

Synapse

Volume 14, Issue 3

Summer, 2011

Newsletter of the Spastic Paraplegia Foundation



2011 Annual Conference Mission Completed



Letter to the Editor,

April 21, 2011

My name is Gretchen Gibson from Ocala, Florida, and I have HSP. The condition originates on my father's side of the family. Those who have endured the disease include my dad, his grandmother, my dad's sister, and a number of my cousins, and me. For each family member, the symptoms are different and the age of onset varies. In my case, it kicked in about age 37. I am 62 now.

Of all the family members, I am the only one who has diligently dealt with what could be done for "quality of life." I accept my limitations, but am doing very well. I exercise every day for about two hours. I have devised my own little program with many different exercises and therapies. Three days a week, the exercises I do involve extensive stretching and strengthening of muscles and also help with flexibility issues. Three days a week, I use a stationery bike and walk one mile (long strides) which stretch bundles of muscle spindle tissue. I obtained all of this information from the 2011 Winter *Synapse*.

I visit my pain management specialist every three months, and he continues to be enormously pleased. As indicated in your newsletter (listed above), "Exercise may not be fun, but it is certainly good for you." It is my PRIORITY to keep up with the exercises. One cannot sit around, make excuses for not following through, and nobody is going to do it for you!

I must tell you I LOVE YOUR PUBLICATION! I find so much useful information. Keep up the good work! Thank you for all of the positive elements you have contributed to my HSP dilemma.

Gretchen Gipson

Your questions and comments are welcome. Please contact me via e-mail at badsp.f@wildblue.net.

Beth Anne Shultz, Editor

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Synapse

Volume 14, Issue 3 - Summer 2011

The Spastic Paraplegia Foundation Inc. (SPF) is a national, not-for-profit, voluntary organization. It is the only organization in the Americas dedicated to Primary Lateral Sclerosis (PLS) and Hereditary Spastic Paraplegia (HSP).

Synapse Editors

Beth Anne Shultz Senior Editor

Robin Grossbier Events

TBD Medical Updates

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Please Send Donations to:

Spastic Paraplegia Foundation

P.O. Box 1208

Fortson, GA 31808

Please direct correspondence to:

Spastic Paraplegia Foundation

7700 Leesburg Pike, Ste 123

Falls Church, VA 22043

(877) 773-4483

information@sp-foundation.org

www.sp-foundation.org

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SPF News from the Board

President's Letter:



Annette Lockwood
SPF President

Our 2011 Annual Conference was held on June 11th in Houston, TX. Thanks to everyone who was able to attend. It was a wonderful meeting with engaging speakers and time available to share stories and experiences with other participants. A summary of the meeting is included in this issue.

The Board of Directors also met in Houston and below are some of the items discussed that you will be hearing more about.

Million Dollar Campaign – In 2010, SPF revenues were approximately \$800,000. This year our goal is \$1,000,000 with our *Million Rays of Hope* campaign. Please help us reach that goal.

Online HSP Community – Through a project sponsored by the National Organization of Rare Disorders (NORD) and its European equivalent, EURORDIS, a rare disease social network for patients & families was established. This multilingual network provides a platform for patients to connect with others and share experiences on living with a rare disease. In May, Hereditary Spastic Paraplegia was added as one of the communities. Go to www.rarediseasecommunities.org to sign up.

Expanding SPF – In anticipation of future clinical trials, we want to increase the number of SPF community members. We currently have approximately 2,600 in our database which is only 10% of the estimated HSP/PLS population in the US and Canada. Please encourage other patient family members to join SPF at www.sp-foundation.org.

Regional Meetings – In an effort to bring the benefits of the Annual Conference to more of you, we will be looking at putting together a simple meeting organizational tool. This tool will include potential speakers and help streamline the steps to hosting a SPF meeting.

Enjoy your summer,

Annette
SPF President

Updates and New Frontiers

HSP / PLS NEALS Task Force

Committee Report – May 16, 2011

Edited by Beth Anne Shultz

The NEALS PLS/HSP committee is dedicated to improving care and quality of life while furthering scientific understanding that may lead to potential treatments for upper motor neuron (UMN) disorders, including Primary Lateral Sclerosis (PLS) and Hereditary Spastic Paraplegia (HSP). These are rare neurodegenerative disorders that are progressive and have no effective treatment or cure. Chaired by Nazem Atassi, MD MMSc of Mass. General Hospital (Boston, MA) and Jinsy Andrews, MD MSc, of Hospital for Special Care (New Britain, CT), the committee includes 31 NEALS members from 24 different NEALS clinics across the United States.

Since its inception in 2010, the committee has pursued the goals of the organization with tenacity and determination. Their efforts have included the following:

- Created a comprehensive list of institutions that welcome PLS and HSP patients. This list was generated through surveying 92 member clinics of the NEALS consortium. Fifty clinics were identified that welcomed PLS patients and thirty-six were identified that welcomed HSP. This list was also published in *Synapse*.
- Developed a scientific advisory board (SAB) to evaluate potential compounds early in development as possible candidates for clinical trials in PLS or HSP. The group had a meeting in February 2011 to develop potential candidates for therapy.

At the 2011 Annual NEALS Meeting, NEALS will host a ½ day symposium dedicated to the genetics of UMN Disease; guest speakers include Dr. Robert H. Brown (UMASS) and Dr. Charlotte Sumner (John Hopkins University). We also hope to develop another full day workshop to continue the interest and enthusiasm in the scientific community.

