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# EHDN *News*

EUROPEAN **HUNTINGTON'S DISEASE** NETWORK

***Red letter day – Venezuelan families are invited to meet the Pope – see story page 3***

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# Looking back on 2016

Jean-Marc Burgunder, Chair, EHDN Executive Committee

2016 was a year of consolidation where EHDN's leadership was concerned. There is now a clear separation between operational work and strategic leadership, as befits a large and growing network such as EHDN, and both the network's staff and its membership embraced the need for this shift in culture.

Channels of communication are now wide open within the network, and this is in no small part thanks to the language area coordinators (LanCos). They showed themselves ready to step into new roles whenever necessary, but especially in the context of the One Study Team initiative, which aims to identify the most efficient ways for EHDN and CHDI to collaborate in the running of clinical studies and trials. >>

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The transition of Registry to Enroll-HD progressed less smoothly, in 2016, but strategies have been implemented to re-invigorate the process, giving us reason to hope that it will be completed in 2017. In the meantime, we can take solace from the fact that EHDN sites that have undergone transition are as active as they were in Registry, if not more so.

2016 saw the emergence of a strong patient group which proved its readiness to advise industry partners who came enquiring about patients' needs and concerns relating to clinical trials. European companies involved in clinical research are also increasingly aware of the benefits of collaborating with EHDN, especially when it comes to site evaluation.

Last but not least, in 2016 EHDN played a central role in the preparation of the European Reference Network (ERN) in rare neurological disorders, an initiative of the European Commission. The success of the application owed much to our expertise and experience, and the ERN will in turn provide more visibility for HD at a European level.

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## HD Clinical Trial Site Certification scheme is up-and-running

Jenny Townhill and Tim McLean, Central Coordination

The HD Clinical Trial Site Certification scheme, an initiative of the HD Clinical Trials Task Force (HD-CTTF), has recently been opened to sites in the following regions: Australia, New Zealand, Europe, Scandinavia, Russia, South America and North America.

The aim of the scheme is to encourage sites to formally register their interest and capability to conduct HD clinical trials. The HD-CTTF will assess these clinical centres for their suitability as trial sites, and those that it certifies will become more visible to potential sponsors via the HD-CTTF's centralised clinical trial feasibility process. The HD-CTTF collaborates with CHDI, EHDN and the Huntington Study Group to review and endorse clinical trials, which may be offered to the certified sites.

As well as raising the profile of existing HD clinical trial sites, the scheme will increase the visibility of potential trial sites, while providing sites that have little trial experience with guidance and support in becoming trial-ready. The hope is that by creating a central repository of information about sites, it will reduce the administrative burden both for them and for sponsors during trial set-up.

Certification of a site involves assessment of its capability and performance according to a set of industry-agreed criteria that include general site information, clinical trial infrastructure, availability of an appropriate HD cohort, and staff training, education and experience. A prerequisite is that site information has been entered into the HD Global Site & Investigator Database (GSID-HD), but since this is already the case for most HD centres, that information should only need reviewing and updating at most.

All HD clinical research sites in the regions mentioned above are eligible to apply for the scheme by completing a simple questionnaire that is available along with instructions on the HD-CTTF website. Once submitted, applications are reviewed for completeness and for meeting the minimum criteria. Sites that do not meet these criteria will be advised of any deficiencies and will have an opportunity to re-apply once they have corrected them. Successful applicants receive a certificate and are added to the database. Certification is renewable annually upon submission of a streamlined re-application and updated GSID-HD entry.

*Please direct any queries about the application process to: hdsite@euro-hd.net*

*Brenda (right) is one of the lucky few who will go to the Vatican in May*

# HDdennomore

Laura Spinney

On 18 May 2017, Pope Francis will bless 16 members of South American families affected by HD, including patients, carers and at-risk individuals.

The unprecedented event marks the first time that any pope has mentioned HD, let alone met HD patients. Among those who will travel to Rome to receive the pontiff's blessing will be Brenda, a 15-year-old Argentinian girl from his native city of Buenos Aires who has Juvenile HD. Others hail from Colombia and Lake Maracaibo, Venezuela. The participation in research of families from the Lake Maracaibo region contributed to the isolation of the HD mutation in 1993.

*Brenda with dramatist Eugenio Zanetti and clinical geneticist Claudia Perandones*

On 6 January 2017, Epiphany, the 16 received large red envelopes containing an invitation to meet the Pope. The date is significant because for Hispanic Catholics, Epiphany is one of the most important festivals in the religious calendar. It marks the arrival in Bethlehem of the three kings bearing gifts.

