July 2001 -

Newsletter Contents –

In Memory of Ethel (Deater) Sutton

- Second oldest of the 12 children of Alvin and Ellen Deater
- Birthdate: August 5, 1909
- Married: Lawrence David Sutton (November 13, 1926)
- Died: May 31, 1932
- Children: Roberta Sutton Mahoney and Joan Sutton Elston
- 7 Grandchildren
- 15 Great Grandchildren
- 6 Great, Great Grandchildren

The Gene Causing the Deater Disease Is Identified! Important Research Results Published

Ellen Burns, Vice President and Medical Liaison

In the March 2001 edition, Volume 27, of the prestigious scientific journal Nature Genetics, two articles were published that were the culmination of years of research involving the Deater family and other families with a degenerative neurologic disease.

One article, *Mutations in SPLTC1, encoding serine palmitoyltransferase, long chain base subunit-1, cause hereditary sensory neuropathy type I,* was submitted by Jennifer Dawkins and her team at the Neurobiology Laboratory of University of Sydney, New South Wales, Australia, under the leadership of Garth Nicholson. For some years, now, this Australian group has been collaborating with the research group from the Day Neuromuscular Laboratory in Charlestown, Massachusetts to find the exact gene that causes the disease that affects the Deater family. This disease is known in medical circles as HSN I (Hereditary Sensory Neuropathy type I). In fact, some medical textbooks and research articles specifically refer to earlier published research on our family.

In the *Nature Genetics* article, the Australian researchers identify the specific gene, **SPTLC1**, on chromosome 9 (more specifically: 9q22.3), that is mutated, or different, in people who have HSN1. These researchers studied 11 families and found three different mutations in the gene, among all the affected family members. Everyone who had the disease had a gene mutation in this gene. Because of the collaboration with the Day Lab research team, these researchers had access to the DNA samples from members of the Deater family, and to previous research done by Khemissa Bejaoui and others in the Day Lab.

The gene with the mutations associated with HSN1, identified as **SPTLC1**, is a gene that had been previously studied, and therefore the researchers know what the gene does. Genes make proteins; proteins make enzymes. **SPTLC1** encodes subunit 1 of the serine palmitoyltransferase enzyme. This enzyme is known to affect the production of a fatty substance (glycosylceramide) in the body. In the article, the researchers speculate that the increased production of this fatty substance causes the death of certain cells and so may destroy nerve cells and cause degeneration of the nerves resulting in the disease HSN1.

The other article in the March 2001 *Nature Genetics* that is of particular interest to the family is *SPTLC1 is mutated in hereditary sensory neuropathy, type 1*. This article was written by Khemissa Bejaoui as a result of the research done at the Day Neuromuscular Laboratory at Massachusetts General Hospital, Charlestown, Massachusetts. Dr. Bob Brown is the Director of the Lab. In this article, Khemissa reports on research done on the DNA provided by members of the Deater family, and other families also affected with HSN1. The Day Lab, through Khemissa's research, reports co-discovery with the Australian group that the gene SPTLC1, which encodes a subunit of serine palmitovltransferase is mutated in HSN1.

The Day Lab research found mutations in two different areas of the gene, and demonstrated complete linkage with the disease in our family; that is, everyone who had the mutation of the gene had the disease, and everyone

who has the disease has the mutation. There were no mutations in people who did not have the disease.

Khemissa also explains that the gene produces a protein product (LCB1) which forms a complex with at least one other protein (LCB2). It is known that the enzyme made by these protens is made active primarily by LCB2. Khemissa surmises that the mutant LCB1 protein has either (1) acquired a new action, or that it (2) somehow changes the levels of SPT activity. Since SPT affects the production of a fatty substance (glycosyl ceramide) in the body, it is possible that LCB1 may either promote, or fail to inhibit, the action of LCB2. The result may be an increase in the production of the fatty substance that then causes nerve cell death, resulting in the disease HSN1. Not all the families studied by the Day Lab researchers demonstrated linkage to this gene. The Deater family did show a mutation in this gene. Another family also showed a mutation in this gene, but at a different location (base) on the same gene. Khemissa indicates that more work needs to be done to examine the gene (on chromosome 14) that is responsible for LCB2. The research is continuing.

