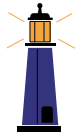


PHAROS SPOTLIGHT



This newsletter is especially for PHAROS participants and their families.

Volume 3

July 2005

PHAROS...A Roadmap to the Future for HD

Dear PHAROS Participants and Families,

Welcome to our third edition of the PHAROS Spotlight newsletter. Many of you have been participants since 1999 while others joined our research study in 2004. Whether you are nearing your 4th visit or your 9th visit, you are providing a unique window into what living at risk for HD means.

We cannot thank you enough and so we thank you every chance we get—here in our newsletter, handshakes and face-to-face smiles and words of thanks. In this issue we put the spotlight on those who analyze the PHAROS data, Hongwei Zhao and David Oakes, both working behind the scenes to help us understand all the important data you have provided.

Past drug studies [CARE HD, MINO, RID-HD], current observational studies [PHAROS, PREDICT, COHORT] and future drug studies are all conducted under one umbrella we call the HSG or Huntington Study Group. Read about the HSG in this issue and keep up-to-date on-line. Take your time to introduce yourself to the organizations that support the many paths of HD research.

We hope you will let us know your questions and concerns. Contact your site investigator or study coordinator and let them know how we can do a better job. Stay in touch! And, thanks again!

Sincerely,

*Ira Shoulson, MD
Principal Investigator*

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

Newsletter Articles

- **What's New? (pg 2)**
- **Meet the Researchers (pg 2-3)**
Interviews with the PHAROS Biostatisticians
- **Topics of Interest (pg 3-5)**
What is the Huntington Study Group?
What is the Huntington Society of Canada?
What has your study team published recently?
- **New Studies on the Horizon (pg 5)**
Upcoming studies in HD
- **Upcoming Events (pg 6)**
National HD events
- **For More Information (pg 6)**
Phone numbers and informative websites on Huntington's Disease
- **Upcoming Issues (pg 6)**
A preview of our next issue
- **Map of Sites (pg 7)**
PHAROS Study sites around North America

What's

We have made the PHAROS Spotlight newsletter available online. Volumes 1 and 2 are now posted on the Huntington Study Group website for easy access. As subsequent issues of the newsletter are published, be sure to check the website for an electronic version. A printable PDF file of each newsletter is also available on the website.

The newsletters can be found at: www.huntington-study-group.org/PHAROSNewsletterVolumes.htm

Meet the Researchers

This issue we will feature two additional members of the PHAROS Steering Committee: the biostatisticians. David Oakes, PhD (*chief biostatistician*) and Hongwei Zhao, PhD oversee data analysis in the PHAROS study. Both individuals are part of the Department of Biostatistics at the University of Rochester.

Responsibilities of the biostatisticians include involvement in protocol design, providing input on the sample size of participants, establishing guidelines for safety monitoring, and deciding how to analyze the data variables collected. In studies involving blinded treatment groups (active drug vs. placebo), the biostatistics department creates a plan that determines randomly (like the “flip of a coin”) whether a participant will be in an active or a placebo study medication treatment group.

Throughout the study, the biostatisticians manage the analytic database and check to ensure quality control of the data. When subjects complete study participation and the database is locked, biostatistics analyzes the outcomes of the study and reports them to the Steering Committee. The study results are then incorporated into a manuscript that will later be published for the public. The results are only reported as group data, names are never used to protect confidentiality.



Hongwei Zhao, PhD

University of Rochester, Rochester, NY

Hongwei Zhao was born in China and attended Beijing University for undergraduate study. She came to the U.S. in 1990. Enjoyment of mathematics and an interest in the application of statistics in the medical field led her to study biostatistics. She received her Sc.D in Biostatistics from Harvard in 1997. After graduation, Hongwei came to the University of Rochester where she currently serves as an associate professor in the biostatistics department

“I have been involved in Huntington’s Disease research for seven years. I became interested in HD from participating in the Huntington Study Group. My primary goal is to make contributions toward finding a cure for HD.”



David Oakes, PhD
University of Rochester, Rochester, NY

Dr. David Oakes was born and grew up near Manchester, England and was educated at Cambridge and London Universities. He received his PhD in Statistics in 1972. After holding faculty positions at Harvard University and the London School of Hygiene and Tropical Medicine he moved to the University of Rochester in 1983, with joint appointments in the College of Arts and Science and the School of Medicine and Dentistry. He has served as Department Chair of Statistics (1989-1995) and of Biostatistics (1995-2002). His interest in Huntington’s disease began in 1987 in collaboration with Dr. Ira Shoulson in the “Baclofen” study (baclofen as protective therapy in Huntington’s disease). While this medication did not show any benefit over placebo in slowing disease progression, the study itself contributed to our knowledge about how to do clinical trials in Huntington’s disease. Dr. Oakes has published two books and 150 research papers, about equally divided between contributions to the theory of statistics (yes, there really is a “theory of statistics”, and it is fascinating!) and collaborative work in Huntington’s disease, Parkinson’s disease and other disorders. He currently directs the Biostatistics Center of the Huntington Study Group and is involved with both PHAROS and PREDICT. Dr. Oakes is also involved in planning new HSG studies like TREND and PHEND.

