



# PHAROS

# SPOTLIGHT

*This newsletter is dedicated to our PHAROS participants and their families.*



*Volume 7*

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

*Dear PHAROS Participants,*

*We are excited to announce that we have received the Notice of Award and funding from the National Institutes of Health (NIH) allowing us to extend the PHAROS study 3 more years until 2010. However, study visits will be completed by December 2009.*

*Based on recent research in HD, new activities have been added to the PHAROS visits. These include a blood and urine sample that will be collected for measuring HD biomarkers, you will be asked to complete quality of life surveys about your physical, leisure, social, behavioral and employment activities, a questionnaire on seeking advice about HD and a unique identification number will be assigned to you so that your data may be linked to other HD studies in which you may choose to participate. You will be asked to sign a consent form explaining the study procedures.*

*The knowledge generated from the PHAROS study extension and your continued participation will better help:*

- To define the very early clinical signs of HD*
- To improve the understanding of genetic and environmental variables that may have an effect on the onset of HD*
- To provide clinical research methods pertaining to the design and conduct of therapeutic trials with the goal of postponing the onset of HD*
- To enhance effective care and counseling for adults at immediate (50:50) risk for HD.*
- To provide biological resources for future HD research.*

*Thank you for your contributions of time and support of the PHAROS study. We look forward to your ongoing involvement for the next few years and the invaluable information that will be collected to enhance future HD research.*

*Sincerely,*

*Ira Shoulson, MD  
Principal Investigator*

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

**PHAROS Spotlight Newsletters  
can now be found online at:  
[http://www.huntington-study-group.org/  
PHAROSNewsletterVolumes.htm](http://www.huntington-study-group.org/PHAROSNewsletterVolumes.htm)**



*PHAROS  
"A National Treasure"*



## Diet and Huntington Disease

### Cross-Sectional Assessment of Diet in Individuals at Risk for Huntington's Disease (PHAROS)

The purpose of this study was to examine the dietary intake in individuals at risk for Huntington disease (HD) who are unaware of their gene status and are participating in the PHAROS study.

We previously reported significantly lower body mass index (BMI is an indicator of body fatness that depends on a person's weight and height) in 361 people with HD whose data was included in the Huntington Study Group (HSG) database. We chose only those people with mildly impaired movements and compared them to people without HD. Results of this study suggested to us that weight loss may occur early in people with HD (Djousse et al.).

Two other studies have shown that the total energy or calorie expenditure in HD participants was 11-14% higher than controls and was attributed to increased physical activity associated with the movement disorder.

We had the unique opportunity in PHAROS of examining people who were at risk for HD but did not have any involuntary movements. This would be an opportunity to determine whether weight loss occurs during the pre-symptomatic stage of HD, and it would be less likely to be attributed solely to movement or physical activity alone.

The Block Food Frequency questionnaire was included in the baseline assessment of 1001 PHAROS participants. The answers to these questions help to estimate a participant's protein, fat and carbohydrate intake from a wide variety of nutrients and food groups and the total number of calories they consume. The gene (+)s and gene (-)s were compared using statistical tests for association and trends. In a separate analysis, individuals diagnosed with HD during the 3 years of follow-up were excluded.

After excluding those subsequently diagnosed with HD, increased caloric intake was associated with being gene (+). In all analyses, despite higher caloric

intake, gene (+)s had lower BMI, even when those who ultimately were diagnosed with HD over 3 years were excluded. Gene (+) and (-) did not differ in the distribution of protein, carbohydrates, and fat adjusting for age, gender, education and total caloric intake.

We concluded that even among participants who had no evidence of HD, they had to eat more to maintain their weight and still had a lower BMI. This suggests one of two possibilities, either participants are burning more calories because of subtle types of physical activity such as fidgetiness or participants at-risk for HD have an alteration in metabolism (how we derive energy from food) before the development of the movement disorder.

We hope that by continuing to study diet in our participants we may gain clues about the etiology of HD, specifically if there are fundamental changes in energy efficiency that may be linked to the powerhouse of the cell, the mitochondria.



Karen Marder, United States and Huntington Study Group PHAROS Investigators. Cross-Sectional Assessment of Diet in Individuals at Risk for Huntington's Disease (PHAROS) *Neurology* 2007; 68(Suppl 1):A230.

PHAROS is supported by NIH HG02449, High Q Foundation.

Body Mass Index (BMI) is a number calculated from a person's weight and height. BMI provides a reliable indicator of body fatness for most people and is used to screen for weight categories that may lead to health problems.



