HD 101—2012

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Presenter Disclosures

Martha Nance

The following personal financial relationships with commercial interests relevant to this presentation existed during the past 12 months:

Lundbeck Advisory Board
Thank you to...

George Huntington

Nancy Wexler

Ira Shoulson
Clinical features of HD

- Clinical aspects
  - Movement disorder
    - Involuntary movements
    - Voluntary movements
  - Cognitive disorder
  - Emotional disorder
    - Wide range of symptoms
  - (weight loss)
Clinical features of HD

- Onset age
  - Average onset 35-50 years (range 2-90)
  - Average duration 15-20 years

- Prevalence 4-7/100,000
- ?30,000 affected in US
- 150,000+ at-risk
- Seen in all ethnic groups
  - ?higher incidence in Caucasians
Dominant inheritance

Each child of a person with HD has a 50% chance of developing HD.
What causes HD

- Caused by a mutation in the Huntingtin gene
- Type of mutation: “CAG repeat expansion”
  - 10-35 CAG repeats is normal
  - 36- above is not normal and can cause HD
- A blood test can “diagnose” HD
- Everyone with HD has a CAG repeat expansion in the HD gene
- CAG repeat expansions between 36-39 may not lead to symptoms within a normal lifespan
CAG repeats in a family

Normal repeat numbers don’t change much; abnormal repeat numbers tend to get bigger when passed from parent to child.
MRI Scans in HD

Normal Subject: Age 38

HD Subject: Age 31
**Care-defining characteristics of HD**

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
</table>
| Neurologic disease        | • Movement disorder  
                           | • Cognitive disorder  
                           | • Psychiatric disorder |
| Adult-onset disease       | • (usually mid-adulthood)  
                           | • (occasionally childhood or old age)                                      |
| Chronic disease           | • 15+ year course  
                           | • Degenerative, ultimately fatal                                           |
| Genetic disease           | • Autosomal dominant  
                           | • Family disease                                                          |
## Shoulson-Fahn Total Functional Capacity Scale

<table>
<thead>
<tr>
<th>Work</th>
<th>Money</th>
<th>Chores</th>
<th>ADLs</th>
<th>Residence</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 3-regular work</td>
<td>• 3-manages independently</td>
<td>• 2-full capacity</td>
<td>• 3-independent</td>
<td>• 2-home</td>
</tr>
<tr>
<td>• 2-difficulties</td>
<td>• 2-manages with help</td>
<td>• 1-impaired</td>
<td>• 2-needs some help</td>
<td>• 1-home with services</td>
</tr>
<tr>
<td>• 1-volunteer</td>
<td>• 1-makes simple purchase</td>
<td>• 0-unable</td>
<td>• 1-assists caregiver</td>
<td>• 0-long term care</td>
</tr>
<tr>
<td>• 0-none</td>
<td>• 0-unable</td>
<td></td>
<td>• 0-does not participate</td>
<td></td>
</tr>
</tbody>
</table>

Stage 1 (11-13)—work, relationships, diagnosis
Stage 2 (7-10)—diagnosis, driving, work, enjoyment
Stage 3 (3-6)—transition time: personal help needed
Stage 4 (1-2)—in-home help vs. nursing home
Stage 5 (0)—dignity in late stages; terminal/Hospice
Medications for HD

• Chorea
  – Neuroleptics (haloperidol, thiothixene, chlorpromazine)
  – Atypical neuroleptics (risperidone, olanzapine)
  – Tetrabenazine (FDA-approved for HD)
• Depression, anxiety, paranoia, explosive behavior, irritability, hallucinations
  – Many drugs
• Cognitive dysfunction
  – (Alzheimer’s drugs: donepezil, memantine, others)
• Weight loss
  – Eat!
### Vitamins (and other unproven treatments)

- **Probably won’t hurt, might help**
  - Multivitamin, B, E (<400 IU), Coenzyme Q10 (>1000mg—expensive), omega fatty acids, creatine
- **Probably won’t hurt, probably won’t help**
  - Blueberries in human doses, most nutraceuticals, blue-green algae, acai berries,…
- **I don’t know what it is or why it would help**
  - Mangosteen, vinpocetine, homeopathy, etc etc
- **Sure, why not?**
  - Yoga, massage, acupuncture (if appropriate symptoms), tai chi, “Eastern medicine” (done appropriately)
- **And there’s exercise, eat right, sleep right, avoid excess caffeine, nicotine, alcohol…**
Principles of management: team-based care

Neurologist or psychiatrist
Psychology, neuropsychology
PT, OT, speech
Nurse-case manager
Social worker
Genetic counselor
Dietitian

Chaplain
Medical doctor
Dentist
Research team
Nursing home staff
Lay group volunteers
HD care team