“Initially my interest in HD was largely accidental. My predecessor Charlie Odoroff, the founding Director of the Biostatistics unit at Rochester, had become incapacitated and he asked me to take over the statistical analysis of the baclofen study. I have since come to appreciate both the scientific challenges in HD research and the urgent need to develop better treatments for this devastating disease. Obviously, all of us who work in HD want to see a cure, and soon. Failing that we must fall back on what, in a different context, has been termed “the patient accumulation of successes”. Small, but incremental, advances may result in significant progress over time. For this reason I would like to see as many promising agents as possible studied in rigorously designed clinical trials. It is important also to avoid blind alleys and to distinguish immediate relief of symptoms, valuable as this is, from true slowing of disease progression or delay of disease onset.”

Topics of Interest

H • S • G
HUNTINGTON • STUDY • GROUP

You may have heard the name HSG mentioned in connection with the PHAROS study, but what is the HSG? The HSG, or Huntington Study Group, is a group of scientists, physicians, nurses and health care providers experienced in the care of Huntington patients and dedicated to clinical research in Huntington’s Disease (HD). The group was formed in 1993 by Ira Shoulson, Jack Penney, Anne

Young, Nancy Wexler, and Jim Guzella. It now includes more than 269 active investigators, coordinators and scientists from approximately 62 HSG sites in the United States, Canada, Australia and Europe. Research is conducted at all of these sites in an effort to find new treatments for HD, as well as new ways to diagnose HD and related neurological disorders. The Unified Huntington's Disease Rating Scale (UHDRS) Natural History's database was the first cooperative research study undertaken by the HSG and contains data on over 7,000 research participants. The HSG has conducted a number of clinical studies, INTRO-HD, CARE-HD, RID-HD, MINO, Creatine, PHAROS, PREDICT, TREND, and PHEND, with many more on the horizon. The HSG works with private foundations, pharmaceutical companies and the

National Institutes of Health (NIH) to conduct trials. All of the group's research efforts are actively published in internationally recognized peer-reviewed research journals.

Every year the HSG holds an annual meeting to bring all the members of the HSG together in one place to share ideas, present scientific findings in HD, and to brainstorm ideas for the future.

HSG Annual Meeting 2004

The 12th Annual Huntington Study Group (HSG) Meeting was held from November 4-7, 2004 in St. Louis, Missouri. The atmosphere, as always, was enthusiastic. More than 200 scientists, researchers, investigators, coordinators, and guests attended making this one of the largest annual meetings yet.

Members gathered to attend committee meetings, scientific and poster presentations, working groups, electronic data capture demonstrations, training sessions and more. The scientific session "Neuroprotection Strategies: Where do we go from here" focused on how to implement clinical studies in the at risk presymptomatic HD population. Speaking out on their perspectives were representatives from NIH (Bernard Ravina and Kurt Fischbeck), Lilly Corporation (Eric Siemers), Harvard (Merit Cudkowicz) and HDSA (James Trethaway).

Those attending this 12th annual HSG meeting are extraordinarily dedicated to "stay the course" for a treatment and cure to be found.



In addition to the many participating Canadian sites that are members of the Huntington Study Group, Canada has its own organization focused on Huntington's Disease: The Huntington Society of Canada or HSC.

Volunteers Ralph and Ariel Walker founded the Huntington Society of Canada in 1973. Ralph Walker became the Society's first Executive Director and held this position for 24 years, and through his vision, the Huntington Society of Canada has grown from Ralph and Ariel's kitchen table to an internationally recognized and respected organization. The Huntington Society of Canada is a national network of volunteers and professionals working together to find new treatments and, ultimately, a cure for Huntington disease; and to improve the quality of life of individuals with Huntington disease and their families. The Society's goals are: Research, to provide hope for the future; Services, to meet the urgent needs of the HD community; and Education, to promote improved understanding and awareness of HD.

The Huntington Society of Canada remains committed to helping Canadians living with Huntington disease and to supporting the worldwide effort to defeat HD.

HSC Annual Convention 2004

The Huntington Society of Canada (HSC) held its Annual General Meeting and Conference in Winnipeg, Manitoba, from October 28-30, 2004. The full three days allowed the Board members, volunteers and staff to re-focus all efforts to their ultimate goal: *A World Free from Huntington's*. The theme for the Conference was *Road to Triumph: Driven by Commitment*.