*The success of PHAROS depends critically on follow-up research visits.*

## Transition to COHORT

COHORT—Cooperative Huntington's Observational Research Trial. Like PHAROS, COHORT is a long-term observational study of individuals who are part of an HD family. Forty sites throughout USA, Canada and Australia are currently participating in COHORT. Unlike PHAROS, the visits occur only once every 12 months. As your participation in PHAROS comes to a close we would like to invite you to participate in COHORT. COHORT will allow us to learn more about HD and to plan future research studies of experimental drugs aimed at postponing the onset or slowing the progression of HD. The COHORT brochure can be found at: <http://www.huntington-study-group.org/Resources/COHORTBrochure.pdf>

## Attitudes & Beliefs in Huntington Disease

### Living at Risk: Concealing Risk and Preserving Hope in Huntington Disease.

This article is the first in a series of papers that examines the experiences of people living at risk for Huntington disease (HD). The Prospective Huntington At-Risk Observational Study (PHAROS) aims to establish whether experienced clinicians can reliably determine the earliest clinical symptoms of Huntington disease in people with a 50% risk for HD and have not had genetic testing.

Only a few studies have explored the meaning, significance, experience and communication of hereditary risk. The results of these studies conclude that telling family members about genetic risk was usually considered a family responsibility. If, when and how to communicate this risk was looked upon differently between families. How certain a person felt about his or her own risk effected what he or she could tell other family members. While some people are able to talk openly about hereditary risk, others find it difficult to discuss.

The purpose of the current study was to gather information about the everyday experiences of a selected group of PHAROS participants living at risk for HD. Five PHAROS investigators and coordinators were chosen and trained in interview techniques (active listening,

minimal direction for answers, conversational initiators and summarizing techniques). Fifty five PHAROS participants (38 women and 17 men) from six PHAROS research sites across the United States participated in this study. The participants were chosen for their ability to actively talk about their HD experiences. The interviews lasted about one hour. Participants were encouraged to describe their personal experiences with HD, their relationships with affected family members, their involvement in care-giving, their attitudes toward telling others about their HD risk, and their motivation to participate in research. Thirty seven of these interviews were analyzed for the results of the study.

*Living at risk* was the pattern demonstrated from the two main themes of the study: 1) careful concealment as an act of self preservation and 2) preserving hope.

Concealment (hiding HD risk does not happen with only one person. People at risk for HD must consider if or when to tell their employers, potential spouses, friends, health care providers, insurance carriers, attorneys, and children about their risk of HD. Some people are very open about their risk, others make a great effort to hide the fact that HD is in their family.

Hope is an important factor in living at risk for HD. Participants

hope that they will not have HD, or that their risk will decrease with age, keeping open the possibilities of a disease free future for themselves and their children. Hope is one of the reasons that participants do not get tested.

Revealing or hiding HD at risk status is a complex decision that participants have to make. Choosing to be tested is in a way, a decision to reveal one's real risk to oneself. Choosing not to be tested is not denial but a positive way to preserve both hope and identity as a person with a future. Discussion of genetic risk within the family especially between parents and their children is very difficult. Nearly every participant with children experienced terrible difficulty in talking to their children about their risk, even when their children were grown. Doctors could and should find ways to help people at risk develop plans for educating their children at an appropriate age.

Each person at risk for HD needs to make the decision about testing for him or herself freely. Doctors need to be aware of their patients attitudes and beliefs about testing, being supportive of whatever choice the patient makes. For several participants the interview for this study was their first opportunity to talk about the emotional side of HD.

Quaid KA., Sims SL., Swenson MM., Harrison JM., Moskowitz C., Stepanov N., Suter GW., Westphal, BJ., The Huntington Study Group Investigators. Living at Risk: Concealing Risk and Preserving Hope in Huntington Disease. *Journal of Genetic Counseling*, Published on line October 18, 2007.

Funding for this study was obtained from the Ethical, Legal and Social Implications (ELSI) program of the National Institute for Human Genome Research of the National Institutes of Health (H602449).



*The longer you participate in PHAROS the more valuable you and your data become to future planning of HD research studies.*



## HSG Study Updates

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**RESPOND-HD:** An Examination of Responses to Potential Discrimination from Individuals At Risk for Huntington's Disease.

... Recruitment for RESPOND is in progress...

The RESPOND-HD observational trial is looking at issues of potential discrimination in those affected by Huntington disease (HD). The information gathered in this study will allow researchers to examine the experiences of persons who have undergone genetic testing for HD or those persons who are at risk for HD. RESPOND-HD will seek answers to questions such as “How is knowledge used after genetic testing?”, “What experiences occur following genetic testing?” and “Why might outcomes differ in persons undergoing genetic testing?”. Study participants from the PHAROS and PREDICT-HD research trials are being recruited for this study. Participants for this international, multi-site study are being recruited from domestic geographical areas where there are differing discrimination laws for employment and insurance, and also from foreign sites where health care systems may be different from domestic sites.



**DIMOND:** A Multi-Center, Phase 2, Randomized, Double-Blinded, Placebo-Controlled Study of **Dimebon** in Subjects with Huntington's Disease

... Recruitment for DIMOND is in progress ...

