EMBRACE
A newsletter for anyone touched by the rare genetic disease CADASIL

The mission of CureCADASIL/CADASIL Association is to raise awareness of CADASIL, ensuring it will be universally recognized and understood by the medical community, enabling patients to be correctly diagnosed. We are dedicated to helping patients, families, caregivers, and other supporters touched by CADASIL. We aim to unite patients and the medical community toward the common goal of treatments and ultimately a cure for this rare genetic disease, by promoting Communication, Advocacy, Research, and Education.

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Please join us in raising awareness!
cadasilassociation.org/raise-awareness

We are:
cureCADASIL.org
5th Annual CADASIL Awareness Day
November 16th

Want to tell your story? Have a question for the doctor? Planning an event? Upcoming newsletters will feature CADASIL patients and their loved ones sharing personal stories of living with CADASIL or caring for someone with this rare genetic disease. We welcome your submissions of stories, questions, news, memorials, and events. Please email them to: embrace@cadasilassociation.org

Please support our research funding drive in November!

The EveryLife Foundation for Rare Diseases will match every $10.00 donation for the month, up to $1,000,000!

Your donation receipt will show "4RareDiseases"

Text "Rare" to 85944
During November 2014
Please help!
Every donation will support vital ongoing CADASIL research at Harvard Medical School.
OUR STORIES

Marie Deets  
Neosho, Missouri  
Diagnosed at age 51

I was once asked to write an article for EMBRACE, but I declined not only because of my mental state but also because I don't have typical CADASIL. Then I decided I should write it simply because I am not typical.

My history with CADASIL began in 2007. I was working in the operating room of my local hospital when I thought I was having slurred speech. An hour later I could not speak at all and was taken to the emergency room. I was admitted and a battery of tests were given to determine what was wrong with me. I actually typed in all my symptoms online and kept coming up with CADASIL. I finally asked my neurologist if CADASIL was a possibility, but it wasn't until all other diagnoses came up negative that he agreed to do the testing. After testing, I was told by my neurologist that I did have CADASIL and was recommended to a genetic counselor. For five years I was treated for the symptoms of the disease, for memory and speech problems, for headaches and migraines, and for loss of sensory feelings in my limbs. I also had repeated MRIs showing extensive white matter lesions. Multiple sclerosis was discarded by the testing.

In 2012, I went to the CADASIL Family Conference in Salt Lake City, Utah. I happened to bring my genetic results with me. After the meetings I had one of the guest speakers from France look at my results. What a shock to be told that I did not have CADASIL, that my genetic mutation was not one recognized as CADASIL! That evening my test results were discussed more fully by the medical personnel attending the conference. Some said it was not CADASIL while others argued that it could still very well be. Needless to say, I was very upset. I had become a part of the CADASIL community and now felt I no longer had a diagnosis at all. Maybe I didn't belong there with other CADASIL patients and family members. A number of my friends at the conference, who are leading CADASIL advocates and showed great concern for me, said I was indeed part of the community and I should stay.

The next year I went to the 2013 CADASIL Association Family Conference in Boston, Massachusetts. I made arrangements to see Dr. Anand Viswanathan and have repeat tests done. Once again my genetic testing came back with an unknown mutation that at the current time is not considered CADASIL. However, after examining me and looking at my medical records, Dr. Viswanathan believed that I did indeed have CADASIL despite what my test results showed, and he decided to label my case as non-traditional CADASIL. He stated there are still many unknowns with the disease.

Since that time my health has continued to deteriorate with balance issues, continued memory issues, more lesions, and migraines 2-3 times a week. I was forced to make the choice to leave my job, as I could not foretell when I would be able to work. I lost my health insurance due to that decision. With the help of an attorney and Dr. Viswanathan, I am now trying to get disability. They feel I have a good chance. My new neurologist, Dr. Donald Hopewell of Joplin, MO, also believes I have CADASIL.

If you have been told that you do not have the mutation for CADASIL but you still have many of the symptoms, don't jump to the absolute conclusion it cannot be CADASIL. Hopefully your physician will be able to ascertain what the cause of your symptoms are, but there is still so much to learn about this and other rare diseases. Perhaps you are like me, one of the rare among the rare!

I am still active in the CADASIL community and continue to be a part of CureCADASIL/CADASIL Association.
OUR STORIES

Mel Messer
Fulton, Missouri
Diagnosed at age 49

When I was a young boy, I remember eating breakfasts consisting of buckwheat pancakes or French toast covered with butter or margarine and Karo syrup. I drank whole milk. For lunches and dinners I often had canned vegetables along with a salad and some kind of meat, usually pork or beef. I drank a variety of beverages, depending on my age and what was offered.

After my mother died when I was 13, my diet changed considerably, although I still consumed a large amount of sugar. I weighed about 162 pounds as a teen. As I got older, my metabolism slowed and I started putting on weight at an alarming rate until I was about 225 pounds at age 50. I had my first TIA (transient ischemic attack) at age 36.

