Synapse
Volume 21, Issue 3 Fall 2018
Newsletter of the Spastic Paraplegia Foundation

Letter from the President

Dear Friend,

As we approach the fourth quarter of the year, we are faced with a big challenge. As you may know, the fourth quarter is when most of our funds come in for making a huge difference in the lives of over 100,000 people worldwide with HSP and PLS. I don't want to be illusive! Those funds don't come from someone else. If we want to cure HSP and PLS, those incredibly important funds need to come from you and me.

I remember, when I was growing up, every year the classic movie, The Wizard of Oz, would show on television. Do you recall when Dorothy, The Scarecrow, Tin Man and Lion decided to go to the Wizard to get all their problems solved? That is what a lot of us with rare diseases do. We want to go to others, whether they be other donors or the government to cure HSP & PLS. Well, I think the message of The Wizard of Oz, was that we all need to bring back that "broom" to make things happen in our own lives. That "broom" could be voluntarism like being a State Ambassador. That "broom" could mean a generous donation to SPF. In this time, when the economy is booming and many of us have things to be grateful for, shouldn't we show that gratitude by making a donation to cure HSP & PLS?

This is not a religious organization but I wonder why we cannot approach this problem with at least a religious fervor. Why can't we approach this with an excited demand that HSP and PLS be taken seriously in the scientific world? The problem is that with all the new neurological science that is excitingly developing the hand is dealt to us and we need to decide how we want to participate. All sorts of new neurological techniques are developing. Multiple genetic sciences are in the hands of neurologists that want to make a name for themselves. If we want to be in the game, we have to at least put up an ante and if we want to play the game toward a very happy ending, we need to put in a few dollars toward the outcome or cure that we are all striving for.

I read recently that fund-raising is either transformational or transactional. Transactional fundraising is when you sell something like cookies or a pancake dinner to raise funds. Transformational fundraising is when you ask people to become transformed into giving toward such an incredibly worthwhile and good cause as curing HSP and PLS. This is a time when we should all write our friends and relatives to transform or remind them to be a part of this mission. An example of a good letter to write them can be found on our website. They all want to give. They just need to be asked.

We can't do it without you. Flip Wilson once said that "you can't expect to hit the jackpot if you don't put a few nickels in the machine." I'm positive that the research we are painstakingly supporting each and every year will hit the jackpot big time with a cure or treatment. How soon the cure happens depends mostly on how much research we can afford to support. Even small donations add up quickly when enough of us make them. Please send in your donation today?

All the Best,

Frank Davis

Frank Davis, President

PS: If you lose the enclosed reply envelope, our address is The Spastic Paraplegia Foundation, 1605 Goularte Place, Fremont CA 94539.

Synapse

Volume 21, Issue 3 - Fall 2018

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).

Published three times a year, Winter, Spring and Fall, for the HSP/PLS community. It is also available online at www.sp-foundation.org

The SPF is a non-profit 501(c)3.
Tax ID # 04-3594491
Combined Federal Campaign CFC #12554

Send Correspondence & Donations to:
Spastic Paraplegia Foundation
1605 Goularte Place
Fremont, CA 94539-7241

Contact the SPF at:
(877) 773-4483
information@sp-foundation.org
or www.sp-foundation.org

Support Synapse, the Newsletter of the SPF

By John Staehle, Senior Editor, Synapse

Three times each year the Spastic Paraplegia Foundation publishes its newsletter, *Synapse*. Our printed subscription list has the names of about 2,000 SPF members in the U.S. & Canada who have asked to subscribe. Each issue is full color and printed on high quality glossy paper to get the sharpest text, photos and graphics possible. The size of the last five issues has ranged from 16 to 28 pages and averages 22 pages. Each issue costs SPF more than $3.00 per copy which is a bargain considering the authors and editors are all volunteers and the publisher doesn't charge SPF for their graphic services.

Upon examination of the *Synapse* mailing list, there were almost 700 people receiving a printed copy of the newsletter for more than 5 years who had never made a single donation to SPF. Frank Davis, SPF President, sent them an email in which he asked each to demonstrate their interest by responding with their choice of either asking to continue receiving the printed newsletter for free, sending a donation to SPF or viewing/downloading future *Synapse* Newsletters on the SPF website. They were given 3 weeks to respond. Two responded, one chose to read it online and the other sent a donation. Those that did not respond were deleted from the mailing list and will not be receiving this issue of *Synapse* in the mail. They may, however, read the online version that is posted on the SPF website, https://sp-foundation-org.presencehost.net/news-resources/newsletter.html.

We're asking all recipients of printed copies of *Synapse* to send at least a $10 donation to SPF to cover the publishing and mailing costs of their copies for a year. A donation envelope is included with this issue. Please use it to send your donation to SPF and write "Synapse" on the memo line of your check. If you prefer to donate using a debit or credit card, please write "Synapse" on the inside flap of the envelope. **DO NOT SEND CASH.**

Your donation will allow SPF to increase its allocation of funds for research grants instead of diverting funds for the newsletter. In the 2017 Annual report, Frank Davis presented some of the highlights of the progress that is taking place with the research SPF is sponsoring

plus the new research projects the Foundation is funding to the tune of $900,000. More grants could have been made if the Foundation had more funds to grant. Every donation, regardless of the amount, helps to make a cure for HSP and PLS more within our reach.

Make No Cost Donations to SPF

By Jackie Wellman, Iowa State Ambassador, SPF Board Member

Most of us shop at Amazon. I do often because I cannot get out to do any shopping for household items anymore. It is so convenient. If you shop at Amazon, please go to Amazonsmile. Just type Amazonsmile in your browser. It will ask you what charity you want to support. Select Spastic Paraplegia Foundation. Every time you want to buy something from Amazon, just type in Amazonsmile and Amazon will donate 0.5% of your purchases to SPF. It costs you nothing. Please tell your friends and family. Share it on Facebook, too.

amazonsmile
You Shop. Amazon Gives.

Other online shopping stores will donate to SPF if you do the same thing with Goodshop. There are many stores on the Goodshop site, from Walgreens to Target to Dell Computers to Land's End. Each store will donate a percentage of your total purchase, some as high as 5%.

goodshop

When you need to use a search engine, use Goodsearch. Set up your charity as SPF and then every internet search you make will generate a penny for SPF.

goodsearch
simply do good

Tell everyone you know about these simple, cost-free ways to help fund research. If everyone reading this *Synapse* along with their friends and family use these sites, we could fund another research grant.

Ambassadors Needed

By Jackie Wellman, Iowa State Ambassador, SPF Board Member

Does anyone want to help others with HSP or PLS to feel welcome? That is basically the SPF Ambassador's job. We need volunteers in Hawaii, Maine, Mississippi and Idaho to serve as their state's Ambassador. It is a very easy but important job. We all know how lonely having a rare disease can be. When a new person in your state joins the Foundation, an email will be sent to you with all of their information. You contact them and welcome them to the SPF. I give them my contact information and let them know they can contact me at any time. Only a few ever do. In fact, in all the years I have done this, only a few have ever responded. When you sign up to be an ambassador, you will be sent an Excel spreadsheet of all the members in your state. Add the information about this new person. In Iowa I get a new person every 4 or 5 months on average. I tell them about the SPF Facebook page... lots happening there.

I do have a get together once a year where I just send a group e-mail to all the Iowans in SPF. We meet for a casual lunch and everyone buys their own. It is a social gathering. You can do this or do something more official...it's up to you.

I also send out a group email every now and then.

There really are no specific rules. We just want people to feel welcome and not so alone. If you are interested there is information on the SPF website or you can contact me at any time. Hoppywell@gmail.com or (515) 971-3012.

Some of the larger populated states have more than one ambassador. Here in Iowa, Bruce Stolba lives a few hours away. He is going to have a lunch gathering in his area of the state. We figure there are many folks in his area who would love to meet others without having to drive two hours to do it.

It is not a time-consuming job and helping people feels good. If you are interested, let me know.

Spread the Word and let your friends and family assist the Spastic Paraplegia Foundation raise money for scientific research.

The Combined Federal Campaign or CFC is a fundraising campaign the Federal Government offers its employees. The 2018 campaign begins September 1st and goes through mid December. Federal employees are allowed to pick from over 200 registered nonprofits to contribute to. Many CFC fairs will be held at Federal facilities throughout the US. This allows employees to learn about the nonprofits and make their selections.

The Spastic Paraplegia Foundation CFC number is **12554**.

Examples of Federal employees are: law enforcement, mail personnel, VA or Veteran's Administration employees, Medicare, Medicaid, military and many types of governmental jobs. If donors want to know more, please have them log on to www.sp-foundation.org

Millions of dollars are raised each through the CFC. The SPF's contribution is on the smaller side since little is known about HSP and PLS. Those affected need your help so the SPF gets a bigger piece of the pie. Please let your federally employed friends and family know about SPF.

If you have any questions or suggestions, please contact Jim Sheorn at jimsheorn@gmail.com or 615-479-7369.

Please help us generate more financial resources for research.

2018 Annual Conference Recap

Pittsburgh, Pennsylvania

June 22-23, 2018

ATTENDANCE

Conference registrations and attendance at the General Sessions were **60% higher** than at last year's Conference in Atlanta.

- Total number of registered participants at the 2018 Conference was 223, of which 84 were spouses and 12 were children.
- Dinner on Friday evening was served to 234 people, Saturday's plated breakfast was also served to 234 and the plated lunch on Saturday was served to 220.
- General Sessions on Friday and Saturday were each attended by 234 people.
- Children's Breakout Sessions on Friday and Saturday were attended by 14 children.
- The Appreciation Reception for donors and sponsors was attended 60 people.

See all the great pics on pages 14 & 15 inside this issue!

A Big "Thanks" to Our Conference Sponsors

Kris Brochinni — The SPF Community would like to express our sincere gratitude and appreciation to you for the generous support and contributions that you give to the Spastic Paraplegia Foundation — Thank You!

MNG Laboratories™ provides expert diagnostics through clinical services, complex biochemical testing and sequencing. Our Next Generation Sequencing panels are the most cost effective and comprehensive available, particularly for cellular energetics defects, muscular dystrophies, epilepsy, cardiomyopathy and intellectual disabilities.

