

Record of Meeting of SP Group Leaders, Madrid, 1–2 June 2015

All presentations made at the meeting have been uploaded to, and can be accessed at the Euro-HSP website www.eurohsp.eu

Meeting Purpose:

To come together as the leaders of Spastic Paraplegia groups to leverage our separate efforts in the best interests of people with SP conditions everywhere.

Desired Outcomes:

- to build relationships
- to identify and deliberate on the most important issues of mutual interest
- to begin developing ways to work together, and
- to establish the basis for ongoing collaboration.

It is only SP support and advocacy groups whose primary mission is serving the interests of people with SP conditions.

Attendance:

Jean Benard (France), Dorthe Lykke, Charlotte Olesen (Denmark), Ian Bennett (UK), Fina Mateo, Marcos Guadalupe, Paco Rodriguez (Spain), Tommaso Amelio, Pasquale Masala, Marina Zapparoli (Italy), Peter van Aken, Hermien Rimmelink (Netherlands), Cornelia Ott, Martin Ott (Switzerland), Frank McKeown (Australia), Frank Davis (USA).

Meeting Facilitator Rob Camp. Guest Speaker Dr. Rebecca Schüle.

Apologies: Ingerid Ringheim (Norway), Peter Barrefors (Sweden).

Support groups represented from France, Denmark, the UK, Spain, Italy, the Netherlands, Switzerland, Australia and the USA.

Monday, 1 June 2015

Meeting Convenor, Frank McKeown, made some introductory remarks that included:

- as support groups, we are facing a different future from either our current or past situations
- this is causing us to reflect on our vision, our strategies, our priorities and how we allocate resources
- we can have a voice, and we both need and are expected to, with clinicians and researchers, with industry and regulators
- the logistics of staging definitive clinical trials are now broadly apparent, with the inescapable conclusion that our efforts need to be collaborative, combined and multinational to create the potential for there to be an approved treatment someday
- it was high time that we all got in the same room and shared information, thoughts, viewpoints and ideas
- there are important issues of mutual interest and relevance between all support groups on which clear thinking and good sense demands that we are aligned, and on which we work together.

Mission and Purpose of Support groups

France: Association Strumpell Lorrain <http://asso.orpha.net/ASL/index.htm> (1992)

- the group is 23 years old and has 600 families, which represents about 25% of the projected HSP population in France
- raise about €25,000 annually
- give around €20,000 annually to HSP research, mainly genetics and physiopathology studies

Denmark: Foreningen for ATAKSI / HSP www.sca-hsp.dk (2005)

- the group is about 10 years old
- the original goal was to fund research, but have not done so to this point
- not just HSP; the formal group includes Ataxia (except Friedreich's Ataxia)
- Have 200 members including about 80 with HSP. The projection is that there are about 400 with HSP in Denmark, so about 20% are members

Spain: Asociación Española de Paraparesia Espástica Familiar <http://aepef.org/> (2001)

- the group began with about 20 families with HSP 14 years ago
- now about 230 families
- part of a bigger neuromuscular organisation in Spain, ASM, with about 4000 people in Spain affected overall
- have produced a good manual on HSP that has been sent to all medical centres in Spain
- Dr Susi Sobrido has been an adviser to the group for a long time
- support Latin American countries, as they do not have their own support groups
- see two problems - 1. Money/funding 2. 50 genes, so a lot of people said to have HSP are not a good diagnostic fit
- trying to create reference centres for HSP
- €26,000 per year is spent on keeping a centre in Madrid with a social worker where the focus is on social and mental health support work
- there is a program to support children and adolescents working with the National organisation to try new treatments; there are 10 kids in this program at present
- there is a national gene study with public subsidies for people who need it to be tested
- a training course for 2-4 physiotherapists has been prepared and a manual will be one outcome of this program

Italy: Associazione Italiana Vivere la Paraparesi Spastica Onlus <http://www.vipsonlus.it/> (2010)

- hold a Congress on HSP awareness every two years; Congress in Milan and Rome with the theme of what is HSP and promotion of wellness/quality of life
- Psychological project : Quality of life and promotion of wellness in people with HSP
- began with 10 families with SPG11
- Nulvi in Sardinia has a special situation where there is a high prevalence of HSP through inbreeding; for example in one HSP family, 75/200 members are affected
- 180 families have now joined (how many individuals with HSP?)
- annual budget of €10.000
- estimate of 2,000 people in Italy with HSP
- there are two rare disease groups in Italy – Uniamo and MIR; they are associated with MIR
- Trying to get started a project with Yerko Ivanovic Barbeito, an acupuncturist with a special interest in HSP and ataxia. Meeting participants spoke of the benefits of his acupuncture, which he recommends before physiotherapy sessions. Continuous

treatment is needed with acupuncture/physiotherapy recommended every two weeks to help with quality of life.