At age 38 I experienced a major ocular migraine that affected my vision. I started taking a magnesium supplement. After a major ischemic stroke at age 52, I decided to lose weight to further reduce my risk of heart attack and further strokes. I was prescribed the aspirin-based blood thinner Aggrenox. I had no more TIAs. When I had a migraine with aura at age 57, it was verified that I did not have diabetes (my blood sugar was normal). CADASIL was identified as present. My employer placed me on disability watch, I was denied by Social Security, and I returned to work.

In 2014 at age 60, my diagnosis of CADASIL was revealed to the VA (Veterans Administration). I am still being considered for military disability, but CADASIL is now more of an organizational annoyance (a basic lack of CADASIL knowledge). I still take Aggrenox and minor magnesium as part of a multivitamin. I am down in weight, close to my teenage body weight. I enjoy my CADASIL fraternity.

I believe my early aspirin regimen prepared me for later CADASIL manifestations, giving me an advantage I enjoy today, with little to no symptoms present, and that the magnesium helped me to deal with the migraines. I like to think that other CADASIL patients can be helped by such simple strategies, and that beginning them early can help younger patients manage the disease.

Recently, I started shorting my prescription of Aggrenox to save money. I experienced a non-TIA manifestation of minor incoherence, resulting in an employment issue and a resulting agreement made between me and my employer to maintain my complete prescription and no longer try to save money. I am certain this will result in no further employment concerns regarding my diagnosis of CADASIL. At this time I have no pain from the disease, and I am lighter in weight, thus raising my personal life expectancy. Life is good.
ASK DR. JOE ARBOLEDA

Read more about him at:
http://www.schepens.harvard.edu/arboleda
Joe is on CADASIL Association’s Scientific Advisory Board:
cadasilassociation.org/scientific-advisory-board

Q: Is CADASIL a neurological disease or a DNA genetic disease?
A: CADASIL is both a neurological disorder and a genetic disease. CADASIL is a neurological disorder because its primary manifestation in both symptoms and signs involve brain functions. CADASIL is a genetic disease because it is caused by mutations in a gene named Notch 3.

Q: Can the lesions in our brains heal over time, or will the damage always be there?
A: The brain has a remarkable capacity to heal itself and try to repair the damage. Unfortunately, in most cases it appears that the disease outperforms the ability of the brain to recover, and this is more the case as we age.

Q: Can brain disorders such as CADASIL cause more vivid dreams and nightmares?
Patients report dreams where they wake up suddenly and are still experiencing the feeling of falling, tumbling backward, being hurled into space, etc.
A: This has not been properly investigated in CADASIL, but it is worth studying. If you are suffering from sleep problems you should consult with your doctor.

Q: We know that stress is bad for everyone. Does stress actually do significant/specific damage to our brains as CADASIL patients?
A: Stress management is essential for all of us regardless of whether or not we suffer from CADASIL. There are a number of effective methods to deal with stress, and your doctor should be able to recommend specific ways that may work for you.

Q: Is there any known benefit to taking drugs such as Axona for CADASIL? (Axona is sometimes prescribed for Alzheimer’s disease.)
A: CADASIL is a disease very different from Alzheimer’s disease, and thus taking medications for it should be done in close consultation with your physician. It is sometimes reassuring to just be taking something. However, because we know so little about the disease, this may not be recommended, as it is impossible to predict potential effects of the drugs.

Do you have questions for Dr. Joe? Send them to embrace@cadasilassociation.org and we will contact him. Chances are we will publish the question and answer in an upcoming newsletter.
May 16, 2014: Anne McGuinness met again with Rare New Jersey at Bio NJ in Trenton, NJ.

May 19, 2014: CADASIL Association launched its campaign for a course in Rare Diseases in Medical Schools. Janice Ragazzo and Robert Davis were part of the team that set this campaign in motion with an online petition and a conference with NORD to discuss the most productive venues to advocate our message.

June 17, 2014: Anne McGuinness attended a Biosimilars Lunch and Learn at the Wyndham Garden in Trenton, NJ. This conference focused on biosimilars that can be used instead of biologics in the treatment of certain diseases. Biosimilars will be just as effective and less costly. Europe is using biosimilars. The US is lagging behind. Hopefully, when a treatment/cure for CADASIL becomes available, a biosimilar will be developed so it will be readily available.

June 17, 2014: Janet Mills and Barbara Hunt attended the RDLA (Rare Disease Legislative Advocates) Conference Call to go over current issues involving the Rare

June 18, 2014: Janet Mills was a call-in guest on Gary Garver’s “Controlled Chaos” Radio Show in Loma Linda, CA (Los Angeles area). Janet shared information on CADASIL and how CADASIL Association is striving for a cure, as Gary’s brother was recently diagnosed. http://www.kcaaradio.com

June 24, 2014: Alisa Jo Middleton and Janet Mills participated in the WEGO Health Rare Disease Chat on Twitter. Anyone who “tweets” and is a member of the global CADASIL community (patients, family members, friends, doctors), please consider joining these discussions to help promote awareness of CADASIL. The chats are held every Tuesday at 3pm EST at: twitter.com/wegohealth

July 8, 2014: Barbara Hunt attended a NORD webinar on relationships with Congress.