Jinsy Andrews, MD
Nazem Atassi, MD MMSc

To read entire article, please visit: www.alsconsortium.org/NEALS_PLS_HSP_Committee_Update_v1.0pdf

Events

Spring Connection Dallas-Fort Worth

April 9, 2011



L to R: Jeff Smith, Joyce Overstreet, Lanny Jones, Ashton Hecker, Mike Petrey, John Staehle, Meg Price, Dani Leugers, Bob Price, Dianne Hecker

We met at a local restaurant, Buck n' Loons, located in Arlington, TX. Ten of us enjoyed a casual gathering that started with introductions, included lunch and involved much conversation about coping with our varied conditions. Ashton Hecker, SPF Board Member and Conference Chair, gave us an update on the SPF Annual Conference. Dani Leugers, a senior Biology major at Texas A&M, who is also a research member of a team examining the pathogenesis of HSP (by focusing on the function of the maspardin protein and its possible contribution to this group of diseases, specifically the mast syndrome), briefed those present on the work the team has been doing for the past 8 years. His discussion also included what is currently being studied and where that may lead. John Staehle presented information concerning the SPF Ambassador program. Texas now has three Regional Ambassadors. This will, in turn, facilitate more local activities for those with HSP and PLS. He also led a discussion on individual fundraising and what each of us can do to become more effective at this important task. We had a great time meeting new friends and renewing old acquaintances. At the end of the meeting, we agreed to continue meeting twice a year. Our fall gathering will be held on Saturday, October 15th, 2011 (alternate date is October 22nd, 2011).

Spring Fling – The DELMARVA West Virginia Connection Frederick, MD

May 14, 2011

Spencerfamily2@comcast.net

The 11th Annual Spring Fling event entertained over 50 people from MD, VA, WV, DE, NC and OH. It was an informative and entertaining day. The presentations addressed a variety of speech and air flow techniques, occupational therapy devices, tips and advice on how to minimize injury when falls occur, some of the latest research developments with regards to upper motor neuron diseases (*Andrea Corse, MD—John Hopkins University School of Medicine*), and last but not least, a wonderful and interactive discussion about the physiological and psychological benefits that come from laughter, humor, and a positive attitude. A special thank you to Ronnie Grove, who started this great tradition in 2001!



Iowa Connection

June 11, 2011



Karen Powers (HSP) (Jackie's Aunt), Jennifer Bailey (HSP), George Bailey (Jennifer's Dad), Chris Yost (HSP, Laurel's son), Dixie Yost (Chris's wife), Laurel Yost (HSP), Linda Gibson (David's wife), David Gibson (HSP), Jackie Wellman (HSP)
Front...Denise Boots (HSP)

Ten Iowans showed up in Ames, Iowa for our informal Connection Lunch. We enjoyed some delicious barbecue at Hickory Park and chatted for several hours. It was a great time to make new friends and visit with old acquaintances. Go Iowa!

Teamwalks

Pennsylvania TeamWalk Magee Rehab Hospital Sept. 10, 2011

Helen Kienlen: hmk17@comcast.net
Our TeamWalk will be held on September 10th, 2011. Lunch will be held after the walk. Please join us at 1513 Race Street, Philadelphia, PA 19102. Please contact Helen at (484) 270-8317 or by e-mail: HMK17@comcast.net for specific details or if further information is needed.

New York TeamWalk Mt. Kisco, NY September 18, 2011

Ann Lakin: alakin90@gmail.com
The Team Walk will be held in the same location as previous years, which is by the Gazebo on Moger Avenue, across from Starbucks (and by the train station).

The Magnificent Mile – Hillsborough Street Raleigh, NC September 18, 2011

Sarah Witt: srwitt@yahoo.com
The 6th Annual Magnificent Mile will be held on Sunday afternoon. If you are traveling to Raleigh for the event, discounted rooms (\$79/night) are available for Friday and Saturday nights at the Clarion Hotel. Call 919-832-0501 and ask for a room in the Magnificent Mile block.

California TeamWalk - Cures & Connection Weekend Pleasanton, CA Sept. 30 – Oct. 1, 2011

Linda Gentner: lkgentner@aol.com, 510-651-5676
A PLS & HSP Welcoming Dinner will be held Friday night -- pay for your own dinner. There will be discussion time with dessert and coffee following dinner. Get an early start on the weekend and stay at the hotel Friday night with no need to get up early on Saturday morning. The TeamWalk, lunch, and raffle will be held at the Valley Community Church.

Golf Outing – Manorville, NY (Eastern Long Island) July 14, 2011

Meredith Gattuso: sweetpea1971@verizon.net
The golf outing is in honor of Meredith's late Grandmother Rosella Vigliotta. All proceeds will be donated to the Spastic Paraplegia Foundation. For more information, please contact Meredith Gattuso.

Southern California Connection Lunch Rancho Palos Verdes, CA Aug. 20, 2011

Malin Dollinger, MD: malind@cox.net
The next Southern California Connection will be held Saturday noon, August 20th, 2011, at the home of Malin & Lenore Dollinger - 26235 Birchfield Avenue, Rancho Palos Verdes - 90275. We will share lunch. Sandwiches, salads, and refreshments will be served. Cost per person will be approximately \$18. Please join us for sharing of victories, problems, solutions, and ways we cope with our illness. It will be a great opportunity to meet old friends and make new ones. If you plan to attend, please e-mail us at malind@cox.net [or phone 310 378 4059] with the number of persons attending, and any special food needs. Please e-mail us for directions as Mapquest and Yahoo routes are incorrect.

We are excited about this important gathering, and hope it will provide mutual benefits and assistance for all of us. I'll also have some input and feedback from the annual conference in Houston, for those who were not able to attend. We look forward to seeing you.

Patient Connection Lunch Austin, TX August 27, 2011

Marlene Doolen: mdoolen512@aol.com
Lunch will be held at the Brick Oven in Austin, TX from 12:00 noon through 3:00 pm. Please contact Marlene if you are interested in attending.

Autumn in Carolina Rural Hall, NC October 8, 2011

Don Wilson: don-wilson@earthlink.net
Autumn in Carolina will be held once more in Rural, North Carolina. We will utilize the same motel as in 2010. The Holiday Inn Select (Madison Park, Winston-Salem) has reserved a block of 10 rooms, including five accessible (one with roll-in shower), all under the name of Autumn in Carolina. The rate for the rooms will be \$90.00 plus tax per night – no increase from 2010. The toll free number is 1-800-553-9595 and be sure to ask for rooms in the Autumn in Carolina block. The motel will hold these rooms until midnight on September 16th, so call early and be sure to get your confirmation number.

(Continued next page)

Living with HSP/PLS

ADAPTING TO LIFE WITH PLS

Judith & Joe Osbourne - Ohio

As a couple, we have, and are still, learning to live with Primary Lateral Sclerosis (PLS). I am a nurse and taught nursing for many, many years. One of the things I have learned is that teaching students about living with a chronic disease is much easier than the actual living of that life. I am much more comfortable teaching about being a caregiver than I am being that care-giver.

