Deater Foundation, Inc.

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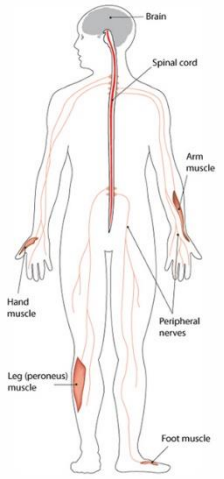
Hereditary Sensory and Autonomic Neuropathy Type 1 (HSAN1) is a dominantly inherited neuromuscular disease. It is sometimes misdiagnosed as Charcot-Marie-Tooth (CMT) disease, which is the most commonly inherited peripheral nerve disorder. Like CMT, HSAN1 causes damage to the peripheral nerves, which relay sensations such as pain and touch to the spinal cord and brain from the rest of the body and carry signals from the brain and spinal cord to the muscles.



Research in this disease in the Deater family began in 1938 and continues today. The family established a non-profit Foundation in 1990 to support research to find the cause and cure for HSAN1. The gene and its likely mechanism have been identified.

We are hopeful for a cure. We encourage you to join with us with your contribution, no matter the amount, to continue the research to put an end to this life altering disease.

Randomized Trial of L-Serine in Patients with Hereditary Sensory and Autonomic Neuropathy Type 1

(Vera Fridman, MD, Saranya Suriyanarayanan, PhD, Peter Novak, MD, PhD, William David, MD, PhD, Eric A. Macklin, PhD, Diane McKenna-Yasek, BSN, Kailey Walsh, BS, Razina Aziz-Bose, BA, Anne Louise Oaklander, MD, PhD, Robert Brown, MD, DPhil,* Thorsten Hornemann, PhD,* and Florian Eichler, MD* Neurology® 2019;92:e1-e12. doi:10.1212/WNL.0000000000006811)

The findings from the 2-year clinical trial involving L-serine therapy in patients with HSAN1 were recently published in *Neurology*. Between August 2013 and April 2014, 18 participants (aged 18-70 years) with symptomatic HSAN1 were enrolled and randomized in the study. Participants were randomly assigned to receive either L-serine (400mg/kg/day) or a matching placebo (identical in taste, appearance, and smell) for 1 year. Both "treatments" were in powdered form, dissolved in water, and administered by oral ingestion. During the second year, all participants were given L-serine. Of the 18 participants, 16 completed the study.

After 1 year, the group treated with L-serine demonstrated a significant improvement relative to the placebo group when assessed using the Charcot-Marie-Tooth Neuropathy Score version 2 (CMTNS) scale. (CMTNS is a scoring system that evaluates things like symptoms, signs, and neurophysiological tests – each item is scored, and the overall sum total provides a method for measuring disease severity, with higher scores indicating worsening function.) At the same time, a decrease in deoxysphinganine levels was also reported in L-serine treated patients versus the placebo group. Both groups improved on the CMTNS scale with L-serine treatment during the second year, and placebo participants who crossed over to L-serine treatment in the second year also experienced a decline in deoxysphinganine levels as well.

No serious adverse effects were observed with L-serine treatment during this study, and the results indicate that oral L-serine supplementation is a safe therapy for patients with HSAN1 and is potentially effective at slowing disease progression.

For the full article, please visit our website at www.deaterfoundation.org

Thank You!

The Deater Foundation is deeply grateful to Dr. Florian Eichler, who has pursued research on the mouse model of HSAN1 leading to the supplementation of L-serine as a treatment for this disease. Dr. Eichler began his HSAN1 journey in Dr. Robert Brown's Day Lab at Massachusetts General Hospital (MGH). From his own lab at MGH Dr. Eichler has collaborated with other researchers from around the country and around the world. He continues to advocate for therapy by encouraging manufacturers to develop a long acting L-serine.

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Spinal Cord stimulator by Amber Wetrosky

The neuropathic pain drowned out any happiness I had. The shooting pains, the burning...
My neuropathy had been steadily increasing in severity. I had reached the therapeutic maximum on the medication gabapentin. I rejected other pain medication. As a nurse, I have seen the throes of opiate addiction in patient care and I swore that I'd never venture down that path myself. The intense burning and shooting pains in my feet were stealing my sanity and I had contemplated suicide many times. If it weren't suicidal plots, I'd often drum up ways to amputate my feet myself. I knew that the pain had pushed me too far into the dark zone of insanity.

