MS.
CADASIL/RESEARCH UPDATE INFORMATION

My lab has identified additional proteins that bind to the Notch3 protein, and we are trying to find out what these proteins may be doing in vessels when they combine with Notch3. We think some of the proteins may slow down the natural removal of Notch3. We are also trying to identify chemical sequences that may accelerate the natural removal of Notch3.

I want to personally thank all of the brave patients and families of patients who have participated in brain donation for research purposes. Your contributions are truly invaluable and will help research into CADASIL in very substantial ways. You are stars.

Michael M Wang M.D., Ph.D. Assistant Professor
Department of Neurology, Molecular & Integrative Physiology Ann Arbor, Michigan

We got a CADASIL-related manuscript accepted in 'Annals of Neurology'. I presented part of these data at the CADASIL meeting in DeKalb, and thought you might be interested. In this paper, we identify an enhanced susceptibility to cortical spreading depression in CADASIL transgenic mice. Cortical spreading depression is the electrophysiological event underlying migraine, and our findings suggest that enhanced susceptibility to cortical spreading depression might be a mechanism for the high incidence of migraine in CADASIL patients.

Kind regards from Boston, Katharina Eikermann-Haerter, MD, Instructor Stroke and Neurovascular Regulation Laboratory, Department of Radiology, Massachusetts General Hospital and Harvard Medical School, 149 13th Street, Room 6403 (CNY149-6403) Charlestown Navy Yard, MA 02129 USA

Recent advances in molecular genetics have enabled identification of several other CADASIL-like conditions involving small vessels predisposing to ischemic and haemorrhagic strokes and diffuse white matter disease. These have been useful to compare and learn about CADASIL. However, CADASIL remains the most common hereditary small vessel disease. Reports from several countries shows that CADASIL is much more prevalent than first realized. CADASIL occurs equally in men and women, and genetically verified cases in small to large (>600) families worldwide suggest no particular predilection of the disease in different communities. The estimated frequencies of CADASIL cases in Western European countries where several hundred families appear to be described can be calculated to range from 1.5 to 5.0 per 100,000. To date we know that it results from over 190 different mutations in the NOTCH3 gene, the product of which is a cell-signalling receptor. Mutant NOTCH3 causes degeneration of small arteries and arterioles leading to recurrent small strokes. The variability in CADASIL cases seems to be by and large independent of the type of mutation. Furthermore, the remarkably different clinical picture in monozygotic twins, points out that environmental factors may significantly modify the clinical symptoms. The youngest symptomatic CADASIL patient with deficits in several aspects of executive functioning and in verbal learning, was diagnosed at the age of 8 years and the youngest patient experienced his at first-ever stroke at the age of 11 years. The oldest known CADASIL patient died at the age of 96 years with onset at 68 years. While the exact mechanisms how NOTCH3 gene mutations lead to the degenerative changes in arteries at the cell and molecular levels are not fully understood, we are also learning much from different mouse models where different mutants of NOTCH3 protein are expressed. In few mutant mouse models the disease is well replicated helping to build a complete picture how the disease is caused. Meanwhile, keeping active is advocated for CADASIL patients. Information
I am pleased to report the publication of new research findings in the Journal of Alzheimer’s Disease showing changes in notch receptors and insulin growth factor receptors in the brain arteries of patients from our CADASIL tissue bank. Many thanks to the CADASIL families for their generous contributions to the Brain Bank. These contributions are making an important difference in the fight against CADASIL. Working with Athena Diagnostics we recently reviewed the results of CADASIL testing in more than 10,000 patients in the United States over the past 7 years leading to the discovery of 115 CADASIL mutations not previously reported. These findings provide new insights into the molecular changes taking place in the notch protein. This paper is currently under review for publication.  

