NEWSLETTER

HUNTINGTONS QUEENSLAND

December 2012

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FROM THE PRESIDENT

Dear Friends

The festive season is now with us and it is worth noting some of the challenges we face for 2013 and beyond. Last month we received a letter from Queensland Health advising that they had applied an 'efficiency dividend' to our Association of 5% as from February 2013. This effectively means a 5% cut in the grant we receive from Queensland Health. However, this is offset by an indexed increase of 3.75%, but most of this will go on the increase in wage costs as granted to the Union in 2011 and spread out over five years. The grant from Queensland Health is to provide services for a three year term which expires 30 June 2013. Early next year we will commence work on applying for the grant for the following three years. We are also conducting a six month budget review to ensure we continue to operate as efficiently as possible.

The Sunnybank Community & Sports Club has been a very generous sponsor over the last few years and they have written to us advising that the State Government has also increased the gaming tax the Club must pay by $330,000 per annum. This will affect what Sunnybank Community & Sports Club can provide in their Community Grants Program.

This is happening at a time when the pressures and demands placed on those affected by HD and their families have never been greater. We are not alone in this challenging financial world as all not-for-profit organisations are facing similar issues. Though I am sure with the help of our sponsors, supporters and families we will meet and overcome the challenges that face us.

As Christmas is nearly with us I would like to wish you all a very merry Christmas and a prosperous and successful new year.

Gerry Doyle, President

Season's greetings from the Management Committee and Staff at Huntingtons Queensland

FROM THE EXECUTIVE OFFICER

I am pleased to say that my goal of meeting many of the Huntington's families has mostly been achieved and at the date of writing the only group I am yet to visit is the Sunshine Coast for their Christmas get together. It has been very special for me to meet with everyone and be able to put a face to the many names who cross my path during the days of my work. I am now nigh on three months in my role and a great learning curve it has been but I am becoming more conversant in our provision of advice, advocacy, information and referral. You have a wonderful team here at Huntingtons Queensland, all working for the same goals and aspirations and I am proud to be leading such a dedicated group of people.

As Gerry has mentioned in his article we have had our funding from Queensland Health cut. We are doing all we can to ensure this will have a minor impact on how we deliver our service. On the proviso that we do obtain recurrent funding in June 2013 we would not be expecting any increase to the amount we currently receive, meaning we will have less and want to do more. This will then require us to take a very close look at how we can further 'streamline' our services and how we can best manage our support to all. One of the areas which would help us to contain some costs would be for our Newsletter to be e-mailed to anyone who has an e-mail address and as such if you could please send an e-mail to admin@huntingtonsqld.com we can add you to our e-mail mailing list and save postage costs. Our membership contributions are an important part of our financial well being so if you haven't paid your 2012-2013 membership which was due 1 July 2012, we would appreciate your doing so as soon as you can.

Any fundraising ideas that you might have would be greatly received. Any people you know who would be able to join us to brainstorm some fundraising ideas again would be greatly appreciated. The higher the profile we can give HD the more hope we have of increasing our fundraising objectives.

Maybe a group of friends could hold a Huntington's High Tea as a fundraising venture. One has to remember that small amounts add up to large amounts. If we had twenty High Teas and raised $100 at each we now have $2,000 we did not have before. Merrilyn Brown raised $500 at our inaugural High Tea in September.

Maybe you know of someone who is in a sporting club, motor racing etc or any organisation that could conduct a fundraising event on our behalf. Maybe a group associated with your family or friends, or maybe you have a friend or associate who is a fundraising 'guru' who could bring some ideas to our table. I am sure there are a myriad of ideas if we could just tap into a few – so thinking caps on – PLEASE.

We had a surprise donation of $5,000 this month from Sullivan Nicolaides Pathology. This organisation no longer sends Christmas presents to their clients but instead consolidates those funds into Christmas charity donations. The staff of Sullivan Nicolaides nominate charities and then a committee determines the recipients. This year we were one of eight charities to receive funds. Ben Lundie spent some time here at our respite centre as a university placement student some years ago and was so impressed by the work we do that he nominated us as a recipient. Ben we thank you so very, very much.

Throughout the year we are always looking for volunteers for a number of projects. We need lawn mowing, gardening and hedges trimmed, drivers to assist with day respite transport and outings and as I mentioned earlier fundraising ventures arranged with assistance given by volunteers. So please call me for a chat should you be interested.