- the website is www.vipsonlus.it

Netherlands: Spierziekten Nederland <https://www.spierziekten.nl/> (1967)

- HSP is part of an umbrella group representing 100 diseases that is run by members and was started in 1967
- it is a very big organisation with a national headquarters and 275 executives, who are all volunteers; there are also regional groups
- there are 320 HSP members, with an estimated 1700 with HSP in Holland (so about 20% of the population are members)
- there are plans for a best practice roadmap manual for management and treatment of HSP
- an e-learning program is available for when diagnosed, especially with respect to social services, issues relating to work etc; there are six modules and it is specific to Holland

Switzerland: Informal group (2007)

- the group is only for German-speaking Swiss; French-speaking Swiss go to the ASL and Italian speaking Swiss to the Italian group
- the group is informal, not being an association or foundation
- there is a geographic cluster of HSP in the centre of the country
- there are 42 members from 30 families

UK: The Hereditary Spastic Paraplegia Support Group <http://hspgroup.org/> (1990)

- the UK group was founded 25 years ago
- the primary mission is to support our members and that has not changed
- recently as surplus funds have accrued, there has been some funding of research
- there are 350 members with HSP whose information is contained in a good database that includes some medical/genetic information volunteered by members

USA: Spastic Paraplegia Foundation <http://sp-foundation.org/> (2002)

- SP stands for spastic paraplegias with coverage of both HSP and PLS (Primary Lateral Sclerosis)
- there are 12,000 members including a mix of people with HSP, donors, supporters etc
- this last year \$600,000 went to fund research, with \$800,000 the previous year
- there is a 12 person international Scientific Advisory Board to review applications for funding and make recommendations to the SPF Board, who make the final decisions
- a promising program, CReATe, has been initiated at the University of Miami including Stephan Züchner and his colleagues in the amount of \$1.2 million per year for five years to investigate the connections between ALS, CMT, HSP and about three other conditions

Australia: HSP Research Foundation <http://www.hspersunite.org.au/> (2005)

- called a Foundation, but legally a charitable association like many other support groups
- all-volunteer, e-based virtual organisation
- dual focus and function... facilitating and funding research; and information, education and support for the HSP community
- over 600 members with around half estimated to have HSP
- raise around \$80,000 annually (no membership fees), >95% of which goes directly to fund HSP research
- vision is to have effective treatments widely-available, affordable and used by people with HSP everywhere

- values include fairness, inclusion, collaboration, geography doesn't matter, professional, competent, businesslike
- core competencies - effective organisation and communication; strategic appreciation and strategy development; collaboration and partnership

Day 2 – Tuesday, 2 June 2015

Establishing effective treatments – patient registries and clinical trials.

Dr Rebecca Schüle, University of Tübingen, University of Miami

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Rebecca and her colleague, Prof. Ludger Schöls, hold an HSP clinic at the University in Germany two days/week and see 8 – 10 patients/week, with a waiting list of 2 to 6 weeks.

The work Rebecca is doing at Miami is mainly genetic, with some cell and animal models being used to investigate the association of different genes with HSP pathogenesis. The overall aim of the work is translational bridging between research and clinical therapies and treatments. The University in Germany is dedicated to translational research and works closely with the Hertie Institute where the focus is on basic brain research.

The following notes are associated with the presentation:

Clinical trial process

The clinical trial process for orphan drugs has recently been examined to make it more practical and feasible. It is regulated by special acts in the US (FDA) and Europe (EMA). Study designs are changing to cater for orphan drug/rare disease trials.

If biomarkers are used for outcome measurement in clinical trials on HSP, they may need to be measured longitudinally e.g. Matching cell impairment status with the level of symptoms over an extended period. A biomarker will be used for the upcoming SPG5 research that will be both cross-sectional (a number of measurements on different participants simultaneously) and longitudinal (measurements on the same participant over time). It is of the order of 2-4 years to obtain useful results from longitudinal data on HSP.