I began seeing a pain specialist. Given my stance on opiates (their mainstay for service), I was at a loss. The pain specialist did however mention a spinal cord stimulator as an alternative to my request to ablate (destroy) the nerves. My first stimulator leads (wires) are placed near the spine in my upper back at the area of Thoracic vertebrae #8 and are connected to an implanted battery. I had the unit re-programmed many times as the coverage area only changed the sensation from my upper-waist down to my knees. The desired target area was still burning. My pain was just as severe as before, but then I had an unnecessary tingling sensation from my waist to my knees.

I scheduled an appointment with a very successful neurosurgeon to see if he could remove the unit. He instead talked with me about the DRG stimulator. It is a stimulator that sits atop the dorsal root ganglia, the portion of the spine that is responsible for bringing sensation signals back to the brain. A DRG stimulator scrambles the pain message from my feet back to my brain without sacrificing motor ability. I researched it. At that point, I had nothing to lose. We went for it!

The DRG stimulator has leads placed near my spine in my lower back at the lumbar #4 and #5, and sacral #1 levels. They are also attached to an implanted battery. Everything is completely internal with both units. The DRG stimulator gave me my life back! Things aren't 100% pain free and I don't expect this holiday to last forever. I'm also very aware that the stimulator is simply a means to control the way my brain perceives pain. The DRG stimulator--any stimulator for that matter, has no impact on the course of this disease.

I have both simulators running simultaneously, at all times. They produce a deep buzz. One so subtle I can't feel it without concentrating. To give someone an idea of how a spinal cord stimulator works, I would loosely compare it to a TENS unit (a transcutaneous electrical nerve stimulation device which is external and sometimes used to relieve back pain). I still take medicine though. I switched from gabapentin to Lyrica (100mg 3X daily).

For the most part I feel pretty good. I can't run, and descending stairs is troublesome, but over-all I'm doing well enough to be a mom and to work full time.

Chris' Decision

Hello, let me introduce myself. I am Chris Deater Christensen, daughter of Harvey Deater. On December 23, 2018 I had a below knee amputation of my right leg. Anyone with HSAN1 could be faced with the same decision. Here is the backstory of how I arrived at this decision.

I came home from vacation in January 2018 with a heel ulcer. I have no idea how it started as I check my feet every night due to my HSAN1 neuropathy. Somehow during the course of one day something caused a hole in my foot. I saw a podiatrist the week after I got home; he had me non-weight bearing for a while and then put me in an off-loading boot. By the end of March, the hole was the size of a pin, so I went back to normal shoes. In June the hole (ulcer) started to get larger so back to the podiatrist. He put me back into the boot. At this time, I had no x-rays or MRI to look for infection and consequently no antibiotics. I was seeing this doctor every three weeks for debridement. By mid-July my foot and leg were very swollen. The podiatrist told me to elevate it. At the end of July, I was feeling sick and sleeping all the time. When I had to drive a short distance on August 1st, I couldn't stay awake. The next few days I got extremely sick: nausea, neck pain, fever, and headache. I was working and didn't get to a doctor until I became so sick I wasn't sure I could drive. My husband, Pete, took me to Urgent Care where they diagnosed me with a kidney infection and possible stones. They prescribed me a broad-spectrum antibiotic. I took that for two days and did not feel any better. At this point I couldn't get out of bed. After the two days with no improvement I went to our local ER. They drew blood and results were within normal limits. I was given fluid for dehydration and sent home; I couldn't keep food or water down. The next morning I started shaking uncontrollably. That really scared me, so Pete drove me to the hospital. By the time we got to the hospital the shaking had stopped so I had him turn around and drive us home. The next evening I felt the shaking start again and made him take me back to the hospital. Something was not right. Even though my shaking stopped, we went into the ER. I waited two hours in the waiting room and prayed that someone would call us next. I was feeling so bad. When we were finally called back Pete answered all their questions. Blood was drawn and things started happening. My white blood cell count was very high, and I was diagnosed with septic shock. I was in ICU for seven days, then transferred to a regular floor for 3 days. They found that I had an infection in my calcaneus, the bone in my heel.

While I was in ICU my podiatrist told me, "we need to amputate your leg on Tuesday". WHAT??? From the man who never even put me on antibiotics? OH NO!! I couldn't wrap my head around that. The orthopedic surgeon said he thought we should try IV antibiotics before doing something drastic. And so we did.