Stephen Salloway, M.D., M.S., Director of Neurology and the Memory and Aging Program, Butler Hospital, Professor of Clinical Neurosciences and Psychiatry, The Warren Alpert Medical School of Brown University, 345 Blackstone Boulevard, Providence, RI 02906

**Mouse Genetic Model**

**Cerebrovascular dysfunction and microcirculation rarefaction precede white matter lesions in a mouse genetic model of cerebral ischemic small vessel disease** This article was published this year and was presented at the CADASIL Symposium in detailed by Anne Joutel, M.D, from Paris France,  

http://www.jci.org/articles/view/39733

**SYMPOSIUM AND FAMILY CONFERENCE WAS HELD IN JULY, 2010**

Thank you to all the medical professionals and appreciation to all who attended or presented at this scientific symposium and or the family conference, especially Swati Sathe, M.D., M.S. hard work for the chairperson for the conferences. In this newsletter are summaries about the conferences. On the website www.cadasilfoundation.org we were fortunate the Medical Professionals who presented volunteered to give us a copy of their presentation for you to view. Not all professionals could provide their presentations due confidentiality. These were the presenters:

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<th>Paula Brazeal, President ULF</th>
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<td>Anne Joutel, M.D (INSERM, Paris, France)</td>
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<td>Sonioa Reyes, Psychologist (Hospital Lariboisiere, Paris, France)</td>
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<td>Kathyn Gardner, M.D. (University of Pittsburgh, PA)</td>
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<td>Luisa Iuela Arispe (ULCA, Los Angeles, CA)</td>
<td>Professor Arndt Rolfs, M.D. (University of Rostock, Rostock Germany)</td>
<td>Ann Moser, ULF Vice Chairman (Kennedy Krieger Institute, Baltimore MD)</td>
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SUMMARY OF THE SCIENTIFIC SYMPOSIUM
The symposium was unbelievable. I’m still in awe over everything which transpired. Doctors from across the globe attended the symposium. They were not just there to present, but to learn. I was blessed to have the opportunity to present data from our foundation's database which mirrored other presented scientific data on age ranges, symptoms, countries, etc. A big thank you is extended to all who signed the registry. Your support was vital. Rest assured that names and e-mails were not shared...only statistical data. Your information is secure as confidentiality is paramount to the foundation. It has been 13 years since I dreamed of this event and am still pinching myself that it finally happened. I never heard the word "CADASIL" so much as I did during this symposium. The medical committee was very complimentary of the foundation’s hard work, dedication, encouraged and our continued efforts. Due to confidentiality reporting on this conference is not permitted to summarize as the medical profession has not yet had their presentations published, etc.

CADASIL Family Conference participants comments:
Sara: When I first heard that there would be a conference specifically focusing on CADASIL, I thought immediately, “that’s where I have to be”! For so many reasons: to learn, to question, to get support, but most importantly: to network with people in the medical & research communities as well as to form supportive relationships with other families! And now reflecting back (after attending both the Professional & the Family symposia days), I was not disappointed. I used to think that very few doctors knew anything about CADASIL and that there was virtually no research work being done. It was a very bleak outlook. But after attending the conference, my outlook has completely changed. There was a two or three year period after initially discovering my test results where I knew that I just had to re-prioritize my life and stop letting everything and anything regarding CADASIL control it. I always felt connected to updates and the “CADASIL community” to some regard during that time period. But it had become just too consuming and overwhelming and I knew I needed a break. Attending the conference has given me a new sense of optimism and encouragement that hadn’t really ever been there before. I was very fortunate to have my local neurologist also attend the conference; as well as my sister and husband for support. I had debated whether or not to physically attend or to just watch the live webinar. I’m so glad we decided to make the commitment to be there in person. It was wonderful meeting other family members who have similar concerns and frustrations. I know that I wouldn’t have gotten everything out of the conference as I did if I hadn’t have been there. Leaving the conference, I haven’t felt that I have all the answers or that everything is now magically solved. In fact, I believe that I left the long weekend having more questions than when I arrived (but that’s good!). But I do have a clear plan of what I need to do and who will help me to get there. I’ve realized over the years that I may not have all of the answers that I need when I need them. More importantly for me than getting an answer is just having a plan. If I don’t have a plan on how to acquire an answer, I’m a wreck! And that is exactly what the conference provided: an opportunity to receive the education and meet the researchers and clinicians who will help provide the answers. Upon leaving the conference, my plan was in place!