Volunteer Delegates from across Canada participated in Volunteer Training and Development Day that included a day of strategic plan updates, working groups and training workshops in all areas of their volunteer work.

Family Day began with a Science and Research Session which included a presentation by Dr. Janice Braun, associate professor in the Department of Physiology and Biophysics and the Faculty of Medicine at the University of Calgary, and a keynote address by Dr. Blair Leavitt, associate professor in the Department of Medical Genetics at the Department of Medicine at the University of British Columbia. Huntington disease family members participated in Families in Focus Forum teaching us all about caring with compassion through stories about how caregivers took care of their partners and themselves. The weekend showed all our members how we need to celebrate what we have accomplished and to make plans for the future.



What has your research team published recently?

Penelope Hogarth, Elise Kayson, Karl Kieburz, Karen Marder, David Oakes, Diana Rosas, Ira Shoulson, Nancy S. Wexler, Anne B. Young, Hongwei Zhao, the United States-Venezuela Huntington's Disease Collaborative Research Group, the Huntington Study Group. Interrater Agreement in the Assessment of Motor Manifestations of Huntington's Disease. *Mov Dis* 20:293-297, 2005.

Elise Kayson, Elaine Julian-Baros, Christine Weaver, Aileen Shinaman, Connie Orme, Joseph Weber, Susan Daigneault, Anne B. Young, Ira Shoulson and the Huntington Study Group (HSG) PHAROS Investigators. Recruitment Strategies for the Prospective Huntington At Risk Observational Study (PHAROS). Published in the program booklet of Huntington Study Group 12th Annual Meeting 2004, Abstract # 8.

Visit the HSG website, www.huntington-study-group.org, to review the published abstracts online.

New Studies on the Horizon

As we learn more about the courses 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.

PHEND (Phenylbutyrate Development for Huntington's Disease - Multi-center, Double-Blind, Placebo-Controlled Study with Open-Label Follow-Up to Determine the Safety & Tolerability of Phenylbutyrate in Subjects with Huntington's Disease) is a study of phenylbutyrate supported by the National Institute of Neurological Disorders & Stroke (NINDS) and HP Therapeutics Foundation, Inc.

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.



Upcoming Events



U.S. Events

- The 21st 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 or toll free at **1-800-345-4372**.

For more information on national or local events see www.hdsa.org



Canadian Events

- The Huntington Society of Canada's annual conference will be held November 3-6, 2005, at the Delta Meadowvale Hotel in Mississauga, Ontario. For more information call the HSC toll free in Canada **1-800-998-7398** or email info@hsc-ca.org

For more information on national or local events visit: www.hsc-ca.org/english/events.htm



World Events

- World Congress on Huntington's Disease (WCHD) will hold its bi-annual conference in Manchester, England. It will take place **September 10-13, 2005** at the Crowne Plaza Midland Hotel. The Congress 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.hda.org.uk/congress/

For More Information



"Huntington Study Group"
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 or contact HDSA toll free at 1-(800) 345-HDSA (**1-800-345-4372**)

"Huntington Society of Canada"
www.hsc-ca.org or contact HSC at **1-800-998-7398**