July 9, 2014: Anne McGuinness and Barbara Hunt attended the Global Genes Foundation Alliance webinar. CADASIL Association is a member of the Global Genes RARE Foundation Alliance. This meeting went over the latest developments in the rare community; rare-related research, industry, and legislative updates; Global Genes initiatives; and tools for the nonprofit community. globalgenes.org/foundation-alliance

July 22, 2014: Barbara Hunt attended the NORD webinar "How to Have a Successful Meeting with Congress."
MORE RECENT NEWS

Summer 2014: CADASIL Association frequently receives phone calls from people wanting more information about this genetic condition. During a recent call, Janet Mills spoke with a woman living in the Virginia area who is originally from the country of Kuwait. She requested information for a friend residing in Kuwait who has CADASIL. The friend wishes to come to the United States for a consultation. Janet was able to recommend doctors in the USA from the association’s Doctor Directory. We continually strive to keep the list updated. Please view our directory at: cadasilassociation.org/Doctors

If you wish to add a name (or if you have information to share about any name on our list), please contact us at: info@cadasilassociation.org

Summer 2014: RDLA (Rare Disease Legislative Advocates) organized In-District Lobby Days – also called “Legislative Fly-Outs” – where anyone in the US Rare Disease community could register to meet with congressional representatives from their regions. Through RDLA webinars prior to the meetings, participants learned about general “Asks” for the Rare Disease community (ie: current health legislation, requests to join health committees, etc). We could provide a one-sheet information page about us personally and our stories concerning CADASIL. We hope to have this opportunity again next summer, with more people from the CADASIL community taking part.

August 4, 2014: Anne McGuinness met with Congressman Holt's staff in West Windsor, New Jersey.

August 7, 2014: In-District Lobby Day at Senator Menendez' Barrington Office in Barrington, NJ.

L-R: Anne McGuinness (CADASIL Association/Cure CADASIL), Ronnie Bradbury (CADASIL Association/Cure CADASIL), Carla Herbert, Lisa Schill, and Nancy Masters met with Vanessa Lawson (front row, center). Vanessa Lawson is the Deputy Director of Constituent Services for Senator Menendez.

August 18, 2014: Janice Ragazzo and Barbara Hunt met with Congressman Maloney's staff in Newburgh, NY.

September 3, 2014: Janice Ragazzo and Anne McGuinness met with Senator Booker's staff in Newark, NJ.
MORE RECENT NEWS

September 3, 2014: Janice Ragazzo and Anne McGuinness met with the Rare Disease Report organization to discuss the need and importance to raise awareness of CADASIL in the medical community, especially among neurologists and emergency room physicians.

September 11-13, 2014: Pam Scott represented CADASIL Association/Cure CADASIL during her attendance at the Global Genes Rare Patient Advocacy Summit and the Tribute to Champions of Hope Gala held in Huntington Beach, CA. Read her story starting on page 9.

September 13, 2014: Janice and Tony Ragazzo participated at the Town Community Day in East Fishkill, NY with a CADASIL Awareness Booth.

September 17-19, 2014: Janet Mills donated a basket of her fiction books for the silent auction held during the Public Health in the Rockies Conference in Fort Collins, CO. Pamphlets about CADASIL were sent with the basket to be displayed and picked up by interested attendees during the conference. To download CADASIL Association’s tri-fold colored information brochures for handouts and displays, and for other awareness materials, go to: cadasilassociation.org/raise-awareness

September 21, 2014: The CADASIL Association was invited to attend The Non Profit Forum sponsored by The National Institute of Neurological Diseases and Stroke. Anne McGuinness attended on behalf of the association.

September 2014: CADASIL Association members participated in the PCORI patient survey.

September 30 - October 2, 2014: Barbara and Joe Hunt and Anne McGuinness attended the American Association of Critical Care Nurses Conference in Valley Forge, PA, and put up an exhibit for display.

October 2, 2014: Dr. Swati Sathe from the CADASIL Association Scientific Advisory Board gave a presentation on CADASIL to the nurses at the American Association of Critical Care Nurses Conference in Valley Forge, PA.

October 3, 2014: Janice Ragazzo and Barbara Hunt joined the Brain Initiative Twitter Chat and tweeted about CADASIL with the NIH.

October 14-15, 2014: Anne McGuinness attended the Bio Conference in Washington, DC.
CADASIL RESEARCH UPDATE

Research Summary – Summer 2014

Mark Graham with Dr. Joseph Arboleda

Harvard Medical School

CADASIL is caused by mutations in a gene that makes a protein known as the Notch 3 receptor. These mutations lead to early onset of stroke, transient ischemic attack and migraine.