This year our staff are taking a well earned break over the holiday period during which time the office will be closed. Our last day in the office will be Friday 21st December 2012 and we will reopen on Monday 7th January 2013. If you have an emergency during this period would you please consult with your general practitioner or dial 000. There will be no facility to leave a message on our telephone system during this period.

I wish you all a happy, healthy and prosperous Christmas and New Year and I look forward to meeting with you all during the coming year.

Cheryl Miller, Executive Officer

FROM THE WELFARE DESK…

Hello families and friends

As the year is coming to an end, the Welfare Team is out and about catching up with family support groups and doing some regional trips. It's that time of year when we see an increased attendance at the events and from what we hear, families appreciated the opportunity to catch up with others. Some of the most commonly asked questions are about research, "What is currently going on? What is coming up? What are the goals of the research?" and most commonly, "How can I get involved?" We try to get as much information into our Newsletters about research as we can, with help from some great websites such as hdbuzz.net who 'translate the technical jargon' so that we non-scientifically inclined people can understand what's going on. This year we brought you the exciting news about the REACH2HD project and also regular news about the upcoming ENROLL-HD project.

Aside from these, there are still some other projects that continue today that need research participants. PREDICT-HD is a clinical research study that is looking to find 'predictors of HD onset'. The following information comes from the PREDICT-HD 2.0 brochure:

Why is PREDICT-HD 2.0 studying people at risk for HD?

- To determine the **earliest signs** of HD
- To find and validate **tests** clinicians can use when detecting early symptoms
- To **reduce** the number of volunteers needed to complete a clinical trial of drug treatment for HD.

Who can participate?

Men and women who:

- Are 18 years of age or older
- Are able to commit to yearly evaluations
- Have a companion who can attend visits or complete surveys by mail
- Are able to undergo an MRI scan
- Have tested **gene positive** or **gene negative** for the HD gene; specifically those at risk for HD who have been tested for the gene mutation but have not been diagnosed with HD (CAG≥36 for CAG-expanded group or CAG<36 for CAG-norm group)

Will my participation in PREDICT-HD prevent me from volunteering for clinical trials of possible new treatments?

No. There are several clinical trials for diagnosed and pre-manifest HD currently ongoing with others being planned. All participants enrolled in PREDICT-HD will be eligible to participate in other clinical trials.

What can I expect at a PREDICT-HD visit?

The PREDICT-HD study uses a variety of tests to help examine the nature and pattern of brain changes that occur in the period leading up to an HD diagnosis. Changes in thinking skills, emotional regulation, brain structure and brain function are measured through computer tasks, paper and pencil tests, motor examinations, survey questions, yearly blood samples and MRI scans.

How do I get more information about participating in the PREDICT-HD study?

Visit the website www.predict-hd.net or contact Dr Anita Goh who can answer any questions you may have:

Dr Anita Goh (Site Investigator) Email: goha@unimelb.edu.au or Phone: (03) 9816 0513

If you would like a copy of the PREDICT-HD 2.0 brochure or would like to know more about this or other research, feel free to give us a call or even better…..call Anita Goh.

Have a very merry Christmas and safe New Year.

Christine Fox (Senior Welfare Officer) along with Theressa Byrne and Fiona Kerr (Welfare Officers)

EHDN2012: On the shoulders of giants

(7th Plenary Meeting of the EHDN in Stockholm Sweden)

The following article has been reproduced from EHDN News (November 2012 – Issue 17) with kind permission from EHDN (European Huntington's Disease Network) and CHDI Foundation Inc. This article provides a good summary of the state of play in HD research – not as good as being there in person - but very informative nevertheless. Our thanks to the EHDN News Editor.

The 7th Plenary Meeting of the **European Huntington's Disease Network** (EHDN) took place in Stockholm, Sweden, from 14 to 16 September 2012, in conjunction with the 15th European Huntington's Disease Association (EHA) meeting, and drew 657 delegates from Europe, the Americas and beyond. The venue was Münchenbryggeriet, a former brewery on the island of Södermalm, across the water from Stockholm's City Hall. Anyone wandering out for a blast of autumn sunshine could therefore gaze upon the venue for the annual Nobel banquet before returning to the conference hall freshly inspired.

