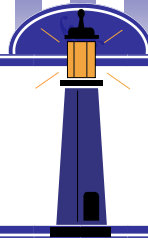


# PHAROS



# SPOTLIGHT

*This newsletter is designed for PHAROS participants and their families.*



## ***PHAROS...A Roadmap to the Future for HD***

### ***Volume 4***

February 2006  
(rev. 3/10/06)

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*Dear PHAROS Participants and Families,*

*Welcome to our 4th edition of the PHAROS Spotlight newsletter. We extend our appreciation to you for your continued dedication to this important study of persons at risk for HD. In this new year we are seeking additional funding from the National Institutes of Health (NIH) to continue PHAROS through 2010, and we hope we can count on you to continue your participation through that time. The value of participation becomes more important with time as we acquire more data that will help us design clinical trials in unaffected individuals who may or may not carry the HD gene.*

*The investigator and coordinator at your research site are prepared to answer any questions you may have about the continuation of PHAROS and its research procedures. We look forward to a year of new discoveries.*

*Sincerely,*

*Ira Shoulson, MD  
Principal Investigator*

*Anne B Young, MD, PhD  
Co-Principal Investigator*

## **World Congress on Huntington's Disease 2005**

The 2<sup>nd</sup> meeting of the World Congress on Huntington's Disease, together with the International Huntington Association, took place in Manchester, England on September 10-14, 2005. Over 400 attendees from all over the world were present to hear about the latest advances in Huntington's Disease. Presentations varied including models of drosophila (fruit flies), developing pre-symptomatic trials, and discussions regarding public policy. PHAROS presentations were given on current research findings. Kim Quaid, PhD presented two posters on the life events of at-risk's persons. One poster described the qualitative interviews (personal conversations) with a subset of PHAROS participants. The other described attitudes towards genetic testing for Huntington's

Disease in PHAROS participants. Elise Kayson, MS, RNC gave a platform presentation to the group on monitoring the safety and well being of the PHAROS cohort. This talk was a report of the PHAROS baseline data on depression and suicide. The next World Congress meeting is scheduled for September 8-12, 2007 in Dresden, Germany. Visit [www.worldcongress-hd.net](http://www.worldcongress-hd.net) for additional details.



**PHAROS Spotlight Newsletters can now be found online at:**

**<http://www.huntington-study-group.org/PHAROSNewsletter-Volumes.htm>**



## Topics of Interest

### **Genetics 101**

There are 23 pairs of chromosomes in each cell in the body. The HD gene was discovered on chromosome 4. The HD gene is made up of a specific piece of DNA, which repeats in units of three, called the CAG (cytosine-adenine-guanine) trinucleotide repeat. Nucleotides are the building blocks of DNA. People who inherit the gene that causes HD have more CAG repeats than someone who doesn't have HD, usually more than 40.

Two special groups focus on the genetic aspects of HD: medical geneticists and genetic counselors. Medical geneticists are physicians or scientists with advanced training in genetics. In North America, both the American Board of Medical Genetics and the Canadian College of Medical Geneticists grant board certification to these individuals. Genetic counselors have completed an accredited master's degree program in Genetic Counseling. In North America, accreditation is received through the American Board of Genetic Counseling or the Canadian Association of Genetic Counsellors.

## Meet The Researchers

This issue features two members of the PHAROS genetics team: Martha Nance, MD and Richard Myers, PhD who have been involved in the area of HD genetics.



*"I have felt that it is important to keep the genetic nature of HD firmly in mind as we design and execute clinical trials."*



**Martha Nance,**

### **Martha Nance, MD**

*Park Nicollet Clinic Department of Neurosciences, St. Louis Park, MN*

#### ***What experience sparked your interest in HD?***

My father was a geneticist, so I grew up with an interest in genetic diseases and issues. I finished my neurology residency in 1988, shortly after the HD gene had been localized (but before it had been identified), and as a genetics fellow, I was part of the team that set up a process for HD predictive testing at my institution. I began attending the monthly HD clinic at that time, and took over as the Clinic Director in 1991. By then it had become my passion!

#### ***When did you first become involved in HD research?***

I had done a small amount of research on my own, but it was by joining the Huntington Study Group (HSG) that I really began to do any meaningful work. As a member of the HSG, it certainly helped that I was fluent in both "neurology" and "genetics", as most of the other neurologists in the group did not have formal training in genetics. I have felt that it is important to keep the genetic nature of HD firmly in mind as we design and execute clinical

trials, as it adds an extra twist to our work that is not seen in Parkinson's, Alzheimer's, Multiple Sclerosis, epilepsy or other diseases.