After almost two months on a very strong IV antibiotic I felt good. I got to wear a regular shoe for a day. Then my foot and leg started to swell again so back into the boot. I did OK in the boot until early December when the swelling made my leg ache too much to go shopping and I was getting sick again. The nausea was almost constant. On Dec. 21st I had Pete take me to our local freestanding ER. They sent me to the hospital to be admitted. The ambulance ride was cool.

On Dec. 22nd the same surgeon who I had seen before stopped by and asked what I wanted to do. Antibiotics or amputation? Pete and I had discussed the decision at length and decided getting rid of the infected bone was the right solution. I assumed I would be sent home and return later for the surgery. I asked what his schedule was like and he said he could do it at 10:30 the next morning. We were speechless for a minute, then said sure, let's do it! I woke up in recovery and felt great. That night was the only time I had any pain. By Jan 15th I was totally healed. Now I am walking with a prosthetic leg.

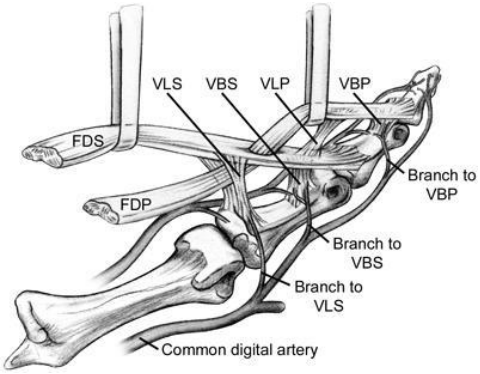
I have no regrets regarding not having the amputation in August. Pete and I needed the time to process everything and talk about how things would be different in the future. It is a very permanent solution and we had to be very sure we were ready. It has been a pretty smooth transition so far and we look forward to the next chapter.

Do It Yourself tip for HSAN1- from Chris Christensen

Have trouble grabbing that Velcro? Well NO MORE!
Punch a hole in the end of the Velcro.
Attach a heavy-duty key ring large enough to put a finger through.
Voila! no more struggles. My husband got me one with bling!

∞♥∞

Successful Surgery for Finger Contractures



Many people with HSAN1 experience contractures of muscles and tendons in the fingers. Paul Clemow is happy to report that the surgery he had on his hands is helping him to regain flexibility in his fingers. He is working hard on strengthening his grip.

His surgeon, Dr. Joshua S. Gluck, explains the procedure this way, starting with "a brief anatomy lesson: each finger has two flexor tendons, one to bend the tip and one to bend the middle. The tendon to bend the tip is a bit more important/ useful because it can also bend the middle. So, if you cut the tendon to the middle, you lose a bit of grip power, but everything still works.

"The surgery we did cut the flexor tendon to the middle of the finger (called flexor digitorum superficialis) and reattached it to the longer tendon to the tip (flexor digitorum profundus). This procedure is referred to as an "FDS to FDP transfer". It essentially sacrifices the tendon to the middle of all four fingers in order to gain length of the tendon going to the tip. It's generally a surgery used for hand and forearm spasticity, especially in patients with cerebral palsy."

The MacTel Project by Marin Gantner, PhD, Lowy Medical Research Institute

The Lowy Medical Research Institute (LMRI) is a non-profit research organization that studies macular telangietasia type 2 (MacTel). MacTel is a rare inherited retinal degenerative disease that affects central vision. For the past year, LMRI has been studying a connection between HSAN1 and MacTel. This link was discovered through an individual who enrolled in the MacTel registry and was later diagnosed with HSAN1.

Thanks in large part to the outreach efforts of the Deater Foundation, LMRI has made connections to members of the HSAN1 community. This has enabled researchers affiliated with LMRI to do comprehensive ophthalmological exams, genetic sequencing and metabolomics research on HSAN1 patients. We are also studying the link between HSAN1 and MacTel. As LMRI is a global research organization, we have extended our studies to HSAN1 patients in Australia and London, as well. Our ability to connect with HSAN1 patients has been instrumental to advancing MacTel research. We hope that our work is also raising awareness of eye health in the HSAN1 community and encouraging individuals to receive ophthalmological exams. LMRI continues to recruit HSAN1 patients to participate in the MacTel Project, a research project that includes eye exams and blood tests for genetics and metabolomics. None of this work would have been possible without the participation of patients. We hope that our research will lead to potential treatments for both diseases.