Those behind the initiative, which is sponsored by Teva Pharmaceuticals among others, hope that it will draw attention to the difficult conditions in which South American families affected by HD live, but also that it will send a message to the wider Catholic community—some 1.2 billion people worldwide—that HD should be "HDdennomore".

*A website dedicated to this initiative has just been launched. Please visit HDdennomore.com for information.*

# Update: Clinical trials

Jenny Townhill and Tim McLean, Central Coordination

**LEGATO-HD:** Recruitment is ongoing into this Teva-sponsored, phase 2 safety and efficacy trial of laquinimod at sites in the Czech Republic, Germany, the Netherlands, Italy, Portugal, Spain, the UK, Russia and North America. The study was originally expected to finish recruiting in 2016, but the introduction of urgent safety measures led to screening being put on hold in January 2016, causing delays. Sites were re-activated upon receiving regional approvals of the amendment implementing the safety measures, and recruitment is progressing smoothly, the majority of sites having been re-activated. Recruitment is now expected to be completed in 2017. EHDN is assisting with participant identification and pre-screening by providing participating sites and referral centres with listings of potentially eligible participants derived from Enroll-HD. LEGATO-HD sites that wish to request a list of potential participants for pre-screening should contact Jenny Townhill: jenny@euro-hd.net

**Pride-HD and Open Pride:** Topline results from the Teva-sponsored, phase 2 study of pridopidine, Pride-HD, were presented at EHDN2016 in The Hague in September 2016, and summarised in the November 2016 edition of this newsletter. The full results are expected to be published in 2017. All those who completed Pride-HD were potentially eligible to take part in the open-label extension study, Open Pride, in which all participants receive pridopidine. Open Pride completed recruitment in September 2016 and treatment will continue for up to 24 months.

**Amaryllis:** This trial of a PDE10 inhibitor, sponsored by Pfizer, enrolled 271 individuals with HD at 46 sites in Germany, Poland, the UK and North America. Pfizer's preliminary analysis of the data, which revealed negative results on the primary (motor) and secondary (chorea, clinical global improvement and safety/tolerability) endpoints, were disclosed to investigators in December 2016. Analysis of exploratory endpoints, including quantitative motor, cognitive, behavioural, quality of life and imaging, is ongoing. The open-label extension, in which all the original study's participants were invited to take part, has been halted. Full analysis of the data is ongoing and the results are expected in the coming months.

Photo: ARTIFOX, Gabriele Stautner

**HD-DBS:** This investigator-initiated trial of pallidal deep brain stimulation for HD, which is sponsored by the University of Düsseldorf and which was described in depth in the July 2016 edition of this newsletter, is currently recruiting at six sites in Germany, a site in Switzerland and a site in Austria. Another site in France is in set-up. Twelve participants have been randomised to the study to date (the target is 50) and no safety issues have been reported. Sites wishing to identify potential participants from the Registry or Enroll-HD databases should contact Pauline Kleger: kleger@euro-hd.net

**IONIS:** Recruitment continues into this phase 1 trial of the antisense drug IONIS HTTRx, which is enrolling early manifest HD patients at a small number of sites in Canada, Germany and the UK. The focus is on safety and tolerability and there have been no issues reported to date. It is expected to run throughout 2017.

*For queries or feedback regarding these studies, please contact Jenny Townhill: jenny@euro-hd.net*

# Enroll-HD launches clinical training platform

Olivia Handley, EHDN Global Platform Manager

The Enroll-HD clinical training platform was released in January 2017 to approximately 1,000 users.

The e-learning system provides a central repository for training materials and resources, as well as a training log. It is available to all Enroll-HD sites, including Registry sites that will transition to Enroll-HD, but also to researchers and clinicians who are not involved in Enroll-HD.

A need for such a system was perceived because, while many studies and clinical trials use the same clinical rating scales and outcome measures, training requirements have not been standardised, meaning that investigators and their staff are often required to recertify for different training platforms as they become involved in new research projects. The Enroll-HD clinical training platform provides a "one-stop shop" where they can complete their training.

To date, the platform makes the Unified Huntington's Disease Rating Scale (UHDRS) Motor Certification 2017 module available to all approved users, while Enroll-HD site staff can use it to access the Barnett Good Clinical Practice modules. Plans are afoot to roll out other training modules, including behavioural, cognitive, functional and HD Clinical Characteristics.