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

"Hereditary Disease Foundation"
www.hdfoundation.org

"International Huntington Association"
www.huntington-assoc.com

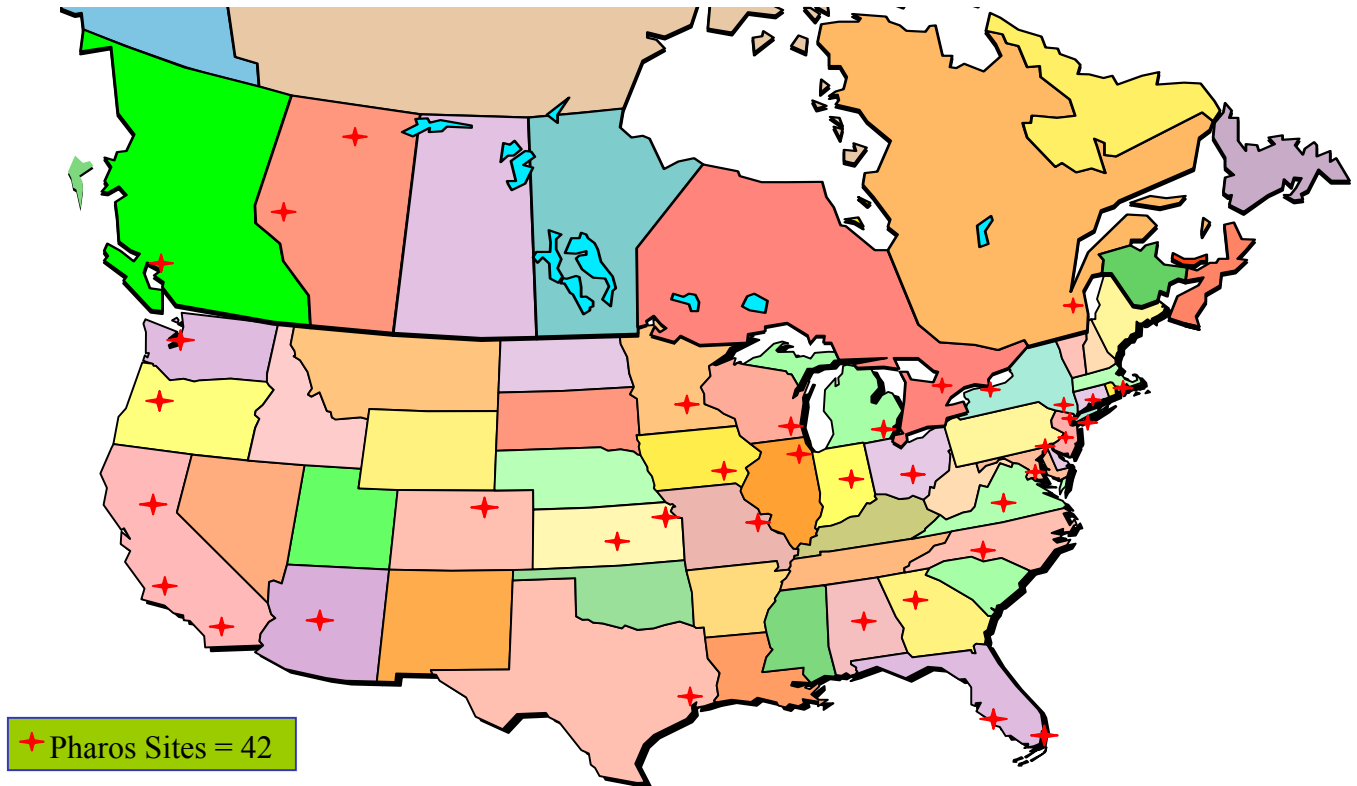
Upcoming Issues

- **What's New in PHAROS?**
- **Topics of Interest**
- **HD Research Update**
- **New Publications**
- **WCHD 2005**

Editorial Board

Melissa Diggin (Boston University)
Jody Goldstein (University of California at San Diego)
Carolyn Gray (University of Kansas)
Vicki Hunt (Wake Forest University School of Medicine)
Elaine Julian-Baros (University of Rochester)
Elise Kayson (University of Rochester)
Mary Lou Klimek (University of Calgary)
Lety Laskowski (University of Rochester)
Carol Moskowitz (Columbia University Medical Center)
Aileen Shinaman (University of Rochester)
Greg Suter (Hereditary Neurological Disease Centre)

PHAROS Participating Sites



University Of Alabama At Birmingham, AL (17)
 Mayo Clinic Scottsdale, AZ (28)
 University of California Davis, CA (27)
 UCLA Medical Center, CA (22)
 University of California, San Diego, CA (35)
 Colorado Neurological Institute, CO (25)
 Institute for Neurodegenerative Disorders, CT (13)
 University of Connecticut, CT (3)
 University of Miami, FL (7)
 University of South Florida, FL (20)
 Emory University School of Medicine, GA (35)
 University of Iowa, IA (34)
 Rush University Medical Center, IL (6)
 Indiana University School of Medicine, IN (31)
 Hereditary Neurological Disease Centre, KS (58)
 University of Kansas Medical Center, KS (46)
 Boston University, MA (4)
 Massachusetts General Hospital, MA (28)
 Johns Hopkins University, MD (4)
 University of Maryland School of Medicine, MD (5)
 University of Michigan, MI (23)
 University of Minnesota, MN (37)

Washington University, MO (23)
 Wake Forest University School of Medicine, NC (36)
 UMDNJ, NJ (16)
 North Shore University Hospital, NY (19)
 Albany Medical College, NY (10)
 Columbia University Medical Center, NY (33)
 University of Rochester, NY (29)
 University of Pennsylvania, PA (14)
 Ohio State University, OH (36)
 Oregon Health & Science University, OR (28)
 Brown University, RI (26)
 Baylor College of Medicine, TX (20)
 University of Virginia, VA (17)
 U of Washington/ VA Puget Sound Health
 Care System, WA (30)
 Medical College of Wisconsin, WI (30)
Canada
 Hotel-Dieu Hospital-CHUM, QC (36)
 The Centre for Addiction and Mental Health, ON (19)
 University of Alberta, AB (21)
 University of British Columbia, BC (21)
 University of Calgary, AB (20)

(Number in parentheses indicates number of participants enrolled at site.)