Treasurer's Report

Nancy Newcomer, Treasurer

Nancy newcomer, Treasurer, reports the following regarding the treasury of Deater Foundation, Inc.:

2000-2001 Finances	
Balance as of 1/1/2000	$20,530.10
2000 Contributions	15,700.00
2000 Interest	349.69
2001 Contributions (1/1/01 to 5/31/01)	1010.00
2001 Interest to 5/31/01	131.06
Total Income	$37,720.85
April 2000 Expenses	8000.00
March 2001 Expenses	8000.00
March 2001 Appreciation Lunch for Day Lab Expense	192.79
Total Expenses (1/1/2000 to 5/31/2001)	-16192.79
Balance as of 5/31/2001	$21,528.06

Sharing Experiences

Submitted by: Ellen Burns

Deater Family gatherings take place throughout the year, not just at the reunion. But for many of us who are far away, it is not possible to make the trip "home" more often than yearly. When the family was smaller and geographically closer, the get togethers for Decoration Day, Independence Day and Christmas were times of sharing experiences with the disease, as well as other family stories.

I remember a large family meal in Mona and Carl's basement when they were building their "new" house. A cup of coffee was being passed hand to hand down the table to Russell. Harvey sat next to him, and as he passed the cup and saucer asked, "Where do you want it? On your head or in your lap?" With that, his crippled hands failed to retain their grip and the hot coffee spilled on Russell's pants. Without missing a beat, Russell turned to Harvey and said, "I thought I had a choice!"

They, and other family members, discussed their symptoms and treatments. Since the Deater family now covers the country, it is less easy to have those discussions. I have received permission from some folks to share what they have learned about the disease.

Charcot foot

A complication of many neuropathies is injury to the bones of the foot. This is caused by repeated trauma- the pounding of the foot against the ground- and the inability of the individual to recognize pain and rest the foot. Ulceration and infection in the feet also contributes to the injury to bones and supporting tissues. Sometimes the bones suffer fractures and displacement from their usual positions in the foot. This condition is known as "Charcot foot", named after the same doctor who was one of the first to describe the neuropathy Charcot-Marie-Tooth disease.

Most of the literature about Charcot foot describes a diabetic's foot, as diabetes is a very common cause of neuropathy in the feet and legs. The arch of the foot falls and the bones spread out. Sometimes this is so pronounced, the result is called "rocker foot", because the bottom of the foot bulges out and takes on the appearance of a "rocker".

Chris Deater Christensen developed Charcot foot after years of ulceration and bone infection in her foot. It was after she finally had surgery to remove bone to get rid of the infection that the condition developed. She was recovering well from the infection, but developed pain in her foot. This was a good warning sign for her, but not everyone gets pain with this condition, or they may assume the pain is just a continuation of the neuropathy pain that they usually

have. Chris has recently had surgery to correct her Charcot foot. This involves re-aligning bones and holding them in place with plates and screws. Her doctor anticipates that her foot will be "nearly normal" in appearance. The surgery should also reduce the likelihood of pressure areas on the bottom of the foot. She will have to watch closely the areas where the appliances are located.

Orthotic devices to relieve pressure

Pressure areas on the feet of someone who has lost feeling is a potentially dangerous situation; you could even say life threatening. Pressure leads to ulceration, which can lead to infection, which can cause sepsis or infection throughout the body. Paul Clemow has found a place in Santa Barbara, California called "The Good Foot Store". At the store they have a device to determine pressure points on the foot, and sell inserts that even out the pressure, so that no one point (such as the ball of the foot) is supporting most of the weight of the body. Many family members who have had ulcers have custom made orthosis for their shoes. But for others, this may be a good preventative measure. There are undoubtedly other stores that provide a similar product.

Paul also recommends Aquaphor cream to prevent rough spots and calluses on the feet. He has tried several different products and finds this one works best for him. Those with impaired feeling know that ulcers often form under calluses.

Larry Deater has suffered for years with a hiatal hernia and reflux esophagitis, the condition in which stomach acid splashes back up the esophagus. You can tell by television commercials that many people have this problem, and it may or may not be related to the neuropathy. Larry's condition has progressed to a pre-cancerous stage known as Barrett's esophagus. Since there is a history in the family of esophageal cancer, this is a condition to watch closely. Avoiding spicy food, alcohol, soda pop, and not smoking are key factors in keeping this condition under control.