Rebecca explained that trials can be categorised in three ways. Those that target:

- symptom level e.g. Cholesterol impairment in SPG5
- gene level e.g. Ataluren for nonsense mutations, and
- pathway level e.g. Trialling a treatment that would be effective on all forms of HSP associated with axon degeneration.

In discussing the 'Valley of Death' for drug development, Rebecca commented that a lot of money is spent either side of the valley... on discovery in the early stages of research, often with government funding, and commonly pharmaceutical industry funding on the other end that is spent on commercialising treatments. Successful drug development is that which adequately manages the five areas of risk... scientific, funding, regulatory, intellectual property and market risk. Key stakeholder groups include scientists, regulators, clinicians, industry, patients and funding providers/sources.

Alliance proposal

Rebecca then introduced the Alliance idea and proposal and provided an overview of it. The HSP community globally owes much to the seminal work of neurologist Anita Harding whose paper published in 1983 brought the condition back to the attention of neurology professionals. There

are 10 members currently in the Alliance, a critical mass to get things started, with the option to add as needs and circumstances dictate later on. Olaf Reiss is an expert on the therapy structure for rare diseases. Stephan Züchner has a particular interest in mega-scale data sharing, organisation and analysis... both clinical and genetic. Hans Lochmüller is an adviser to the Alliance on trial-ready infrastructure, chair of the interdisciplinary committee of IRDiRC and chair of the NMD Foundation, whose excellent “Treat NMD” initiative is a good benchmark for HSP interests to adopt in the quest to present as a partner of choice for clinicians and industry.

Rebecca then discussed the ideas and proposal for a global HSP/PLS registry. Human Phenotype ontology developed by Peter Robinson will probably be used. One of the major challenges is developing a workable and compatible global unique identifier system (UID). Different algorithms exist and different global UID’s exist. In the NIH, the UID system “is a lost cause”. It is thought at this point that the one adopted by RD Connect will probably be used by the Alliance.

SPATAX originated as a genetic database with a focus on special HSP situations e.g. The Middle East, where a significant proportion of HSP is caused by inbreeding. One of the major challenges in establishing a global patient registry concerns datasharing. The ownership stakes tend to be high as often people have initiated and developed their databases for a significant part of their professional careers. Datasharing needs to be skilfully negotiated with consultation, trust, collaboration and the valuing of sharing all being required to create the potential for success.

For trial ready infrastructure, the Alliance organisation will have the following workgroups:

- clinical standards
- imaging
- biobank and biomarkers
- IT implementation
- regulations.

Role for Support Groups

There is a place for patient-entered data, especially in attracting motivated potential candidates for trials. The purpose of a patient-created registry is primarily to attract large numbers and can provide, as a minimum, contact information on individuals as well as basic permissions from them for use of the data provided. It could be that the one interface is used by all support groups globally through their separate websites, but with their own “shopfronts” and dominant language, so that it feels familiar to each community accessing it. There needs to be a joint project to develop a universal interface that will be at the heart of the global system. Possibly as a separate project, there needs to be an exploration of what it would take to harmonise the patient-entered database with the professional registry, and this would include, amongst other aspects, the need for verification and validation, and in many cases clinical/genetic data collection.

Support groups also have a role to play in attracting and consolidating joint funding to undertake the above initiatives.

Another appropriate role is the development of a professional interface... web presence and publicity... that makes the SPs attractive as a partner for clinicians, researchers, regulators and the pharmaceutical industry. As mentioned earlier, ‘Treat NMD’ would be a good benchmark for this undertaking.

Rebecca said that it may be desirable to work with Peru and Brazil as many North American-based clinical trials carry out phase I and II in South America. The Spanish AEPEF have relationships with Latin America through support provided to them over the years. There may be

potential to develop this relationship, with global support, given that early-stage HSP clinical trials may be held in South America.

People with SP conditions are often dissatisfied with the outcomes of their involvement in research... commonly complaining that they never get the results of their test and never hear anything about the results of the research. There is a potential role here for support groups to provide and be the interface with members of their community regarding the use of samples taken from them for research and updates/progress reports on the research in which they have been involved in the sampling/data collection phase. There is also a role for support groups in educating their communities about the nature of research studies and the separation of personal results from research data due to ethical considerations relating to privacy and anonymity. This role could extend to information about how personal results can be obtained from samples provided for research. These are all legitimate needs and concerns, but the use of researchers' time and resources on such communications with study volunteers cannot be justified.