Welcome

Sven Pålhagen (Stockholm) of the local organising committee opened the meeting and introduced a man who clearly needs no introduction in Sweden. **David Lega** (Gothenburg), one-time Paralympian, businessman and politician, injected energy and optimism into the fledgling plenary, as he presented model number five of his own wheelchair design and adroitly manipulated a bottle of water with his mouth (if he always had to carry straws around with him, he said, he would be that little bit more disabled). Lega, who was born with paralysed arms and limited use of his legs due to a congenital condition called arthrogryposis multiplex congenita (AMC), talked about the importance of adapting to disability—choosing your battles, not being afraid to fail, and taking strength from a support network that continually boosts your self-esteem. He was lucky enough to have been born to young parents who hadn't yet learned defeatism, he said, and he grew up surrounded by "happy eyes". Of course, disability comes in many different forms, and Astri Arnesen, speaking for EHA President **Beatrice De Schepper** (Moerbeke-Waas), reminded delegates of the devastation that Huntington's disease (HD) can inflict on a family. Thus armed with a goal and hope, the conference got down to business.

Hot topics

Following a hallowed plenary tradition, the scientific part of the meeting opened with a round-up of hot topics. First **Michael Hayden** (Vancouver) reminded the meeting that as many as five per cent of the general population may carry an "intermediate allele" or "grey area" HD gene, with 27 to 35 CAG repeats. The offspring of these people are at risk of inheriting an expanded CAG tract, with repeats in the 36-39 range, meaning that they could develop the disease in old age. In the past, this group of carriers may not have lived long enough to reach diagnosis, but in an ageing population that scenario is becoming increasingly common. The prevalence of HD is going to have to be revised upward as a result, genetic counselling will have to be made available to a broader category of people, and clinicians will have to adapt to the fact that the disease presents differently in late-onset patients.

Cristina Sampaio (Princeton) advocated smaller, more flexible clinical trials that will produce results more quickly—"gazelles" as opposed to "mastodons". This means improving trial methodology, something her organisation, CHDI Foundation Inc., is investing a great deal of effort in. Assessing the risk-benefit ratio for a putative therapy is all-important, she said, and based on what is currently in the pipeline, the first treatments likely to come online will target the premanifest or manifest stages of the disease, not the earlier preclinical or presymptomatic phases. There is a

difference between the reality and the dream, of course, and in an ideal world, said **Alexandra Dürr** (Paris), care should begin as early as possible, and be multidisciplinary. That is at least a theoretical possibility, since many studies have now documented changes long before diagnosis, including metabolic—reflected in early weight loss—and brain structural changes.

New frontiers

What light can basic biological research shed on HD? This session was designed to present the disease in a broader scientific perspective in the hope of suggesting new research leads. **Hugo Aguilaniu** (Lyon) kicked off with the notion that targeting longevity genes could prove a fruitful therapeutic approach. The molecular mechanisms mediating the body's response to stress in the form of caloric restriction, for example, could potentially impact on the functioning of such genes and provide protection against age-related disease.

Włodzimierz Krzyżosiak (Poznań) raised the possibility that not only the protein product of the mutant huntingtin gene, but also its RNA transcript, could be toxic to cells. The critical experiments have not been done to test this, but if the RNA does turn out to be toxic, there are methods available for blocking it.

What does the normal huntingtin protein (Htt) do? This is the $64,000 question, and **Ray Truant**'s (Hamilton) answer was that it is probably involved in the cell's response to stress. He presented his "rusty hinge" hypothesis, according to which the protein's glutamine or CAG tract acts as a hinge, allowing it to fold. Expansion of that tract, combined with overphosphorylation of Htt, could cause the hinge to "rust" or become less flexible, impairing the protein's movement about the cell and, as a result, the cell's ability to respond to stress.

Elena Cattaneo (Milan) offered clues about the function of the huntingtin gene (*htt*) from its evolutionary history. This gene has been around in some form or other for 800 million years. Her experimental manipulations, which involve knocking it out in mouse embryonic stem cells and replacing it with its homologue from species belonging to different branches of the tree of life, suggest that one of its more ancient functions is to inhibit apoptosis, or programmed cell death. More recently, however, it may have acquired a role in regulating neural development. This function seems to be associated with the relatively youthful N-terminus of the protein, where the CAG tract lies. Cattaneo hypothesises, provocatively, that over the course of evolution, the expanding CAG tract may have acted as a driver of brain evolution.