Our adventure began approximately ten years ago when Joe developed vague symptoms affecting his speech and his walk. Being the nurse in the family, I wondered if he was having mini-strokes. We had both retired early so that we could indulge in our love of travel, both in the United States and abroad. The early symptoms concerned me but I was not unduly worried. However, over the next four years, Joe continued to have trouble with his walk and his balance. When the diagnosis of PLS was finally made at The Ohio State University Medical Center, we were stunned! Neither of us had ever heard of this condition so we were thrown into a steep learning curve and had to absorb things quickly.

One of the decisions we made, then, was to continue to travel as we had originally planned. This has been a wise and fulfilling course of action. In the beginning, Joe used a walking/hiking stick as a means to stabilize his balance. He did well until someone bumped into him. Though he usually fell when this happened, he continued to enjoy our travels. Once, in the middle of a street in Madrid, Spain, he fell but three men appeared immediately and seemingly out of nowhere, and helped him up. We have found that people everywhere, regardless of location, are usually very quick to offer their help when needed.

After a period of time, the walking stick was no longer adequate and Joe made the decision to purchase a walker. The first walker he used had small wheels and it was quickly replaced with one that had bigger, eight inch wheels. The bigger wheel size made rolling over the cobblestone streets in Europe much easier to navigate. At this point in time, Joe must use the walker constantly and even that does not prevent falls from occurring. He has also purchased an electric scooter which makes getting around much easier as we continue to travel, and fatigue has become more of a problem.

Since Joe's diagnosis, we have been to Europe numerous times, traveled in Alaska by bus and ship, and celebrated our 50th wedding anniversary on a Caribbean cruise. Each fall we journey back to a small village in the Austrian Alps for Joe to attend an annual woodcarving school. Joe was

the second "handicapped" person to attend the school and progress has been made. There is now a small elevator and ramps in addition to the stairs! Interspersed with these travels abroad, we have traveled extensively within our own country as well.

I am not sure we have any profound "tips" for traveling with PLS, but I have learned that it is imperative to notify the airlines, the cruise ships, or the tour operators when your traveling companion uses an alternative method of mobility. Asking for a wheelchair, for example, gets you through security and customs very quickly. I have also had to learn to become more assertive when moving through crowds of people to minimize potential injury to Joe. And finally, I must say that we have found people throughout the travel industry – airlines, cruise lines, and tour operators – to be helpful in making our travel as stress-free as possible. Happy Traveling!!

Mobility Marvels

SEGWAY: Improved Mobility!!!

by Jean Brunet

I was diagnosed with HSP 14 years ago and every year, I lose a little bit more of my mobility. I am still mobile with the use of a cane and walls inside the house and the use of 2 forearm crutches outside our house, but "walking on my hands" is not something I can do for long periods or great distances. Also crutches and a cane have their limitations, especially on surfaces that are not smooth: ends up the world is mostly uneven surfaces...But read on...



A year ago, I was traveling on a cruise ship and by luck, I met a one legged man (*Vietnam Vet*). That meeting was really fortunate for me...he was traveling around on a Segway. I asked him about it and he was happy to say that he went everywhere with it and that he even used it

in airports right to the door of the plane. He said that it had made the trouble and pain that came from reduced mobility a real pleasure. He is no longer limited to where he could go with crutches (*my problem also*) but could go on ANY surface, including rough trails in the bush (*fishing and hunting*), beaches, etc. I was amazed and wanted to find out more about the Segway. So I started to do a little research.

Dean Kamen was the inventor of the Segway (*Google the name "Dean Kamen" for more information*), a technology that he developed after witnessing a disabled person come up against a wheel curb with a wheelchair, and then later, once that disabled person was inside the store, seeing how awkward a conversation between the clerk and the person was (*different eye level*). You have probably seen the wheelchair that resulted from that: it stands up and can go up and down stairs. The wheelchair was produced by Johnson and Johnson at a cost more than \$30,000. The price point made it a very limited success. Part of that technology was brought over to the Segway. Over \$100 Million were invested in the Segway, a truly incredible technology that was proclaimed by Jeff Bezos and Steve Jobs to be a revolution in personal transportation.

On my return from the trip, I was lucky to find a Segway dealer that was not far from me (*Segway dealers are far and few*) plus I had the good fortune of falling on one who was trained by the Canadian Army to help returning war vets who have suffered an amputation regain some mobility. Double bonus, he was able to install a seat on the Segway for me to use when my legs get tired. The US army have a similar program, for more information go to www.segs4vets.com.

My wife and I rented two Segways for a long weekend to see if the technology was for us. It was superb: I could go everywhere for long periods of time and as a bonus, I could do it with my partner. Usually, I have to bow out of any trips or event that includes long walks. We were able to use bike paths everywhere and go to museums (*only the disabled person can use it inside*) for that weekend. The learning curve was short (*in their safety video they say from 5 to 15 minutes and that is correct*). The learning curve is short because the Segway mimics what you have already done: walking. For more information on this, go to www.segwaysafety.com

Since then, I have been to Europe three times, have used it to "glide" through 11 airports (*Rome, Munich, Frankfurt, Venice, Washington, Boston, Miami, Fort Lauderdale, Montreal, Toronto and Ottawa*). I have used it to

go over the cobble stoned streets in Italy, Spain, Turkey, Greece and San Juan and on the beaches of Costa Maya in Mexico. On my last trip, I used it in Istanbul and in the Grand Bazaar, on a few Greek Isles and in Venice, (*my brother was with me and pulled the Segway over the many bridges in Venice, otherwise the city is a pleasure to Segway around and explore*). The more I use it, the more relaxed I am with it. The sensation is best compared to gliding as the machine keeps you upright and balanced at all times. If you are going up a hill, it leans you back a little so you are standing perfectly straight; same thing when you are going downhill: it keeps you in continuous balance.