Currently there are no therapies for this condition and developing one requires proof of concept with the use of clinical trials. Depending on the type of clinical trial, many outcomes can be used to measure the effect of a therapy. Many groups have tried to relate MRI scans but these are time consuming for the patient and incur greater costs when compared with proxy markers. The potential use of proxy markers or biomarkers of CADASIL disease status found in the blood could offer a great alternative and increase the feasibility of a clinical trial.

Given that the mutations that cause CADASIL are associated with the Notch 3 receptor, our group set out to develop a test that could be used in the lab to measure the levels of circulating proteins in the blood.

Previously Dr. Joseph Arboleda had collected blood samples from CADASIL families in Colombia. These families had a variety of mutations associated with CADASIL and had a large range of ages. Using these blood samples they compared levels of circulating proteins in CADASIL patients, with people who do not have CADASIL.

From our preliminary results we see a general trend suggesting that specific proteins may serve as biomarkers of the disease because their levels in the blood of patients with CADASIL appears to be different than that in individuals without the disease. This find was validated in mouse models of CADASIL carrying identical mutations than that of the patients. These mice show a very robust change compared with our human blood samples. This is not surprising given the huge variation in age seen in our patients and the incredibly controlled environment the mice live in. As such we would love to expand our study to include more patients in a larger, more controlled patient screen including patients from the US. Such a screen could validate circulating proteins as biomarker in CADASIL.

The full scientific report has been submitted to CureCADASIL/CADASIL Association, which includes the data generated during the CADASIL summer fellowship and an overview of the science behind the use of biomarkers in CADASIL.

CureCADASIL/CADASIL Association awarded Mark Graham with a $4,000 grant to conduct this research in Dr. Joseph Arboleda's laboratory at Harvard Medical School during the summer of 2014. Donations will help continue funding for this vital research.

Want to help? Please see our donation options at: http://www.cadasilassociation.org/donate

Photo at left: Dr. Joseph Arboleda in his Harvard lab presenting Mark Graham with the CureCADASIL grant check
**EVENT SUMMARIES**

*My Experience at the Global Genes Rare Disease Patient Advocacy Summit by Pam Scott*

I attended the Global Genes Rare Disease Patient Advocacy Summit and Gala on September 11-13, 2014 in Huntington Beach, California, as a representative on behalf of Janet Mills for CADASIL Association. This event was very eye opening for me about rare diseases and the challenges patients, families, and doctors face in dealing with rare diseases. As is the case with other serious conditions, finding a good doctor who knows about CADASIL is one of the biggest challenges we face; the second is finding a treatment that can help ease our symptoms; and a third challenge is having our rare disease get enough attention for much needed research funding to enable breakthroughs in treating our symptoms and, God willing, ultimately find a cure.

I met so many good people there! A lot of them are parents of children with rare diseases, as well as doctors, care workers, and other angels on earth who care that the voices of the rare disease community are heard. It is through these parents and others with rare disease that I’m learning the frustrations of our health care shortcomings.

So much needs fixing in our system. The parents I met at the summit are looking for support, and they want to be heard. All the health care advocates I met also want to be heard, and they came to share ways they have learned to get a foothold in the rare disease world, to gain attention for their conditions, and to have patient needs met.

By speaking out and uniting as a rare disease community, we can be strong enough collectively to have our needs be heard and invoke changes in the health care system; otherwise, we are just trying to fit into a mold already in place.

I attended a number of the workshops offered. (Please see my notes later in this article from some of the Deep Dive Discussions.) I learned that patients and their families can be involved at basic levels by sharing their data through sanctioned and safe sites.

I feel I am lousy at lobbying, but now I know from talking with another woman about this first-hand that it is a one-step-at-a-time process -- going up the ladder one rung at a time. She just posted her success the other day on Facebook, for her non-profit organization being recognized by the State of Texas. To me, this is proof that anything is possible!

An important take-away for me is that everyone at the Summit was there for the betterment of those afflicted with rare disease and their families, and that this community coming together for all aspects of rare disease was bound by love. There was a particular moment in the afternoon of our first day as Christina Waters (founder & CEO of RARE Science) was giving her lecture, when she had to stop and pause for a moment, overcome by emotion. She was talking about how patients suffering from rare diseases don’t have time to wait. She said, “Individualized medicine holds the key to finding treatments and cures for rare diseases. (We/you/they) don’t have time to wait for a 15-year drug development program...when other means can provide therapeutic solutions today. It’s so important to keep this...
**EVENT SUMMARIES**

**Pam Scott - continued**

momentum of advancement going, for the hope it gives patients to know somebody cares for them, are working with their best interests in mind, to help them keep looking forward at a positive ‘someday’ for breakthroughs in their treatment…” It was at that moment when I realized how special this Summit and its guest speakers really were.