Patient Family

Research nurse
Dietitian
Speech therapist
Occupational therapist
Physical therapist
Neurologist/Psychiatrist
Neuropsychologist
Psychologist
Social worker
Genetic counselor

And: Students, Clinic staff, chaplain, Nurse coordinator, general practitioner, dentist
# Management of HD

<table>
<thead>
<tr>
<th>Health professional</th>
<th>Role in HD management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neurologist</td>
<td>Team leader, movement disorder, initiate referrals</td>
</tr>
<tr>
<td>Psychiatrist</td>
<td>Psychiatric/behavioral symptoms</td>
</tr>
<tr>
<td>Psychologist</td>
<td>Behavioral symptoms; family counseling</td>
</tr>
<tr>
<td>Neuropsychologist</td>
<td>Cognitive assessment and recommendations</td>
</tr>
<tr>
<td>Speech therapy</td>
<td>Assess, treat dysphagia, communication problems</td>
</tr>
<tr>
<td>Physical therapy</td>
<td>Gait disorder, assistive equipment, exercise program</td>
</tr>
<tr>
<td>Occupational therapy</td>
<td>Safety, functional assessment, equipment</td>
</tr>
<tr>
<td>Dietitian</td>
<td>Healthy eating; altered food textures; high calorie foods</td>
</tr>
<tr>
<td>Social worker</td>
<td>Identify community resources; assist with legal, financial issues</td>
</tr>
</tbody>
</table>
Management of JHD

<table>
<thead>
<tr>
<th>Type of professional</th>
<th>Role in HD management</th>
</tr>
</thead>
<tbody>
<tr>
<td>General practitioner</td>
<td>General, age-appropriate care</td>
</tr>
<tr>
<td>Dentist</td>
<td>Age-appropriate care</td>
</tr>
<tr>
<td>Lay organization</td>
<td>Support for patient and family</td>
</tr>
</tbody>
</table>
Centers of Excellence

- Designated by HDSA
- 21 Centers throughout the country with special expertise in HD
- COEs have multidisciplinary care, support services, research
- Excellent care can also be found outside of COEs
Principles of care

- Never "nothing I can do"
- Care from beginning to end
- Support and education
- Proactive care
- Nobody can "do HD" alone
You are not alone…

- Care
- Family support
- Genetic testing
- Advocacy
- Fundraising
- Research
- Community
## Developing a new drug

<table>
<thead>
<tr>
<th>Phase</th>
<th>Preclinical</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lab/animal</td>
<td>Lab/animal</td>
<td>Early clinical, safety testing</td>
<td>Patient safety testing</td>
<td>Efficacy, Safety</td>
</tr>
<tr>
<td>No humans</td>
<td>No humans</td>
<td>Small number healthy subjects</td>
<td>Multiple studies, small to moderate # of subjects with disease</td>
<td>Large # of subjects with disease</td>
</tr>
<tr>
<td>10-20 years</td>
<td>3-5 years</td>
<td>3-5 years</td>
<td>2-5 years</td>
<td></td>
</tr>
</tbody>
</table>

New drug application FDA review Approval
Kinds of clinical research

**Type**
- Observational
- Interventional

**Size**
- Small-scale
- Large-scale

**Duration**
- Brief
- Long-term

**Sponsorship**
- Government/nonprofit
- Pharmaceutical/for profit
Target Enrollment of Studies in Progress or Planning

<table>
<thead>
<tr>
<th>Year</th>
<th>Study</th>
<th>Participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>2008</td>
<td>CREST-E (Creatine)</td>
<td>650 pts</td>
</tr>
<tr>
<td>2009</td>
<td>2CARE (Co-Q)</td>
<td>680 pts</td>
</tr>
<tr>
<td>2010</td>
<td>PREQUEL (Co-Q)</td>
<td>90 pts</td>
</tr>
<tr>
<td>2011</td>
<td>PREDICT 2.0 (1,000 +)</td>
<td></td>
</tr>
<tr>
<td>2012</td>
<td>CAB Beta Study (250)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>REACH 2HD (100)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ENROLL (30,000+)</td>
<td></td>
</tr>
</tbody>
</table>

Thousands of trial participants are needed!
RESOURCES

• Huntington’s Disease Society of America
  http://www.hdsa.org/research/clinical-trials.html
• Huntington Study Group (HSG)
  www.huntington-study-group.org
• HD Trials
  www.hdtrials.org
• National Institutes of Health (NIH)
  www.Clinicaltrials.gov
• Centerwatch Listing Service
  (617-856-5900) or www.CenterWatch.com
Other Good On-line Resources

• CHDI
• HD Youth Organization
• European HD Network
• Stanford Hopes
• Genetests.org