LIVING WITH HUNTINGTON’S DISEASE
Overview

- History
- Background
- Genetics
- Diagnosis
- Treatment
- Resources

History

- 1872 - George Huntington described a family from Long Island in his first paper "On Chorea"
- 1908 – William Osler said of this paper: "In the history of medicine, there are few instances in which a disease has been more accurately, more graphically or more briefly described."
- 1993 – Huntington gene was identified, located on short arm of chromosome 4
Epidemiology

- The frequency of HD in different countries varies greatly
- Occurs in ~ 1/10,000 people in US
- Higher prevalence
  - Lake Maracaibo region in Venezuela
  - The island of Mauritius off the South African coast
  - Tasmania

Background

- Huntington's disease is a inherited, degenerative brain disorder
  - Movement
  - Cognition (Thinking, memory etc)
  - Behavior
- Caused by a genetic defect resulting in the loss of cells in a part of the brain called the basal ganglia
- Symptoms onset bw ages 30-50
- Disease duration ~ 20 years

Phillips et al. 2008
Genetics - How do you get HD?

- All people have the Huntingtin gene
  - Gene is made up of a stretch of genetic material (CAG repeats)
- When the length of this repeated section reaches a certain threshold, it produces an abnormal or "mutant" huntingtin protein

<table>
<thead>
<tr>
<th># CAG repeats</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;36</td>
<td>Unaffected</td>
</tr>
<tr>
<td>36-40</td>
<td>Intermediate +/- symptoms</td>
</tr>
<tr>
<td>&gt;40</td>
<td>HD symptomatic</td>
</tr>
</tbody>
</table>

- Number of CAG repeats inversely correlates with disease onset
  - More repeats = Earlier onset
  - Fewer repeats = Later onset

Phillips et al. 2008

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Genetics – continued

- Autosomal dominant inheritance
  - Mutation is passed from parent to child
  - Each child has a 50% chance of inheriting the gene
- Almost always a family member with disease
  - 10% of HD pts have a (-) family hx
  - Adoption, early death, etc
- Those who inherit the gene will eventually develop the disease
- Those who do not inherit the gene are not at risk
- Must be born with the gene in order to develop this disease

Phillips et al. 2008
Diagnosis

- Clinical
  - Based on thorough history and physical exam findings

- Individuals with a typical clinical exam and genetically confirmed family history
  - Do NOT need genetic testing for dx

HD – Imaging

Phillips et al. 2008
Genetic testing

- Readily available blood test
- Should be performed under 3 circumstances
  1. To confirm diagnosis, if family history is unclear
  2. “At risk” or unaffected individuals
  3. At risk individuals wishing to conceive a child
     ○ “prenatal” or “pre-implantation” genetic testing
- Testing does NOT predict exact age of onset or severity of the disease progression
- Despite the availability of pre-symptomatic testing, only 5-10% of those at risk of inheriting HD choose to do so

Phillips et al. 2008

Genetic Counseling

- HD affects everyone in the family
- Counseling of “at risk” individuals is needed before proceeding with DNA testing
- Advice on the implications of a confirmed diagnosis
  ○ Impact on an individual's psychology, career, family planning decisions, relatives and relationships

Phillips et al. 2008
Clinical features of HD

- **Movements**
- **Behavior/Psychiatric**
- **Cognition**

**HD – Movement disorder**

- **Chorea**
  - Greek *choreia* – “dance”
  - Involuntary movements occur at rest and increases with distraction
  - Resolves during sleep
  - Typically starts in distal extremities (fingers, toes) and facial muscles
  - “Restlessness, fidgeting, twitching”
  - Individuals are often unaware of movements
- **Motor impersistance**
  - Inability to maintain an ongoing activity
  - Ex: Holding tongue out, maintaining grip (“milkmaid grip”)
- **Eye movement abnormalities**
Over time, movements progress to involve more proximal muscles (neck, trunk, arms/legs)
Choreic movements become constant and interfere with walking
Talking and swallowing become more problematic as the disease progresses
   - Choking, aspiration
In late stages
   - Movements gradually change from HYPERkinetic to HYPOkinetic
     - Slow and rigid
     - Severe dysarthria/anarthria
   - Gait instability and frequent falls

Roos et al. 2010

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**HD – Behavior & Psychiatric sx**

**Behavior**
- Personality changes may be the earliest sign, often occur prior to onset of motor symptoms
  - Apathy
    - Diminished concern for things you used to care about
    - Lack of initiation of activities, conversations etc
  - Irritability, aggression
  - Rigid thinking
  - Impulsivity