With a little bit of Velcro tape, I have been able to customize the Segway so I can easily attach either my crutches or my cane to the control shaft for use when I stop. On my new Gen 2 machine, I had a seat installed so I can use it for extended periods. www.segsaddle.com

The technology (*Dynamic Stabilization*) is incredible: it balances you 100 times a second, which is actually more than the human brain can do. The Segway is completely redundant: it consists of 2 computers, 5 gyroscopes, 2 tilt sensors, and 2 electrical motors that are actually wired as 4. So any failure by one part will be backed up and corrected by its "redundant" partner to stop you safely. It has no accelerator or brake and it works on the same basic premises that a person walking uses: lean forward and move forward, stand or sit in your neutral balance point and remain stationary, lean back and go back. A Segway weighs between 85 lbs and 95 lbs. (depending if it is a generation 1 or a generation 2 machine). Both generations rely on the same technology (*dynamic stabilization*) but the one preferred by people with disabilities is the older Generation 1 machine. Unfortunately, you can only buy those used. Ebay or your local Segway dealer are great sources to get one. The Generation 1 model can be bought for anywhere from \$1,000.00 to \$3,000.00 dollars, the second generation model sells for about \$6,000.00 brand new. It is considered a green machine, has zero emission and is safe for indoor use. Its width is 25 inches so it can very easily be manoeuvred through doorways, into and out of elevators or busy pedestrian areas.



In a major development, on March 15th, 2011, the American Disability Act (ADA) recognized the Segway as a mobility device and its use is now protected under the Act. Consequently, it can be used in most public locations (*like a wheelchair or a scooter or other mobility devices*) and cannot be discriminated against. For more information either refer to the ADA act or go to www.segs4vets.com.

To travel by plane, you must use a Generation 1 with Nimh batteries (*dry cells*). The second generation units all have Lithium Ion batteries and these are considered hazardous material and are not allowed as cargo by airlines. The basic difference between the batteries is range: a Nimh battery can only travel between 12 and 14 miles on a full charge (*4 hours*) while a Lion battery can travel from 18 to 20 miles on a full charge (*8 hours*).

I am not selling this product and just wanted to share with you how great it has been for me. In many ways, I wish that I would have been made aware of this technology sooner and how it can assist mobility-impaired people. It's a whole new life. Here are some areas where you can do more research on the product and get answers. Look at www.Segs4vets.com, or www.Segchat.com (*check the forum on special needs, mobility and Disabled Use*), Segway.com, segsaddle.com and many videos that have been posted on YouTube about the Segway and the adaptation of Segway technology for mobility impaired people. There was also a great book called "Code Name Ginger" written on the technology and its creation: the book was written by Steve Kemper. Furthermore, if I can answer any other questions, please feel free to contact me at yjbrunet@gmail.com.

There is only one drawback to the Segway: it is hard to stop smiling when you are gliding around on it !!!



Exercise And You: Stand Tall!

Contributed by Liz Wroblewski, MPT, PT

A standing frame, or stander, is a piece of equipment that provides standing support for those unable to do so on their own. There are health consequences due to immobility for those who remain seated for most of their day. This column addresses those consequences and the benefits that standing provides.

People who cannot or do not stand are at risk to develop osteoporosis, a loss of bone mineral density. This loss increases fracture risk. Bone density is maintained or increased by weight-bearing stresses on the skeletal system. Standing is an activity which accomplishes this objective.

Prolonged sitting without a position change is a risk factor to develop a pressure ulcer in the "sit" area. The best management of this is prevention. Wheelchair users are advised to "unweight" the area for up to 60 seconds every sitting hour. A seated push up unweights the bottom allowing for blood flow into the compressed tissue. Daily use of a stander would be another approach to pressure relief.

Prolonged sitting puts us at risk to develop joint contractures, especially in the 2-joint muscles of the hamstrings and the calf. The iliopsoas, or hip flexor muscle, can shorten making it difficult to stand erect. A shortened muscle will develop an increased sensitivity to stretch. This will increase spasticity. Weightbearing and lengthening muscle are techniques of spasticity management.

Daily standing improves bowel and bladder emptying. Less urinary retention will result in fewer urinary tract infections. Sitting, especially in a slumped position, can restrict rib cage recursion leading to decreased oxygenation throughout the entire body. Efficient respiration is compromised.

In summary, standing as a daily activity is important to all body systems. Use the words standing frame or stander in a web to search for more information.

Thank you to Jane Anne King for allowing me to use her picture as an illustration. She is demonstrating straight knees and hips!



Annual Conference Bytes

John K. Fink, M.D.

University Michigan Dept. of Neurology

Dr. Fink's presentation highlighted several exciting new ideas in the area of genetic research. He discussed, in detail, the significance these new research approaches will have in discovering and uncovering important new information about the evolution of motor neuron diseases. This new direction in genetic research also has implications in the identification process, and treatment of, Hereditary Spastic Paraplegia and Primary Lateral Sclerosis.

Due to the vast amount of information relayed and to the technicality of that information, the following summary of Dr. Fink's presentation is more of an outline of his presentation rather than a simple explanation of it.

- Spasticity and Spastic Gait (*Neuroplasticity*)
- Genetic Analysis
- Evolving Concepts in HSP and PLS

Spasticity and Spastic Gait (Neuroplasticity):

Spasticity, long determined to be one of the outward "hallmark" symptoms of HSP and PLS, is undergoing a change with regards to its meaning and to its significance for those of us suffering from these two conditions. Spasticity (*increase in tone*), as it is assessed in the clinic, is difficult to measure during action and is also highly variable. In other words, one's spasticity on any given day can increase to a certain degree due to numerous factors: posture, fatigue, pain, emotional stress, activity, and medication can all play a factor in the variability of spasticity.

Spastic Gait on the other hand, is a complex symptom that reflects "upper motor neuron" deficits in bilateral lower extremities. It is important to note that Spastic Gait usually understates the neurologic abnormality. In other words, a "spastic gait" is almost never simply a "gait" that is abnormal because of spasticity alone. Rather, it almost always includes elements of increased muscle tone, slowed movements, decreased precision, and weakness. These are important distinctions to make because evaluating these components is very important in designing individualized treatments.