Frédéric Saudou (Orsay) explained that Htt facilitates the transport of vesicles containing important chemicals through neurons. His work using microfluidic devices, which allow him to study different cellular compartments in isolation, suggests that Htt acts as a scaffold that recruits GAPDH to the vesicular surface. GAPDH is the all-important molecule that provides energy for vesicular transport, so this might explain why cell signalling is disrupted when mutant Htt (mHtt) fails to do its job properly.

Where next?

The biannual plenary is a chance to take stock and look to the future, and presenting EHDN's scientific strategy for 2011-2015 (http://www.euro-hd.net/html/disease/huntington/pubdocs/strategic-plan-full.pdf), **Juliana Bronzova** (Noordwijk) said that among the network's goals were improving the design of clinical trials so as to expedite them to useful

conclusions, stimulating scientific collaboration and refocusing the objectives of the network's working groups (WGs), of which 20 are currently active. To that end, two new committees have been created which along with the existing Scientific and Bioethics Advisory Committee (SBAC), will interact with the WGs and answer to the Executive Committee (EC). These are the Scientific Planning Committee, chaired by Gill Bates, and the Clinical Trials Task Force, chaired by Cristina Sampaio. EHDN has also instigated a medical writing support facility and, soon, a biostatistical support facility. Its new fellowship programme will be up-and-running by early 2013. The EHDN website will be revised to make it more visible.

Oliver Quarrell (Sheffield) gave an update on the work of the juvenile HD (JHD) WG. JHD, the onset of which occurs before the age of 20, accounts for five per cent of HD. It is associated with very large CAG repeat numbers—over 60 in about half of cases—and preliminary findings from magnetic resonance imaging (MRI) studies suggest that bigger expansions are associated with more rapid brain shrinkage, lending support to the idea that JHD has a shorter duration than adult-onset HD. If that is the case, Quarrell said, then the JHD population might be of interest to those designing clinical trials, because the effects of drugs might also be demonstrated more rapidly in this population. A new substudy of the European observational study REGISTRY is currently enrolling JHD patients in Europe, with 40 having been recruited to date.

Katia Youssov (Créteil), a member of the Advanced HD WG, described a version of the Unified Huntington's Disease Rating Scale (UHDRS) that has been adapted for advanced HD patients. The UHDRS-FAP was developed on the basis of a pilot study with 70 patients, and the group considers it superior to the UHDRS for this category of patient. It is more sensitive to remaining capacity, for example, while pushing back assessment of progression and floor effects to later in the disease.

Simon Brooks (Cardiff) explained that his group had found a "clear and beneficial" effect of exercise in the R6/1 mouse model of HD. This effect, which he thinks is cognitive rather than motor—affecting thinking speed—is reflected in reduced striatal atrophy in the mice. The optimal exercise dose has yet to be determined. However, **Monica Busse** (Cardiff) said that the evidence is now so clear that exercise is beneficial for HD patients, that the Physiotherapy WG, which she heads, is developing an evidence-based home exercise DVD for patients, called "Move Exercise".

Understanding the disease process

Gill Bates (London) described her group's attempts to find out how mHtt gets cleaved into pathogenic fragments in the cells. **Ellen Nollen** (Groningen) has identified genes in the worm *Caenorhabditis elegans* that prevent the harmful build-up of alpha-synuclein, the protein that accumulates in cells in Parkinson's disease (PD). Protein aggregation is a problem in both PD and HD, only in HD the protein in question is mHtt. One of the genes Nollen has identified, *tdo-2*, produces a protein whose human homologue, TDO, she thinks could be an interesting target for an HD drug. Interestingly, TDO is related to the enzyme KMO, which is already being investigated as a potential target. **Erich Wanker** (Berlin) described his group's attempts to map, systematically, all the cellular interactions of proteins known to be involved in potentially related neurodegenerative diseases, including Alzheimer's disease, PD and HD. And **Nicholas Perentos** (Cambridge) gave an update on progress in a new sheep model of HD. Due to its large brain, which is anatomically more similar to the human brain than that of a mouse, this could prove very valuable in studying HD-related brain changes, and in testing therapies that require some kind of special brain delivery, such as an injection.