Phillips et al. 2008
**HD – Behavior & Psychiatric sx**

- **Psychiatric**
  - Anxiety ~ 34-61%
  - Depression ~ 40%
    - Suicidality
      - 8 – 17 times more common than in general population
      - Risk highest at time of diagnosis and when sx interfere with independence
  - Behavioral and psychiatric symptoms do not necessarily progress like motor symptoms but rather fluctuate over time

- Phillips et al. 2008

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**HD – Cognition dysfunction**

- Subtle changes occur early, often before motor symptoms occur
  - “Executive dysfunction”
    - Poor planning & organization
    - Difficulty setting priorities, problem solving
    - Poor judgment
  - As disease progresses, individuals with HD will develop “dementia”
  - Impaired insight

- Phillips et al. 2008
Not all dementia is Alzheimer’s

- **AD**
  - Primary memory problem
  - Unable to learn and store new information
  - Unable to freely recall memory

- **HD**
  - Executive dysfunction
  - Slow to process but usually accurate
  - Slow to learn but able to do so
  - Free recall of memory slow but can answer with choices
    - Give cues

Stages of HD

- **Early**
  - Chorea most prominent
  - Cognitive and behavioral sx affecting employment and relationships
  - Independent in ADL

- **Middle**
  - Obvious involuntary movements impairing walking
  - Speech and swallowing begin to be affected
  - Thinking and planning more impaired, no longer able to hold a job
  - Partial dependence

- **Late**
  - Severe movements now become more rigid → unable to walk or speak
  - Complete physical dependence → Nursing home or hospice care
Treatment

- Mutidisciplinary Team Approach
  - Movement Disorders Neurologist
  - Psychiatrists
  - Nurses, social workers, dieticians
  - Therapists (PT/OT)

- Treatment aimed at treating symptoms to improve quality of life
  - Movements/Chorea
  - Cognitive dysfunction
  - Behavior/Psychiatric

Pharmacologic treatment

<table>
<thead>
<tr>
<th>Drug</th>
<th>Mechanism of action</th>
<th>Indications</th>
<th>Side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Levodopa</td>
<td>Block vesicular monoamine transporter, inhibiting uptake of monoamines into synaptic vesicles; also blocks postsynaptic dopamine receptors</td>
<td>Hyperkinetic movement disorders</td>
<td>Dyskinesias, Parkinsonism (around 20%), depression, anxiety, acute dystonia, rarely confusion, autonomic dysreactions, hallucinations. No NAs for postural hypokinetic, but cerebrovascular malignant syndrome has been reported.</td>
</tr>
<tr>
<td>Progressine</td>
<td>Sympathetic (Sy) antagonist</td>
<td>Hyperkinetic movement disorders</td>
<td>Postural QP interval, postural hypotension, Parkinsonism, tremor, dyskinesia, Parkinsonism (similar to postural), etc.</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>Sympathetic (Sy) antagonist</td>
<td>Hyperkinetic movement disorders</td>
<td>Postural QP interval, postural hypotension, Parkinsonism, tremor, dyskinesia, etc.</td>
</tr>
<tr>
<td>Clonazepam</td>
<td>Selective serotonin reuptake inhibitor (SSRI)</td>
<td>Depression</td>
<td>Cognitive dysfunction, serum, hypothermia, dementia, syndrome of inappropriate antidiuresis (SIADH), postural hypotension, confusion, etc.</td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>SSRI</td>
<td>Depression</td>
<td>Cognitive dysfunction, syndrome of inappropriate antidiuresis (SIADH), postural hypotension, confusion, etc.</td>
</tr>
<tr>
<td>Methocarbamol</td>
<td>Prexypaginic (Sy) antagonist, increases central monoamine and serotonin function</td>
<td>Depression, weight loss</td>
<td>Cognitive dysfunction, syndrome of inappropriate antidiuresis (SIADH), postural hypotension, confusion, etc.</td>
</tr>
<tr>
<td>Sodium valproate</td>
<td>Antiepileptic, anticonvulsant, and X-linked sodium channel and potassium channel conductance</td>
<td>Mood swings</td>
<td>Sodium valproate, sedation, muscle cramps, migraine, cognitive dysfunction, etc.</td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>Inhibition of voltage-gated sodium channels. Anticonvulsant activity, and GABA-A receptor conductance</td>
<td>Mood swings, weight loss</td>
<td>Sodium valproate, sedation, muscle cramps, migraine, cognitive dysfunction, etc.</td>
</tr>
<tr>
<td>Lamotrigine</td>
<td>Inhibition of voltage-gated sodium channels. Anticonvulsant activity, and NMDA receptor conductance</td>
<td>Mood swings</td>
<td>Sodium valproate, sedation, muscle cramps, migraine, cognitive dysfunction, etc.</td>
</tr>
</tbody>
</table>
Treatment - Movements