MNG LABORATORIES
Neurogenetic Answers™

CHRISTOPHER & DANA REEVE FOUNDATION
TODAY'S CARE. TOMORROW'S CURE.®

The Christopher & Dana Reeve Foundation provides a Paralysis Resource Center that educates and empowers those with paralysis with a host of FREE programs that include information services, peer mentoring, community education program, grants for non-profits that serve individuals with paralysis and a lending library. All of our services can be accessed through christopherreeve.org or by calling 800-539-7309.

permobil FOUNDATION

The Permobil Foundation is dedicated to enhancing the quality of life by empowering strength and independence through community support, employee engagement and grant funding. We work in partnership with non-profit organizations and agencies to provide support and services so individuals can live a life without limitations.

SAOL THERAPEUTICS

Each patient with a rare disease is a patient who needs to be heard and who deserves to be treated. And that is why Saol Therapeutics exists. We bring therapies for these serious and often life-threatening conditions to market and to the life of the patient who desperately needs it. Addressing the needs of patients with rare diseases and under-served neurological conditions are our passion and focus at Saol. Supporting patients with high un-met needs by offering promising treatment options is what drives us.

INVITAE

Invitae Corporation (NYSE: NVTA), one of the fastest growing genetic information companies, today announced an expansion of its network of rare and ultra-rare patient registries in its Patient Insights Network™ (PIN) program to include a collaboration with the Spastic Paraplegia Foundation. The program is designed to empower patients to be active participants in their network and further expand Invitae's work to connect patients with rare genetic disorders to research, clinical trials and information on managing their condition.

BEMER

BEMER, **B**io **E**lectro-**M**agnetic **E**nergy **R**egulation, is a device that releases pulsed electro-magnetic energy to strengthen the body's own capacity to heal itself. Activating the body's own regenerative abilities, it supports the natural regulatory processes of the body. It is not a substitute for a healthy life style, but it allows the cells of our body to do what they were designed to do.

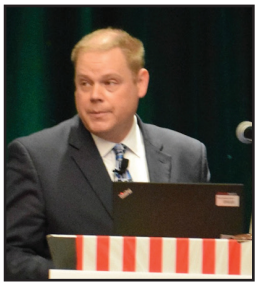
2018 Annual Conference Presentation Summaries

Editor's Note: *The videos of Dr. Statland's presentation and Dr. Lange's presentation were not available at press time. The written summaries of their presentations will be included in the Winter issue, pending the availability of those videos.*

Cell Therapy Update

Corey Braastad, Ph.D., Vice President & General Manager of Genomics at Covance Drug Discovery

This is a high-level overview of Dr. Braastad's very timely, important and informational presentation made at SPF's Annual Conference this past June. To reap the full benefits of his presentation, you are urged to watch its video, which is posted on the SPF website (see details at the end of this overview). Space limitations in this issue do not allow for the many important educational slides that complemented his spoken words.



He began by listing approved cell therapies, including antisense oligonucleotides, CAR-T for two types of cancer, and Gene replacement therapy, all of which have been approved by the FDA. Important themes to the cell therapy update this year include the willingness of the FDA to approve innovative therapies, financial investment – over $2.5 billion to date – and approval of drugs to treat rare diseases. Cell therapy includes gene therapy to target enough correct cells to treat the disease, the delivery of therapeutic genetic material via an adenoviral vector, and the use of CRISPR, a derivative of a natural process in bacteria now adapted to use in human diseases. There are four types of change in DNA, fully explained in the video of the lecture. These are deletion, translocation, inversion, and single gene changes. He also discussed cell therapy themes in 2018, phases of a clinical trial, and gave examples of cell therapies.

Mentioned above are four types of cell therapy already approved by the FDA. Studies not yet approved include gene replacement, CRISPR gene editing, and induced pluripotent stem cells. He discussed the four phases of clinical trials, Phases 1, 2, 3, and 4, their end points and types of studies performed in each phase. [*See the Spring 2018 issue of Synapse, pages 18-19, for a description of each phase. Medical & Research Editor.*] He also described the basis of genetics and how viral vectors deliver genetic payloads to cells. Editing DNA sequences in a cell is a very important capability for both research and therapy. For research, CRISPR/Cas9 can create cells in the laboratory that have the same DNA mutations as those that cause genetic diseases like HSP or PLS. Studying these cells can discover a therapeutic target. For therapy, CRISPR/Cas9 can edit the DNA sequence of cells to benefit a patient. The first CRISPR/Cas9 human clinical trial, approved in 2016, is focused on safety. Risks of such gene editing include off-target mutations. CRISPR treatment would not alter germline cells – sperm and eggs – so the genetic condition can still be passed on to children.

One important condition treated by antisense oligonucleotides is spinal muscular atrophy (SMA), a motor neuron disease that is the number one genetic killer of children under 2 years of age. Disease progression is often halted and even reversed. He discussed SMA genetics and therapeutic approaches and listed many research drugs/pathways in the SMA drug pipeline. Gene replacement therapy has been used to treat a genetic condition causing blindness. A 24-year old woman with congenital blindness had marked vision improvement after treatment. Treatment costs $425,000 for each eye! A listing of the CRISPR therapeutics drug pipeline was also presented.

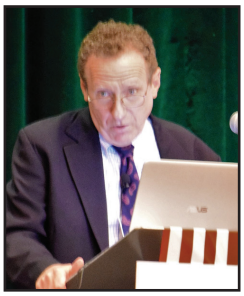
This talk was chock-full of important and comprehensive information. This summary simply introduces the topics presented which will be much more extensively understood when the reader views and listens to Dr. Braastad's presentation. The video of Dr. Braastad's complete presentation may be viewed on the SPF website at https://sp-foundationorg.presencehost.net/what_we_do/annual-conference-recap.html.

This presentation overview was prepared by Malin Dollinger, M.D., Synapse Medical & Research Editor.

Transforming Remarkable Genetic Advances into a Path Toward Treatment for PLS and HSP

John K Fink, M.D., University of Michigan Department of Neurology

Dr. Fink gives us the gift of his annual very helpful enlightenment about the status of HSP and PLS research and treatment. This year was no exception, and I encourage you to view the lecture on the SPF website, from which this brief highlight summary was prepared. Throughout this summary, "he" refers to Dr. Fink.



Dr. Fink commented that "Everything I learn now, I learn from you! – you are the experts." It is clear to this reviewer that this emphasizes our responsibility to ask questions, share information, and support research. He emphasized the need to now chart a course toward therapy, using the research findings and advances we already have. He discussed the philosophy of managing science, in that there may be multiple important research directions. Some of the primary ones are abnormal gene structure, forming abnormal proteins, and the similarities and differences between different forms of HSP. But the different forms of HSP are more similar than they are different.

There are also derivative research questions resulting from primary basic research, such as how best to determine symptomatic treatment and how to classify different forms of HSP and PLS. He commented that some of these questions and research directions may be controversial, but that does not diminish the importance of each one. For example, some people thought to have PLS actually have HSP, and vice versa, since both conditions have complex forms that may resemble one another. But they are more similar than they are different. Treatment for one may also be treatment for the other. Treatment is now specifically directed at subjects having symptoms. There are thus far at least 90 different HSP genes. An important research question is, "Is the problem one of active degeneration of nerves already formed or is it some failure in the nerve formation and development process?" He used the analogy of a pencil and a hammer, each having two functions, and pointed out that the HSP protein spastin has at least four different functions, like a Swiss Army Knife! Thus, any treatment must depend on research to begin with, a decision as to which research direction to follow and then figuring out the best and optimum target of therapy.

HSP proteins have multiple functions so the answer is not simple. An example of treatment to supply a missing substance is the use of L-dopa for Parkinson's disease where we are treating symptoms by indirectly supplying a missing chemical, dopamine, resulting in improvement, but not treating the cause of the disease. He would be ecstatic if such a "replacement" therapy existed for PLS. Dr. Fink was very excited about the successful treatment of Type 1 Spinal Muscular Atrophy in children. There has been substantial improvement after a single intravenous injection of the gene/viral vector. In that situation we can assess the results of treatment with a muscle biopsy or a blood test. There is no corresponding test where we can objectively measure the results of a gene trial in HSP.

HSP involves the descending motor pathways in the spinal cord, as well as the ascending sensory pathways. PLS involves only the descending motor pathways. Dr. Fink discussed six different pathways to finding therapy which are extensively discussed in the video of his lecture available for viewing on the SPF website.

Following his formal presentation, Dr. Fink opened the floor to questions. The following comments represent his answers to some of the questions posed by the audience.

- Although cannabis can reduce spasticity, he has not yet prescribed it. Baclofen, which works by a different mechanism, of course, reduces spasticity whether taken orally or intrathecally [into the spinal area]. He recommended starting treatment with conventional drugs. Botox causes weakness of the injected muscle with decreased spasticity, but works only in the spot of muscle injected with the needle. Its effect lasts about three months and then the Botox must then be repeated. SPG4, the most common form of HSP,

Continued on next page

is usually uncomplicated with involvement of only the legs, but in some persons, there are other problems as well. PLS should be termed "PLS Syndrome," since different persons with PLS have different degrees of problems with their arms, their legs, their speech, and their swallowing, as well as the course of the disease over time.