One of the most important "new ideas" with regards to spasticity is this: Spasticity requires maturation and integrity of both the central nervous system and peripheral nervous system. What does this mean, exactly? Well, traditionally medical professionals have viewed spasticity as visible "proof" that something within the body isn't working well, or properly. However, due to the fact that spasticity requires a certain level of maturation and integration of both the central and peripheral nervous system, the thought now is that perhaps spasticity can be an outward symptom that something in the body is working TOO well. This perspective would then have numerous implications that would be looked at completely differently in a research setting.

If it's possible then, that spasticity can worsen in non-progressive disorders, then the question becomes, "Does emergence of spasticity and spastic gait represent an evolution of a static lesion or does it represent emergence of a progressive disorder?" This

is a crucial question that must be answered but is difficult to do so. Is there progressive weakness? Does physical therapy help? Is there the appearance or worsening of other neurologic signs?

This is where the term, "neuroplasticity" comes into play. Neuroplasticity is a factor in spastic gait. Neural reorganization ("*plasticity*") within motor cortex (*and presumably also in cerebellum and spinal cord*) occurs in subjects with chronic upper motor neuron impairments. The spastic gait phenotype represents the complex outcome of neurologic impairments (*of variable nature and degree*); in the context of preserved neurologic function and relative maturation; and as influenced by the variable nature and extent of motor reprogramming.

In summary, spasticity in and of itself may or may not indicate a progressive and neurological disorder. But when the complexity and presence of Spastic Gait (*and the accompanying neuroplasticity*) is considered, the probability of a neurologic impairment is at once more clearly evident, and yet immediately more difficult to treat and/or cure.

Genetic Analysis: Whole Exome Sequencing

Genes are divided into coding portions (*exons*) and non-coding portions (*introns*). The exome refers to all exons, collectively. And if that's not confusing enough, consider this: the exome only represents approximately 1% of a person's entire DNA. So why then, is this an exciting new direction in genetic testing? Simply put, whole exome sequencing analyzes all coding sequences of all genes. It takes 4 weeks to complete the analysis and the cost is around \$4,000. One HSP gene profile analysis can cost up to \$12,000. Wow! Whole exome sequencing is rapidly identifying new mutations and new genes responsible for inherited disorders.

While whole exome sequencing is a significant development in the area of genetic testing and analysis, there are several issues that must be considered before this road is taken. First, this process has two major limitations. The first is that whole exome sequencing does not analyze non-coding regions of genes. For example, a condition known as Friedreich's ataxia is due to a mutation in a non-coding region of the Frataxin gene. This gene mutation, therefore, would not be discovered by whole exome sequencing. The second "hitch" with whole exome sequencing is the fact that it requires ongoing reassessment pertaining to the significance of discovered gene variations. Each year, for example, at least one new gene is usually discovered that causes HSP. In order for that new gene to be included in a person's profile, he or she would have to redo the whole exome sequencing each time a new HSP gene was discovered.

Evolving Concepts in HSP and PLS:

Concept Evolution 1: There is a gradual disappearance of "uncomplicated" HSP as a genetic category. With more intensive evaluation, "complicating features are increasingly evident in some subjects with types of HSP that were previously considered "uncomplicated."

Concept Evolution 2: There is a school of thought that is beginning to challenge the traditional and central dogma that PLS is a pure upper motor neuron disorder and HSP involves upper motor neurons and dorsal column fibers (*vibration sensation*).

PLS and HSP: Building a Path Towards the Cure

Jinsy Andrews, MD, MSC.

Director of Research & Clinical Trials Unit
Hospital for Special Care - New Britain, CT

Dr. Andrews began her presentation with an overview of three diseases: Hereditary Spastic Paraplegia (HSP), Primary Lateral Sclerosis (PLS), and Amyotrophic Lateral Sclerosis (ALS). As most of us are aware, all three share at least one common denominator: upper motor neuron involvement. And, we also learned that some facts concerning HSP and PLS haven't changed. A PLS diagnosis still requires a four year waiting period and the number of genetic tests for HSP is still seven, though there are now 25 genes known to cause the disease.

The crux of Dr. Andrews' presentation however, was what a crucial impact the NEALS and SPF PLS/HSP consortium has had on the HSP, PLS, and ALS communities. Specifically, a small group of researchers and clinicians realized that if they were to treat these diseases in the most effective manner possible, three things needed to happen: increase awareness among researchers and clinicians about the existence of PLS, HSP and the similarities with ALS, thereby laying the foundation for 'ease of diagnosis'; standardize the care for PLS, HSP and ALS by encouraging the use of multi-disciplinary clinics; and develop a cohesive manner in which to treat the symptomatic problems that occur with each disease.

Thanks to the inception of the NEALS and SPF PLS/HSP task force that was created in 2010, these important goals and objectives have begun to be implemented across the nation. In essence, researchers, clinicians, doctors, scientists, and neurologists are trying to bridge the gap between the laboratory and the clinic in order to better identify and treat patients with PLS, HSP, and ALS. This new approach in trying to bridge the gap between the lab (*genes, cell mechanisms, how disease is caused in a sterile environment*) and the clinic (*understanding who gets the disease, how it progresses and defining different types of the disease*) is called Translational Research.

Dr. Andrews concluded her presentation by outlining the current and future direction of PLS, HSP and ALS research programs. They are as follows: Northwestern (Siddique) – studying the genetics of ALS and related disorders; Columbia (Mitsumoto) – multi-center study investigating exposures and their relationship to ALS and PLS; NIH (Floeter) – collection of blood samples for DNA analysis in motor neuron diseases; University of Michigan (Fink) – HSP registry; Natural History Study PLS – planning stages via NEALS SPF PLS/HSP consortium.

Thank You!!

The Spastic Paraplegia Foundation is proud to announce that it has received a \$2,400 Quality of Life grant from the Christopher & Dana Reeve Foundation. The Quality of Life grant is awarded to nonprofit organizations throughout the nation that help people living with paralysis and their families become more integrated members of society. This is the second grant that has been awarded to the Spastic Paraplegia Foundation.

"The Quality of Life program recognizes and supports organizations that assist individuals living with paralysis, their families and caregivers in ways that more immediately provide them with increased independence, well being, and improved access," said Peter T. Wilderotter, president and CEO of the Christopher & Dana Reeve Foundation. "Throughout the past ten years, we have had the privilege of being able to impact the lives of thousands of people living with paralysis through these deserving organizations. As Dana Reeve used to say, 'our Quality of Life program is about freedom' and we are pleased to do our small part to assist the Spastic Paraplegia Foundation in fulfilling its mission."