The Huntington Study Group (HSG) is conducting a study of the research medication **Dimebon** in persons 18 years of age or older who have mild to moderate Huntington disease (HD). DIMOND is designed to determine safe and tolerable doses of Dimebon and also to determine the effect of Dimebon on cognitive (thinking) and motor (movement) signs and overall functioning of subjects with HD. Approximately 15 research centers in the United States and in the United Kingdom will enroll up to 90 research subjects and will last about 3 months. The study will enroll research subjects with early to moderate signs of HD who are independently ambulatory (walking) and self-sufficient in activities of daily living, such as eating, dressing, and bathing. Enrollment began in the Summer of 2007. This study is sponsored by Medivation, Inc.



**COHORT:** **C**ooperative **H**untington's **O**bservational **R**esearch **T**rial. A long-term study in individuals who are part of an HD family.

... Recruitment for COHORT is in progress...

This long-term observational study will initially take place at 40 North American and Australian Huntington Study Group (HSG) sites. The goal of COHORT is to collect information in order to learn more about HD, potential treatments, and to plan future research studies of experimental drugs aimed at postponing the onset or slowing the progression of HD. This study will recruit both adults and children who have clinically diagnosed HD and adults who are a part of an HD family. Individuals who choose to participate will have one study visit every year for as long as they are able and choose to participate. This study is sponsored by HP Therapeutics Foundation, Inc.



For more information visit the Huntington Study Group website at: <http://www.huntington-study-group.org> or call the toll free number at 1-800-487-7671.



## HSG Study Updates

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### **PREDICT: Neurobiological Predictors of Huntington's Disease**

#### **... Recruitment for PREDICT is ongoing ...**

In September 2001, the Huntington Study Group, under the direction of Jane Paulsen, Principal Investigator (University of Iowa), received funding from the National Institutes of Health (NIH) to study healthy men and women at risk for HD, who have been tested for the HD gene mutation. Eligible individuals must be 18 years of age or older, are able to undergo a MRI and have the commitment of a companion to attend visits or complete surveys via mail.

The PREDICT-HD study uses a variety of tests to examine the nature and pattern of neurobiological changes and neurobehavioral changes that occur in the period leading up to a diagnosis of HD. The intent of the study is to learn more about the beginning changes in thinking skills, emotional regulation, brain structure and brain function as a person begins the transition from health to HD. As of December 3, 2007, the PREDICT-HD study has enrolled 1000 participants. It is our goal to continue to enroll additional participants.



### **2-CARE: Coenzyme Q10 in Huntington's Disease.**

#### **... Recruitment for 2-CARE will begin in 2008...**

The HSG is funded to conduct a definitive phase III clinical trial of high dose coenzyme Q10 (CoQ) in Huntington disease (HD). The HSG-run CARE-HD study (led by Dr. Karl Kieburtz) demonstrated evidence that CoQ might have a potential benefit in slowing the decline of functional capacity in HD. We therefore began the important process to determine the best dosage, obtain funding and obtain FDA approval to conduct a definitive clinical study. Please continue to visit the HSG web site for further developments as we get closer to starting this exciting new study.



### **CREST-E: Creatine Safety, Tolerability, & Efficacy in Huntington's Disease**

#### **... Recruitment for CREST-E will begin in 2008...**

This trial will test the safety, tolerability and efficacy of creatine in persons with HD and is scheduled to move ahead. As of November 2007, funding has been secured from the National Center for Complementary and Alternative Medicine (NCCAM) and the FDA Orphan Products Division. Steven Hersch, MD, PhD is the Principal Investigator.



- For more information on eligibility criteria and the
- locations 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)





## Upcoming Events



### 23rd Annual Huntington's Disease Society of America (HDSA) Convention

June 6th - 8th, 2008, Pittsburgh,

The Huntington's Disease Society of America (HDSA) Convention each year is dedicated to bringing together physicians, researchers, patients and care givers from the HD community, sharing knowledge, expertise, personal experiences and advancements in therapeutic research. For further information visit <http://www.hdsa.org>.

The 22nd Annual convention was held June 15-17, 2007, in Oklahoma City and celebrated the 40th anniversary of the HDSA. The theme for the 2007 convention was "Impact of HD on the Family Unit: Structurally, Economically and Socially".

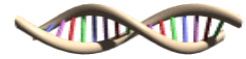
Presentations from the 2007 convention can be found on the HDSA website. <http://www.hdsa.org>.



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## For More Information



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<http://www.hdfoundation.org>

International Huntington Association  
<http://www.huntington-assoc.com>

The HD Lighthouse  
<http://www.hdlighthouse.org>

HOPES: Huntington's Outreach Project for Education at Stanford  
<http://www.stanford.edu/group/hopes/>

EURO Huntington's Disease Network  
<http://www.euro-hd.net>

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<http://clinicaltrials.gov/>

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