Observing HD

Olivia Handley (London) described how REGISTRY and its sister study COHORT—which covers America, Australia and New Zealand—will be merged as of 2013 into a new study called ENROLL-HD. As ENROLL-HD's Global Project Manager, she told the conference that the new study already has three sites that are actively recruiting, and 37 participants, and

continues to roll out to new sites all over the world. Meanwhile, the number of participants in REGISTRY was announced to be tantalisingly close to the 10,000 landmark, at 9,982.

Sarah Tabrizi (London) gave an update on the major observational study TRACK-HD, which will now be succeeded by TRACK-ON. TRACK-HD completed 36 months in December 2011, and the as yet unpublished 36-month data show significant change on a range of motor, cognitive and brain imaging tasks in those premanifest HD gene carriers who were less than 10.8 years from their predicted onset at baseline (where onset is predicted on the basis of age and CAG repeat number). This means that, for the first time, it is possible to assess a premanifest individual using such tests, and accurately predict their onset.

Andrea Varrone (Stockholm) and **Rachel Scahill** (London) told delegates that the brain imaging techniques positron emission tomography (PET) and MRI had now proved their worth as robust and meaningful markers of disease progression. **Michael Orth** (Ulm) reported that changes in activity in the brain's default mode network—that circuit which is active when our brains are "idling", and which goes quiet when we execute a task—might be sensitive to disease progression, starting pre-diagnosis. He has conducted a small, cross-sectional study using functional MRI (fMRI), and finds that, in premanifest carriers, unlike in healthy controls, the network doesn't completely shut down during performance of a task. **Nellie Georgiou-Karistianis** (Clayton) reported that working memory tasks can be used to detect change in the relevant brain networks over 18 months, using fMRI in premanifest patients.

Julie Stout (Clayton) described her group's efforts to develop a brief, sensitive cognitive assessment test battery for clinical trials in early HD, based on what has worked in large observational studies like TRACK-HD. Those tests need to reflect growing understanding of HD pathophysiology and progression, and to be clinically meaningful and relevant to affected individuals' day-to-day functioning and quality of life, she said. **Anne-Catherine Bachoud-Lévi** (Créteil) said that there was room for new cognitive tests that were even more sensitive to disease progression than existing ones, and that could be administered more rapidly. Based on an ongoing pilot study that her group is conducting, she suggested that very simple tasks—ones involving picture-naming and basic arithmetic, for example—could be appropriate. Meanwhile, **Ellen 't Hart** (Leiden) has found cognitive and general functioning differences between the two motor subtypes of HD—choreatic and hypokinetic-rigid—with the former performing better on both.

Therapy: bright hopes

Fetal grafts continue to show therapeutic promise, **Patrik Brundin** (Grand Rapids) told the conference, but a less morally fraught alternative, induced pluripotent stem cells (iPSC), are causing much excitement—if not yet as a therapy, then as a valuable tool for understanding HD. These cells can be made from a person's skin cells, then reprogrammed to develop into a wide range of other cell types which can later be grafted back into the person—without risk, in theory at least, of immune rejection. In the case of HD gene carriers, iPSC will need to be genetically "corrected" before being grafted. But the uncorrected cells could also be of interest, as **Leslie Thompson** (Irvine) explained. The National Institute of Neurological Disorders and Stroke (NINDS)/CHDI stem cell consortium, which she heads, has generated iPSC lines from HD gene carriers and healthy controls, and shown that many cellular processes in uncorrected iPSC are affected by the HD mutation in a CAG repeat number-dependent manner. The cellular assay that appears to be most sensitive to the number of CAG repeats is the calcium signalling response to stress. This could potentially be used, therefore, in testing new HD drugs. **Lisa Ellerby** (Novato) presented a multicentre, collaborative effort to study HD using iPSC. Not only has her group shown that it is possible to correct the HD genotype, she said, but that correction is reflected in a corrected cellular phenotype. Levels of brain-derived neurotrophic factor (BDNF), which are low in HD cells, return to normal in the corrected ones, for example.

The next step for her group is to transplant the corrected cells into a mouse model of HD, to see if this corrects the phenotype at the level of the organism.