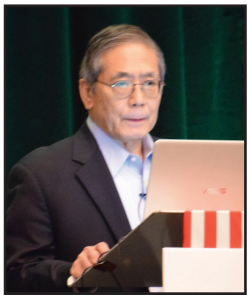
- When should genetic tests be done? Not as the first test, but rather to confirm a clinical diagnosis after other possible diagnoses/ diseases have been excluded. There is no reason to repeat a recently-done genetic test if other diagnoses have been excluded. To prevent genetic transmission to our offspring, prenatal testing can be done using the same methods as used for other diseases, such as removal of amniotic fluid – amniocentesis- to obtain genetic material. If positive for HSP, the pregnancy can be allowed to continue or that embryo could be aborted. Another method of prenatal disease determination is by studying fetal tissue at a very early stage, specifically, a method used in in-vitro fertilization to determine the presence or absence of certain diseases. In the 8-cell or 16-cell very early stage of the embryo, there is simply a clump of identical fetal cells. Under a microscope one cell can be removed and studied for a genetic abnormality. If implanted into the uterus, the remaining cells still develop into a normal embryo and subsequent child. We thus have a unique pathway to determine certain genetic defects in the very early embryo without harming it. Other aspects of genetic variation include the rare skipping of generations and the occurrence of different degrees of severity in different people in the same family, called incomplete penetrance. X-linked forms of HSP are not passed from father to son. Gene testing also includes other diseases that may cause muscle spasticity, which may help resolve clinical confusion. He discussed unusual/rare forms of HSP, called Silver Syndrome and Troyer Syndrome.
- HSP and PLS muscles are usually spastic (for example reflexes are overactive). If muscle flaccidity exists (the loss of muscle tone), then it means that lower motor neurons are involved rather than upper motor neurons. In the rare forms of HSP, only a few families have been described. What about the person with classic clinically-diagnosed HSP, with a negative gene study, who has no living or deceased relatives with HSP? What should we call their disease? He prefers the term, "Apparently Sporadic Paraplegia." It looks like HSP, but gene study is negative and there are no HSP relatives. Within the same genetic type of HSP, there is still a lot of variation in symptoms and problems from one patient to another, even in the same family. Some patients reach what is called a "plateau" in their clinical status. That means that although they may still be having some deterioration over the years, that loss of function is at the same rate as occurs simply with the normal aging process.
- He repeated his standard advice: exercise is a good idea. If muscles are tight, they need to be stretched. If muscles are weak, they need to be exercised. Thus, the exercise program needs to be individualized.

A video of Dr. Fink's complete presentation may be viewed on the SPF website at https://sp-foundationorg.presencehost.net/what_we_do/annual-conference-recap.html.

This presentation summary was prepared by Malin Dollinger, M.D., Synapse Medical & Research Editor.

PLS Research Projects Update

Hiroshi Mitsumoto, M.D., DSc., Wesley J. Howe Professor of Neurology at Columbia University Medical Center



Dr. Mitsumoto has been the Director of the MDA/ALS Clinical Research Center since 1999. He has expanded his research to include PLS and, over the past nine years, has received multiple grants from the SPF to fund his PLS research.

Dr. Mitsumoto explained why research on PLS is needed. Until recently it has been completely ignored by the research community. That has changed with funding from the SPF. PLS has never been included in ALS clinical trials. It is exceedingly rare and

therefore, difficult to investigate. There have been only retrospective studies until recently when there have been neuropsychological studies, neuroimaging studies [*see Dr. Paganoni's presentation summary elsewhere in this issue*] and a 5-site, SPF-funded prospective and clinical study completed two years ago. It's time for more prospective and clinical studies.

In 2017, Dr. Mitsumoto applied for a National Institutes of Health (NIH) grant but it was not funded. He resubmitted the application earlier this year with more detail: 100 total cases of early PLS and established diagnosis; improved diagnostic accuracy; biomarkers that have been developed but need further proof they are accurate and repeatable; establish the validity and reliability of the PLS Functional Rating Scale (PLSFRS); investigate the natural history of PLS; and ensure PLS is ready for future clinical trials.

Dr. Mitsumoto stated the ALS Functional Rating Scale-Revised (ALSFRS-R) is the most validated and widely used scale for ALS. However, ALS is a rapidly progressive disease and PLS is not. Average rating scores for studied ALS patients declined an average of 0.8 points per month while PLS patients declined only 0.05 points per month. ALSFRS-R is not sensitive enough to detect meaningful clinical changes in PLS. The development of a disease-specific clinical scale for use with PLS, the PLSFRS, was funded by the SPF and Mr. David Marren and Family. The 66-point PLSFRS scale (ALSFRS-R is a 48-point scale) was the result of a 20-site study involving 75 PLS patients over a 6-month period. Changes to individual scores were measured over time at 12 weeks, 24 weeks and 48 weeks to study test-retest reliability as well as internal consistency and construct validity. The results showed internal consistency, construct validity and test-retest reliability had been established for PLSFRS.

The new PLSFRS showed significant changes over time in bulbar, fine motor and gross motor sub-scores and total score. It revealed greater sensitivity to detect changes in PLS compared to ALSFRS-R. PLSFRS also showed significant changes in a period as short as 24 weeks which suggests it may shorten future study periods to perhaps one year. If the clinical trial readiness project in PLS proposed earlier this year is funded by the NIH, it will confirm that possibility. PLSFRS will be useful in future clinical trials, for clinical research and to assess patients at MND/ALS clinics.

Dr. Mitsumoto said PLS is an exceedingly rare, mysterious and enigmatic disease with no cure that has generally been neglected. There have been very few PLS studies to date, partly due to its rarity and the shortage of participants. Clinicians are told to wait three years after the onset of symptoms before making a diagnosis of PLS. To overcome these frustrations, Dr. Mitsumoto said we need to stimulate and encourage new PLS research. One way to do so is to hold a highly scientific international conference on PLS. He further said we have to make PLS a top priority of MND research and clinical trials and show that research in PLS would improve the understanding of ALS and MNDs in general.

Dr. Mitsumoto closed his presentation with the plans to hold a PLS International Scientific Conference in 2019. National and international experts on PLS (or ALS) will meet in one place to discuss what is known in PLS research and how to push the field forward. Drs. Atassi, Elman, Floeter, Paganoni, Siddique and Mitsumoto make up the conference organizing committee. There will be 25 domestic and 11 international speakers/moderators. PLS topics will include the clinical spectrum, cognitive functioning, electrophysiology, neuroimaging, genetics, neuropathology, biology and biomarkers, outcome measures, PLS clinical trials, revisiting the diagnostic criteria and the international PLS registry. The conference will be held May 3-4, 2019 at the Philadelphia Airport Marriott.

The conference committee will be seeking support from the National Institute of Neurological Disorders and Stroke (NINDS), the National Center for Advancing Translational Sciences (NCATS), the Spastic Paraplegia Foundation and a couple of pharmaceutical companies.

A video of Dr. Mitsumoto's complete presentation may be viewed on the SPF website at https://sp-foundationorg.presencehost.net/what_we_do/annual-conference-recap.html.

This presentation summary was prepared by John Staehle, Synapse Senior Editor

PLS Research Updates

Sabrina Paganoni, M.D., Ph.D.

This important talk is the follow-up to Dr. Paganoni's talk at our national conference a year ago. In that talk, she outlined the four goals of her SPF-sponsored fellowship: improve our knowledge of PLS; discover PLS disease mechanisms; promote PLS clinical trials; and create a community of PLS researchers. Since last year, she has made important progress in the first two goals and this year's talk summarized that progress. To read the summary of her 2017 SPF Annual Conference presentation in the 2017 Fall *Synapse*, you can download the issue at the SPF website, https://sp-foundation-org.presencehost.net/news-resources/newsletter.html. This summary will only emphasize the new research findings.

Dr. Paganoni is also working on HSP as well as PLS. Her sophisticated MRI/PET imaging equipment can offer information on other types of upper motor neuron (UMN) disease. HSP and PLS are both upper motor neuron diseases, in the brain, that send a distorted message to the muscles by way of the spinal cord. Her estimates of the number of people in the US, with four UMN diseases, are: ALS 20,000; PLS 1000; HSP 10,000 to 20,000; and SMA (spinal muscular atrophy) 10,000. SMA represents the first example of successful treatment using gene-modifying therapy.

As part of her Virginia Freer-Sweeney Fellowship, granted by the SPF, she discussed NEALS, a consortium of 120 research organizations studying ALS. Previous PLS studies included only 10 to 50 PLS patients, whereas the current NEALS registry has 250 patients. Dr. Paganoni will publish her current research so we will have the opportunity to read the actual results ourselves. The retrospective registry includes research sites in 21 academic centers in three countries - Canada, the USA and Israel. Important natural history statistics have been recorded in the PLS registry. Males were 50.8% of the patients, the age of onset of symptoms averaged 53.1 years, and the age at diagnosis was 59.4 years (earlier than ALS). The average time from onset of symptoms to time of diagnosis was 6.3 years. She presented additional statistical information showing the wide range in the length of time from onset to diagnosis for individual patients.

There are two types of registries: retrospective and prospective. As stated above, a retrospective registry is based on patients' natural past histories, and a prospective registry is "from now on," and is populated with "new history" based on verifiable real time events along the progression timeline (usually from patients being part of a study group). Often, PLS is a "diagnosis of exclusion," one that is made after other possible diagnoses have been considered and ruled out. As expected, this type of diagnosis takes a longer time to make. The incidence of PLS symptoms is: spasticity/stiffness 90.4%; difficulty walking 88.4%; speech difficulty 55.2%; difficulty swallowing 38%; fatigue 32.4%; bladder urgency 29.8%; pain 24.8%; emotional liability 22.8%; depression 22.8%; and shortness of breath 20.8%. Regarding the degree of mobility at the time of diagnosis: 38% were independent, no devices needed; 38% needed partial assistance, such as a walker, cane, brace, splint, or crutches; and 24% needed a wheelchair or power scooter.

An important finding from her research on PLS patients using a specialized MRI+PET scanner, a new and unique combined diagnostic device at Massachusetts's General Hospital, is the discovery of areas of inflammation in the brains of PLS patients. The inflammation was found in the same area as the motor neurons, it was very reproducible and consistent, and the shape of the inflammation area was different between ALS and PLS. Thus, this test can differentiate and distinguish these two conditions, a great dilemma which often was resolved only by observing the patient for several years. She expects that this new test will shorten the time from the onset of symptoms to the time of diagnosis. Importantly, HSP patient's brains showed no inflammation, at least none so far in the three HSP patients already examined, two with SPG4 and one with SPG7. She needs to scan many more people, to discover and establish the presence or absence of inflammation in various upper motor neuron diseases, including subtypes of HSP.

[*Medical & Research Editor's Note: The following explanation is provided to assist the reader's understanding of the scanning procedure. The MRI scan shows "anatomy," that is, the shape and size of various structures and organs. The PET scan shows "activity," in other words, "what's going on." A good analogy is the weather map on TV. There are also two parts to that image. One is a view of the states, cities, rivers and boundaries (analogous to the MRI scan) and the other part of the image shows high- and low-*

pressure systems - "where's the storm?" (analogous to the PET scan). So, using both the MRI and PET at the same time on the same machine gives the same sort of comprehensive information as that TV weather map - what's going on and where it is. The "ordinary" tracer injections given in your x-ray/radiology department, with MRI and PET scans, are tried-and-true formulas that have been in use for a long time. In this research, a new chemical tracer is used, called PBR28, which specifically finds the inflammation in the brain. This chemical tracer lasts only a short time and must be prepared the same day as the scan.]

