

HIND-Sight

Huntington's Information & New Discoveries

What is the UHDRS?

The Unified Huntington's Disease Rating Scale (UHDRS) is a clinical research tool developed by the Huntington's Study Group (HSG). The purpose of the scale is to grade HD symptoms and make comparisons between patients over time. The scale provides a rating formula of HD clinical components such as motor, thinking and emotional skill. The rating scale was shown as accurate; accordingly, it is used as an outcome measure by the HSG in controlled clinical trials. Currently, more than 10,000 individuals have taken the UHDRS, helping us learn more about HD each time.

What does it measure?

The UHDRS is divided into five sub scales. The motor assessment is typically administered by a neurologist or a certified motor rater. He or she will rate movements of the eyes, tongue, hands and arms, as well as assess walking and balance. The ratings are added together to get a total score and to determine a diagnostic confidence level (DCL). The score measures the rater's view of the patient's motor signs. A "0" equates to no abnormalities on a motor examination, a "1" is non-specific motor abnormalities mean-

ing less than 50% confidence that the person has HD, "2" indicates abnormalities that may be signs of HD (confidence level of 50-89%), "3" indicates abnormalities that are likely signs of HD (90-98% confidence) and "4" indicates motor abnormalities that are 99% likely to be signs of HD.

The cognitive section of the scale comprises three tests that require concentration, flexibility in thinking and speed.

The behavioral assessment asks about sad mood, anxiety, and other emotional challenges.

The functional assessment asks about the person's ability to perform certain tasks of daily living. Examples include asking if the person is gainfully employed, doing laundry or supervising children.

The independence scale looks at how the person functions independently in activities of daily living (ADL).

How is it helpful?

In a clinical or observational study, participants are re-evaluated over time to see if their UHDRS scores change. In an observational study, like PREDICT or PHAROS, the

*HDSA Center of Excellence
University of Iowa*



*volume 6 number 3
Summer 2005*

difference in scores over time help identify subtle changes in moving, thinking and feeling that may be associated with early disease. When drug studies use the UHDRS, scores are compared for participants that are on a study drug versus on a placebo (or sugar pill). Researchers are looking for differences between the study drug and the placebo.

Please remember that this scale is a tool that helps doctors understand HD symptoms. It cannot replace the interaction between you and an HD qualified professional. Feel free to share your experience and insights with health care professionals.

MUSIC at the MILL

October 7th at 8 pm

Please help to improve the care for persons with HD.

It's time to listen to some good music, do a dance or two and support the University of Iowa's HDSA Center of Excellence. **big wooden radio** (BWR) is our headliner this year. With three highly acclaimed CDs, they have both a regional and national following. **University of Iowa President, David Skorton, and musician, Dan Moore**, will also entertain with some Latin tunes. Stay tuned for more information, and put the date on your calendar. Call Anne (319-353-4307) to donate an item to our silent auction.

Annual HDSA National Convention

The 20th Annual Huntington's Disease Society of America (HDSA) National Convention took place June 24-26, 2005 in Atlanta, GA with approximately 500 people attending the events. Professionals, researchers and families came together to discuss important topics such as relationship issues, how to talk to kids about HD, symptom management, and other topics of importance to families. Additionally, there were forums on research advances and future clinical trials. The University of Iowa's HDSA Center of Excellence staff was well represented at the convention with highlights from Jane Paulsen and Elizabeth Penziner. The two day conference highlighted a dinner/dance on Saturday evening giving all attendees a chance to relax and enjoy the food, music, awards and company. Many families found support when interacting with hope and inspiration.

Research 101: Basic Science, Translational Research Clinical Trials... What does it all mean?

HD research aimed at finding treatments and a cure for HD can be divided into three primary phases: basic research, applied or translational research and clinical trials. Although these three phases of research occur in the order listed, HD research is currently occurring in all three phases.

Basic Research: The primary goal of basic research is the identification of targets for possible intervention. Scientists who conduct this type of HD research work at the level of individual brain cells. They work to understand the process of brain cell malfunction and death in HD. Once steps of this process are understood, interventions can be identified that prevent the process from occurring. A specific goal of this research is to understand biochemical differences that occur with HD and which of these differences are critical in the disease.

Applied/Translational Research: The primary goal of applied or translational research is to discover interventions that "hit" the targets identified by the basic researchers. Researchers working in this phase of research screen potential compounds for their ability to stop or prevent the disease process from occurring. These compounds are first tested on HD cells in a test tube and later in the animal models of HD. Once a compound succeeds at this level, it moves to the clinical phase of research. Lessons learned from mouse models and fruit flies are helping us to better understand HD in humans.

Clinical trials: The primary goal of clinical trials is to determine whether potential interventions are successful in the treatment of HD in humans. Clinical trials occur are monitored by the Food and Drug Administration (FDA). Four phases of clinical trials are required before a drug can be made available to the general public. See the back page of this newsletter for more information about these phases.

For more information:
HDSA: www.hdsa.org

CHDI (Cure HD Initiative) update

New at the HDSA convention this year was the introduction of a biotech company that has a single disease focus, namely HD. This not-for-profit company fits in the applied/translational research definition in the column to the left. An anonymous gift of \$2,000,000 was given to help launch the project. The company's main goal is to rapidly discover and develop drugs that will prevent or slow the progress of HD. They hope to have medications ready for clinical trials within 3-5 years. We look forward to 2006 HDSA national convention in Milwaukee to hear about the company's progress. Robert Pacifici, PhD, the chief scientific advisor of CHDI, was the speaker at the convention and was on his way to California to manage this new endeavor.