The other bright hope for future therapy is huntingtin-lowering drugs, aka gene silencing technology. Htt can be lowered in cells, either by blocking the DNA of the mutant *htt* gene, or by blocking its RNA transcript, and keynote speaker **Beverly Davidson** (Iowa City) and colleagues have focused on the latter. In HD mouse models treated with so-called RNA interference (RNAi) techniques, they have shown that the mice live longer, and show less neuronal damage and better neurological function than untreated controls. Moving a step closer to the clinic, they have now shown that the technique is safe in rhesus macaques, while reducing Htt levels by half. An alternative approach, based on antisense oligonucleotides (ASOs) has been shown by Donald Cleveland's group in San Diego to produce improvement in HD mice, when injected directly into the brain, and to spread further through the brain than RNAi-based drugs. The question remains, however, whether ASOs are able to reach the deep basal ganglia, which are affected early in HD. The first clinical trials of RNAi-based drugs are due to get underway in 2013.

The drug pipeline

Douglas Macdonald (Los Angeles) described seven different Htt-lowering technologies that CHDI is actively pursuing, some of which are close to clinical trial. These include DNA-based drugs that are injected into the spinal fluid, and RNA-based ones that are injected directly into the brain. **Andrea Caricasole** (Siena), presented Siena Biotech's drug Selisistat, which is being tested in the European PADDINGTON study. In theory, and in preclinical studies, Selisistat prevents mHtt from accumulating in cells by inhibiting the enzyme sirtuin 1. Sirtuin 1 removes the acetyl tags from mHtt, where the tags act as a signal to the cell to get rid of the harmful protein. **Chris Schmidt** (Groton) described an inhibitor of PDE10A that is currently being tested, in a collaboration between CHDI and his company, Pfizer, in mouse models of HD. PDE10A is a subtype of the phosphodiesterase PDE10, an enzyme that clears away signalling molecules from neurons once they have been received from nearby neurons via a synapse or chemical junction. Preventing it from doing so could increase the intensity of the signal and so, potentially, compensate for the impaired synaptic function in HD. A clinical trial will hopefully get underway next year. **Frank Gray** (Stevenage) is interested in a different phosphodiesterase, PDE4, which is also involved in signalling at synapses. In neurons grown *in vitro*, a PDE4 inhibitor made by his company, GlaxoSmithKline, produced improvements in functions related to learning. Gray thinks the inhibitor will potentially be useful for treating the cognitive symptoms of HD. **Josef Priller** (Berlin) described a trial called Action-HD which is designed to test the effects of the drug buproprion—marketed as Wellbutrin—on apathy in HD. Apathy, or lack of motivation and emotional blunting, is a major problem in HD. Action-HD began recruiting in May 2012 at four sites in Germany. Last but not least, **Julie Stout** presented Reach2HD, a phase 2 trial of the copper-reducing drug PBT2, produced by Australian company Prana Biotechnology.

Business meeting

There was plenty of network business to discuss, beginning with the approval of amendments to the constitution (http://www.euro-hd.net/html/network/project/constitution). Following the network's 2012 elections, **Bernhard Landwehrmeyer** (Ulm) and **Joaquim Ferreira** (Lisbon) were re-elected to the EC, while **David Craufurd** (Manchester), **Ralf Reilmann** (Münster) and **Sarah Tabrizi** (London) were elected to it for the first time. **Gill Bates** (London), **Pierre Krystkowiak** (Amiens) and **Sheila Simpson** (Aberdeen), rotating out, were thanked for their valuable contributions. **Bernhard Landwehrmeyer**, who was re-elected as committee chair, announced that, though he will stand for the full four years of his second term, he will only be available as chair for two. **Jean-Marc Burgunder** (Bern) replaces **Gill Bates** as co-chair. **Chris Frost** (London), **Flaviano Giorgini** (Leicester), **Andrea Nemeth** (Oxford), **Hugh Rickards** (Birmingham), **Jennifer Thompson** (Manchester) and **Patrick Weydt** (Ulm) were elected to the SBAC, replacing **Lesley Jones** (Cardiff), **Anne Rosser** (Cardiff), **David Craufurd** and **Ralf Reilmann**, who along with **Bernhard Landwehrmeyer**, were thanked warmly for their input.