The Spastic Paraplegia Foundation is grateful for the support that the Christopher & Dana Reeve Foundation have given.



9 DAY FULLY ESCORTED ACCESSIBLE TOUR OF ISRAEL

**Mark your calendars! This exciting tour is
March 13th - March 21st, 2012**

This 9 DAY FULLY ESCORTED tour is for people with disabilities, slow walkers and wheelchair users and their companions. The tour will include airport transfers, accessible hotel accommodations, two meals a day, transportation in a wheelchair accessible vehicle, an English-speaking tour guide and sightseeing. The tour will visit both Jewish and Christian sites.

The price will begin at \$2,570 per person, but the more people there are the lower the price. This price does not include airfare.

**Detail Brochures are now available! For
more information, please contact
Bonnie Guzelf at 480-838-1184 or
e-mail her at bguzelf@cox.net**

2011 Annual Conference

A well deserved thank you to Ashton Hecker, committee chair, his family and friends and to his fellow committee members: Ashley Aniol, Marlene Doolen, Ida Park, and Joshua Robnett. The conference provided both an educational platform rich in diversity and the opportunity to develop sense of fellowship and support with others. A thank you goes out to our speakers, as well. They presented a wide array of informative and interesting topics.

Friday evening began with the registration process and time to greet other attendees in a casual and friendly atmosphere. After a delicious dinner was served, a representative from a local law firm provided a detailed overview of the disability process. Saturday sessions began with a lively and interactive presentation by Dr. Jinsy Andrews concerning specific treatment options, or lack thereof, for PLS & HSP. Dr. John Fink's presentation followed with a detailed analysis of exciting new approaches being implemented in research and clinical studies regarding upper motor neuron diseases. Afternoon sessions began with a well-received Chair Yoga session. The hour was filled with demonstrations of specific yoga stretches and lots of laughter. A detailed analysis of acupuncture and its uses was presented by Mr. John Paul Liang, a licensed acupuncturist in Texas. The day's formal presentations concluded with a brief history of the Spastic Paraplegia Foundation, presented by our own Kathi Geisler. Saturday events wrapped up with three breakout sessions: Orthotics and WalkAides, Service Dogs, and The Benefits of Aquatic Therapy. If you would like to receive a copy of the Aquatic Exercise Booklet that Katie was kind enough to put together, please contact me via e-mail or phone.

Thanks to our Sponsors

The Spastic Paraplegia Foundation greatly appreciates the financial donations made by Athena and the Sundt Foundation in support of our 2011 Annual Conference.

ATHENA

Athena Diagnostics (*Thermo Fisher Scientific*) is a reference laboratory dedicated to the development and commercialization of diagnostic testing for neurological disorders. Using innovative technologies, Athena provides neurologists and other physicians with diagnostic answers that can improve the quality of health care for patients in a cost effective manner.

Athena is a leading provider of advanced neurological diagnostic assays. Our expertise includes diagnosis in the areas of: peripheral nerve disorders, neurogenetic disorders, Alzheimer's disease, paraneoplastic syndromes, movement



disorders, neuromuscular disorders, and ataxia. Our technologies are licensed predominantly from the academic research environment and represent our commitment to cutting-edge technology and our close relationships with world-renowned experts in neurology and genetics. The technical staff at Athena Diagnostics performs over 200 assays for neurological diseases using a variety of sophisticated laboratory methods. Assays are performed in our laboratory located in Worcester, Massachusetts, and are available only to physicians.

Athena graciously donated \$5,000 towards this year's Houston Event! Their willingness to help sponsor the SPF Annual Conference year after year demonstrates their commitment to The Foundation and its members. Thank you, Athena! Your continuing dedication towards the Spastic Paraplegia Foundation is of great importance.

The Spastic Paraplegia Foundation proudly announces a new sponsor – the Sundt Foundation! Their generous donation was received with much delight. Many thanks! We look forward to the opportunity to work with you again.

THE SUNDT FOUNDATION



SUNDT
FOUNDATION

**Building Integrity –
Building Communities**

The Sundt Foundation is proud to announce its \$5,000 donation to assist in sponsoring this year's Spastic Paraplegia Foundation's National Conference in Houston, Texas. Since it was founded over a century ago, Sundt has been dedicated to improving the communities where it operates. In 1999, Sundt expanded this effort by creating the Sundt Foundation, a separate non-profit organization focused on the needs of disadvantaged children and adults. The Foundation receives most of its funding through employee contributions, which are matched by the company. To date, the Sundt Foundation has provided more than \$4 million in aid to community organizations in Arizona, California and Texas.

The Sundt Foundation supports individual volunteer projects undertaken by its employees for various worthy organizations. Committees, made up of employees who work in the cities where Sundt has an established office, review grant requests and make recommendations to the Board of Directors. The Board meets quarterly to act on grant requests and provide support for communities in which it works.

The Sundt Foundation is excited to support the Spastic Paraplegia Foundation in its efforts to increase awareness, and raise funds for research. Motor neuron disorders hit close to home for Sundt.

Medical Updates

Dealing with Drooling

Getting rid of excess saliva goes high-tech

When 61-year-old Deborah Clark first experienced trouble swallowing, she didn't think much of it. But six months later, when she began having symptoms like slurred speech and difficulty projecting her voice, she visited a neurologist. Diagnosed with amyotrophic lateral sclerosis (ALS, also called Lou Gehrig's disease) in February 2008, Clark quickly discovered how integral the muscles in her mouth were to her quality of life. Not only did she have difficulty speaking, but she also experienced excess saliva pooling in her mouth. At its worst, Clark found herself changing clothes up to four times a day because she had drooled down the front of her shirt.

"I was reluctant to be in public or around strangers--especially when a meal was involved," says Clark. "People were always offering me tissues to control the drooling. It was embarrassing."

Drooling, or sialorrhea, can be a major problem for people with neurologic conditions ranging from Parkinson's disease and cerebral palsy to certain types of stroke and ALS. People with these conditions may not have the brain control to coordinate movements in the face and mouth.