Pain

The pain that comes with neuropathy is perhaps the most life altering aspect of the disease. Pain can keep people from using a limb, which leads to further muscle weakness and deterioration. Pain can limit work and social activities and interfere with sleep. It can cause irritability and personality changes. It is ironic that a disease that prevents people from feeling pain causes so much pain itself. The pain has been described differently by different people, and often people will have several different types of pain, either at different times in the disease or concurrently. Many people become so used to the "dull ache" that they fail to describe it as pain after a time. Other pain is described as "burning" or "like frostbite" or "shooting" or "lancinating." For some people the

"restless leg syndrome", often described as legs "jumping" in bed at night, is very distressing because it prevents or interrupts sleep.

People who suffer from pain need to talk about it with their doctors. Only the person who has the pain is the expert in this aspect of the disease! No one can guess what your pain is like, they have to be told. There are no medals for suffering needlessly! Ask your doctor what pain scale he or she uses, and then tell the doctor how you rank your pain at its chronic level and during a more severe attack. Don't make the mistake of using your daily pain level as the baseline! Compare everything against NO PAIN.

There are many drugs on the market, not just the "usual" pain medications. Doctors can prescribe medications usually used for other diseases that will help with nerve pain and other problems. For example, Sinemet, a drug associated with Parkinson's disease treatment, is sometimes given for restless leg syndrome. Some types of antidepressant medications have been proven to be valuable in alleviating nerve pain. These medications work on chemicals in the brain that have various effects on the body. Some medicine given to people with epilepsy, anti-convulsants, have also been helpful. Neurontin is an anti-convulsant medication that can be given in small doses and increased to much larger doses with few side effects. Paul Clemow has received relief with this drug, used in combination with others prescribed by his neurologist.

Traditional pain medication continues to be most helpful for many folks. The current treatment of pain emphasizes keeping the pain under control at all times. People used to suffer "as much pain as they could stand" and then take pain medicine. The problem was, the medicine had to be given in large doses to conquer the severe pain. Often people would feel "drugged" in order to relieve the pain, and then the cycle of pain and "drugging" would start over again. Now doctors strive to use low doses of pain medication routinely- every day or several times a day. The person may not be pain free, but does not suffer from the intense "peaks" of pain that require large doses of drugs. Sometimes people are resistant to taking "pain pills" when they don't have acute pain, but the consistent treatment of pain is much better and safer.

Some people have discovered methods other than medications to provide some pain relief. Gloves to warm the hands and provide a gentle pressure have helped some. Others agree that some kind of pressure to the area, such as clenching the fist, provides short term relief. If you have "tricks" that have worked for you, talk about them or let me know and we will share them with others.

Excerpts from Grandma's Diary (July 1942)

Preparation for the first Deater Reunion?
Submitted by: Beulah Womer

Friday 3--It rained hard at night. Mona, Carl, and Dad went to town. Helen came up from Mona's this morning. She and I mowed the lawn; then I got the potatoes ready for salad. Helen cleaned and mopped the kitchen; then we made the salad. Verna finished her mopping up-stairs, while I did the lamps. Isabel, Lynn, Henrietta, Rudy and the children came. June and Bob came. Mona and Carl went to Berwick for Tom and Lois. Beulah and Donnie went up with June for the night. Lynn, Isabel, Henrietta, Dad and I went to Wilkes-Barre for Harvey. We didn't get home until daylight, and the rooster was crowing.

Saturday 4--It showered towards night--nice showers at night. Well, we had a clam bake by the creek and had a very nice time. About nine o'clock at night Tom, Anna, Lew, Mae, Ruby, and David came in. It was late when they left. Isabel, Lynn, Henrietta and Rudy stayed all night with June. Lois and Tom with Mona again.

Research Funding

Submitted by: Ellen Burns--Vice President

Research costs a lot of money. The Deater Foundation was established to help pay for research into the cause and cure of the Deater disease, HSN 1. Muscular Dystrophy Association has generously supported research for neuromuscular diseases including HSN 1. Dr. Khemissa Bejaoui, the primary researcher at the Day Lab for HSN 1, has spent many long hours researching for and writing for grants of money to support her work. Recently, she has submitted a grant request for a substantial amount to the National Institutes of Health. Please keep these efforts in your prayers.

