After starting out as a Huntington disease researcher and clinician in the 1990s, Dr. Jane Paulsen began to notice a common theme in discussions with HD patients and families. “They would tell me that before their loved one was diagnosed with manifest HD, they were noticing changes in the way he or she behaved,” said Paulsen. “Or maybe their once-punctual family member was now frequently late for appointments. It’s the families that really brought these early changes to the forefront and drove me to start the PREDICT-HD study.”

The study that set out to identify those earliest changes and signs of HD so the course of the disease could be better understood and treatments could be targeted to keep people healthy longer was first funded by the National Institutes of Health (NIH) in 2001. Thousands of participants, 90-plus medical journal articles and 13 years later, PREDICT-HD, as it is currently constituted, is concluding.

Thirteen years of sustaining support

Over the life of the study, hundreds to thousands of research visits were conducted each year at as many as 32 worldwide study sites. This immense data collection effort has been funded by multiyear grants from the NIH as well as grants from the private HD research-funding CHDI, Inc. The term of the final NIH grant to fund the multisite, annual visit data collection ends on Aug. 31.

Paulsen, PREDICT-HD’s principal investigator, said she is very pleased with the support PREDICT-HD has received from the NIH over the years. “Studies come and go all the time, so in that respect, we’ve been very fortunate,” Paulsen said. “To have had the support of the NIH, CHDI and of our participants and collaborators for 13 years is really quite extraordinary.”

“There’s always more we want to learn about the earliest signs of HD and we intend to do so going forward. But if you had told me in the beginning we would’ve conducted a multisite study like this for 13 years, I would’ve been thrilled at that opportunity, as I am at the end of the multisite study this year.”

A collaboration of participants, families and researchers

Dating back to those early conversations Paulsen had with HD family members, PREDICT-HD has focused on its participants and their families, the people who make it what it is. If you thumb through the pages of the first PREDICT-HD participant newsletter, it is evident there. “Partnership among HD families and scientists has never been so critical,” the newsletter reads. “Today’s goals toward an improvement for HD require collaboration among scientists and family members.”

Though she has always believed in the HD community and their willingness to participate in research, Paulsen says having 500 people (the original PREDICT-HD participation goal) give up a day or two of work or travel many miles to take part in research seemed like a daunting prospect at times. However, participants from all walks of life signed up to be a part of the new study, and the original goal was tripled, with more than 1,500 participants over the life of the study.

“Our participants give their time, their energy, their effort and concentration, and provide biological samples like cerebral spinal fluid,” Paulsen said. “Without that aspect of selfless participation, we could assemble the most brilliant HD researchers in the world, and we wouldn’t get anywhere toward our goal of making a difference in the lives of people with HD. It’s really the participants that have taken this study to great heights.”

Furthermore, participants have
CONCLUDING continued from p.1

contributed by way of providing feedback that has helped the study evolve. Study tasks have been added or removed based on participants’ comments and suggestions. In 2011, a research participant came to study staff with the idea of making a video showing what a PREDICT-HD research visit is like. That participant later starred in the video that was filmed and posted on YouTube as a way to take the mystery out of participating in a study like PREDICT-HD. And at the 2013 Huntington’s Disease Society of America National Convention, study participants were at the PREDICT-HD booth to tell people what participating in the study was like.

And whenever participants have been asked to take part in a new aspect of the study like cerebral spinal fluid collection, Paulsen says they have been very willing to do whatever it takes to contribute further to HD research. “We are so appreciative of people’s willingness to take part in all the different things we ask of them as part of the study,” Paulsen said. “It’s heartening to us as researchers when people want to do whatever they can to contribute to the study.”

Impactful findings

Much more is known about the course of the disease in general and the prediagnosed “prodromal” phase of the disease as a result of PREDICT-HD findings. Numerous early signs of HD in the areas of brain imaging, cognition (thinking ability), psychiatric symptoms and movement symptoms have been identified, some occurring decades before a traditional motor diagnosis would be expected to occur. These early signs could also be outcome measures for therapeutic trials aimed at slowing or preventing HD, according to a review article about PREDICT-HD by Dr. Edward J. Wild and Dr. Sarah J. Tabrizi in *The Lancet Neurology* in 2006 (for recent results detailing potential outcome measures, see Page 3).

PREDICT-HD findings touch on a variety of topics beyond early disease signs. Results indicate cognitive reserve may delay the onset of changes in the brain caused by HD, and a separate report shows couples used positive coping strategies that they found to be effective in dealing and living with HD like acceptance and planning.