Frank McKeown raised the issue of POs (patient organisations). The word "patient" reflects a traditional, legacy medical/research approach and perspective. It is the terminology that medical professionals use for support groups. It is what they call us, but there is no compulsion that this is what we should call ourselves, just the same as we need not call ourselves "sufferers". Support group is a good descriptor for our role, even as it is changing, because while the support might take a different form, it is support nonetheless. Instead of 'sufferers' or HSP 'patients', feel free to adopt the coined term 'HSPer' that is used in Australia, or create one of your own that fits your culture and context. We need to rename ourselves first, then try to influence other stakeholders such as researchers, clinicians, the pharmaceutical industry and rare disease groups such as Eurordis to get used to referring to us as 'support groups'. When it comes to clinical trials, patient registry is appropriate as it is an accurate descriptor in that context.

The group thanked Dr Schüle enthusiastically not just for the excellent and highly relevant presentation, but also for choosing to make the trip from the US specifically for this session.

Public Awareness: Potato Pants

Lori Renna Linton, High School Teacher, HSPer, Klosterneuburg, Austria
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As largely unknown rare conditions, name recognition, public awareness and political leverage of the SPs is low everywhere. An initiative in Austria in 2014, 'Potato Pants', may well represent an excellent unifying narrative for SP groups and people with SPs everywhere.

The session opened with a video <https://www.youtube.com/watch?v=56XdjtrpZlo> explaining where the idea and the term "potato pants" originated. Lori then introduced herself and Constanze and gave some background about the frustration they both felt seeing the endless stream of celebrities tipping ice buckets over their heads to publicise ALS. What could they do to get HSP in the spotlight?

The meeting then watched the 2nd video <https://www.youtube.com/watch?v=K8oQ8BnU-Vo> that recorded the experience of kids in the high school having fun racing each other around the school gymnasium while wearing 'potato pants'. It proved to be a powerful experience for all involved, a significant fundraiser for HSP research, and provided a visceral appreciation for the able-bodied students who gained some insight into what walking might be like for those with HSP.

There was a brief question and answer session with Lori, following which discussions were had about the potential for the central idea to become the universal symbol for HSP globally. People also came up with ideas for publicising HSP using potato pants in various ways. The outcomes of these discussions follow:

- Keep the English wording 'Potato Pants' for everyone.
- The following countries were in favour of adoption of the concept as the global symbol for HSP – US, Denmark, Netherlands, Italy, Switzerland, Spain, UK. Jean (France) was not attracted to the concept and will discuss it with his group.
- Apart from the idea of adoption of an international image and symbol for HSP, ideas for application that were mentioned include schools initiatives such as the one in the video; public events; celebrity figures wearing potato pants such as from TV, the arts and politicians; have a potato pants race on Rare Disease Day; initiate a “go to work in Potato Pants day”.
- Advice from a PR professional is that the central theme has all the ingredients to make a meaningful and sustainable symbol as it is a good, appealing story behind the name that can easily be related to by the general public who may never have heard of HSP. It demystifies HSP and makes it accessible, as in “having HSP is like walking around with your pants full of potatoes”. It was thought that the logo that was developed, with a focus on potatoes, may not work so well and perhaps should be revisited.
- Volunteers for a working group to take the concept forward are Ian Bennett, Frank Davis, Marina Zapparoli, Hermien Remmelink and Frank McKeown.
- Next steps include the working group determining how to get alternative designs to consider and come up with recommendations for support groups to adopt and simultaneously launch the concept globally. Frank McKeown undertook to document a proposal that will be circulated separately to members of the working group.

Moving Forward Together

- Setting priorities... what does each group see as the highest priorities of mutual interest.
- Collaboration... how best to work together.
- Next Steps... how and where to move forward from this point.

Setting Priorities – the leader from each group nominated what they believed to be the most important mutual priorities emerging from the meeting:

France

- form a formal international group of HSP support groups/patient + advocacy groups linked to the Alliance described by Dr Schüle
- this group would work in parallel to the clinician group of the Alliance

Denmark

- build a database of HSPers in Denmark

USA

- have an international patient registry; need to work out:
 1. How to begin?
 2. Partners and consultants?
 3. Costs
 4. Make a yes/no decision
- Implement the Potato Pants design contest

Italy

- develop the global database
- implement Potato Pants
- new priorities for funding??