My impression after leaving the Summit is that there is much to be done in the rare diseases’ world, especially in two dominant areas: research for symptom treatments and cures, and funding for this research. There are many facets to explore: symptoms, diagnosis, name of diseases, treatment, research, funding, and acknowledgement in the world. There are many branch-offs within these areas, but they all are heading in the same direction: toward the cure.

The emphasis is that rare diseases are better treatable for young children: research programs prefer to start with youngsters and see the progression through childhood. There are few opportunities for adults to experience these treatments, even on a research level. There are treatments for some that make life longer and symptoms become negligible or at least disappear just enough for some better quality life.

For adults, the best things we can do with our resources are bring awareness to our disease and fundraise, fundraise, fundraise! Also “Take it to the Hill” meaning write to and/or meet your representatives on Capitol Hill. Get these people involved and help direct funding to research for our disease.

Pam Scott with Carrie Ostrea of Global Genes

Pam attended a number of sessions at the Patient Advocacy Summit on topics that include:

- Caregivers: Strategies to Stay Afloat; Making Peace With What You Cannot Control; 10 Qualities of Resilient People; The E-Patient Revolution; The Power of Putting Information into the Hands of the Patient; Patient-Centered Benefit-Risk Assessment: Why It Matters to You; Mobilizing Your Community for Patient-Focused Drug Development; The Unstoppable Charity; Mission, Goals, and Strategic Planning; Where the Needs of Families and Healthcare Professionals Intersect

For Pam’s notes to these sessions, email us what you are interested in reading at: info@cadasilassociation.org
UPCOMING EVENTS

CureCADASIL.org
ENVISION THE CURE
EMBRACE THE CHALLENGE

5th Annual CADASIL Awareness Day
November 16th

Raise awareness everyday by checking out our ideas at:
cadasilassociation.org/raise-awareness

Have suggestions and ideas? We’d love to hear them! Please email us at: info@cadasilassociation.org

Save the date!

The ULF/United Leukodystrophy Foundation is planning their next Scientific Meeting and Family Conference in Omaha, Nebraska from July 15-18, 2015. CADASIL will be one of the conditions included in the conference. Dr. Fabrice Dabertrand of the University of Vermont, who received the ULF’s $25,000 CADASIL Research Grant earlier this year, will be reporting on his work. The ULF plans on inviting additional doctors knowledgeable about CADASIL, and there will be a concurrent session during the conference that focuses on CADASIL. We will update you as we learn more about this opportunity to gather as a CADASIL community. http://ulf.org/conferences

Please support our research funding drive in November!

CADASIL Association is a 501(c)(3) tax-exempt non-profit organization
MORE UPCOMING EVENTS

Cure CADASIL/CADASIL Association will have this ad (below) published in the 60-page Rare Disease Resource Guide, to be distributed to over 60,000 clinicians and key stakeholders interested in rare diseases. These Guides will be mailed to 15,000 physicians and geneticists and an additional 45,000 physicians and nurses via e-mail. The Guide will be on their website for the entire year.

Coming up on February 23, 2015: Tony and Janice Ragazzo, representing the CADASIL Association, are collaborating with the New Jersey Devils for a fundraiser at Prudential Stadium in Newark, NJ during the NHL/National Hockey League New Jersey Devils vs. Arizona Coyotes game.

CADASIL Association is a 501(c)(3) tax-exempt non-profit organization
PARTICIPATE

Opportunities for you to help the Association!

Bravelets™ bracelets are worn to help you be strong and brave in tough situations. Order a Bravelet™ and CureCADASIL/CADASIL Assn will receive $10 of your purchase! www.bravelets.com/bravepage/cure-cadasil

Tax-exempt donations are always appreciated and acknowledged by the CADASIL Association. Some ways the association is planning to use funds raised and donated in the near future include:

Developing educational materials for patients, caregivers, and healthcare professionals that are accurate, comprehensive and current. We have a full-color tri-fold brochure printed and available for distribution. Other items are also available. Please request materials from: info@cadasilassociation.org

The summer of 2014, CADASIL Association sponsored a college graduate student for a research project, assisting Dr. Joe Arboleda at Harvard Medical School. This first award was given for $4,000. It takes $16,000-$20,000 to sponsor one undergraduate student for a year. Please see page 8 for a summary of this ongoing research.

Providing awareness materials to anyone interested in helping educate the public about CADASIL. We have banners to loan for events, business cards and denim ribbons to hand out, informational letters, and donation request letters available. Please contact us about any of these items.

CADASIL Association is a recognized charitable organization of iGive, where you can sign up to have a small amount of each item you purchase donated (at no extra cost to you) to your

Please consider signing up for Amazon Smile and listing CADASIL Association as your charity. Your Amazon account benefits and prices will remain the same, and 0.05% of each purchase is donated. http://smile.amazon.com/ch/45-5242623

CADASIL Association is a recognized charitable organization of GoodSearch and its affiliates. Go to: www.goodsearch.com/nonprofit/cadasil-association.aspx

Once you sign up and choose the association as your designated charity, every time you do a search with GoodSearch or use GoodShop, GoodDining, or their other choices, CADASIL Association earns money. Consider joining GoodSearch instead of Google or other search engines. You can bookmark the weblink or put it into your browser's toolbar so it is easy to find every time to search or do a little online shopping!