Bernhard Landwehrmeyer announced that an iPad would be awarded to the site that recruited the 10,000th participant in REGISTRY, to be used in study-related activities. The winning site turned out to be Münster in Germany, the landmark being reached just a few days after the meeting, on 18 September.

Daniela Rae (Aberdeen) presented the guidelines that were published by the Standard of Care WG early in 2012. The result of the group's systematic documentation and appraisal of all the care models available in Europe, the guidelines are based on the principle of a multidisciplinary managed care network.

Matt Ellison (Coventry), who watched his father lose his battle with HD and founded the Huntington's Disease Youth Organization, HDYO (pronounced "HD-Yo"), in February 2012, made a plea for better access to the HD community and information for young people affected by the disease. HDYO already has a 70-strong team and over 1000 friends on Facebook, and is growing fast.

Charles Sabine (Gloucestershire), HD gene carrier and advocate, echoed Ellison's sentiments as he closed EHDN2012 with a moving reminder to delegates of the importance to affected families of their continuing efforts to understand and treat the disease. Little by little, he said, understanding was diluting fear, and each generation had less to fear than the last. In 2012, it was no longer possible for a doctor to tell a gene carrier, at the point of diagnosis, that his or her disease was incurable.

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Go to http://www.wheelieplanet.com/index.html for more information.

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Targeting oxidative stress in Huntington's Disease

This article is courtesy of hdbuzz.net

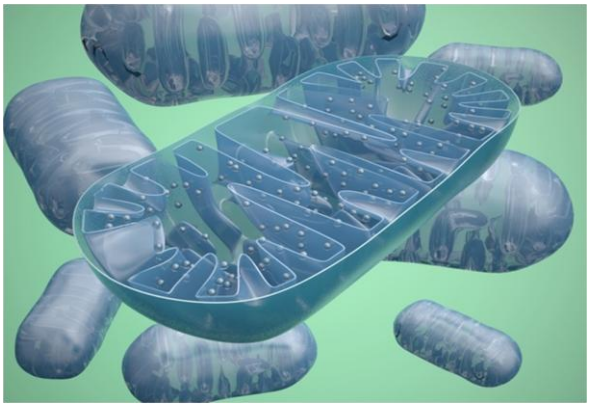
Damage to cells caused by oxidative stress is part of HD - could a new targeted drug help reduce this problem?

By Dr Jeff Carroll on December 03, 2012. Edited by Dr Ed Wild.

Some Huntington's disease researchers believe that drugs protecting against 'oxidative damage' could help HD patients. Existing drugs come with some problems, so a team of scientists have tested a new drug in a mouse model of HD, with encouraging early results.

Mitochondria and oxidative stress

All cells in the body require energy to work. We consume energy-containing food, and our bodies must convert those consumed chemicals into usable energy. This process of consuming food and making energy with it is known as 'metabolism'.



The 'mitochondria' serve as the powerhouse of cells, but produce a lot of stressful molecules in the process.

Cells from animals have an interesting way of making the majority of the energy they need to function. Tiny structures called **mitochondria**, which are like miniature cells inside our cells, produce the vast majority of energy used by each cell — chewing up fat and sugar and spitting out usable energy.

But there's no such thing as a free lunch. As a by-product of turning chemicals into usable energy, mitochondria also produce a stream of damaging, highly reactive, molecules. These molecules are called **reactive oxygen species**, or **ROS** for short, because they're composed of different types of oxygen and are highly reactive.

We are all familiar with the damaging power of oxygen molecules, in the form of rust. Rust is a product of reactive oxygen and iron, and — can destroy even mighty machines.

Many years of evidence suggest that excessive oxidative damage is occurring in cells and tissues from Huntington's disease patients. This has suggested to some scientists that reducing oxidative damage, using chemicals called **anti-oxidants** might be helpful in HD.

Problems with existing anti-oxidants

In fact, many Huntington's disease patients already participate in trials of molecules intended to protect against oxidative stress. A nutritional supplement called 'coenzyme-Q10' is thought to work, in part, by serving as an anti-oxidant molecule.

Many HD patients have taken coenzyme-Q10 as a supplement, either within or outside clinical trials. The CARE-HD study, which ran from 1997 to 2000, studied the effects of coenzyme-Q10 but did not show that it was beneficial. The 2CARE study, currently ongoing, is studying Coenzyme-Q10 in the largest ever HD trial — involving over 600 participants observed over 5 years.