Continuing Research in HSAN1

Robert H. Brown, Jr., D.Phil., M.D.
Department of Neurology, S5-753
UMass Medical School

We have been fortunate to recruit a new doctoral student, Huiya Yang, to join us in studying HSAN1 here at UMass. She is an outstanding molecular biologist who will work with me to generate two new models of HSAN1 in mice. The new mouse models will be knock-in instead of transgenic mice. That is to say, we will replace one of the two mouse SPTLC1 normal genes with the gene bearing a mutation. Then, using those models, will work on strategies to silence the offending genes. Huiya brings lengthy preliminary experience to the project, having worked extensively on suppressing other types of disease genes in mouse models of other neurological disorders.

Two developments in the field are noteworthy over the last year. First, it is now well established that the same gene defects that trigger HSAN1 can also cause a form of macular degeneration, characterized by unusual vascular changes in the retina. For this reason, we are setting up a collaboration to evaluate the retina of our existing, transgenic HSAN1 mice. It is possible that this will provide a sensitive, early readout of pathology in the mice. In turn, such a readout may facilitate testing of therapies.

The second development of interest is that it has been discovered that a set of mutations in the HSAN1 gene (called SPTLC1) that do not cause HSAN1 can nonetheless cause a form of early childhood Lou Gehrig's disease. This is not directly related to HSAN1 but nonetheless holds enormous interest as it provides further insight into the central importance of SPTLC1 as a determinant of normal neuronal development and function.

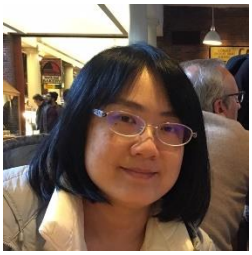
These developments heighten and intensify the level of interest in the biology of HSAN1. We look forward to working closely with the Deater Foundation on these and related topics over the coming year and are deeply grateful for its support. Hopefully, we will be able to work with the Deater Foundation to assemble another consortium meeting in early 2020. That will provide an excellent venue to draw these research themes together and plan our next steps forward.

Deater Foundation Inc. Treasurer's Report

Balance as of 4/1/18	**$24,578.56**	**Balance as of 3/31/19**	**$46,641.17**
Income		**Expenses**	
Contributions 4/1/18 to 12/31/18	20,133.38	PayPal Service Charges	-1.70
Interest 4/1/18 to 12/31/18	2.28	Network for Good Service Charges	-0.00
Contributions 1/1/19 to 3/31/19	1,927.60		
Interest 1/1/19 to 3/31/19	1.05		
Total Income:	22,064.31	Total Expenses	-1.70

Your donations allow the Deater Foundation to continue the important work to eliminate HSAN1

My HSAN1 Story



I'm a Taiwanese, born and raised in Taiwan. As a toddler, I was as healthy as other kids. One day when I was 5, my mother discovered something wrong with me while she was bathing me. I stepped into a bucket filled with bathing water, as soon as I sat down, I screamed and jumped out of the water "it is too hot, mom!" "but your feet were in the water first before you sit down, how come you didn't feel it then?" I did not know how to explain it.

My mother soon took me to see pediatricians, but no one knew what's wrong with me. "your daughter is fine!" said most of doctors. "She is just a little skinny, feed her more milk!" Another said.

I started to have club feet and my calves looked thin when I was in 4th grade. My mother took me to hospital after hospital looking for answers. After I went through the prescribed lab tests, NCV, EMG, and nerve biopsy, a pediatric neurologist in National Taiwan University Hospital said that I have CMT. He recommended my parents take me to other countries where more medical resources are available.

My parents took me to Japan when I was age 10. We visited two very well-known hospitals in Tokyo. After repeating many tests plus the muscle biopsy, both hospitals gave the same diagnosis of CMT. Braces were made for the first time in my life to support my ankles. Very soon, I started to develop ulcers on my ankles because club feet cause uneven pressure when I walk. The next year I had two surgeries on my ankle, tendon transfer and bones shaved to fix the problem. The ulcer issue was finally gone and I was able to walk again without bleeding, with braces, of course.

Symptoms on my hands started to progress at the beginning of my teenage years. The tap water no longer felt as cold as before, and my fingers no longer have enough strength to use clippers or staplers. I got bilateral cataracts when I was 17, severe enough to have them removed at age 22. Around the same time, I noticed I couldn't stand up from a squat down position. I realized muscle atrophy and weakness were coming to my lower thighs.