Enroll-HD site staff (principal investigators, site coordinators, motor raters and others) may access the platform using the same login credentials they use for the electronic data capture (EDC) system, and the two systems share information, allowing them to synchronise automatically. The training platform imports a user's Enroll-HD site name and rater ID, for example, while the EDC imports their certification status.

The website is easy to navigate on both desktop and mobile devices, and the modules have been designed to walk the user through the various steps. Once a user has successfully completed a step, a certificate is emailed to them as a pdf, and an e-copy is stored in the "My Certificates" section of the website. Automatic email notifications remind them about new releases, upcoming or completed training, and expiration or renewal of training.

Our hope is that the platform—which is the product of close collaboration between EHDN, CHDI and the HSG—will enable faster, more cost-effective start-up of clinical studies and trials, improve the quality of training and hence the quality of data, and reduce frustration at Enroll-HD sites.

*Please visit https://hdtraining.enroll-hd.org/ or email websitesupport@enroll-hd.org for more information about the clinical training platform.*

In other news, Enroll-HD made its third periodic data set available to the public on 15 December 2016. Enroll-HD Plus PDS3, to give it its correct name, includes data from 8,714 participants, including 3,598 from Registry. It can be accessed at: www.enroll-hd.org/for-researchers/access-data/. Enroll-HD principal investigators who already have access to the EDC can login with their existing account details. To set up a new account, please contact: accountsetup@enroll-hd.org

## HDBuzz turns five

HDBuzz celebrated its fifth birthday in 2016. Launched in 2011 by HD researchers Jeff Carroll and Ed Wild, with the guidance of Emmy Award-winning journalist Charles Sabine, the plain-language HD research news website has grown exponentially to become the biggest provider of HD research news worldwide. Wild and Carroll now lead a team of 25 writers and over 100 volunteer translators to make their award-winning content available in 14 languages. HDBuzz gets about 150,000 article views per month and has tens of thousands of followers on social media. Since all HDBuzz content is freely syndicated via news feeds, any website can make use of it free of charge.

## #ILoveMyBrain

On 14 February 2017, Valentine's Day, the European Brain Council (EBC) launched the logo and hashtag #ILoveMyBrain as a communication channel to bring together all the work being done in Europe to promote brain health and reduce the prevalence of brain disorders. The EBC doesn't "own" the logo or hashtag and encourages others to use them far and wide, to promote any activity related to brain health. The organisation hopes that over the next few years the logo will become as recognisable as other symbols that have drawn attention and resources to specific diseases, such as the pink ribbon for breast cancer and the red ribbon for HIV. Spread the word!

## Funding opportunity

There's still time to apply for the Huntington's Disease Society of America Berman/Topper HD Career Development Fellowship, a three-year grant to provide support for young scientists to work collaboratively with their mentors and other committed HD health professionals to develop the fellow into an independent HD leader. The awards, of up to US$80,000 a year, are open to young scientists and clinicians from around the world, who are interested in a career in HD research or care. The deadline is 17 March 2017. More information and an application form can be found here.

Photo kindly provided by Marco Marcegaglia

## Introducing your intelligent friend, the sheep

At the EHDN2016 plenary meeting in The Hague, Jenny Morton of the University of Cambridge presented her pioneering work on a sheep model of HD. Among the attributes of sheep that mean they lend themselves easily to HD research, Morton explained, are their complex social behaviour, their willingness to follow their handler but also to be tested singly, and their ability to perform two-choice discrimination tasks designed for humans. Shaun the Sheep did much to improve the image of his species, but feeling that it continues to be misunderstood, the Cambridge group has been on the lookout for clean, funny sheep jokes that show them in a more positive light. We decided to launch a competition to help them. The winning entry was supplied by Jenny Townhill of Central Coordination, and her friends, whom we salute with a chorus of baaas:

A man finds himself sitting next to
a sheep at the movies.
"Are you a sheep?" the man asks.
"Yes," says the sheep.
"What are you doing at the movies?"
"I liked the book," replies the sheep.

# Three new seed grants awarded

A pathological hallmark of HD is the accumulation of mutant huntingtin (mHtt) protein into large aggregates, but intermediate Htt species that are formed prior to or in parallel with those aggregates have also been proposed as a source of neurotoxicity. In a project that EHDN approved for seed funding in 2016, Willianne Vonk of Utrecht University in the Netherlands and Steffen Sahl of the Max Planck Institute for Biophysical Chemistry in Göttingen, Germany, will study the pathogenic nature and cellular fate of these intermediate Htt species at different stages of HD pathology, using super-resolution optical nanoscopy. They will also investigate their potential modulation by molecular chaperones and protein clearance mechanisms, generating knowledge that could fuel the design of future disease-modifying therapies.