There is some controversy amongst scientists at how much coenzyme-Q10 gets to the brain when it's taken in pill form. The brain is protected by a water-tight layer called the 'blood-brain-barrier', which blocks many drugs from entering the brain, potentially includingcoenzyme-Q10. Taking higher doses is one option, but that can cause increase the risk of unwanted side-effects.

'Designer' anti-oxidants

Rusty machines don't work as designed - cellular machines damaged by oxidative stress are also a problem.

Because coenzyme-Q10, and other drugs like it, have a hard time getting where they're needed, scientists have been working on developing new and improved versions of them. In 2005, the group of Valerian Kagan at the University of Pittsburgh described new and improved anti-oxidant molecules. The special feature of these drugs is that they included a chemical signal that tells the cell: "Take me to the mitochondria!"

When these drugs get into cells they are rushed directly to the mitochondria, thanks to this tag. Having the drug there is beneficial because mitochondria generate most of the reactive oxygen species in a cell — it's like building a fire station next to the fireworks factory!

XJB-5-131 in mice

Cynthia McMurray's research group, at Lawrence Berkeley National Laboratory, decided to test one of these new anti-oxidants called, **XJB-5-131,** in a mouse model of HD. They reasoned that this drug might help cells cope with the increased oxidative damage found in HD.

After first testing the drug in isolated brain cells, mice were injected with XJB-5-131 three times a week for over a year, to study the effect the drug had on symptoms that resemble human HD.

Like human Huntington's disease patients, the mice used in this study lose weight and have problems with coordination. Both of these symptoms were strikingly improved in mice being injected with XJB-5-131. HD mice and humans also accumulate damage to their DNA, thanks in part to oxidative stress. Giving mice XJB-5-131 reduced this DNA damage.

Given these beneficial results, the team turned to studying directly the effects of XJB-5-131 on mitochondria they had isolated from brains of mice. They found that XJB-5-131 had a number of beneficial effects on these little powerhouses, and proposed that this is why the drug seemed so beneficial when given to HD mice.

Future directions and reservations

These positive findings in mice provide early evidence that XJB-5-131 might be worth looking at in people with HD. But, as always, there are some hurdles and reservations that are worth understanding.

In this trial, XJB-5-131 was injected into the mice, rather than being taken in the food or water. Given that this drug needs to be used for many years, taking regular injections is probably not feasible. Would a pill would be a suitable way of getting this particular drug into the bloodstream?

As we said, one of the problems with anti-oxidant drugs is that it's not clear how much of them crosses from the bloodstream into the brain. It's certainly not clear how much XJB-5-131 reaches the brain. This will be an important thing to work out using mice before we think about using this drug, or related ones, in people.

Finally, scientists are taught always to question their assumptions. It's easy to think of oxidative stress as bad, which makes anti-oxidants good. But we've learned important things about oxidative stress, including the idea that it can sometimes be a good thing.

As an example, researchers have recently discovered that oxidative stress in muscle cells may actually help turn on many positive changes that occur after exercise. In fact, taking anti-oxidant vitamins blocked the beneficial effects of exercise in muscle tissue of human volunteers! As ever, biology has ways of surprising us with its complexity.

So, while this study of XJB-5-131 shows very compelling benefits to HD mice, mice aren't patients, and a lot of work remains before we can know for sure how the drug was beneficial, and translate these findings into people.

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Huntingtons Queensland
is a not-for-profit service organisation.
Established in 1976.

Our Mission is:

To provide professional support and advocacy for all persons affected by Huntington's Disease in Queensland.

Our Services Include:

- Providing individual and family support
- Facilitating the HD Day Respite Program
- Facilitating support group meetings
- Recreational activities for families with young children
- Organising respite holidays
- Providing information to families and health professionals
- Distributing a regular Newsletter
- Co-ordinating the annual HD Awareness activities
- Fundraising activities

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This Newsletter has been printed free of charge by the office of Graham Perrett, Federal Member for Moreton. Our kind thanks to Graham & Staff.


The Songs of Christmas
By: 365greetings
Silver bells are ringing
Choirs merrily singing
"Hallelujah, hallelujah
To the King!
Children running joyfully
Colored lights lit so brightly
Chorus singing merrily
Glory to the Child Most Holy!
Merry Christmas