#### ***What are two major issues for HSG researchers to address as we prepare for therapeutic trials that may have preventative outcomes?***

When we begin clinical trials in presymptomatic people with drugs that we think might slow the course of the disease we have an important job. We must communicate both with at-risk people and with genetic counselors to ensure that people only get a predictive test if they perceive a benefit from knowing their results, not as a ticket to get into a research study.

We also need to communicate very carefully the results of our studies to the public and to our HD families. People tend to want quick answers, and results that are black-and-white, but research often doesn't work that way. We need to work together with our families; communication is a critical part of working together.

*(continued on pg 3)*

Martha Nance, MD *Continued*

***As one of the leaders in the genetics of HD, what do you see as the next important goal?***

In research, we are looking beyond the HD gene to other genetic factors that might influence the onset or course of the disease. This will give us additional insight about the processes that lead to nerve cell degeneration. Although it is difficult to identify the tools to study them, identifying "outliers"--people with much earlier or later onset of HD, or unusually fast or slow rates of progression--may also lead us to a better understanding of the disease.



Richard Myers, PhD *Boston University, Boston MA*

***What experience sparked your interest in HD?***

After undergraduate school I took a job working in a school with autistic children. That sparked my interest in neuroscience, and I entered a graduate program focusing on neuroscience. After the first year of that program, Dr. Arthur Falek came seeking a graduate assistant to work with him on his Huntington's research in the Human Genetics section of the Department of Psychiatry at Emory. I jumped at the opportunity, changed my emphasis to neurogenetics and I've never looked back.

***When did you first become involved in HD research?***

Working in Dr. Falek's lab, as a doctoral student from 1975 through 1980, I came to know Marjorie Guthrie, Mike Conneally, Harold Klawans, Nancy Wexler, Ted Bird and many other HD investigators. At some point, Marjorie asked me if I would consider making HD my career path. I did my doctoral dissertation on the genetic epidemiology of HD, and on muscle tremor physiology as a possible presymptomatic test for HD. The latter, I actually demonstrated did not work. But nonetheless I gained important experience in working with persons at risk for HD that I later applied to developing protocols for the HD presymptomatic testing program that I have directed at the Massachusetts General Hospital since 1986.

***What are two major issues for HSG re-***

***searchers to address as we prepare for therapeutic trials that may have preventative outcomes?***

Developing therapeutic trials that may postpone or prevent onset is the ultimate goal for HD investigators. However, in developing therapeutic trials, how do we best allocate the resources available? Should efforts be focused on trials using existing agents that have shown some promise? Or should we wait to develop trials on agents in the pipeline that hold promise for greater beneficial effect, but may be three to five or more years in testing before they can be used in clinical trials? How do we balance wanting to help those in need today, with the longer range goal of developing potentially much better agents for the future?

A second major issue is that we still have very limited understanding of how and why the expanded polyglutamine repeat causes the specific patterns of cell death seen in HD. While we have many tools to test potential therapeutic agents in transgenic animals (worms, flies, fish, mice), creative cell cultures and high-throughput screening mechanisms, there remain potentially important differences between the disease as it is expressed in the animal models and the human disease. An appreciation for the significance of HD brain banks has waned, but other human tissues for biomarker studies have gained increased interest. We continue to need strong human research in HD to cross-validate the animal models and we need to acknowledge more readily where the animal models fall short. *(continued on pg 4)*



**Richard Myers,  
PhD**



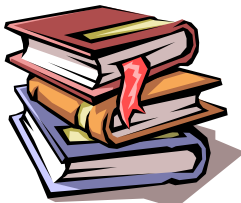
*"How do we balance wanting to help those in need today, with the longer range goal of developing potentially much better agents for the future?"*

## Richard Myers, PhD *continued*

### *As one of the leaders in the genetics of HD, what do you see as the next important goal?*

I believe that there are opportunities for genetic research to provide new classes of treatments for HD that will target the damaging effects of the HD gene. By understanding the role of the HD gene and the biological mechanisms that influence how it causes cell death, we can use the body's own defenses to ward off the disease. We recognize that persons with identical repeat sizes can develop the initial symptoms of HD at dramatically different ages. There is overwhelming evidence that other genes have powerful influence on the way the HD gene is expressed and leads to disease that go far beyond repeat size alone. If we understand why one person begins to show symptoms at age 30 and another, with the same repeat size, at age 65, we might begin to understand how to postpone the onset for everyone with HD.