Spain

1. encourage communication between the head of the clinical/genetic database in Spain, Dr. Sobrido, and Dr Schüle
2. direct research funding to develop an effective treatment for SPG4 HSP
3. incorporate Potato Pants activities into Rare Disease Day next February
4. Latin America is important but it is difficult to include at this point given available resources
5. Joint funding of Euro-HSP groups needs to be considered.

Question: Who is going to head global research for HSP under the Alliance?

Answer: No one. Things would work as they work now with researchers still applying to, and access funding grants, through their normal channels. They would then apply to a steering committee formed by the Alliance seeking access to suitably qualified participants for their clinical trials.

Netherlands

- database Alliance
- encouraging neurologists to contribute data to the Alliance

UK

- communicate information about the Alliance to our community
- contribute to database information – do what we can
- form an alliance between every SP support group in the world
- adopt a uniform sub logo; this needs coordinating (but I am not volunteering)

Switzerland

- we need to think globally and act locally
- we need to make our national group strong
- fostering the establishment of an HSP reference centre in Switzerland

Australia

- support the establishment of the global HSP registry under the Alliance
- benchmark 'Treat NMD' (and perhaps other groups) and create a single, global attractive proposition with whom clinicians, researchers, industry and other key stakeholders want to partner
- explore models and ways of doing joint funding
- develop a global support group interface that facilitates working together in general and on joint projects in particular
- Regular sharing of initiatives, activities and progress reports from each support group to all SP groups globally.

Collaboration – as this gathering of global leaders is new, a discussion was had about how best to collaborate, given that in many cases, working on joint projects will be in different locations and widely differing time zones. The special challenges that this presents need to be addressed. The following ideas emerged from discussions:

- Potato Pants is a low risk initiative to develop ways of working together. The self nominated working group is Ian Bennett, Frank Davies, Marina Zapparoli, Hermien Rimmelink and Frank McKeown

- hold international events sponsored by this group; do exchanges of people e.g. Potato Pants international e.g. Student exchanges to raise awareness and share knowledge about HSP. Question on how to fund this?
- the group needs a virtual office facility e.g. Skype, Dropbox, Google groups or similar technologies to enable working together non-simultaneously and non-co-located.

Next Steps – how to move forward from here? The following ideas were put forward:

- that the presentations made at the meeting be shared and available on the website of Euro-HSP (kindly offered by Dorthe and to be uploaded by Rob Camp)
- that the photos/videos taken at the meeting be shared and available. Pasquale to create an online album space and advise the group how and where photos and videos can be uploaded
- that a summary of the meeting be collated and distributed to participants, together with information about accessing presentations and videos. Frank McKeown to undertake
- that a schedule of meeting costs be distributed, including the relevant invoices and details for making a contribution towards costs. Frank McKeown to undertake.

Communiqué

(group photos were taken of both all meeting participants and separately of elected group leaders)

What messages would we like to send to ourselves as leaders of support groups after these two days of deliberations?

The sentiments expressed by people were of encouragement, optimism and challenge. Resolve to collaborate and be inclusive, not just between support groups, but to also foster collaboration and inclusion with other stakeholder groups such as clinicians and researchers was also generally shared.

Specific comments included:

- Fina: this is the beginning of an encouraging working period. We will need to work very hard. I am no longer VP of Euro-HSP but I will check the Euro HSP email address or you can send to my private Gmail address
- Peter: we should gauge our own national groups' reactions to what we are now thinking of doing as a result of this meeting and feed that information back to everyone here
- Jean: we need to ensure an international group that is ongoing. We also need to foster the collaboration with clinicians because this is a first... It has never happened before, and we need to maintain it

What messages do we want to send to our respective SP communities?

- our shared commitment to collaboration
- the rationale/reason/need for collaboration (if we remain national organisations without collaboration, there will never be enough people for proper clinical trials, and without that, no effective treatments can be developed)
- “it is the beginning of a very exciting future” Fina
- Frank Davis was asked what is the SPF motto? Something about “reason for hope”. Frank agreed to provide the motto
- the Alliance is a top team of quality world leaders in their field
- we are entering a new era; we must collaborate internationally to get what we all want.

The meeting closed at 4 PM.