Alice: I am so glad that I attended that seminar. I liked the informal way it was held. I didn't really hear a whole lot that I hadn't already heard, but was happy to hear that everyone is on the same note. Meeting and visiting with so many victims was an experience. Some of the Docs that were there I have talked with and corresponded with in the past. It was great meeting them finally, as it was to finally meet you. I think my son also enjoyed being there. Wish some of my other family could have attended. I will definitely
plan on attending again in the future, I also realized, after hearing about the other peoples
conditions, how very lucky my sons are. They are still able to be employed and live a normal
life.

**Andrew:** “The CADASIL conference the first ever but not the last”. Was a great opportu-
nity for CADASIL suffers and their care givers to get information and connect with others who
suffer from or love someone who does have CADASIL. Billie Duncan-Smith who founded To-
gether We Hope and Paula K. Brazeal who founded the ULF assembled the world’s experts on
CADASIL. The doctors got to meet with each other and share their ideas. We CADASIL suf-
fers got to meet with and ask doctors questions in a relaxed and friendly environment. I be-
lieve that getting the word out about CADASIL is a major step in finding a cure"

**Phyllis:** I attended the conference this July 31st with my husband Steve Carter. He was the
guy with the camera. We have been dealing with this disease since 1999. Actually, that’s
when he was diagnosed. We had been dealing with it way before then, just didn’t know
its name. How amazing it was to meet and see so many CADASIL patients gathered
together in one place. To have the chance to meet their family, caregivers, and friends, as
well, was a gift. It was a very emotional experience but at the same time, the room just
emanated hope. We never anticipated seeing so many people living with this disease and
doing relatively well. It was a great opportunity to share with others and hear their stories.
I am grateful to the doctors who took the time to attend. Their knowledge is invaluable.
Personally, I could have spent more time discussing caregiver issues and maybe meeting
with other spouses & caregivers. But that can be for another time. Steve and I don’t spend a
lot of time worrying about his CADASIL. It is what it is. We try to enjoy life now. For us, that
means movies, theater, museums, travel, etc. But it was wonderful meeting everyone.
Thanks to Billie, who makes all this happen. Thanks to the ULF for collaborating with the CA-
DASIL Together We Have Hope. Steve and I wish you all the best.

**Bob:** Lisa and myself attended the CADASIL family conference this past summer in DeKalb
Illinois. It was nice to get together with other families that were going through the same sort
of things that our family is going through. We were able to ask a lot of questions of the guest
speakers about CADASIL, and with some very good answers. It is nice to know that we are
not alone with this disease, and together we do have hope! There are way too many people
out there in the country/world with misdiagnosis mirroring Multiple Sclerosis (MS) symptoms.
There needs to be more blood testing laboratories in the USA. Also there needs to be a study
on, why it cost so much just for a blood test. It is time to get the word out there about CA-
DASIL, so we can get the research and grants that other diseases get, even if we have to
raise the money through fund raisers and informational conferences. It was a great confer-
ence and very well put together. I would like to thank all of the people that work so hard to
put the conference together. I do believe this can work. Bob Leslie, CADASIL supporter for
the Hoffman family group from MN. Together We Have Hope!

**Janet Mills:** An incredible opportunity at this family meeting was the ability to talk to doc-
tors and other medical professionals at the end of each of their sessions, to spend part of
lunch chatting with those who didn’t have to rush away to meet other obligations, and to ask
any remaining questions of the few who were able to stay after the end of the conference.
The doctors were friendly, approachable, and available to everyone. Their attention, respect,
and honesty toward the CADASIL patients and families were greatly appreciated. (see web-
site for full summary from Janet)
How do I get purchase a DVD from the conference? To obtain a DVD from the CADASIL family conference send $ 30.00 to United Leukodystrophy Foundation, 2304 Highland Drive, Sycamore, Illinois USA 60178, Phone: (800) 728-5483

Will there be another conference? Yes, when we have more information and research data as it is redundant to have a conference without new information.

