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HDSA encourages all attendees to consult with their primary care provider, neurologist or other healthcare provider about any advice, exercise, medication, treatment, nutritional supplement or regimen that may have been mentioned as part of any presentation.
Presenter Disclosures

Holly Shill

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

No relationships to disclose or list
History

- 1872- “On Chorea” by George Huntington
  - clinical symptoms
  - hereditary nature of the disease
- 1955- Lake Marachaibo, Venezuela
  - Americo Negrette
- 1967- Woody Guthrie dies of HD
  - HDSA
- 1981- Wexler begins field work in Venezuela
- 1983- Gene located - chromosome 4p16.3
Genetics

- Autosomal dominant
- Each child has 50% chance inheritance
- CAG repeat or expansion
- Excessive glutamine in Huntington protein
- Normal  CAG 10-35
- Borderline CAG 27-35
  - may expand if passed by male
- Low abnormal CAG 35-39
  - may develop disease
- Abnormal CAG >40
  - will develop disease
Other genetic concepts

- CAG repeats correlate with age of onset
- CAG repeats may expand
  - Paternal transmission
- Absent family history
  - 2-5%
    - Non-paternity, new mutation
- Diagnostic testing
  - Patient has symptoms
- Predictive testing
  - AHSC, Tucson
Pathology

- Basal ganglia
  - Caudate > putamen
- Loss of GABA
- Increases in dopamine/adrenalin
- NMDA increased “excitotoxicity”
- Mitochondrial inhibitors (3-NP)
  - Animal model
Course and Prognosis

• Average age onset = 40 years
  – 10% <20, 10% >60
• Average survival 15-20 years although varies
• Initially, mood changes and subtle cognitive issues
• Chorea more prominent in middle stages
• Advanced stages with dementia and parkinsonism
Clinical Features

• Motor symptoms
• Cognitive symptoms
• Behavioral symptoms
• Psychiatric symptoms
Chorea

- Restlessness
- “piano playing” fingers; “milkmaid’s grip”
- Can be suppressed
- Increased with stress or paying attention
- Ranges from not interfering to incapable of walking, speaking or eating
Chorea

• Treatment:
  – When socially or physically disabling

• Medications:
  – Dopamine reuptake inhibitors (tetrabenazine)
  – Dopamine blocking drugs (haloperidol)
  – Muscle relaxants (diazepam)
Incoordination

- Motor sequencing - fine motor
- Bradykinesia - slow movements
- Dysarthria/Dysphagia - speech/swallow
- Gait instability and falls
- Leading cause of nursing home placement
- More difficult to treat
  - PT/OT/ST
Cognition

- Subcortical dementia
- Different from Alzheimer’s disease (cortical)
- Testable by neuropsychological tests of memory, language ability, visual spatial skills, attention and concentration, and judgment
<table>
<thead>
<tr>
<th>Ability</th>
<th>Speed of processing</th>
<th>Speech output</th>
<th>Learning new information</th>
<th>Free recall of memory</th>
<th>Motor memory</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alzheimer’s Disease</td>
<td>Slow, often inaccurate</td>
<td>Normal in clarity and rate; often the incorrect word</td>
<td>Rapid forgetting, defective storage of information</td>
<td>Impaired: memory store is defective; cannot recognize, cues don’t help</td>
<td>Intact: can learn and retain motor memories</td>
</tr>
<tr>
<td>Huntington’s Disease</td>
<td>Slow, but relatively accurate</td>
<td>Slurred and slow, but accurate</td>
<td>Disorganized and slow, but can learn</td>
<td>Impaired: cannot find the right word; can recognize with choices, benefits from cues</td>
<td>Impaired: cannot learn or recall motor memories</td>
</tr>
</tbody>
</table>

Personality

- Suspicious
- Aggression/Irritable
- Eccentric
- Untidy
- Excessively religious
- False sense of superiority
- Impulsive
- Sedentary
Behavior

• Outbursts of temper
  – Hunger, thirst, pain, inability to communicate, frustration with failing abilities, boredom, changes in routine

• Fits of despondency

• Jealousy

• Sexual promiscuity/Paraphilias
  – (voyeurism, exhibitionism)

• Alcoholism
  – 17% in males
  – 6% in females

• Smoking
  – Cardiovascular mortality high
Behavior

• Divorce
  – No good studies
  – Experience suggests it is more common
• Decreased ability to manage household
• Work performance
• Jail
• Total functional capacity (work, home, self-care)
Psychiatric issues

- Mood disturbances
  - Depression
  - Anxiety
  - Mania
- OCD
  - Mild obsessiveness can be seen
- Psychosis
  - Hallucination rare
  - Delusion more common but still rare
Depression

- Studies suggest about 40% of the 40% meet criteria for MD
- 22% of the 40% meet criteria for MD
- Not correlated with disease severity
- Can predate HD by years in "at risk" population but can occur at any stage of the disease
- Apathy in NOT depression
- Treat if necessary
- Suicidal attempt 7.3%-12%, greater than average risk
Anxiety/OCD

- Anxiety
  - Excessive worry
  - Irritability
  - Poor sleep
  - Can respond to treatment

- OCD
  - SSRIs
  - Psychotherapy is difficult
Mania

- Small number of patients 4.8-10%
- Presents with
  - Elevated or irritable mood
  - Grandiosity
  - Impulsivity
- May be confused with bipolar illness
- Treatment: Avoid lithium, use valproate or carbamazepine
Disease modification

- Studied, not helpful
  - Remacemide
  - Riluzole
  - Ethyl-EPA
- Still of interest
  - Creatine
  - CoQ10
- Promising?
  - Stem cells
  - Antidepressants, tiagabine, rosiglitazone
  - Specific mitochondrial agents
Living with HD

- Address genetic issues
- Family planning, discrimination
- Address social issues
- Disability, living arrangements, EOL, POA
- Address neuropsychiatric issues
- Mobility aspects
- Participate in research
- Local support groups/community outreach
- Quality of life!
Thanks!

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