Research costs include not just the salary of the researcher, statisticians, and secretarial support, but also the lights, heat, and upkeep of the building; the purchase, updates and maintenance of the huge and costly computer run machinery; the phone bills, paper, and paper clips. Since 1992, the Deater Foundation has provided anywhere from $8000 to $24,000 in a year to the Day Lab. Although the Deater Foundation, by itself, does not come close to providing enough funds to research HSN 1, it serves as an example to other potential donors and "primes the pump" into the well of research dollars.

Now that the gene for HSN 1 has been identified, there will be increased interest in the scientific and medical communities for treatment of the disease.

This is perhaps the most important time to consider giving to the Foundation! The ultimate goal has always been to treat the disease and to prevent it in future generations. As painful as this disease has been for individuals, I have been told by many that the worst pain is seeing your children develop the disease.

Now that the gene has been identified, the researchers plan to make a working model of the disease, in a cell and in a mouse. Then research can be done to determine what the gene defect does in the body to create the disease. At the same time, treatments can be tried at the cellular level. All of this must be done in preparation for treatment of the disease in humans. This is an expensive process.

Thanks to the many family and friends who have supported the Deater Foundation financially and with their prayers, we now know the gene. It has been inspiring to hear how families and individuals have been creative in finding ways to set money aside for the Foundation. Keep your penny jars, or quarter jugs earmarked for the Deater Foundation. Request a contribution instead of a birthday or Christmas present. Encourage your children to think of others with their pennies and their prayers. When you receive solicitations in the mail or at your door for all of those other worthy charities, slip a dollar instead into an envelope for the Deater Foundation. A donation will provide future hope for many of your kin as the researchers develop treatment for this disease.

At the conclusion of the article identifying the gene for HSN 1, just before Khemissa's name, is paragraph headed **Acknowledgments**. It begins, *"We thank G. Nicholson for sharing prepublication results. This work was supported by the Deater Foundation, Inc.,…".* This is to me an affirmation of the work of the generations before us. It is a tribute to those who suffered and sought knowledge about this disease. It is a sign of hope and trust in the Lord and in family. We Deaters, with little material wealth but rich with compassion and love for one another, have made a difference in the lives of so many people around the world! We have much for which to be thankful!

A Poem

By Harvey Deater

Harvey and Russell Deater were hospitalized at Thomas Jefferson Hospital in Philadelphia in 1938. The initial studies on the "Deater Disease" were done at this time. Harvey wrote a poem while in the hospital, following the diagnosis and poor prognosis at that time. Copies of the poem were given to Dr. Bob Brown and Dr. Khemissa Bejaoui to mark the discovery of the gene causing HSN 1. Harvey wrote:

As I lay there on my iron bed
And watched time in its flight
From 5 o'clock in the morning
Until 9 o'clock at night,

How very oft' I wondered
Of the wondrous works of God,
Far past the understanding
Of we mortals on this sod.

Then I wondered if those earthlings,
By some miraculous deed,
Could devise some unknown treatment
That would cure our awful need.

'Till the day they came and told us
'Twas beyond the ken of man;
It had come down through the ages
As a part of God's great plan.

When they told us we'd be crippled
For as long as we drew breath
It really would have been easier
If we'd faced a sudden death.

But our spirit raised and brightened
As out of the door we trod,
For we'll be healed in the future
By the graciousness of God.

If you have any questions, comments, or suggestions about our newsletter, the medical report, etc., or if you are interested in contributing to the Deater Foundation, send your e-mail message to: cdorward@enter.net. Or, you may also write to: Deater Foundation, Inc., PO Box 255, White Deer, PA 17887.

57th Annual Deater Reunion
Saturday, July 21, 2001
At the grove in the Stull

Dr. Robert H. Brown, Jr., Director of the Cecil B. Day Laboratory for Neuromuscular Research and Professor of neurology at harvard medical School, will be joining the Deater Family at the Reunion this July 21st. Dr. Bob Brown was last at the Reunion in 1986 when he, along with then medical student, now Dr. Gordon Shepherd, drew blood and performed medical examinations on many of the Deater family members.

Dr. Brown will be giving a presentation on the research done by Dr. Khemissa Bejaoui and others at the Lab which resulted in verifying the discovery of the gene for HSN 1, the "Deater disease." He says he is very excited about attending the reunion and has looked forward for years to the time he would be able to bring this information to the family. We are so blessed to have Bob and Khemissa interested and involved in such a caring way with our family!