I immigrated to United States right before I turned 20. Entering a school to study English, my fingers were too weak to hold a chalk to write on the blackboard in class. I also had difficulty turning my dorm room key. My fingers got injured as I tried to button up my jeans with all my body strength. Ulcers on my left foot happened again as I walked across campus every day. My feet bled for more than a year. My parents then decided to let me have ankle surgery again, in the United States.

My symptoms seemed stable for a while. I finished college and started to work. Now with health insurance, I visited UCLA neurology. I was prescribed OT, PT, and a new pair of braces. PT helped me a lot. Within a few sessions, my thigh muscles become stronger and my balance much improved. I was excited and thought that I would keep improving if I did the exercises every day. Unfortunately, by 2012, when I visited UCLA neurology the 2nd time, I was having difficulty walking. "If you want to find the cure, you need to find the cause first!" said my UCLA neurologist. Several lab tests and NCV were prescribed to eliminate some of the possible diseases. Two years later, in 2014, a genetic test was done at UCLA. 500 plus genes associated with my symptoms were screened. Unexpectedly, not only one but 3 genes were caught, but none of my loci of these three genes were ever proven or documented to cause disease. I was told that only one is the culprit gene, but which ONE is it?

I sent the genetic test report to a neurologist in Taiwan who has my parents' blood samples and asked him to compare them. He discovered that I inherited the first two genes from my parents and only the third one is my own mutation. My parents are normal. "So it is the third one." I was told. But, can we be so sure that this SPTLC1 is the real culprit gene just by ruling out the other two? What if it is not and the real one is still out there at large? I was concerned.

In 2016 my plasma was sent to Switzerland for testing for deoxysphingolipids, the biomarker of HSAN1. The result was that I have super high amounts of these neurotoxic lipids. In order to confirm this toxic lipid is indeed from my SPTLC1 gene mutation, a cell study was done that finally confirmed that gene as the cause behind my afflictions all these years.

This disease not only affects the muscles and the sensations on my limbs, but also my heart beat intestinal motility, and physical energy. My airway cannot open as quickly as before after I have several coughs and I have a strange burning sensation from my lower back down my legs in a very weird "every other day" pattern. Temperature on both my feet are like riding roller coasters every day, either flaming hot or ice cold. All these symptoms showed up one after another in recent years.

I am taking serine now with a very low dose, only 1.65g a day, which helps maintain strength in my arms, improves constipation, and helps my brain stay awake and focused. A higher dose would cause intestinal discomfort and also brings too much energy to my brain which feels like a huge light shining on the back of my head. I visited MGH last year, and it was suggested to increase the dosage gradually over time in hope that my body can adapt to it. I have been trying to do that.

I'm in a wheel chair now and have lost the ability to hand write. This disease totally changed the course of my life and turned my life upside down. However, I thank God for being with me on this journey, giving me strength and the opportunity to come overseas to seek medical attention leading to the right diagnosis and maintenance of my health at the optimum level. I am also thankful to my doctors, scientists, and the Deater family; without their help and effort, my condition could be a lot worse.

Despite all of these adversities, I do not want to give up. Life is a miracle, worth living and living well. Knowing HSAN1 is a super rare disease, I hope more patients can be identified so that we can support and encourage each other and that may eventually lead to more research. The Deater Foundation did a lot in this, and I hope I can do my part. Recently I got hold of CMT China, sharing my story in their community, hoping to increase their awareness about this SPTLC1 gene which may cause symptoms of CMT and perhaps find patient in their group. I also made a Mandarin website on HSAN1 in hopes of finding patients speaking that language. There are more than 1.3 billion people who speak Mandarin Chinese. I really hope that by providing disease information and hopefully some low to non-cost genetic testing service, more people with similar conditions can get diagnosed.

I do not want to give up. Life is a gift, and I cherish it. This disease may damage my nerves and muscles, but it trains me to be resilient and persevering in character. Looking at the mission on the Deater Foundation website: "Dedicated to finding a cause and cure for HSAN1", I think the word "Deater" has a deeper meaning now.

THE 75TH DEATER FAMILY REUNION WILL BE HELD ON JULY 20, 2019

at 12 NOON at STULL, (near Noxen) PENNSLYVANIA

Same place as last year, behind LeRoy and Isabelle's house

Let us know if you need directions!

The Deater Foundation meets at 10:30 am prior to the Reunion

ALL ARE WELCOME! WE HOPE TO SEE YOU THERE!

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