In total, over 90 medical journal articles have been published reporting findings from PREDICT-HD. But you won’t only find study results on journal pages. Findings have helped inform the Huntington’s Disease Society of America in its advocacy efforts to pass legislation to update outdated federal Social Security Administration definitions of HD and end waiting periods for deserved disability and Medicare benefits.

An ongoing effort

Though the multisite, large-scale data collection configuration of PREDICT-HD is concluding, several ancillary studies funded recently by the NIH are ongoing and will require smaller-scale data collection. Paulsen and her PREDICT-HD colleagues are also pursuing funding for additional HD research projects that would involve the HD community as participants, and more will likely be formulated as researchers continue to analyze the data collected in PREDICT-HD.

“With PREDICT-HD as it’s currently constituted concluding, our HD research continues,” Paulsen said. “With each new finding we report on, we’re moving closer to supporting the development of clinical trials in this early pre-motor diagnosis stage.”

As they have for the past 13 years, PREDICT-HD participants will continue to be a big part of that process. Whether they continue participating in current or future PREDICT-HD related studies, roll their participation into the new worldwide Enroll-HD study or whether their previously collected data continues to inform HD research around the world, Paulsen says their contributions have been (and will continue to be) significant and appreciated.

“I am very proud to call each of our participants partners in this effort to make a difference in the lives of those affected by HD,” Paulsen said. “We look forward to ongoing collaboration between researchers, participants and families to continue working toward this goal.”

---

Study visit amidst cross-country trip

*Erika Bjorklund* (left) combined HD involvement, volunteerism and fun in a whirlwind trip this summer. Pictured with her friend and PREDICT-HD research companion *Querida Bergevin* (right), Bjorklund traveled from Washington state to Louisville for the HDSA National Convention with her sister Melissa. After meeting up with Querida and stopping by Dollywood in Tennessee, the trio headed to Iowa City for Erika’s first PREDICT-HD visit. Thank you to Querida, Melissa and Erika for making PREDICT-HD part of your trip!
Beyond the call of duty for a cure

By Christina Colletta
Public Relations Assistant

Susan Reasor’s daily juggling act consists of being a stay-at-home mother to three active children and helping lead the Huntington's Disease Society of America (HDSA) Greater North Texas Affiliate as vice president and cofounder. She also brought HD research opportunities to others in her region, and is a PREDICT-HD participant.

Some would call Reasor supermom, while others know her as super-advocate for the HD community in Dallas.

“I think the most essential thing is building a community so everyone doesn’t feel alone, I think that cuts out the fear factor for a lot of people,” said Reasor.

A life-changing diagnosis

On June 14, 2011, Reasor’s father was diagnosed with Huntington disease.

“It was a hard hitter,” said Reasor. “Since we didn’t know we had a family history of Huntington disease and since there wasn’t an HDSA Center of Excellence in the Dallas region [where Reasor lives], we hadn’t been educated about genetic testing.”

Six months after her father was diagnosed, Reasor’s sister tested positive for HD.

Before undergoing testing, Reasor wanted to ensure she was prepared to deal with her results. After extensive counseling, she decided to get tested five hours away in Houston at the only HDSA Center of Excellence in the state.

In January of 2013, Reasor tested negative for Huntington disease.

Taking Action

After receiving her results and now knowing she would be helping others who hadn’t been as fortunate, Reasor was inspired to do everything in her power to help find a cure for HD.

“My test results really determined my place in the HD community,” Reasor said.

With a group of individuals in the Dallas area, Reasor helped form the HDSA Greater North Texas Affiliate. Then, at the 2013 HDSA National Convention in Jacksonville, Fla., Reasor was on the prowl for more opportunities to get involved when the PREDICT-HD booth caught her eye.

“I walked up and said, ‘Sign me up! Use my brain and spinal fluid for research, that’s why I’m here!’”

Inspired by her positive experience with PREDICT-HD, Reasor wanted to contribute more to HD research while helping others in Texas achieve the same sense of purpose she felt. Reasor arranged for research staff from the University of Iowa to meet with her support group members in their homes for the HDQLIFE study. The effort was beneficial to both participants and the research team's push to find more participants.

Driven to help find a cure for her HD gene positive father, sister and at-risk nephews and niece, Reasor is steadfastly committed to her mission.

“I will die fighting for a cure,” she said.

Study findings could lead to premanifest treatment trials

By Christina Colletta
Public Relations Assistant

Findings from PREDICT-HD could lead to the missing piece needed to determine whether treatments are effective at the time treatment matters most: early in the disease process.

It is known that changes due to HD begin in people many years prior to a motor diagnosis of the disease. Researchers believe this stage, also known as premanifest, is the most impactful time to try treating the disease, before symptoms begin to have a major impact. Clinical trials to test promising treatments have been limited due to a scarcity of proven outcome measures, which are tests involving human participants to determine whether or not a treatment is effective.