Please note: A number of CADASIL Association Trustees and members travel to conferences and events to promote awareness of CADASIL, to learn more about this condition, to network with others in the rare disease community, to meet with elected officials and medical professionals, to attend workshops and seminars, and for various other reasons important to our mission. **These trips are funded entirely by the trustee or member involved. No monies from the CADASIL Association are used for travel expenses.** In some cases, organizations such as RDLA (Rare Disease Legislative Advocates) and Global Genes offer limited travel stipends, funded by corporate sponsors, for rare disease advocates attending events. CADASIL Association encourages all members to participate in the same manner when possible. We will provide informational materials for your use upon your request.

CADASIL Association is a 501(c)(3) tax-exempt non-profit organization
Please join the CADASIL Association! Here's the link again: www.cadasilassociation.org/join-us

Looking for ideas on how to help raise money for CADASIL Association toward our goals and mission? Here are some suggestions. We welcome yours, so please share them with us and we may publish them in an upcoming newsletter.

**Gifts:** Looking for the perfect gift for someone on your list? Making a donation to CADASIL Association in honor of someone touched by this disease is a loving gesture.

**Cans for CADASIL:** Does your state have deposits on containers? Have a Cans for CADASIL Drive! Ask your friends, family, schools, churches, social clubs, etc. to collect their cans and other recyclables and donate the money to CADASIL Association.

**GoodSearch.com:** Join GoodSearch to raise funds for CADASIL Association! GoodSearch donates money to your favorite cause when you search the Internet, shop online or dine out at local restaurants! Use GoodSearch.com to search the Internet and they donate a penny per search to your cause. Use GoodShop.com when you shop online and they donate a percentage of every purchase and offer over 100,000 coupons to help you save money too! Sign up for their GoodDining program and they'll donate a percentage of your restaurant bill when you eat at any one of thousands of participating restaurants. It's really easy; it's FREE and turns simple everyday actions into a way to make the world a better place. Please sign up today to help CADASIL Association! Go to www.goodsearch.com/nonprofit/cadasil-association.aspx to get started.

**Make Change for Charity:** Toss that spare change from your pocket or purse into a container. Once every few months, locate a Coinstar machine at your local grocery or discount store and donate the cash you receive back to CADASIL Association. This would work well in a school setting as well.

**One Thing I can Do:** Your days are busy, and if you have CADASIL, sometimes filled with painful symptoms. Instead of thinking of all the many ways you can help make a difference, pick just one and follow through on it. One person doing one thing can help toward awareness and ultimately funding toward a cure.

**Know someone who owns a business?** Make a call today and ask if the business could host an event to benefit CADASIL Association. Many businesses in our communities are willing to partner with a good cause. One example: An ice cream shop allowed a charity to display their sign next to a receipt fishbowl by the cash register for one day. Patrons “donated” their receipt. The charity was given 5% of total receipts for the day! Another example: A friend who sells products through home parties donated a percentage of sales at a party organized by a member of the charity. Make that call today!

**Garage sale:** Clean out those closets and pick a date for a garage or yard sale! Enlist friends and neighbors who may want to help, and have fun together while supporting CADASIL Association.

Electronic donations are always appreciated at: www.cadasilassociation.org/donate
The Burden of Knowing by Phil Jones

Is it a privilege, or is it a burden, to have knowledge of what may lie ahead?

Modern medicine brings with it many advantages for modern societies, but – for some people – those advantages also have associated personal costs. One such cost flows from developments in genetics, whereby conditions that might previously not even have been recognised can now be identified and documented … and their likely effect on individuals predicted with increasing levels of confidence and accuracy.

In 1993 an extensive study of 57 adult members of a French family identified a new genetically-based medical condition – still relatively unknown, even today – that came to be called CADASIL. Within three years, the responsible gene was identified. During the past twenty or so years, over 1,000 CADASIL families have been identified worldwide and over 1,000 scientific articles published on their experiences. [The disease was actually first described by a Belgian neurologist in 1955. In 1987, a Nordic case was identified and reported upon. At the time, the condition was generally referred to as hereditary multi-infarct dementia.]