"Any condition that affects the muscles and nerves of the bulbar area (the swallowing mechanism) could cause increased drooling," says Steven Bachrach, M.D., co-director of the Cerebral Palsy Program for Alfred I. duPont Hospital for Children in Wilmington, DE. And if you're not swallowing your saliva, it tends to pool and accumulate in the mouth, and then it starts overflowing.

Beyond the obvious social implication of incessant drooling, the overflow of saliva in the mouth can irritate tissues around the lips and even cause aspiration pneumonia, a serious condition where people breathe fluid (*or other foreign materials*) from the mouth into the lungs. But with recent advances in everything from oral medication to botulinum toxin injections, people have more options than ever to control sialorrhea.

SWALLOWING THERAPY

Speech and swallowing therapy is a great option for people who are mildly impaired and highly motivated to control their drooling. Most neurologists will advise patients to investigate this approach before considering invasive procedures. Through a series of sessions, therapists teach patients a variety of techniques to improve the safety of swallowing and minimize the risks of aspiration.

"There's a lot that a swallowing therapist can do in this area," says Robert Miller, M.D., professor of Neurology at Stanford University and director of the Forbes Norris

ALS Research Center at the California Pacific Medical Center in San Francisco. "If you tuck in your chin when you're swallowing, for example, you'll close up the airway, making it easier for fluid and food to go down."

Even just becoming more aware of when and how to swallow can be effective. With regular training, people can learn to swallow more efficiently and get rid of excess saliva. Unfortunately, none of these techniques actually dries up the spit. If that's your goal, medications or surgery are your best bets.

MEDICATION

When less invasive methods have failed, the next approach is medications. This class of drugs is used for everything from seasickness to overactive bladder. But with dry mouth as one of the main side effects, anti-cholinergics have become a useful tool to control drooling. In fact, studies investigating glycopyrrolate (the most commonly prescribed medication for drooling) consistently find the drug reduces drooling for up to 95 percent of patients who try it.

When Clark started taking glycopyrrolate, her drooling improved within a matter of days. Initially she took one tablet three times a day, but eventually she needed four tablets daily to experience the same effects. Over time, even four tablets didn't reduce her drooling to an acceptable level.

"Even if the drugs do work initially, receptors on the cells and within the salivary glands change, so patients may end up requiring higher and higher doses to get the same result--and then they get side effects," says Scott Brietzke, M.D., M.P.H., director of pediatric otolaryngology at the Walter Reed Army Medical Center in Washington, D.C. While dry mouth is the most common side effect, some people also experience constipation, urinary retention, and cognitive side effects such as confusion and memory impairment.

If the anti-cholinergics stop working--or the side effects are intolerable--some physicians prescribe amitriptyline, an anti-depressant that dries up saliva. A bonus, amitriptyline improves sleep, which is often disrupted in patients with ALS, multiple sclerosis, and other neurologic disorders.

INJECTIONS

If meds can't control drooling, botulinum toxin is another option. Using an ultrasound-guided approach, the physician injects the drug into the major salivary glands to paralyze the muscles that normally squeeze out saliva. In one study of 131 patients, published in the medical journal *Archives of Otolaryngology Head and Neck Surgery* 2010, botulinum toxin injections in the submandibular glands (*the two glands located in the lower jaw that produce most of the saliva*) reduced drooling and improved quality of life among patients who received injections. Two months after

the injections, nearly 50 percent of patients experienced significant improvement, with effects beginning to wear off at the eight-month mark.

Clark started with just two shots into the salivary glands on either side of her face. Within a week, her drooling had dissipated more than it had with glycopyrrolate alone, and the effects lasted for three months. On the heels of this success, Clark's physician gradually increased her dose to a total of six shots (three on each side).

"With six shots, the results were much more dramatic," says Clark. "I have very little drooling and the only side effect is a dry mouth, which is easier to deal with than drooling." After the last round of botulinum toxin, Clark discontinued the glycopyrrolate without any noticeable difference.

Studies suggest that combined injections in both the parotid glands (which are located in the cheeks) and submandibular glands are slightly more effective than injections into the submandibular glands alone. And after repeated injections, there have been some reports that the salivary glands actually stop working, resulting in a permanent reduction in drooling. "You can't count on that," says Dr. Bachrach, "but it does happen in some patients. For other people, though, botulinum toxin is just a trial procedure to determine whether surgery will be effective. "Botulinum toxin deactivates those major glands, so we can see if that helps the patient with either the social problem or aspiration," says Dr. Bretzke. "If there's significant improvement, then we can consider a potentially irreversible procedure, such as tying off the ducts or removing the glands."

SURGERY

Surgical treatment for drooling may be even more effective than injections, without subjecting people to recurrent treatments. Studies show that people who have surgery are generally happy with the results. Unfortunately; there are a variety of approaches and little consensus about which ones work best. The most straightforward procedure involves the submandibular glands: Rerouting the ducts from these glands to the back of the mouth makes it easier to swallow saliva. Alternatively, surgeons can reroute the ducts from the parotid glands or remove the submandibular glands altogether.

"The evidence we have suggests that intra-oral procedures (like tying off the four ducts in the mouth) may not be as successful," says Dr. Brietzke. According to a study he co-authored in *Archives of Otolaryngology Head and Neck Surgery* in 2009, "removal of the submanibular glands and parotid duct rerouting appear to have the highest success rates at 87.8 percent while the success rates for tying off the four ducts varied wildly from 31 to 100 percent."

"The biggest downside is that surgery is not reversible," says Dr. Bachrach. "Once you've tied off the ducts, or removed the glands altogether, you can't undo that." So while you can go from drooling to dry, you can't go back. And dry mouth has its own set of complications.

Even so, treating symptoms like drooling still gets short shrift from some health care providers.

"We tend to think that since some of these [neurologic] conditions are incurable, they're also untreatable," says Dr. Miller. "That's a big mistake. We have many treatments for the breathing issues, the nutritional issues, treatments that slow the progression of disease, and yes, treatments for drooling."

For Clark, that treatment has been invaluable. Today, she no longer carries a napkin with her at all times, she doesn't shy away from social events, even with strangers, and her shirt stays dry throughout the day. "I'm very happy with the results," she says.

Written By: Amy Paturel, M.S. M.P.H.