There was a long discussion and questions from the audience about having this combined scan done in Boston. She offered to create an "easy" appointment pathway; the scan itself takes 90 minutes, but participants should allow a half-day for the entire visit. The scan is for research, which means that there is no charge [except the person to be scanned must get to Boston at their own expense] and there is no report to your doctor, except for a comment about "general results," i.e. there is, or is not any sign of inflammation. There is a group of patients, about 10%, that have a certain blood type to which the tracer does not attach itself. So, there is no point in scanning those people. She will send a kit for taking the blood sample in your own community. After she receives the sample in the mail and tests it for blood type, she can tell you if you are OK for the scan. There is no need for a physician referral. Thus far, Dr. Paganoni has scanned 65 patients with ALS, 10 with PLS, and 3 with HSP and would like to scan at least 35 additional people during the next two years. She would scan ALS and PLS people more than once over time to study the progression. However, she would scan HSP patients only once. She also wishes to scan patients with other types of HSP.

There are the usual MRI rules and exclusions, regarding implanted metal, pacemakers, etc. Most newer Baclofen pumps have no problem with MRI scans, although such patients should see the pump specialist right after the scan since the pump may need to be reset. There is no sedation during the scan, although some patients have taken benzodiazepines, such as Xanax, Librium, and Valium, or the muscle relaxant Baclofen beforehand. If you are interested in participating in this study, contact Catherine Cebulla, ccebulla@partners.org, 617-643-6252.

Dr. Paganoni then discussed more technical information on the nature of inflammation response in the brain, compared with the rest of the body. In the brain, inflammation is dealt with by specialized cells called microglia and astrocytes, not present in the rest of the body. So, the usual anti-inflammatory drugs, like corticosteroids [prednisone] and NSAIDS, like Motrin, would not help brain inflammation as treatment. Wouldn't it be exciting if a drug that could reduce inflammation in the brain would help PLS? She promised to give us updated important research findings at our annual conference next year.

The video of Dr. Paganoni's complete presentation may be viewed on the SPF website at https://sp-foundationorg.presencehost.net/what_we_do/annual-conference-recap.html.

This presentation summary was prepared by Malin Dollinger, M.D., Synapse Medical & Research Editor.

Current Genetics Topics in HSP and Related Diseases and the Promise of 'Big Data'

Stephen Züchner, M.D., Ph.D., Department of Human Genetics, Hussman Institute for Human Genomics, University of Miami

Dr. Züchner was originally trained to be a neurologist, but for the last 15 years he has been a geneticist. He told the audience he was going to give them a genetic education and that some of the slides might be too technical. He also said he would try to explain those to keep everyone "entertained." Dr. Züchner opened his presentation with a quote by Francis Collins, Director, National Institutes of Health, "Except for some cases of trauma, it is fair to say that virtually every human illness has a hereditary component." He told everyone that "genetics is everywhere" and it has become a topic "of great public interest." Dr. Züchner is quite optimistic that something like genetic therapy will come sooner than most think. There are two sides of research that must come together. We must first be able to make a precise genetic diagnosis. This is important to those with HSP because there are so many genetic variations of HSP. The gene therapies developed will therefore have to be

Continued on next page

extremely specific. Most of his presentation will cover the progress being made to reach better diagnoses and at the end, he will touch on where gene therapies are going.

Dr. Züchner then presented several statistics about the human body. We all started as a single cell. That cell divided into 2, then 4, then 8 and so on until our body has about 40 trillion cells that work together. Each cell has a complete exact copy of the genome in the DNA molecule tucked away in its nucleus. The instructions to make a human body are coded in alphabetical letter combinations called bases. A human genome is three billion bases long. All life on Earth, as we know it, carries the same genetic alphabet. That is why biologists think we evolved from lower animals to what we are today. The Government made the decision to initiate a project to sequence the entire human DNA, all 3 billion bases. [*In 1990, National Institutes of Health and the Department of Energy published a plan for the first five years of an expected 15-year project. The project would develop technology for analyzing DNA; map and sequence human and other genomes; and study related ethical, legal, and social issues. In 2003, the Human Genome Project's ambitious goals had all been met or surpassed.*][1]

Subsequently, studies were done on specific diseases, like Type 1 diabetes, to identify the genes in the DNA that increase the chance of getting the disease. They found there are a few genes that carry the highest risks of Type 1 diabetes. There were also many other genes that carry much smaller risks, many with risks near one. All the known risks together only describe about 15% total risk. [*According to the American Diabetes Association, 1.25 million Americans have Type 1 diabetes.*][2] HSP is a rare disease with about 20,000 cases in the United States. The top 3 HSP genes make up more than half the known HSP cases. The HSP genes that are being identified today are very rare and each explains only a "handful" of families. There are still about 30% of cases that cannot be explained by a gene. Geneticists light-heartedly refer to these unknowns as the "dark matter of genetics."

Today the next-generation sequencing industry is very competitive and extremely innovative. In 2001, the cost to sequence one human genome was $100 million; by 2018, the cost was about $1,000. This makes sequencing a large number of people everywhere in the world more affordable. So now there are more and more sequences available to analyze. In one study comparing the exomes of more than 60,700 "healthy" people, they found millions of genetic variations. Most of these variations were seen just once. The second most common variations were seen in only 2 to 10 people. Ninety-nine percent of the variations between people were rare, in other words, they were only seen a few times.

Dr. Züchner presented a number of slides describing the variations discovered in specific diseases and the overlap with those diseases have with each other. Analyzing the large number of whole genomes in multiple databases that don't talk to each other has been a problem for geneticists. There was a need to develop software help researchers scan the different databases. Since 2011, GENESIS was developed as a genomes management platform. It is a free, web-based exome/genome pipeline and matchmaking tool. It is user-controlled sharing data between individuals, consortia and ad hoc collaborators. With GENESIS researchers have access to the largest and most collaborative data repository for HSP. It includes data from 436 whole genome sequences, 5,770 whole exome sequences and 777 targeted panels from 6,026 affected and 913 unaffected patients, and 44 where the diagnosis was unclear.

To maintain the pace of progress, there is a need to further aggregate data from many sources to work/collaborate with scientists in many parts of the world, to fund data platforms like GENESIS and to fund data analysis. Dr. Züchner said, for some reason, nobody wants to fund data analysis. We live in a data-driven world but the role of data in medicine is not yet acknowledged.

A video of Dr. Züchner's complete presentation may be viewed on the SPF website at https://sp-foundationorg.presencehost.net/what_we_do/annual-conference-recap.html.

This presentation summary was prepared by John Staehle, Synapse Senior Editor.

Additional Sources:

1. Genome: Unlocking Life's Code, "A Brief History," https://unlockinglifescode.org/timeline
2. Healthline: "Diabetes: Facts, Statistics, and You", https://www.healthline.com/health/diabetes/facts-statistics-infographic#1

A Letter from Your Handicap Scooter

That's me on the left with my twin brother.

Dear Malin,

I go with you wherever you go. When I can't, my twin brother is my temporary substitute. I know you depend on me, as I depend on you. It's as if we are cut from the same cloth, or the same machinery, or the same spirit. I know your dependence, your hesitancy and your foibles, but with a nightly charge, I am up and raring to go. From time to time you have a friend take me apart to diagnose my acute illnesses. This sudden need for interim minor or major surgery is part of my normal life, similar to your own needs. All I need is to regularly have my umbilical cord inserted temporarily. You call it a charger, but I call it my lifeline.

I enjoy being with you and I accompany you everywhere you go. My gratification is having you sit on me while you go through your day. However, I do frequently take breaks, either while you sleep (I wait by your bedside for your awakening), while you use the toilet or shower (I'm too big and/or fragile to be under you then), or while you drive (then I sit behind you, watching you drive, while I patiently wait for you to sit on me again).

My life with you will be long, I hope, for I know I am the latest in a succession of dedicated scooters, who having done their life work, which is also your life work, have been gently retired and allowed to "rust in peace." I know and am grateful for my special role as part of your own body, so to speak, and I appreciate your concern and hesitation about any other person touching me, handling me, or regarding me as merely metal and fabric parts. I am more than that, a living part of you, and I am blessed, as you are, by our association of mutual dependence and assistance, as well as life-long respect. My batteries are your batteries as well. Thank you for your caring and your devotion to me.

Sincerely,
Your #1 Handicap Scooter

RECUMBENT TRIKE IS FREEDOM FROM HSP!

By Mary B. Schultz, HSP, SPG7

My husband Rob gave me the best gift ever for our anniversary. Rob's gift was a recumbent trike (for riding outdoors), a bike rack, and a hitch for my car. My trike is a Catrike Villager. I can load it on the platform-style bike rack myself, without help, and can take off for a trike ride without waiting for anyone's assistance. It makes me feel independent. I have now ridden several times, and for the first time since I was diagnosed in 2012, I feel free of HSP when riding my recumbent trike!

Jim Brewi wrote an article that appeared in the Spring 2018 *Synapse* about his recumbent trike, a Terra Trike Rambler. At the time, I had no recumbent trike of my own, and had no desire for such a trike. Unfortunately for me, I did not devote much attention to Jim Brewi's article. But now, all I can say is "DITTO!" Like the description of the Black Pearl as more than a ship in "Pirates of the Caribbean", my recumbent trike represents FREEDOM, freedom from HSP!

For more information on the Catrike Villager, go to https://www.catrike.com/villager.

Mary Schultz was diagnosed with HSP in 2012, and through genetic testing has learned that her gene mutation is in SPG7. Mary has been a member of SPF since 2012. Mary lives in Missouri with her husband (of 32 Years) Rob.