***Willianne Vonk***

***Claudio Alonso,***

Another project approved for seed funding in 2016, and led by developmental neurobiologist Claudio Alonso of the University of Sussex in the UK, will explore the role of small non-coding RNA (microRNA) regulation in a fruit fly model of HD. Studies in mice, monkeys and humans have indicated that microRNAs are differentially expressed in HD brains, but their contribution to the disease remains mysterious. Alonso's group believes that the fruit fly is the best model in which to explore the question, because the fly's genetics and neural development are well understood, and it is amenable to imaging.

The third project to be approved for a seed grant last year, which is led by Tom Massey of the Division of Psychological Medicine and Clinical Neurosciences at Cardiff University in the UK, will investigate DNA repair pathways that recent studies have suggested modify the age at onset of HD. It will do so by stratifying the Registry database by actual age at onset against predicted age at onset, and then using exome sequencing to identify DNA changes that alter the protein sequence in DNA repair enzymes.

***Tom Massey***

**Seed funds are intended to support pilot studies that will eventually kickstart larger projects. The next deadline for applications is 1 November 2017. More information about the programme and how to apply can be found here.**

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# EHDN working groups

Jean-Marc Burgunder, Chair, Executive Committee, and Michael Orth, Central Coordination

The new EHDN strategic plan, which the Executive Committee is currently finalising, will pay particular attention to the role of working groups (WGs) within the organisation. These were designed as a forum where members could exchange ideas and conceive projects to test those ideas scientifically, and we would like to take this opportunity to thank all those who have contributed to them to date. Their work has influenced not only how we think about the pathophysiology and phenotype of HD, but also how we measure the disease in the lab, and treat it in the clinic. Since many questions remain unanswered, we encourage the WGs to continue their good work. At the same time, in an effort to simplify and redynamise this core EHDN activity, we will be re-assessing their objectives in light of current knowledge. We also plan to set up task forces that will work on well-defined topics for well-defined periods of time.

*If you have any comments or suggestions with respect to the future role of the WGs, please contact Michael Orth: michael.orth@uni-ulm.de*

Photo kindly provided by Astri Arnesen

# Stronger together

## Profile of Astri Arnesen

**Norwegian Astri Arnesen was elected President of the European Huntington Association (EHA) at the EHDN plenary meeting in The Hague in September 2016. Her main priority for the next three years is a collaborative project between the two organisations called "Stronger Together".**

### *How did you become involved in the HD community?*

When I was 18 my mother was diagnosed with HD and I joined the Norwegian HD association. I drew a lot of support and comfort from that community, first during my mother's illness, and later when other members of my family became ill. My mother died in 2004, and my brother passed away almost two years ago. My sister is currently in a nursing home in an advanced stage of the disease.

### *You yourself don't carry the mutation?*

No, although I didn't know that until I was in my late 40s. I got tested in 2010, because if I did have it, I was approaching an age where I would likely start developing symptoms, and because one of my daughters needed to know. Taking the test was the most frightening thing I have done as an adult, because for me not knowing was a very active choice. It allowed me to hope, and that was my coping strategy. If it hadn't been for my children, I would probably still not know.

### *How did that knowledge change your life, if it did?*

When you get the right result, it's a big relief, of course. I had been living with the father of my children for 25 years, and by way of celebration he proposed to me. We got married and had a fantastic party, but my day-to-day life changed surprisingly little. I had never lived irresponsibly, before, but I had also never let the fact that I was at-risk limit me in any major way. I had children, took out a loan and engaged with the HD community. I was President of the Norwegian association long before getting tested. I suppose there was change, but over time. A few years later, for example, I was thinking about the future.

> *"It occurred to me that I had never made retirement plans before the test. You realise that you were more worried than you knew."*

### *Did your engagement with the HD community make you aware of ways in which life could be improved for people affected by the disease?*

Yes. When my mother finally received her diagnosis, that was helpful because it explained a great deal about her behaviour, but the doctors in Oslo didn't really