So, what is CADASIL? It’s not too hard to guess that it’s an acronym: Cerebral Autosomal Dominant Arteriopathy with Sub-cortical Infarcts and Leukoencephalopathy. Deconstructing the acronym is helpful because of its less familiar terms:

Cerebral - pertaining to the cerebrum or brain;

Autosomal Dominant - a trait or disorder that can be inherited. If a gene is autosomal dominant, a person only need get it from one parent in order for offspring to inherit the condition;

Arteriopathy - a disease of the arteries, usually those of small to medium size;

Sub-cortical Infarcts - areas of tissue death in the subcortical region of the brain (i.e. immediately below the cerebral cortex). White matter and deep grey structures constitute the subcortical region. This is the area involved in thought, voluntary muscle movement, reasoning and memory;

Leukoencephalopathy - a brain disease caused by damage to the white matter.

Put simply, CADASIL is an inherited condition that causes strokes and related impairments. The cause of the condition is a mutation on the Notch 3 gene, which – after birth – has a key role in maintaining the integrity of arterial vessel walls. The mutation (the specific form of which may vary) causes muscle cells in the arterial wall to disintegrate over time, leading to a loss of blood supply in the region supplied by the blood vessel concerned. Arteries throughout the body may be affected, but it is vessels within the brain where the effects of the mutation manifest themselves most seriously. The white matter and deeper parts of the brain are particularly affected, giving rise to the eponymous infarcts of the condition.

An infarct in the brain can lead to a stroke, which is often the symptom with which CADASIL patients first present. In individuals with CADASIL, a stroke can occur at any time from childhood to late adulthood, but typically happens during mid-adulthood. Further, not only does the age of symptomatic onset vary greatly amongst affected individuals, but so does the severity of symptoms.
Phil Jones, continued

People with CADASIL often have more than one stroke in their lifetime; and recurrent strokes can cause cumulative damage. Strokes that occur in the subcortical region of the brain can cause progressive loss of intellectual function (i.e. dementia) as well as changes in mood and personality.

The damaged blood vessels can also lead to some patients experiencing migraines, often with visual sensations or auras, or – though less often – recurrent seizures (epilepsy). Many CADASIL patients also develop leukoencephalopathy, a change in white matter tissue that can be seen with magnetic resonance imaging (MRI). Death generally occurs 10-20 years after the onset of strokes and dementia, typically in the sixth decade, though some patients survive well beyond this.

If one parent is affected, each child of that parent has a 50% chance of inheriting the condition. But, once a child receives the abnormal copy of the gene, the child is certain to develop CADASIL. Although a gene mutation may occur spontaneously, most individuals with CADASIL have a family history of the condition. However, because a genetic test for CADASIL was not available before 2000, many cases were previously misdiagnosed as multiple sclerosis, Alzheimer's disease, or some other neurodegenerative disease.

CADASIL is not associated with the common risk factors for stroke and heart attack, such as high blood pressure and high cholesterol, although some affected individuals might, of course, also have these health problems. Because it is a rare and little known condition, it is often under-recognized and under-diagnosed. Accordingly, the condition may be suggested by a patient presenting with one or more of the following factors:

- (i) One or more of recurrent subcortical ischemic strokes (especially before age 60 and in the absence of vascular risk factors), migraine (especially with aura) and/or early cognitive decline or subcortical dementia;

- (ii) An MRI image showing more white matter lesions in the brain than might be expected for the patient’s age (characteristic changes to white matter are detectable before an affected person is in his or her twenties);

- (iii) a family history of migraine, early-onset stroke, or dementia. The clinical spectrum of CADASIL is broad, and – in some families – migraine may be the only clinical manifestation.

While MRI is not used to diagnose CADASIL with certainty, it can show the characteristic progression of white matter changes decades before onset of symptoms. Once CADASIL is suspected, however, confirmation requires genetic testing, which can nowadays be undertaken simply by using a blood sample.

There is currently no cure for the condition, and medical treatment is aimed at minimising risk factors. Migraine headaches may be treated by appropriate drugs, and a daily aspirin may reduce stroke and heart attack risk. Typically, aspirin and statin therapy will be used jointly. Homocysteine levels tend to be elevated in CADASIL patients and treatment with folic acid is sometimes considered. [Homocysteine is an amino acid in the blood. High levels have been associated with atherosclerosis (fatty deposits in blood vessels) although a causal link has not been established. Folic acid interacts with homocysteine in such a way as to reduce its associated risk.]

Anticoagulation drugs are generally inadvisable because of the ongoing risk of micro-haemorrhages. Other stroke risk factors such as smoking, hypertension and high blood fats should also be treated. Symptoms usually progress slowly. By the age of 65, however, most people with CADASIL will have some cognitive problems and dementia, and some will become dependent following multiple strokes.