Further, by identifying and controlling for the powerful genetic factors contributing to HD expression, other influences, including such things as diet or environmental factors, which we are studying through the PHAROS surveys, might become more readily apparent and may also bring important insights to prolonging health for persons with HD. Weight loss, exercise, caffeine, smoking, alcohol consumption, these other factors may come into better focus once the powerful genetic modifiers are identified, thereby assisting persons who carry the HD gene to live longer healthier lives.



### What has your research team published recently?

K.A. Quaid, M. Swenson, S. Sims, the PHAROS Investigators and Coordinators. Qualitative interviews in a subset of PHAROS participants. *Journal of Neurology, Neurosurgery and Psychiatry* October 2005 76 (suppl 4).

Huntington Study Group PHAROS Investigators (Quaid K.A. primary author). Attitudes towards genetic testing for Huntington's disease in PHAROS participants. *Journal of Neurology, Neurosurgery and Psychiatry* October 2005 76 (suppl 4).

Huntington Study Group PHAROS Investigators (Kayson EP, primary author). Monitoring the mental health and well being of the prospective Huntington at-risk observational study (PHAROS) cohort. *Journal of Neurology, Neurosurgery and Psychiatry* October 2005 76 (suppl 4).



### New Studies

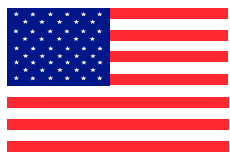
For more information on eligibility criteria and the location of HSG participating sites in the U.S. and Canada, please call the HSG at 1-800-487-7671 or visit the HSG website at [www.huntington-study-group.org](http://www.huntington-study-group.org).

As we learn more about the course of HD, new drugs are being developed to target the pathways in the brain affected by the expanded CAG repeat length. We are pleased to announce the initiation of two clinical research studies for people with manifest HD, conducted by the Huntington Study Group investigators and coordinators.

**TREND** (A Multi-Center, Double-Blind, Randomized, Placebo-Controlled Trial of Ethyl-EPA (Miraxion™) in Subjects with Mild to Moderate Huntington's Disease) is a study of the ethyl EPA compound Miraxion™ supported by Amarin Neuroscience Ltd.

**DOMINO** (A Multi-Center, Double-Blind, Pilot Study of Minocycline in Huntington's Disease) is a study of minocycline supported by the Food and Drug Administration (FDA).

## Upcoming Events



### U.S. Events

The 21<sup>st</sup> Annual Huntington's Disease Society of America (HDSA) Convention will be held **June 9-11, 2006** at the Hilton Milwaukee City Center in Milwaukee, WI. If you have any questions, please contact HDSA at [hdsainfo@hdsa.org](mailto:hdsainfo@hdsa.org) or toll free at **1-800-345-4372**.



### Canadian Events

The Huntington Society of Canada will hold its bi-annual conference in Vancouver in the **fall of 2006**. For more information call the HSC toll free in Canada **1-800-998-7398** or email [info@hsc-ca.org](mailto:info@hsc-ca.org)

For more information on national or local events visit: [www.hsc-ca.org/english/events.htm](http://www.hsc-ca.org/english/events.htm)



### World Events

World Congress on Huntington's Disease (WCHD) will hold its bi-annual conference in Dresden, Germany. The conference will take place **September 8-12, 2007** at the International Congress Center. The WCHD is a joint meeting of the World Federation of Neurology Research Group on Huntington's Disease and the International Huntington Association (IHA).

For more information see the WCHD website at: [www.worldcongress-hd.net](http://www.worldcongress-hd.net)

## For More Information



"Huntington Study Group"  
[www.huntington-study-group.org](http://www.huntington-study-group.org) or contact the HSG toll free at **1-800-487-7671**

"PHAROS Spotlight" newsletter online  
<http://www.huntington-study-group.org/PHAROSNewsletterVolumes.htm>

"Huntington's Disease Society of America" [www.hdsa.org](http://www.hdsa.org) or contact HDSA toll free at **1-800-345-HDSA (1-800-345-4372)**

"Huntington Society of Canada"  
[www.hsc-ca.org](http://www.hsc-ca.org) or contact HSC at **1-800-998-7398**

"Huntington Project"  
<http://www.huntingtonproject.org>

"Hereditary Disease Foundation"  
[www.hdfoundation.org](http://www.hdfoundation.org)

"International Huntington Association"  
[www.huntington-assoc.com](http://www.huntington-assoc.com)

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