SPFoundation's
Annual Conference
Sponsors
Kris Brocchini
INVITAE
permobil
SAOL
BEMER
SPF
SPASTIC PARAPLEGIA FOUNDATION, INC.
Research / Education / Support
HEREDITARY SPASTIC PARAPLEGIA
PRIMARY LATERAL SCLEROSIS
SP-Foundation.org





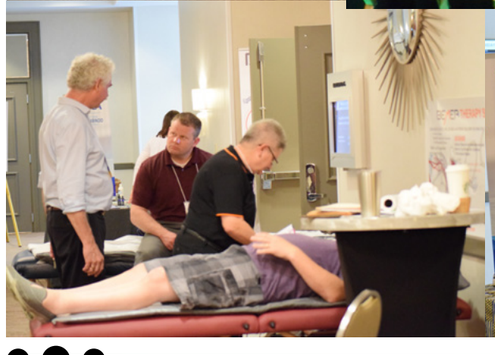



SPF
SPASTIC PARAPLEGIA FOUNDATION, INC.
Research / Education / Support
HEREDITARY SPASTIC PARAPLEGIA
PRIMARY LATERAL SCLEROSIS
SP-Foundation.org

SPFoundation's
Annual Conference
Sponsors
Kris Brocchini
INVITAE
permobil
SAOL
BEMER
SPF
SPASTIC PARAPLEGIA FOUNDATION, INC.
Research / Education / Support
HEREDITARY SPASTIC PARAPLEGIA
PRIMARY LATERAL SCLEROSIS
SP-Foundation.org

SPF
SPASTIC PARAPLEGIA FOUNDATION, INC.
Research / Education / Sup
HEREDITARY SPASTIC PARAPLE
PRIMARY LATERAL SCLEROSI
SP-Foundation.org





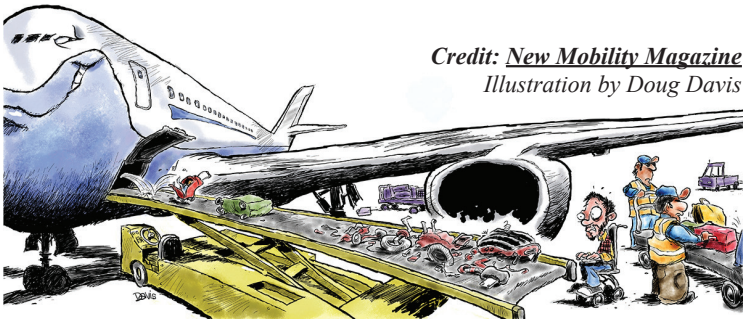
ULTRA
FULL SPECTRUM
ENDOCANNABINOID
SYSTEM SUPPORT
www.zilis.com
zilis

SPF
SPASTIC PARAPLEGIA FOUNDATION, INC.
Research / Education / Support
HEREDITARY SPASTIC PARAPLEGIA
PRIMARY LATERAL SCLEROSIS
sp-foundation.org

SPF
SPASTIC PARAPLEGIA FOUNDATION, INC.
Research / Education / Support
HEREDITARY SPASTIC PARAPLEGIA
PRIMARY LATERAL SCLEROSIS
SP-Foundation.org

TRAVEL TURMOIL
A Compilation of Travel Woes

By Malin Dollinger, M.D., SPG4



Credit: New Mobility Magazine
Illustration by Doug Davis

A new recurring column about travel problems begins with this issue. Each issue will have a specific travel topic that I will introduce followed by related first-hand travel stories that you submit. Each story will describe a travel event with a disability-related problem and how it was solved or not solved. They can also describe a splendid good event or a solution to a particular travel difficulty. Topics will include air travel, hotel stays, rail and bus travel, driving trips, meals while traveling, airport security, and any travel situation where your disability created a problem or required a solution. Kindly submit a concise description/story about your own related experience to me at malind@cox.net. I will select the most relevant submissions and compile them into a Travel Turmoil article for each issue of *Synapse*. Because I want to include as many of different but related travel experiences in the space allocated in each issue, kindly submit a concise summary of your travel experiences, not to exceed 200 words. The stories in this first column are my own. They give you an idea of the kinds of problems and solutions to submit for future issues.

My Scooter Was MIA - I flew home to Los Angeles from Washington DC and United Airlines left my scooter at the airport in Washington DC. They did not tell me until we landed, and then they asked me for my measurements and weight so they could order a temporary scooter for me to use, but it wouldn't arrive until the next day. I had made no plans or arrangements to spend the night at LAX and without a scooter, I could not get to a hotel. As an alternative, I asked to use the "preferred" airline lounge. They said "no." I managed to get myself to the outside pickup area in a wheelchair where my driver managed to get me into my handicap van "by foot." Then on arrival at home, she brought my other scooter to the van. It took a couple of days to get my scooter back from the airline. My letters to the airline's VP were unanswered.

MIA Again! - On a different trip to San Francisco from Los Angeles via United Airlines, my scooter was missing on arrival. I had prearranged to have it brought to the airplane door. I stayed on the plane on purpose rather than follow the airline's request to go to the baggage area in a wheelchair. The airline is still responsible for me as long as I am on the plane. This is not true once I leave the plane. In the baggage area, all I can do is "wait and hope." Finally, the pilot came to me and asked if I needed help. I explained the situation, and he said, "Come with me; I'll get your scooter for you and I will not take off for Vegas till you have your scooter." The next thing I knew, two men in coat and tie promptly appeared with clipboards and spoke with the pilot. I had my scooter in 15 minutes. Then the pilot said to me, "Well, you've got your scooter, I need to leave, 'cause the plane is full and they're waiting." I wrote United a letter commending the pilot for his caring, kindness, and dedication to me.

My Scooter Went to Pieces - Then there was the time upon landing when another airline put my scooter into a tiny elevator and then couldn't get it out. So, they took it apart inside the elevator and I was greeted, sitting in an airport wheelchair, with a vast collection of scooter parts lying all over the airport floor. You need to know how to assemble and repair your scooter; always take the scooter manual with you.

My Scooter Got the Best Seat on the Plane - When you fly, where do you put your small scooter or wheelchair? Usually it goes into the baggage compartment; make sure they also put a *luggage tag* on it, which helps them find it if they lose it. This is in addition to the scooter tag with the size, weight, scratches, etc. Sometimes flight attendants will, if asked, place your folded wheelchair or very small scooter in their luggage locker in the cabin. Once there was no room for my small folded scooter in the cabin, so the pilot put it on the "jump seat" in the cockpit. In any case, ask the flight attendant to make sure your wheelchair or scooter is loaded before you take off.

The subject for the next issue is "Airline Travel" and I need your bad and good experiences, especially how you fixed a problem. Please send your summaries to me at malind@cox.net. Thank you in advance for helping me create an interesting and helpful series of articles about Travel Turmoil.

I Touched the Water!

By Tina L. Croghan, MO State Ambassador, SPF Board Member

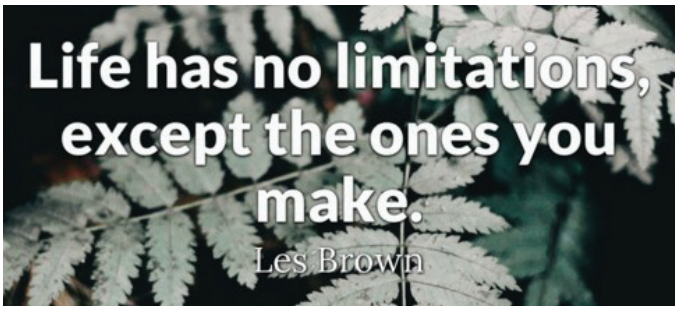
Over the summer, I was invited to spend a few days with close friends at their condo in Florida. My friends know of my limitations, and strive every day to make sure that there are no boundaries for me. Things that I would have just accepted as a "normal situation," they find unacceptable. So, before I arrived, they called or visited restaurants and stores, finding all of the ramps and bathrooms, making reservations and alerting them of my rollator or scooter usage.

My friends knew how important it was for me to "not make a big deal," but they wanted me to enjoy the beach with them, so they did a little Internet research and found http://www.rentabeachwheelchair.com.

I rented the manual wheelchair and had it delivered to the condo, and that afternoon we were off to the beach. After the sheer joy of rolling over the sand, sun on my face and wind in my hair, and finding way too many sea shells, my friends guided the beach wheelchair and me to the edge of the waves, "…just so I could see better." I said, "I just want to feel the ocean." I leaned over and touched the water with my hand and the next thing I realized, I had the waves splashing up and quickly covering my feet. I squealed with pure joy! How did they know? I didn't even know myself!

Creative people have figured out many solutions to help us overcome obstacles, it just took a little bit of internet research to find them and for me to enjoy the beach again.

You can do it, too!



SNAP OUT OF IT!

By Tina L. Croghan, MO State Ambassador, SPF Board Member

"Snap out of it!" Cher screams and slaps Nicholas Cage in the face in a most memorable moment in the 1987 movie, *Moonstruck.* I wish my depression could be cured so easily!

What we need to do first and foremost is accept that depression is not a choice or something that you can just snap out of or just get over. How many times have you heard…or even uttered yourself…I wish he/she would just suck it up, Buttercup!

After the recent celebrity suicides of Kate Spade and Anthony Bourdain, depression and mental illness was thrust into to the national spotlight. At the same time, I had a close friend's sister commit suicide, too. I knew this was as much of a crisis as the opioid crisis, but was going overlooked and shamed.

Perhaps we need to look at the types of depression. I recently talked with Dr. John K. Fink of the University of Michigan and medical advisor to the SPF about this subject. He was glad that I was shedding some light on it, but I soon realized that I was quickly over my head!

"Depression can be caused by several extenuating factors," Dr. Fink says. One factor could be a simple side effect from a drug. Another could be from a debilitating disease or from pain. Sometime a lack of good old sunshine or vitamin D could throw anyone into the "dumps."

Hello, HSP/PLSers, we check the boxes for all three!

It's time to get our head out the sand and be proactive. *Tell* someone how you feel. Start with yourself! Take a survey of yourself. Keep a log or journal just about this. How do I feel today? Do I have any pain? If so, where? Am I gloomy? Have I smiled today? When was the last time I got outside for a breath of fresh air or felt the sunshine on your face?

After you have analyzed your logbook and realized for yourself that you, too, may suffer from a slight case of depression, do something about it! There are many mood elevators out there, but if you are seeking an all-natural alternative, there are a number of "tricks" that you can do to pull yourself out of the "blues."

In the wintertime, my husband will just take me for a drive in the car so that I get some sunshine!

Continued on next page

The Olfactory Sense (sense of smell) can be quite strong. A certain aroma can trigger a desired response. I love the smell of coconut. I have a body lotion that I use when I feel "down" that reminds me of summer and the tropics. Perhaps the smell of doughnuts or who doesn't love the smell of bacon frying or chocolate!