- Anti-dopaminergic therapy
  - Dopamine blockers (neuroleptics)
    - Typical antipsychotics
      - Ex: haloperidol, fluphenazine, thioridazine
      - Undesirable side effects
      - Potential to cause other movement disorders
    - “Atypical” antipsychotics
      - Ex: Risperidone, Olanzapine
  - Dopamine depleting drugs
    - Ex: tetrabenazine

Tx – movements continued

- Atypical antipsychotics
  - Side effects:
    - Prolonged QT interval, postural hypotension, tardive dyskinesia, parkinsonism
- Tetrabenazine
  - Side effects
    - Drowsiness, depression, parkinsonism
- Other drugs
  - Remacemide
  - Riluzole
  - Amantadine

Phillips et al. 2008
Tx – Cognitive dysfunction

- Acetylcholinesterase inhibitors (Donepezil/Aricept)
  - Not beneficial in HD

Tx – behavior / psychiatric sx

- Behavioral modification
- Pharmacologic therapy
  - Depression:
    - Mirtazapine, fluoxetine, citalopram
    - Mood stabilizers (carbamazepine, laotrigine, valproate)
    - ECT
  - Aggression
    - Citalopram, sertraline, propranolol, antipsychotics

Phillips et al. 2008
Nonpharmacologic treatment

Tips for caregivers
- Communication
- Swallowing/Eating/Nutrition
- Behavior
- Bathing
- Sleeping

Communication

- Ability to organize thoughts and present them in an orderly way is compromised
- Speech may vary in volume, be interrupted by grunting sounds and hard to understand
- Patients can use nonverbal communication like anger, withdrawal or short temper
- Tips: It is important to remember that although individuals with HD might not be able to speak, they may still understand you and what is going on around them
  - Be calm, gentle and matter-of-fact
  - Use short sentences
  - Ask questions with yes/no answers
  - Give choices (one or two)
  - Allow time
Nutrition & Swallowing

- Meal time can be difficult
  - People with HD often complain of constantly being hungry
    - Stuffing food in mouth
  - Difficulty coordinating movements needed to bite, chew and swallow
- Serious risk of aspiration
- Risk of malnutrition bc of increased energy expenditure
- Tips: Preventing weight loss
  - Patients often require bw 3500-5000 calories/day
  - Consider giving double and triple portions
  - Supplement meals with high calorie foods and drinks

Swallowing Problems “dysphagia”

- Tips: Reduce risk of aspiration
  - Minimize distractions
  - Sit up right during meal with chin tucked down
  - Remain upright for 30-45 minutes after the meal
  - Double swallow between bites
  - Thicker and colder liquids are better
  - Small bites and sips
- As swallowing becomes more impaired, may not get adequate nutrition by mouth
  - Feeding tube (PEG tube, G-tube) needs to be discussed
Behavioral Problems

- **Tips:** Remember that the patient is NOT deliberately trying to be difficult. The problem is occurring because of changes in his/her brain.
- Establish a routine
- Simplify the environment & remove distractions
- Limit number of activities to one at a time
- Keep number of people in a room at a minimum
- Avoid busy and noisy settings

Behavior – Apathy

- **Tips:** Do not mistake apathy for laziness
  - Remember, individuals with HD have difficulty initiating activities
  - Encourage participation
Bathing

- Many people with HD are reluctant to bathe in a tub or shower
- The individual with HD has to focus on maintaining balance, unfamiliar caregiver, modesty

**Tips:**
- Keep shower time as short as possible
- Use a chair, hand held shower head, bath mits
- Minimize unfamiliar caregivers

Sleep Problems

- Maintain a regular schedule
- Bedroom should be cool, quiet and dark at night, full of light during the daytime
- Avoid excessive napping in early evening
Summary - What can we do?

- People with HD are NOT intentionally trying to be difficult
  - Minimizing Distractions
    - Patients have difficulty organizing and prioritizing information
    - When they are over stimulated, may respond with frustration or anger
    - Very important during meal time
  - Safety
    - Task may become dangerous as the patient loses control over emotions, motor skills and judgment
    - Modify activity rather than completely restrict
  - Identity/Individuality
    - Surrounding patients by the things they most enjoy
    - Videos, pictures, pillows, blankets, books on tape

Resources
Resources – patients and caregiver (HDSA)

Resources – Physicians (HDSA)
HD clinical trials

Welcome to HDTrials.org

There is hope on the horizon for people with Huntington's Disease. There are many Clinical Studies underway, and a number of potential therapies may move into Clinical Trial phases in the very near future. Volunteers are needed for ongoing trials and many more will be needed for future trials.

HDTrials.org has been created to enable clinical trial participation, the HDTrials.org website will provide guidance, notification to Huntington families of opportunities for participation in clinical trials and studies through a confidential email list.