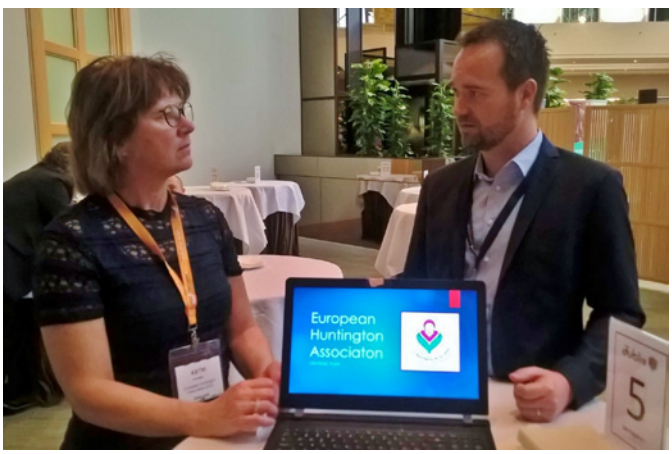


Photo kindly provided by Astri Arnesen

***At the Orphan Drug Conference, November 2016, presenting EHA's objectives to Gerro Struebbe of Novartis***


Photos: ARTIFOX, Gabriele Stautner

*At the EHDN plenary in The Hague, September 2016*

involve us, her family, so we turned to the association for support and information. A lot of HD families don't seek help, however, maybe because they feel ashamed or scared. The stigma attached to the disease is such that even today, when there is so much information out there about it, they can feel very isolated. It's a problem.

### *How do you see your role as President of the EHA?*

I want to improve the world for people affected by HD, but one organisation can't do that alone—not even EHA, which is an umbrella association for 43 national or regional associations—so my role has to be strategic. It's about collaborating with politicians and bureaucrats, about networking and creating partnerships to make the system work better for us as a community.

### *Is it a full-time job?*

Until last September all my HD-related activities were performed on a volunteer basis, and I worked full-time as a special needs educator and consultant here in Norway. Since September, I work full-time for the EHA, and that is possible thanks to CHDI, which is sponsoring the three-and-a-half-year "Stronger Together" campaign.

### *Tell us about "Stronger Together".*

It grew out of my experience as patient representative to the EHDN Executive Committee. Five years in that role have taught me that first Registry and now its successor study, Enroll-HD, are amazing resources, but there is more that we as patients and carers can contribute to them.

### *Such as?*

Slow recruitment often delays start-up in studies and clinical trials. When you analyse the reasons for that you find that a major contributing factor is a lack of information and motivation among HD families. People are aware of the sacrifices they make in terms of time and effort, to participate in such studies, but they often aren't aware of the fruits of that research. We want to improve communication, to help them see the bigger picture: even if it doesn't benefit them, it may benefit their children.

### What else do you hope to achieve?

We believe that our member organisations could help reduce trial drop-out rates by providing patients with "buddies" or partners to accompany them throughout the trial process. And we think that patients and their partners could help improve care at participating centres—which is currently very uneven—by supplying constructive feedback. Overall, the idea is that patients themselves become partners in the scientific process. They contribute more, but they also demand more in terms of information and care. Given that the membership of EHA—that is, of all its member organisations combined—is currently around 30,000, we could really make a difference.

Photo kindly provided by Astri Arnesen

***With former EHA President Bea de Schepper, President of the Danish HD association Charlotte Hold and Bernhard Landwehrmeyer***

### How can those reading this help?

We're still drawing up our action plan, but at this stage we welcome suggestions. For example, we're exploring practical ways that our members could provide feedback to the HD centres where they are enrolled. Could it be via an app? We'd also like feedback on two new sections that we've introduced to the EHA website: "Our Voice", where laypeople and professionals talk about their experiences of HD in videos; and "Ask the Doctor", where our resident HD expert, Alzbeta Mühlbäck, answers medical questions. Are these helpful? And what did you think about the two-minute "Call to Action" that we posted on the site, to mark Rare Disease Day on 28 February 2017? Tell us! We're stronger together...

*Astri can be contacted at: astri@eurohuntington.org*

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By Felix König https://commons.wikimedia.org/wiki/User:Felix_Koenig

## Dates for your diary

Save the dates for

- Brain Awareness Week—Outreach Event, Strasbourg, France, 16 March 2017
- CHDI's 12th HD Therapeutics Conference, St Julian's, Malta, 24–27 April 2017
- The Brain Forum, Lausanne, Switzerland, 29–30 May 2017
- 3rd Congress of the European Academy of Neurology, Amsterdam, the Netherlands, 24–27 June 2017
- European Huntington Association Conference, Sofia, Bulgaria, 22-24 September 2017
- Huntington Study Group Annual Meeting, Denver, Colorado, 1–4 November 2017
- EHDN2018 Plenary Meeting, Vienna, Austria, 14–16 September 2018 (details to follow)