According to Jane S. Paulsen and coauthors of “Clinical and biomarker changes in premanifest Huntington disease show trial feasibility: a decade of the PREDICT-HD study” published in Frontiers in Aging Neuroscience in April 2014, 39 outcome measures were given annually from 2001 to 2012 in 1,013 participants with premanifest HD and 301 gene negative controls. Researchers grouped the gene-positive participants into Low, Medium, and High groups based on their CAP score, a calculation of how close a participant is to an estimated motor diagnosis based on age during the time of the study and their CAG repeat length. Those in the Low group were thought to be furthest from an estimated motor diagnosis.

Findings showed a distinguishable change over time in 36 of the 39 measures examined over the 10-year period. Specifically, outcome measures of imaging (brain volume), motor, cognition (thinking ability), and psychiatric symptoms of HD were thought to be among the strongest in all three premanifest categories.

With these outcome measures in place, the authors say clinical trials could be feasible in the Medium and High premanifest groups, meaning 7-12 years before diagnosis would be estimated to take place.

To read the article and an extended summary, visit www.predict-hd.net.
Study participation gives sense of purpose

Editor's note: After finding out she tested positive for HD, Kasci Brantley decided to take action and do something proactive by participating in PREDICT-HD, and sharing her story with her fellow participants and the general public. Read the full article at www.predict-hd.net.

By Kasci Brantley
PREDICT-HD Participant

About a year ago, I was a normal 25-year-old mother who didn’t know what Huntington disease was. I will never forget the day that all changed.

My husband David and I had just returned home from a trip. We carried our two sleeping babies, ages two and seven, into the house and tucked them into bed. That’s when I read a Facebook message from my biological sister, informing me that our biological father, who has never been an active part of my life, was diagnosed with HD.

I felt like the rug had been pulled out from under me. I Googled HD, and when I learned my children had a 50-50 chance of having the HD gene, it became like every parent’s worst nightmare. As a mother, I want to protect my sweet babies from everything that’s evil or harmful to them, but it broke my heart that I couldn’t protect them from this.

I immediately decided I wanted to get tested. Unfortunately, I couldn’t afford the testing procedure the Huntington’s Disease Society of America recommended, so I called my biological father’s neurologist and was shocked when he offered to do the testing for free.

When the call finally came from the neurologist’s office telling me to come in right away for my results, I knew it was bad news. Everyone close to me was busy that day, so I packed up my kids and we went alone.

When we walked into the doctor’s office, the nurse had tears in her eyes. I could tell it was bad news by the way she was acting, and then she hugged me and said that she was so sorry. I turned to walk down the hall to the exam room like nothing was wrong, not wanting to scare or worry my children.

The neurologist sat across from me at a loss for words, staring at me silently for what felt like forever. I imagine he was looking at how young I was and thinking he was about to say those tragic words that would change my life forever. I summoned up my courage and said, “I have it.” He was stunned for a moment and finally nodded his head as he answered, “Yes, I am afraid you do.” I am grateful the neurologist did the test for me for free, but I left there that day with a dark cloud over my life.

For about a month after that dreadful day, I was depressed. I cried a lot more than I would like to admit during that period. But one day, I decided I wasn’t going down without a fight. There are research groups who study Huntington disease and try to find a cure. I could help them! I could fight this horrific disease with them!

I reached out to the PREDICT-HD study, and University of Iowa study coordinator Bella De Soriano explained every detail of the study and how they use the information to find early predictors in people with HD. I was thrilled to finally feel like I was fighting back against the HD monster that was trying to take over my body.

The night before the study visit, I was so excited to get started with the study the next day. The following morning, we met Bella, who was just as sweet in person as she was on the phone and in emails. She reminded me that she wanted me to be completely happy and comfortable, and that I could back out at any time if I changed my mind. I assured her that I don’t have any other way to fight back against HD and I wasn’t backing down.

Bella led us through the various parts of the study over the next two days. She took great care of me and always had a smile on her face and a warm, loving nature. I was mostly afraid of the spinal tap, but was pleasantly surprised that it was just a little pressure and a small prick. Every person I came into contact with was incredibly kind and caring. I felt like part of their little “PREDICT-HD family.”

Doing the study gave me a sense of purpose. I haven’t felt depressed or sad one single time since. I enjoyed the trip; like a mini-vacation, except that I returned with a sense of purpose. I am helping in the fight against HD. I am helping fight for my future, my children’s future, and the future of everyone affected by this horrible disease. No one has to fight this alone.