Exercise is a great natural endorphin release. I don't mean running a marathon or lifting 250 pounds! Just a simple walk or roll to the corner and back will do. Sing in the shower. It's OK—no one is listening—or judging! Dress—everyday—put on clothes besides sweats. Girls, put on makeup and do your hair. You'd be surprised at how just doing these little things will elevate your mood.

Sometimes it's not enough and we must seek chemical help. If you are like the 16.2 million Americans, according to the National Institute of Mental Health, who have a more severe depression than simple moodiness, perhaps a phone call or visit to your doctor or professional is in order.

How do you know if your depression is "clinical?" Check for these symptoms:

- A persistent sad, anxious or empty mood
- Sleeping too little or too much
- Difficulty concentrating, remembering or making decisions
- Reduced appetite or weight loss or increased appetite and weight gain
- Fatigue or lack of energy
- Loss of interest or pleasure in activities that once brought pleasure
- Restlessness or irritability
- Persistent physical symptoms that do not respond to treatment, including headaches, chronic headaches, constipation or other digestive disorders
- Feeling guilty, hopeless or worthless
- Thoughts of death or suicide

If you have noticed one or more of these symptoms, please seek professional help from your doctor or specialist.

None of the recommendations I have suggested will guarantee you will not have depression. But by reducing anxiety, "... they can keep the inevitable bumps in the road from seeming like monolithic obstacles," says Barry J. Jacobs, a clinical psychologist and family therapist and author of the book, *Emotional Survival Guide for Caregivers*. http://www.emotionalsurvivalguide.com/about.htm

I wish I could just "snap out of it," sometimes! What I have come to realize is that depression comes with HSP just like leg cramps. If we were to treat depression like the disease it is and not try to hide it until it is too late and much more serious, I think we would all be better off.

It's Time to Talk about Frustration

By Lewis Sid Clark, Illinois Co-Ambassador

Ok, I am not a professional psychologist so what I am going to say is about me and what works for me – at times. Words that come to mind, but are not often talked about, that are side effects of neuromuscular diseases include frustration, depression, distress, downheartedness, and if it is a word "give-up-ness." In various degrees we all get frustrated. I get frustrated when I cannot do the things I want to do: things I used to do, things I planned to do, things I see other people do. I can't travel, go to a downtown theater, sports, dance, or play with kids / grandkids like I want to. I get frustrated and, yes at times, down. You can wallow in that mood or move on to something positive. So, what is there to do?

Accept reality. It is not what we want but it is what it is. Do not be angry about it or blame yourself, parents, the environment, or the moon. HSP/PLS/SP are neuromuscular disorders. We are here and able to do a lot. We still have many things left to do and experiences to have. We need to play the hand we were dealt and live life.

What we have is a puzzle to solve. What do we need to carry on as normal a life as we can? Adaptive equipment? Maybe exercise to help certain muscle groups? Certain prescriptions for some of the unwanted side symptoms? Relaxation therapy of some kind? Faith in a supreme being? All these help and are needed.

Another thing is a positive mental attitude. It is not what we cannot do but what we can do that is

important. Follow the old saying: "be positive and count your blessings." We need to be here and now and appreciate what we do have. Think about what we can do and plan those activities. A positive open mind is open to solutions. Visualize positive outcomes.

Break down a frustration into easy victories. It can be true of any problem but to give an example take my desk. I have ideas I want to look at and start, projects started not yet finished, and projects done. However, to others they are just piles of paper, folders and junk. That frustrates me since I want a "clean" desk. So, if I just take one item and file it or throw it away, I will have one victory. If I break the whole mess into individual items and just do one at a time, I will get one victory for each. You cannot do everything at once; simply act and take one action. Do what you can and you will find the solutions to most problems, a step at a time.

It would be the same for any problem. Is there adaptive equipment that would help you do the things you want? Mobility problems? Get and use a rollator, wheel chair, power chair, or scooter. Shower problems? Get a shower bench, hand held shower attachment or offset hinges to widen bathroom door. Problem getting off the toilet? Have grab bars or a toilet riser seat installed. Problem with the car? Get a door cane or adaptive driving controls. Stuck in the house? Get your groceries delivered.

Want help paying for some of these? Look up Medicare or insurance requirements, they may help. Medical supply equipment is tax deductible depending on how you file. There may also be local volunteer organizations that will do medical improvements at no or little cost to you. Furthermore, there are state organizations to help low-income people with disabilities.

Want human contact? Phone your friends, volunteer to help phone for a cause that interests you. Consider fostering kittens or join Facebook. Whatever suits your fancy, there are many, many things that can help. By the way volunteering is good for both physical and mental health. Just take one-step and reach out. The frustration may start to melt away. Just do it. In addition, consider HSP/PLS connections – be around positive people and bond with other HSP/PLS/SPers. Talk to others. Share what works or does not work for you. Listen to ideas that may help you. Even be amazed.

These are some ideas. I am not saying just these suggestions will be the magic bullet to solve any and all your problems. They may help. Be patient with yourself, appreciate, and truly live each day. When needed, ask for help. You may need to stop trying to deal with these serious matters alone. You may need professional help. After all, **you're not alone** - believe me.

NEW MOBILITY: THE MAGAZINE FOR ACTIVE WHEELCHAIR USERS

www.newmobility.com

"New Mobility" encourages the integration of active-lifestyle wheelchair users into mainstream society, while simultaneously reflecting the vibrant world of disability-related arts, media, advocacy and philosophy. Our stories foster a sense of community and empower readers to:

- Participate in all areas of life, including education, work, love, sex, home ownership, parenting, sports, recreation, travel and entertainment;
- Be informed of and take charge of health concerns;
- Obtain appropriate technology; and
- Assert legal rights.

Please consider making a gift to the Spastic Paraplegia Foundation in your Will and Financial Plan.

Sharing Chronic Illness Challenges

By Mary Ann Inman

Photo by Cheryl Breunig

A few months ago, two responsible people walking by the laundromat in Clinton, WI, found me "kissing the parking lot pavement" and they called 911. After I fell, my husband Tom called my cell. I wasn't making sense. I don't remember any conversations or the faces of those who helped me, only bits and pieces of the blurred ride in an ambulance.

I am okay and feeling very lucky to have survived the head trauma with mostly external scrapes and bruises. I am grateful to my unknown helpers and EMT's! My family and friends know I was diagnosed at Mayo Clinic with a rare neurological illness which affects the way I walk and talk. Only about 500 people who live in the United States have Primary Lateral Sclerosis (PLS). The easiest way for me to explain it, is to call it *"slow moving"* ALS (Lou Gehrig's Disease). I hope to stay active. It is disabling but not fatal. Typically, people with PLS die from something else.

Thank goodness for the ice bucket challenge! It raised awareness about many upper and lower motor neuron diseases. During the summer of 2014, donors raised $115 million. It has been reintroduced annually. A third ALS gene was identified by the University of Massachusetts which has been linked to developmental therapy, drug therapy, and hopefully a cure.

I started to lose my balance and fall in 2008. When I was diagnosed in 2011, I went through denial, and continued to fade in and out of stages. My husband, friends, and family have been supportive. It has been a life-altering and humbling experience. I have had to adapt which is my point.

Let me share gold nuggets I have discovered during my journey. Warning, all are easier said than done.

- Good folks want to help, just ask them.
- Life gets easier when pride is set aside.
- Chronic illness is no-fault and no-blame.
- Acceptance opens doors and feels good.
- Talk about your talents, then limitations.
- Thoughtless remarks hurt, but move on.
- Disability awareness is improved today.
- Discover skills you didn't know existed.

Listen carefully to others that have been there, done that. One woman from my online support group turned a light bulb on for me when she said, "When I was diagnosed, I was devastated. Now, due to my progression, I would give anything to be back where I was then."

I have tried to overcome my obvious clumsiness by using humor. I say things like, "I am sure glad my mother didn't name me Grace." When a group was talking about volunteers for Clinton's upcoming Civil War reenactment, I commented, "I could fall down."

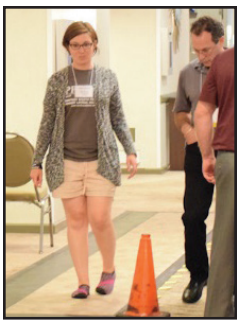
Now, I truly understand the depth of Stephen Hawking's comment about being trapped in his own body. He said ALS freed his mind, so he could fully concentrate on finding the secrets of the universe.

Since acceptance, I have reinvented myself. I set-up a non-profit, the Clinton Public Library Foundation, and serve as one of its co-presidents. I learned the art of grant writing, turned out to be a proficient photographer, continued to teach art on Wednesdays, continued to serve as president of Wisconsin Regional Artists Association with 500 members, created art, judged/coordinated art exhibits, and started to write. Each time, it felt good to contribute!

Walking Test May Assist in Therapies and Trials

By Greg Pruitt, SPF Co-Executive Director and Member of SPF Board of Directors

Dr. Mark Gudesblatt and the South Shore Neurologic Associates Research Team participated in the 2018 SPF annual conference held in Pittsburgh and introduced attendees to the Zeno Mat, developed by Protokinetics. The Zeno Mat is a digital mat which captures and records information such as velocity, base of support, double support and gait variability regarding one's walk. During the two-day conference, sixty-five attendees, both HSP and PLS patients, chose to participate in the team's research regarding the impact of the two diseases on walking at various stages of the disease.



Those who participated signed a consent form and provided basic information concerning their personal histories and progressions in dealing with their disease. Participants' walking would first be measured at their own comfortable, self-selected pace. Subsequently, participants would walk the same distance while being asked to count backward by threes. Following the walking tasks, participants were then asked to answer a questionnaire to gauge their perception of their fatigue and walking disabilities. Two goals of testing are to quantify 1) the relationship of patient perception of disability to actual disability and 2) walking impact to normal walking values. Information gathered through this process may be helpful in determining parameters in future clinical trials.

SPF thanks Dr. Gudesblatt and the team, Jared Srinivasen and Nina Giannuzzi, as well as Michael Rowling, Protokinetics CEO, for their assistance in measuring these walking issues for our Pittsburgh attendees.

Gene Therapy: Legal Issues (Extra Regulation will be relaxed.)