Neurology Now February/March 2011

Scientific Articles More Your Thing? -Take a look at these Eye-Catching Headlines-

❖ Disease severity affects quality of life of hereditary spastic paraplegia patients

PubMed - U.S. National Library of Medicine - National Institutes of Health www.ncbi.nlm.nih.gov/pubmed/21631647
European Journal of Neurology – 2011, June 1
Klimpe S, Schule R, Kassubek J, Otto S, Kohl Z, Klebe, S, Klopstock T, Ratzka S, Karle K, Schols L

❖ Adequate Dose of Intrathecal Baclofen Therapy for Spasticity

(Smaller dose of Baclofen needed in HSP)

Department of Neurosurgery, University of Nara Medical Graduate School (Japan) *No Shinkei Geka* – 2011 April – 39(4) – 345-350
Wajima D, Hirabayashi H, Nishimura F, Motoyama Y, Nakase H.

❖ Corticospinal Motor Neurons and Related Subcerebral Projection Neurons Undergo Early and Specific Neurodegeneration in hSOD1G93A Transgenic ALS Mice

(Similarity of mouse model of familial ALS to human form)
Journal of Neuroscience – 2011 March 16 – 31(11) – 4166-4177
Ozdinler PH, Benn S, Yamamoto TH, Guzel M, Brown RH Jr, Macklis JD

Note from Mark Weber: The SPF has funded the work of Dr. Jeff Macklis of Harvard University for 3 years. Here (in work that the SPF did not fund) he starts with a line of genetically modified mice. These mice have been developed with a human copy of the hSOD1(G93A) gene – instead of the mouse version of that gene. Further, the human hSOD1(G93A) gene that these mice have contains a mutation that causes ALS in humans.

Dr. Macklis and his team show that these mice have the same type of selective neuronal degeneration observed in humans with a mutation in their hSOD1(G93A) gene. Specifically, upper motor and sensory neurons and related association subcerebral projection neurons all degenerate in these mice – as they do in humans. Further, this degeneration begins approximately 30 days after birth (of mice) – before they begin to show symptoms.

By showing the similarities between these mice and humans with this form of ALS, science is another step closer to developing therapies for upper motor neuron degeneration – such as that in PLS.

❖ **NIPA1 mutation in Complex Hereditary Spastic Paraplegia with Epilepsy**

Eur J Neurol. 2011 Feb 22. doi: 10.1111/j.1468-1331.2011.03359.x. [E-pub ahead of print]

Svenstrup K, Møller RS, Christensen J, Budtz-Jørgensen E, Gilling M, Nielsen JE.

Source: Section of Neurogenetics, Department of Cellular and Molecular Medicine, University of Copenhagen, Copenhagen Memory Disorders Research Group, Rigshospitalet, University Hospital of Copenhagen Department of Neurology, Danish Epilepsy Centre, Dianalund Department of Neurology, Aarhus University Hospital, Aarhus Department of Biostatistics, University of Copenhagen, Copenhagen, Denmark.

❖ **Structural and metabolic damage in brains of patients with SPG11-related Spastic Paraplegia as detected by quantitative MRI**

J Neurol. 2011 May 29. [E-pub ahead of print]

Stromillo ML, Malandrini A, Dotti MT, Battaglini M, Borgogni F, Tessa A, Storti E, Denora PS, Santorelli FM, Gaudiano C, Battisti C, Federico A, De Stefano N.

Source: Neurology and Neurometabolic Unit, Department of Neurological and Behavioural Sciences, University of Siena, Viale Bracci 2, 53100, Siena, Italy

Patients Needed for SPG4 Genetic Research Study!!

Researchers at Baylor College of Medicine are enrolling subjects in a genetic research study of type 4 autosomal dominant spastic paraplegia (SPG4). They are studying the way that different types of gene mutations lead to differences in clinical symptoms among SPG4 patients.

If you or your family member has been diagnosed with a “deletion” or “duplication” mutation in the SPG4 disease gene (*this gene is also called SPAST*), you will likely qualify to participate.

If you are interested in participating or would like more information, please contact Philip Boone at pmboone@bcm.edu or at (713)798-6873.

University of Miami HSP Study

Investigators at the John P. Hussman Institute for Human Genomics (HIHG) have made major breakthroughs in the identification of one gene that causes HSP. HIHG Director Margaret Pericak-Vance, Ph.D., was involved in several studies that described new chromosomal locations for HSP and the discovery of the KIF5A gene involved in HSP.

More recently, the HIHG’s Stephan Züchner, M.D., identified the REEP1 gene that is now established as the third most common HSP gene. Dr. Züchner is also leading current studies that focus on cell culture models for HSP to increase understanding of the pathological processes that lead to these conditions. The HIHG is also actively enrolling HSP patients and their families in special studies to identify the remaining genes, which may account for about 40 percent of the disease. This research is supported by grants from the National Institute of Neurological Disorders and Stroke (NINDS) and the Spastic Paraplegia Foundation.

HSP: Research Study Participants Wanted

If you are interested in joining any research study, please contact the Hussman Institute for Human Genomics (HIHG) study coordinators by calling 1-877-686-6444 or by e-mailing: hihginfo@med.miami.edu

For participation in our Hereditary Spastic Paraplegia study, you can also contact the study coordinators directly by using the information below:

HIHG Hereditary Spastic Paraplegia (HSP) Study
PO Box 091932 (M-860) I Miami, FL 33101
1-877-686-6444

Fiorella Speziani – Project Manager (305)-243-2550
fspeziani@med.miami.edu

Please see following links for more detailed information:

<http://hihg.med.miami.edu/hsp/our-team>

<http://hihg.med.miami.edu/hsp/about-hsp>

Excerpts taken directly from web pages of University of Miami’s / John P. Hussman Institute for Human Genomics (HIHG)

Support SPF with One Step a Month

Consider making a monthly donation to help SPF move a step closer to a cure. Our One Step a Month Program is a win-win! Recurring gifts allow us to plan ahead with confidence, making sure we take the best steps towards finding the cures for HSP and PLS. Plus, recurring donations allow you to give in a convenient, safe and secure way.

Go to <http://www.sp-foundation.org/donate.htm>

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