Hope, Heroes and Science

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CHDI Management, Inc.
Where are we going?

- Talk about “hope”
- What we can learn from an English country doctor
- Who are the heroes and heroines of science?
- What is our challenge? Suggestions on how we can address the challenges...
- Come back to hope as a motivation to get involved... NOW
What is HOPE?

Hope, unlike optimism, is rooted in unalloyed reality....

Hope is the elevated feeling we experience when we see - in the mind’s eye- a path to a better future. Hope acknowledges the significant obstacles and deep pitfalls along that path.

True hope has no room for delusion.

J. Groopman, *The Anatomy of Hope*
Today’s Reality

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<th>Societal Realities</th>
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An Uncertain Future
What does our path to a better future look like?
A lesson from history...
The story of the British physician Edward Jenner

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Jenner’s Experiment

- Jenner was curious about the old wives’ tale that milkmaids could not get smallpox.
- A simple hypothesis: Infection with cowpox would give protection from smallpox.
“How do I test this hypothesis?”

Enter our heroes: James Phipps, Sarah Nelmes, and Blossom.
What do we learn from Jenner?

- Power of observation
- The need to test the hypothesis
- Importance of human participation
Let’s look at the heroes and heroines of our story:

- Jenner – courage to explore the observation that “milkmaids do not get smallpox”
- James Phipps
- Phipps’ parents
- Sarah Nelmes – the milkmaid (and Blossom the cow)
- The 23 people who participated in Jenner’s first “clinical trial” which led to publication of results in 1798.

... and in 1980 smallpox was declared eradicated by the WHO
Hope is a resource to generate action...

Science is the effort, based on discovery, whose aim is to increase human understanding of reality.

Research

Clinical Research

Clinical Trials

TREATMENTS

The Collaboration:

Patients & Families

Community Advocates

Researchers/Caregivers

Sponsors & Foundations
The Challenge

- Time is **not** on our side... and delays are common in our system.
- Less than 1% of the 1 million people with Parkinson's Disease participate in clinical trials\(^3\).
- About 5% of patients with cancer enroll in clinical trials.\(^2\)
- If just 10% of cancer patients participated in clinical trials; studies would be completed in one year instead of the current average 3-5 years.

- 50% of trial delays are due to poor recruitment\(^1\).
- 86% of all clinical trials in US fail to recruit on-time\(^1\).

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\(^1\) CenterWatch data  
\(^2\) Tufts Center for the Study of Drug Development  
\(^3\) PD Trials.org
The HD Landscape

**DIMOND**
A Multi-Center, Phase 2, Randomized, Double-Blinded, Placebo-Controlled Study of Dimebon in Subjects with Huntington Disease
17 Centers / 90 patients
5 pts per center over 8 months
0.6 pts/month

**DOMINO**
A Multi-Center, Double-Blind, Pilot Study of Minocycline in Huntington Disease
12 Centers / 114 subjects
9 pts per center over 16 months
0.6 pts/month

Assumptions:
12 centers / 110 pt. study
Comparing recruitment rates of 0.6 and 0.9 pts/month

**Patient Recruitment**
- 12 months
- 17 months

A small change in the recruitment rate can make a big difference!
Studies in Progress or Planning

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<td>2008</td>
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<td>2009</td>
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<td>2010</td>
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<td>Horizon (Dimebon) 350 pts</td>
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<td>CIT-HD (citalopram) 36 pts</td>
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<td>Memantine 60 pts</td>
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2,100+ participants
What can we do?

The Collaboration:

The Best Solution is a Shared Solution:

- Decrease clinical trial delays (e.g. recruitment, contracts, etc.)
- Support the patient registries (e.g. COHORT, REGISTRY)
- Improve access to clinical trials for patients and families
- Ensure quality data from well designed studies
- Education and outreach to the community

HDTrials.org
Some suggestions...

- **Clinical Trial Center Award for Performance and Care**
  - Awarded to centers for their efforts to improve patient care of people with HD through participation in clinical trials.
  - Recognize centers that use best practices in making studies more efficient, improve quality and provide a positive participant experience.

- **HDSA Clinical Trial Ambassadors**
  - An ambassador in every chapter who is a resource and advocate for clinical trial participation.
  - Trained and re-trained to bring reliable and accurate information and news to the community.
  - Know the centers in their area; a “voice” for participants and carers.

- **HDTrials.org**
  - Will serve as an important tool to match subjects with studies!
CHDI Discovery Pipeline

**Active Programs:**
- Energy Homeostasis
- Histone Deacetylases
- Htt Processing
- Modulation of Htt Levels
- Inflammation
- Neurotransmission
- Phosphodiesterases
- Protein Folding
- Transcriptional Dysregulation
- Trophic Factors

42 Projects
CHDI Discovery Pipeline - Highlights

- **HDAC4 – a clear priority**
  - Data for HDAC4 (+/-)-R6/2 genetic cross from Gill Bates are encouraging

- **Antisense Oligonucleotides (ASOs)**
  - Goal to nominate a set of lead ASOs for further pre-clinical testing by the end of the year.

- **PDE4 Modulators for Cognition(...and beyond?)**
  - Evaluation of the published literature on the potential pro-cognitive, neuroprotective, motor, and anti-inflammatory effects of these inhibitors has led to CHDIs interest in evaluating inhibitors for PDE4, PDE2, PDE1/5 and PDE10.
  - Currently evaluating a compound in our in vitro and in vivo assay platforms to assess the potential as an HD therapeutic.

- **MITO-HD**
  - Finding biomarkers for energy defects in HD
Hope begins in the dark, the stubborn hope that if you just show up and try to do the right thing, the dawn will come. You wait and watch and work: You don't give up.

Anne Lamott
Thank you

HD Patients and Families
HD Families who have participated in FuRST Focus Groups

CHDI Colleagues:
Robi Blumenstein
Dan van Kammen
Robert Pacifici
Beth Borowsky

LaVonne Goodman
Louise Vetter

Collaborators:
Ken Evans, OCBN
Anthony Vaccarino, OCBN
Marta Newby, UTSW