By Mary B. Schultz, HSP, SPG7

Gene therapies offer hope to people like us with HSP or PLS who are looking for a treatment or cure that would end our personal nightmare, or at least help future generations. Stem Cell Therapy in particular is now at the forefront of the scientific frontier. In the Winter 2018 issue of the *Synapse*, there was an article titled, "Gene Therapy-Our Latest Potential Treatment", by Malin Dollinger, M.D. and Jim Sheorn. In the Spring 2018 issue of the *Synapse*, there was an article titled, "Gene Therapy: New Developments and Ethical Implications" by Malin Dollinger, M.D. It is my hope in this article to put those issues relating to gene therapies that hold promise for HSP or PLS in the context of a legal framework. However, newly proposed regulations would streamline extra regulation and oversight of potential gene therapies, and render them like any other potential therapy.

As of this writing, there are 49 clinical trials of stem cell therapies alone. There are now two clinical trials for stem therapy targeted at ALS (Amyoptropohic Lateral Sclerosis). One of the ALS clinical trials is a "Phase III" clinical trial with a targeted enrollment of 200 ALS patients. A "Phase III" clinical trial is comprised of testing on patents to assess "efficacy, effectiveness and safety." Therapies that successfully pass a Phase III clinical trial will usually be approved for use in the general population. The success rate for Phase III clinical trials is about 25-30%.

Although we want to expedite therapeutic application of gene therapies, there is need for caution. The legal framework is supposed to balance the promise of rapidly advancing science with safety and ethics, but not interfere with progress. I defer to your own judgment as to whether the law has achieved the proper balance and has allowed for the promise of gene therapy without impeding medical progress.

An Overview of Gene Therapy

Gene therapy is still considered experimental. Therefore if you decide to undergo this experimental treatment, I recommend that you thoroughly research the provider and carefully review your "consent"/"authorization" documents. Unfortunately, patients are now "on their own" for securing safe and effective gene therapy, particularly stem cell therapy. Gene therapy involves introducing genetic material into a person's cells to fight or prevent disease. Please refer to the previous gene therapy articles by Malin Dollinger and Jim Sheorn in the Winter 2018 and the Spring 2018 issues of *Synapse* for a more comprehensive review of genetic medicine. [*If you do not have printed copies of these issues, they are available to download as a PDF file on the SPF website, https://sp-foundation-org.presencehost.net and select Synapse Newsletter. Ed.*]

There are several approaches to gene therapy being tested, but the gene therapy that appears suited for HSP or PLS involves replacement of a mutated gene that causes the disease with a healthy gene. Other types of gene therapies are discussed in the previously referenced article in the Winter 2018 *Synapse*, inactivating a "bad" gene or adding a new gene. Delivery of a healthy gene to a neuron would be by a vector (or "carrier"). Currently, the most common type of vectors are viruses that have been genetically altered to safely carry and deliver normal healthy DNA to target cells (in our cases neurons) so as to remove disease-causing genes and insert therapeutic or healthy genes.

Continued on next page

Who is Jesse Gelsinger?

Gene therapy was dramatically affected in 1999 by the death of 18-year old Jesse Gelsinger in a clinical trial of a gene therapy for a rare metabolic disorder of the liver that had been effectively controlled for Jesse Gelsinger with a specialized low protein diet and medication (32 pills a day). Jesse Gelsinger joined a clinical trial of a gene therapy to correct OTC (ornithine transcaromylase) deficiency. One September 13, 1999, Jesse Gelsinger was injected with a viral vector carrying a corrected gene and died four days later after having a massive immune response to the viral vector. Jesse Gelsinger was the first person identified as having died in a clinical trial for gene therapy.

After Jesse Gelsinger's death, all genetic research (not only genetic research at the University of Pennsylvania) ground to an abrupt halt. An investigation followed by the U.S. Food and Drug Administration, and two civil lawsuits were filed. The family sued in tort alleging a variety of legal theories to recover for Jesse Gelsinger's unexpected death. The government also filed a civil lawsuit alleging false claims had been made to secure approval for the clinical trial. Unfortunately, both lawsuits settled very quickly, and there is very little public information about either case.

Genetic research has slowly resumed; but very cautiously and slowly. There are now additional laws, regulations and oversight of gene therapy over and above the regulation of medical therapies in general. Very recently (as of this writing, just last week), new regulations have been proposed that would relax the additional requirements that have been applied only to gene therapy. The comment period for those proposed regulations commenced on August 16, 2018, and is to continue through October 16, 2018.

Gene Therapy Regulation

Genetic research and genetic medicine are governed by many laws and regulations that apply to all areas of clinical work, but in addition, extra laws and regulations that are unique to gene therapy also govern. Recently proposed regulations would relax the additional requirements that are unique to gene therapies and treat potential gene therapies just like any other potential medical procedure. The comment period for proposed new regulations commenced on August 16, 2018, and will continue through October 16, 2018.

The United States Department of Health and Human Services (HHS) oversees clinical trials. Two organizations within HHS have specific authority over clinical trials of gene therapy, the Office for Human Research Protections (OHRP) and the Food and Drug Administration (FDA). All investigators must comply with the regulations of these two organizations set forth in the Code of Federal Regulations (CFR). The OHRP requires that all research involving human subjects undergo Institutional Review Boards (IRB) review and approval. An IRB should evaluate research risk to subjects and must approve research protocols and informed consent documents prior to beginning a study.

Within the OHRP is the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. The Commission was created as a result of the National Research Act of 1974, and was charged with identifying ethical principles that should guide biomedical and behavioral research involving human subjects. In 1976, the Commission wrote the **Belmont Report**, which set forth ethical principles that the Commission concluded should govern biomedical and behavioral research involving human subjects and set forth guidelines for adhering to those ethical principles.

The National Institutes of Health (NIH) now oversees the conduct of federally funded clinical trials through a series of guidelines that add additional requirements to those specified in the CFR (Code of Federal Regulations). The NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines) detail safety practices and containment procedures for basic and clinical research involving recombinant or synthetic nucleic acid molecules, including the creation and use of organisms and viruses containing recombinant or synthetic nucleic acid molecules. An electronic (.pdf) copy of the NIH Guidelines may be found at https://osp.od.nih.gov/wp-content/uploads/2013/06/NIH-Guidelines.pdf .You may also review current NIH Guidelines and HGT (Human Gene Transfer) protocols at NIHGuidelines@od.nih.gov and HGTprotocals@mail.nih.gov.

FDA and the Center for Biologics Evaluation and Research (CBER)

The Center for Biologics Evaluation and Research (CBER) (within the FDA) is responsible for assuring

the safety, purity, potency, and effectiveness of biologics and related products (which encompasses gene therapies). CBER regulations for clinical trials involving human subjects are set forth in 21 CFR 50.

NIH Office of Science Policy (OSP)

The NIH Office of Science Policy (OSP) advises the NIH on biomedical research policy, including gene therapy and protection of human subjects. One of the five divisions of the OSP is called the "Clinical and Healthcare Research Policy" (CHRP) Division. It recommends NIH policy relating to clinical trials and works with the Patient-Centered Outcomes Research Institute (PCORI), a government-sponsored non-governmental institute established by the 2010 Patient Protection and Affordable Care Act, which influences what types of therapies will be covered by Medicare.

The NIH and RAC

The Recombinant DNA Advisory Committee (RAC) was formed in 1974 to advise the NIH on research relating to the manipulation of nucleic acids, in assessing gene therapy protocols and the review of safety information. RAC review and reporting requirements to the NIH for Human Gene Therapy protocols would be eliminated under the newly proposed regulations. The responsibilities of Institutional BioSafety Committees (local research oversight) would also be revised making their human gene therapy protocols consistent with other research, subject to NIH guidelines.

FDA and NIH: Proposed streamlining of regulation and oversight

The FDA and NIH are supporting trimmed down oversight of relevant clinical trials, specifically eliminating the duplication of oversight related to initial study protocols, annual reports, amendments, and serious adverse event reporting. Senior leaders in both organizations believe that there is no longer sufficient evidence to assert that the risks of gene therapy are entirely unique and unpredictable or that the field requires special oversight over and above the existing framework.

As gene therapies have become reality, the U.S. government is removing some special regulations that had been set up long ago over concerns of safety risks to human subjects. NIH's RAC would no longer be called upon to review all gene therapy applications. The FDA would review proposed gene therapies like any other types of medications. NIH's RAC would have a broader advisory role.

During the comment period from August 16 through October 16, 2018, the NIH will no longer accept new human gene transfer protocols for the protocol registration process under the NIH Guidelines, or convene the RAC to review individual human gene transfer protocols. The NIH Office of Science Policy will also not accept annual reports, safety reports, amendments or other documentation for any previously registered human gene transfer protocols under the NIH "Guidelines." It should also be noted that during this time, IBCs and Institutional Review Boards (IRBs) will not be required to submit documentation to the NIH assessing whether a particular protocol meets the criteria for RAC review.

Big Pharma

Gene therapy poses a threat to big pharmaceutical companies. Rather than waiting for what would appear to be an inevitable disruption in their market might by genomic medicine, many pharmaceutical companies are embracing gene therapy by acquiring assets and entering into collaboration agreements for gene therapies. Such acquisitions and collaboration agreements are beyond the limited scope of my expertise, and therefore beyond the scope of this article.

CRISPR/Cas 9

I do not intend to duplicate my discussion of the patent dispute arising from CRISPR/Cas 9 (**C**lustered **R**egularly **I**nterspaced **S**hort **P**alidromic **R**epeats), but refer you to my articles in the Spring 2016 and the Spring 2017 issues of *Synapse.* Those articles followed articles by Malin Dollinger, M.D. and presentations at the 2017 SPF Annual Conferences by Corey Braastad, Ph.D. CRISPR is possibly the most promising biotechnology of the last century. [*Above referenced past issues of Synapse are available for download on the SPF website. Ed.*]

Conclusion

The original fears of gene therapy have not been realized. The extra regulation and oversight of gene therapy in the interest of safety and protection of human subjects is not warranted. Gene therapy should, and probably will, be treated like any other proposed bio-technology. The way has been cleared for gene therapy to present an opportunity to improve human health.

Continued on next page

Tips for Commenting on Proposed Regulations Published in the Federal Register

The proposed federal regulations are at 83 FR 41082-41093 (12 pages). You may review and comment on the proposed regulations online at https://www.federalregister.gov/documents/2018/08/17/2018-17760/national-institutes-of-health-nih-office-of-science-policy-osp-recombinant-or-synthetic-nucleic-acid. Comments may also be sent via fax to 301-496-9839, or by mail to the Office of Science Policy, National Institutes of Health, 6705 Rockledge Drive, Suite 750, Bethesda, Maryland 20892-7985.