In my own family, the effects of CADASIL can be traced, in all probability, to at least my great-great grandmother, who died in 1877 at the age of 41 because of “Softening of Brain [and] Convulsions”. Following the genetic line, my grandmother died in 1960 at the age of 54 as a result of “Disseminated Sclerosis” (i.e. Multiple Sclerosis). My mother died in 2001 at the age of 69 because of “Cerebrovascular accidents [and] TIA’s”; and her younger sister predeceased her after suffering the same fate at the age of 65. Of some comfort, perhaps, is that my great-grandmother, who must have passed on the faulty gene, survived until age 78. She died in 1947 of “Myocardial degeneration [and] Arterio Sclerosis”, which is consistent with having the gene, despite living to a reasonable old age (though her physical and mental condition prior to death is unknown).
Phil Jones, continued

My own confrontation with CADASIL came two years ago at the age of 60, following an unexplained brain haemorrhage. There was, at the time, some debate amongst the hospital doctors as to whether an MRI was necessary, given that a CT scan had already confirmed a bleed in the brain. But some of the more prescient consultants took the view that the unusual locus of the haemorrhage (the cerebellar vermis), coupled with an absence of established risk factors, warranted further investigation. In the event, the MRI revealed abnormal signals in the sub-cortical white matter, the distribution of which was characteristic of CADASIL. A genetic blood test later confirmed the diagnosis. [The genetic test found what was described as a “classic well described mutation”, with “the exon 4 mutation causing c544C to T mutation with the protein going from arginine 182 to cysteine.”]

It is an interesting psychological challenge when, having lived a reasonably normal, healthy life, one is confronted with the knowledge that something has been quietly and consistently burrowing away, as it were, at one's biological essence. It seems akin to a deceitful bodily self-affront. And yet, why should it not be so? We all – save in the farthest reaches of futuristic speculations – have to die of something; and the proverbial bus could despatch any of us at any time. But somehow there is a quiet finality to it all: the challenges, and possible end, that one may face are suddenly revealed in stark, undeniable simplicity. Given my age and the likely progress of the condition, I am perhaps approaching the end of the race, and a bell may signal the start of the final stretch at any time. The everyday term for the archetypal manifestation of a brain haemorrhage – a “stroke” – well reflects its characteristic suddenness, rather like the ominous appearance of a medieval executioner.

I find that I have a new, heightened sense of awareness. Occasional head pains – too minor and fleeting to be termed headaches – now take on a new significance. A momentary stumble, as I miss my footing, is now something that I note and remember, in case it becomes a frequent occurrence. A verbal hesitancy, if I have to search for the correct word, is no longer something casually ignored. Yet all such events are part and parcel of everyday life – who does not occasionally have a headache; who does not sometimes miss their footing; and who does not sometimes search for a word in their speech? Friends of a comparable age are kind enough to say that they experience similar events too, and I’m sure that they do. And yet, and yet...

There are, too – perhaps inevitably – associated feelings of guilt. The guilt may be unwarranted and illogical, but it exists nonetheless, albeit in a shadowy, background form. No moral blame can be attached when I inherited the gene, and none was involved when I passed it on, as I now know I have. An MRI scan of my elder son has revealed tell-tale signs of white matter lesions in his brain too. In his case, a decision needs to be made about whether he should seek genetic testing as final confirmation. There may be little point in this, and there are insurance implications too – so it’s not an easy decision for someone with family responsibilities. I acquired knowledge of my condition at age 60 – the situation is different for someone in their early thirties, with children of their own. The burden is greater.

Diagnosis of a degenerative condition changes everything, but more so perhaps if the condition is a rare one, because it can be so unexpected. It can fracture plans and dreams, metaphorically knock you sideways, and require ongoing emotional investment as you try to assess what your next steps should be. Further, living with a progressive disease is a profound challenge not just for the affected individual but for his or her family too.

So, is it better to know or not know? Well, the answer may depend both on the medical condition and on an individual’s circumstances. In my case, I think it is a privilege as well as a burden. My diagnosis has not only helped explain what happened to my immediate forebears, but has also helped me to connect with them in a way that would not otherwise have been possible. I understand more now. And, although modern medicine cannot currently provide a cure, it can help mitigate the risks, and identify lifestyle choices that may optimise future wellbeing. Further down the line, my descendants may benefit from advances in gene therapy, which is already making significant strides forward. For my part, I’ll just try to maintain a full and active life, hope for the best ... and keep taking the tablets.
WEB LINKS

These website links may be new, recently discovered, or information we wish to share with the CADASIL community again. If you find some as well, please let us know!

Multiple Sclerosis Differential Diagnoses (including CADASIL)

National Multiple Sclerosis Society – Other Conditions to Rule Out (CADASIL is listed)
http://www.nationalmssociety.org/Symptoms-Diagnosis/Other-Conditions-to-Rule-Out-section-3

5 Ways You’re Not “Living” with Chronic Illness by Ilana Jacqueline
http://www.huffingtonpost.com/ilana-jacqueline/personal-health

Strokes and the Toll They Take on Younger Adults

The Amazing Brain Benefits of Going Grain-Free

From The Netherlands: The development of therapeutics for CADASIL patients
http://media.leidenuniv.nl/legacy/ncd-mc142.pdf

Twitch, a documentary about Huntington’s Disease, deals with the question many people with rare diseases ask: Would You Want to Know? http://twitchdocumentary.com/see-the-film
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