For more information about CHDI, Inc. and its collaborative programs please see <http://www.chdi-inc.org> (a new website) or contact Robert Pacifici at robert.pacifici@chdi-inc.org.

HDSA Iowa's 1st HD Person of the Year

Congratulations to Vickie Mensing who received the Person of the Year award at the Iowa HDSA meeting in Des Moines on July 23, 2005. Thank you Vickie for years of hard work and dedication to increasing awareness of HD in the state of Iowa.

HDSA National Award

The outstanding 2005 fundraiser award from the national HDSA convention went to the Iowa chapter for their success with local hoop-a-thons raising close to \$50,000. Congratulations to the chapter for their hard work and dedication!

Ongoing HD Research

in the laboratory:

- drug screening for treatments
- creating and testing animal models with HD
- basic science exploring the DNA, the protein(s), and the process of cell death in HD

in the community:

- we need a partnership of families and scientists to do this work!
- survey research to document legal and social aspects of genetics research
- clinical trials of new drugs in humans
- rehab therapies to maximize quality of life
- imaging studies to measure disease stage(s)
- clinical research to find new measures of disease for drug studies



HD MAPS STUDY

Study purpose- HD MAPS (HD Modifiers in Age at onset in Pairs of Siblings) is investigating genetic factors that influence the age and severity of symptom onset.

Study facts- Seeking siblings that are **affected** by HD (diagnosed with motor symptoms). The study requires affected brothers and sisters (full siblings) to each contribute a blood sample. Rick Myers, PhD, (Boston University) is the lead investigator on this large collaborative project that has already resulted in 2 publications describing modifying genes for HD.

Inclusion criteria- The siblings will be asked their CAG repeat length and the date they were diagnosed with motor symptoms. Samples are encoded to ensure privacy.

As of December 2002, nearly 1000 sibling pairs from a variety of sites around North America have been registered. Please call if you and one or more of your siblings are **diagnosed with HD** and are interested in participating in this study.

Please contact Anne Leserman at (319) 353-4307 or anne-leserman@uiowa.edu about any of the above studies.

TREND- HD

Study purpose- to investigate ethyl-EPA on chorea symptoms and general clinical improvement. Ethyl-EPA is found in omega-3 fatty acid present in some animal foods (like fish).

Study facts- study participation will last one year and includes telephone and outpatient visits to UIHC. All participants will get study drug in the study's second phase.

Inclusion criteria- 35years old or older, diagnosed with HD, still ambulatory and provide informed consent

Exclusion criteria- some medications are excluded, having an active GI illness and other exclusion criteria may apply.

TREND HD is an HSG study occurring at 43 sites throughout North America. Contact 1-800-487-7671 to find the site nearest you.

PHEND-HD

Study purpose- The study will measure the tolerability of *phenylbutyrate* and its effects on HD symptoms. Phenylbutyrate is an HDAC (Histone deacetylase) inhibitor known to slow or stop neurons from dying in a mouse model.

Study facts- Participation will last 20 weeks and will include telephone and outpatient visits to UIHC.

Inclusion criteria: age 18, diagnosed with HD and ambulatory

Exclusion criteria: some medications excluded, unstable mental illness and other exclusion criteria may apply.

PHEND HD is an HSG study occurring at 6 sites throughout North America. Contact 1-800-487-7671 to find the site nearest you.

HD Support Groups:

DES MOINES

Valley View Village Conference
2571 Guthrie Ave
3rd Tuesday at 6:30 pm

LINCOLN, Nebraska

Perkins Family Restaurant
48th and O St
1st Monday at 7:30 pm

OMAHA, Nebraska

Village Inn Restaurant
78th and Dodge
2nd Monday at 6:00 pm

IOWA CITY

University of Iowa Hospitals and Clinics
Della Ruppert Conference Room
6th floor, elevator H
4th Sunday at 1:00 pm

Clinical Trial Definitions

Clinical trial- A research study in human volunteers to answer specific health questions. The primary focus of clinical trials is to find treatments to improve the health and well being of human with disease or illness. Trials can determine whether experimental treatments or new ways of using known therapies are safe and effective.

Protocol- A study plan on which all clinical trials are based. The plan is carefully designed to safeguard the health of the participants as well as answer specific research questions. A protocol describes what types of people may participate in the trial; the schedule of tests, procedures, medications, and dosages; and the length of the study. While in a clinical trial, participants following a protocol are seen regularly by the research staff to monitor their health and to determine the safety and effectiveness of their treatment.

Placebo- An inactive pill, liquid, or powder that has no treatment value. In clinical trials, experimental treatments are often compared with placebos to assess the treatment's effectiveness. Researchers want to see if the treatment is more effective than the placebo.

Control group-The standard by which experimental observations are evaluated. In many clinical trials, one group of patients will be given an experimental drug or treatment, while the control group is given either a standard treatment for the illness or a placebo.

Phases of Clinical Trials- Each phase has a different purpose and help scientists answer different questions.

Phase I- researchers test a experimental drug or treatment in a small group of healthy people (20-80) for the first time to evaluate its safety, determine a safe dosage range, and identify side effects.

Phase II- the experimental study drug or treatment is given to a larger group of people (100-300) to see if it is effective and to further evaluate its safety.

Phase III - the experimental study drug or treatment is given to large groups of people (1,000-3,000) to confirm its effectiveness, monitor side effects, compare it to commonly used treatments, and collect information that will allow the experimental drug or treatment to be used safely.

Phase IV- after the drug has been shown to work, additional information is gathered including side effects and safety as well as long terms risks and benefits.

information from www.clinicaltrials.gov



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