Comments would be accepted through October 16, 2018 at 11:59 pm EDT. Your comment(s) on the proposed regulation might affect federal action. Even a simple statement of support might influence federal action. More detailed comment(s), with scientific or even anecdotal support, is/are even more likely to impact regulatory decision-making.

Here are a few tips for comments:

- Identify the regulation (word or phrase) that you are commenting on, citing the federal register if possible.
- Read and understand the regulations. If you do not understand a term, provision, or regulation, call the NIH at 301-496-9838. You may also contact Jessica Tucker, Ph.D., Director of the Division of Biosafety, Biosecurity, and Emerging Biotechnology Policy, Office of Science Policy, NIH, at 301-451-4431 or Jessica.Tucker@nih.gov.
- Be concise. (Remember, your comment(s) is/are to PERSUADE!)
- Document your claims. Scientific evidence, or even personal stories (anecdotal evidence), may might support your comment(s).
- Address opposing views "head on".
- A single thoughtful comment might have greater impact than many form letters.
- Be aware of time differences. Comments will be accepted through October 16, 2018 at 11:59 EDT. If you are on the west coast, that time limit would be 9:59 pm. (I do not recommend waiting until the "last minute"; but "last minute" comments might be better than not commenting at all…)

Mary Schultz is a partner is the law firm of Schultz &Associates LLP, www.sl-lawyers.com , 640 Cepi Dr., Suite A; Chesterfield (St. Louis), Missouri 63005, (636) 537-4645. Mary B. Schultz graduated from Northwestern University Law School more than 30 years ago, in 1985, and has been practicing primarily in Missouri ever since. Mary B. Schultz is admitted to practice in Missouri and Illinois. Mary Schultz was diagnosed with HSP in 2012, and through genetic testing has learned that her gene mutation is in SPG7. Mary has been a member of SPF since 2012.

SYNAPSE APPEAL

Synapse costs lots of money to print and mail, and we need your help to keep it going. If you or a loved one enjoyed this issue and would like to support it, please use the enclosed response envelope to make a donation.

Every little bit helps.

SPFIllinois Connection

May 5, 2018

By Sid Clark, HSP, and Hank Chiuppi, PLS
Illinois Co-Ambassadors

Your doctor can (maybe) talk to you about HSP/PLS. You can dig into the literature to read up on living with HSP/PLS. None of this is as good as sharing with others who are living with HSP/PLS: the good, the bad, the hopes, the pain, the anxiety, the frustration, the dos and don'ts of living with these conditions. That is where sharing with others comes in, where a get together or connection comes in. SPFIllinois had our 17th connection over the last 7 years. We openly shared our experiences. Contact your state ambassador or others you know with HSP/PLS and meet. You will be glad you did.

Under the most beautiful skies we discussed many things, such as:

- Home delivery of groceries
- CReATe
- Rare disease research (www.rarediseasesnetwork.org/diseases)
- The Commend Study, a muscle cramp study (http://www.commendstudy.com).

Group Photo includes L to R: Steven Beutelspacher, Rich Fairbairn, Frank Madrigali, Paulette Chiuppi, Annie Sopala, Carol Clark, Sara Kramer, Greg & BJ Irwin, Heidi & Jenny Swanson, Hank Chiuppi., Inside the table Sid Clark, Ed Sopala, Phyllis Madrigali. Not shown is Lynn Staudacher.

- AnswerALS research that has many locations creating unique stem cell (iPSC) lines (http://answerals.org/)
- The why and how of genetic testing and genetic data privacy
- Finding information on drugs ref. NIH list (www.nlm.nih.gov/learn-about-drugs)
- In addition, thanking those who help us.

We discussed these plus more with many different subject sidebar discussions during our lunch. Over the years that we have met as a group, it is surprising how many different subjects we have covered. Not in a theoretical study mode but as we who live it experience it. As I have said many times, it is nice to "know we are not alone".

SPFIllinois Connection

July 28, 2018

By Sid Clark and Hank Chiuppi
Illinois Co-Ambassadors

The comments made for our spring May 5th connection are very true. It is nice to know "you are not alone." Moreover, sharing with each other is invaluable.

On a beautiful July 28 summer day, our 18th connection considered many topics:

1) We reviewed the presentations from the SPF annual conference. Thank you, SPF for putting them online. The presentations showed an extensive amount of knowledge we need and can use.

2) We discussed donating your body for research; there is a need for us to learn more.

3) We kicked around the frustrations of living with a neuromuscular disorder. The sentiment is we just want our lives back; a neuromuscular condition is just no fun. Unfortunately, it is what it is. Accepting reality and sharing with each other helps.

4) We considered SSI (Supplement Security Income) but it is beyond what we know.

Continued on next page

5) What HSP/PLS do we have and what difference does it make? Some HSPers really have PLS and some PLSers have HSP.

6) We also tossed about the need for a definite measure of the HPS/PLS condition and its progression.

7) Will our kids develop HSP/PLS? There is no easy answer. PLS is thought not to be inherited. HSP recessive genes may not passed on but with HSP dominate genes, there a chance.

8) We discussed toe and foot conditions.

No, we did not solve all these and other topics. The conclusions are as we understand them. In talking and sharing our thoughts, feelings and experiences we learn. If you have a connection near you – GO. If you do not, contact your state ambassador or organize one yourself. Let SPF know. You will be glad you did. Our next connection will be on Saturday, October 20, 2018.

Group photo includes L-R: Regina Potts, Sue Tenton, Frank Madrigali, Sara Kramer, Debbie Sexton, Carol Clark, Hank Chiuppi; inside the table L-R Phyllis Madrigali, Chris Sexton, and Sid Clark; Inserts Right Joan Morris, and left Paulette Chiuppi

Houston Connection

April 21, 2018

By Janet Woodham, SPF Ambassador, South Texas Region

On a beautiful temperate Saturday in April, SPF hosted its inaugural Houston patient connection.

We began with a 45-minute Feldenkrais group lesson that was given by Mary Beth Smith, director of the Feldenkrais Center of Houston. Wheelchair, sitting, or lying down, mattered not. Everyone could benefit from this thoughtful, guided, gentle movement practice.

Following the lesson, lunch was provided. Group discussion then ensued with the camaraderie that is only found when sharing a rare condition. Frank Zendejas of the Grief Recovery Institute chimed in when asked questions. He was found to be very helpful in quietly instigating discussion.

Personally, I have found relief in many of my SP symptoms using the Feldenkrais and ABM/ Neuromovement modalities. If you would like further information, please contact me at jdwoodham@comcast.net.

Austin Connection

August 25, 2018

By Marleen Doolen, Texas State Ambassador Central Region

The 2018 Austin Patient Connection was held Saturday, August 25, 2018 at a Texas Land and Cattle Restaurant, in Austin, Texas with eleven in attendance. Former attendees and new friends were made with sharing of experiences, information, and asking questions regarding Hereditary Spastic Paraplegia (HSP) and Primary Lateral Sclerosis (PLS).

St. Louis Connection

August 18, 2018

By Tina Croghan, Missouri State Ambassador, SPF Board Member

An SPF "Connection" event was planned in St. Louis on Saturday, August 18 at 11:30 a.m. at The Brass Rail restaurant, 4601 Hwy. K in O'Fallon. It was an opportunity for a casual get-together to share information, friendship, and support. Shown on the left in this picture are Jim and Rhonda Morley, SPF's newest members. Pictured in the center are Tim and Tina Croghan and their friend, Laura Holzen. Not able to attend were Mary B. Schultz and Pat Hansen. Our next gathering is still TBA. All are welcome to join!

How to Help

We operate out of the strength of our community, caring friends and sponsors. Your help makes a difference!

Please contact us at volunteer@sp-foundation.org to help in one of the areas below or to suggest another way you can get involved.

Support Research to Speed Our Cures by Volunteering

Below you'll find information on some of the ways you can help SP Foundation in their search for a cure to PLS and HSP.

Raise Funds: The primary focus of SPF is to raise funds to support research to find the causes, treatments and cures for Hereditary Spastic Paraplegia and Primary Lateral Sclerosis. Our major fundraising activity consists of a Team*W*alk. Individuals can help organize local fundraisers. People are also needed to secure corporate sponsorships and help with grant applications.

Patient Connection Programs: Organizing a Connections gathering for people to meet, share stories and help one another is a great service. Events can be as simple as meeting for coffee! In areas with large patient populations, SPF seeks to establish Chapters.

Conference Organizers: SPF's conference coordinator gladly welcomes planning and organizing assistance from SPF members living in or near the metropolitan areas selected for annual conferences. These events feature speakers and programs on special topics of interest to our community as well as provide the opportunities for individuals to meet others. Conferences can be half-day or full-day events.

Communications: Individuals with writing, research, website or graphic design skills are needed to assist with various communication initiatives.

Ambassadors: Ambassadors raise awareness about our disorders as well as enhance community building and industry relationships. You can assist with media relations, share your story, speak at local groups or help with grassroots advocacy.

Business and Administrative Support: Volunteers with business and administrative skills can play a valuable role in administering the work of the SPF. Most of the help is coordinated through email correspondence and uses popular Office applications.

SPF SPASTIC PARAPLEGIA FOUNDATION, INC.
Research / Education / Support

NON-PROFIT ORG.
U.S. POSTAGE
PAID
Permit No. 1001
San Antonio, TX

1605 Goularte Place
Fremont, CA 94539-7241

Support the SPF When You Search and Shop Online This Holiday Season!

See Page 3 inside this issue of *Synapse* for more information.

amazonsmile
You Shop. **Amazon Gives.**

AmazonSmile is a website operated by Amazon with the same products, prices, and shopping features as Amazon.com. The difference is that when you shop on AmazonSmile, the AmazonSmile Foundation will donate 0.5% of the purchase price of eligible products to the charitable organization of your choice.

goodsearch
simply do good

goodshop

We donate the lesser of $0.01 per search or 50% of the revenue earned from our partnership with Yahoo! *(i.e., revenue generated from sponsored search results displayed on Goodshop)* when our users select a cause.