REGISTRY DATA

Please sign the registry as we need to have everyone with CADASIL documented for research, etc. and make your number count. All information provided to us is kept strictly confidential!

1061 Confirmed Cases Worldwide as of 12/31/2010

Gender: 54% Females and 40% Males
Average age of diagnosis is 40 to 49 years old

How our database has grown since June 2005 to present

- 200 confirmed cases in June 2005
- 523 confirmed cases in July 2006
- 568 confirmed cases in January 2007
- 702 confirmed cases in August 2007
- 796 confirmed cases in May 2008
- 858 confirmed cases in April 2009
- 1005 confirmed cases in March 2010
- 1026 confirmed cases in June 2010
- 1061 confirmed cases in Dec 2010

AVERAGE VISITORS TO CTWHH WEBSITE IS 70 VISITORS PER DAY

- 25,200 Visitors per year
- 2,100 Visitors per month
IN LOVING MEMORY
with prayers and thoughts for families who had a family
pass away due to CADASIL.

BRAIN FITNESS EXERCISES YOU CAN DO IN 15 MINUTES OR LESS

Throughout your whole life, you're constantly taught how important it is to stay in shape. Being physically fit wards off an array of serious medical conditions. But one thing we often overlook is the importance of staying mentally fit. Just like your body, your mind needs to stay in shape too so that it can fight off serious mental diseases. The older we get, the likelier it is that we'll start forgetting things, and memory retention will begin to deteriorate, and short term memory loss might occur.

Have a Conversation—Many experts believe that social interaction is one of the keys to keeping your mind sharp. For this reason, you should engage in a discussion with others for at least 15 minutes a day. Listening to what others have to say and coming up with thoughtful responses keeps your brain on its toes. It's an easy and fun brain fitness exercise.

Do a Crossword Puzzle—Crossword puzzles aren't just silly games people do to kill time. They're an important brain fitness exercise. A crossword puzzle is a logical activity that will put your mind to the test. If you do these at least a couple of times a week, your mind will stay fit.

Eat with Different Hand—This might sound ridiculous at first, but it really is an effective brain fitness exercise. Your mind is so used to you eating with one hand that switching it up will cause you to really focus. It's the same as brushing your teeth with the opposite hand. It might sound easy, but once you try it, you'll see how much you have to focus to complete the task successfully.

Brain fitness exercises: final word—Never stop exercising your brain. Brain fitness exercises will keep your mind operating at its highest level, and you'll remain healthier until an older age.

How Brain Fitness Games Work—Playing brain games is a proven way to improve brain fitness. Brain games are games which are designed to force the brain into using new neural pathways. Brain fitness is improved by engaging these new cells. Staying mentally active by playing brain games is a simple way to ensure that the brain will not become lethargic and lazy.

Brain Games You Can do When You're Bored—When a person is bored the brain is sending a message that it craves stimulation. Brain games can provide that stimulus. Any game which is new to you can improve your brain fitness. Many web sites offer free, short, fun games billed as brain games to play when you are bored. Brain games can be loaded on PDA's to play whenever one has a spare minute. Word games or puzzles, number games, speed coordination games, and spatial relationship puzzles and games are all types of brain games. Brain Games You Can Play with Others. One can also be social and improve brain fitness. Playing cards or working puzzles competitively are all brain games. Strategy games, chess being the ultimate example, will improve your brain fitness. For those who find chess daunting, the game itself is not the key issue. What is important to make any game a brain game that will improve brain fitness is that it be something new and challenging to the person playing it. A game of solitaire that is familiar and can be played while half asleep is not going to improve brain fitness. Switching to doing crossword puzzles or sudoku for a while will be stimulating. Variety is critical.
