HD 101

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Huntington's Disease Society of America

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Presenter Disclosures

Holly Shill

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

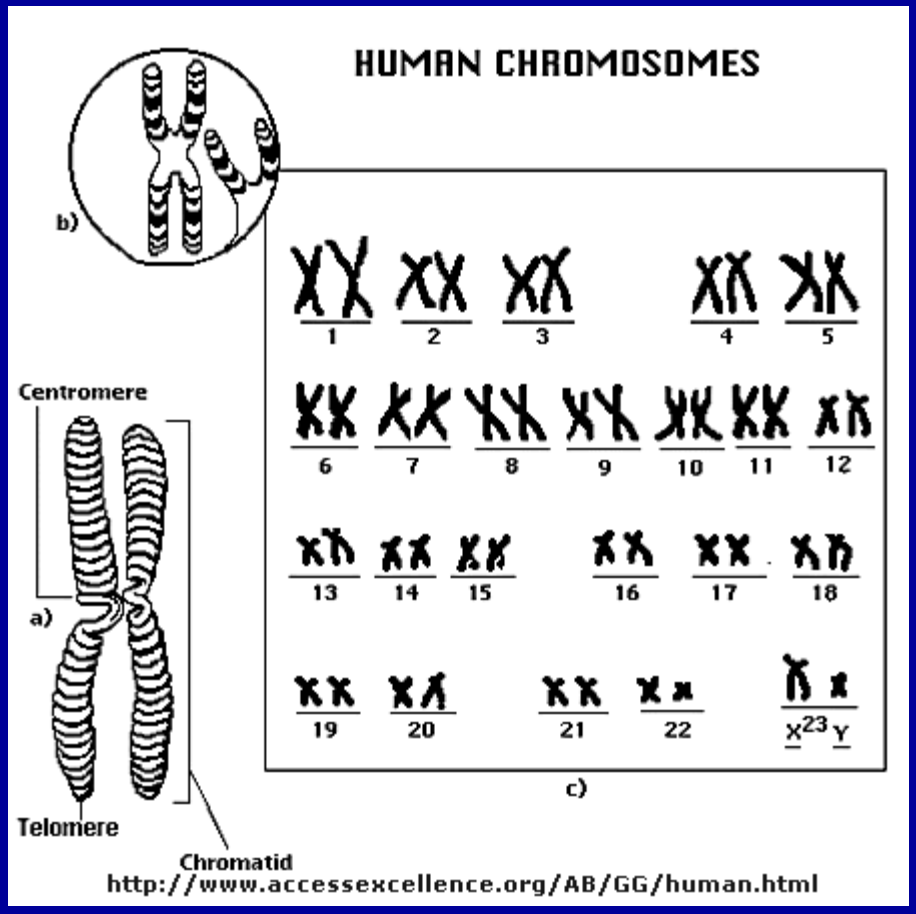
No relationships to disclose
or list

Huntington's Disease Society of America

History

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

Genetics


HUMAN CHROMOSOMES
b)
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Centromere
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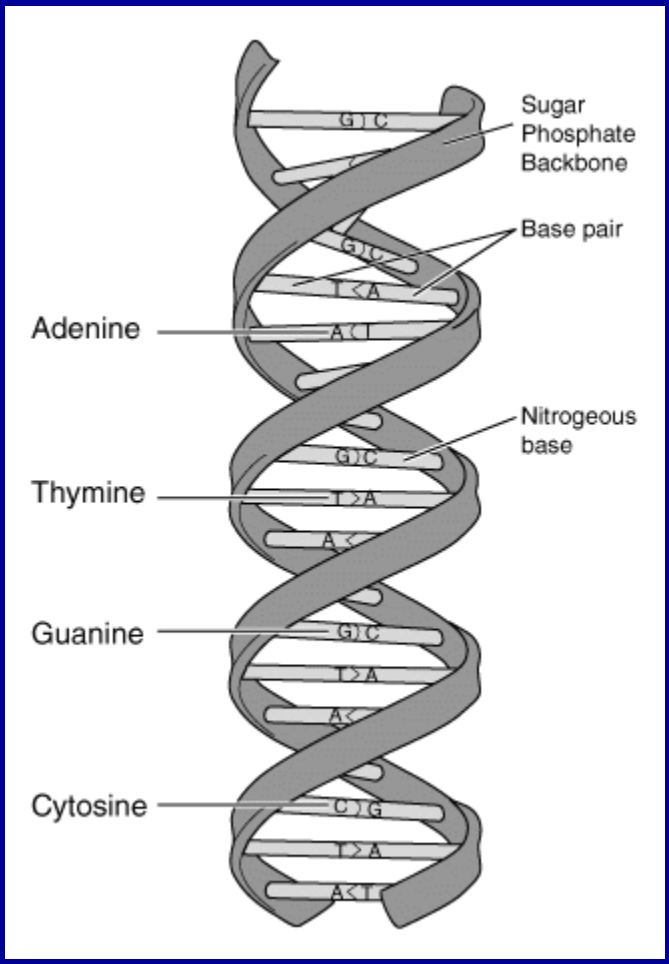
Telomere
Chromatid
http://www.accessexcellence.org/AB/GG/human.html


Sugar
Phosphate
Backbone
Base pair
Adenine
Nitrogeous
base
Thymine
Guanine
Cytosine

Genetics

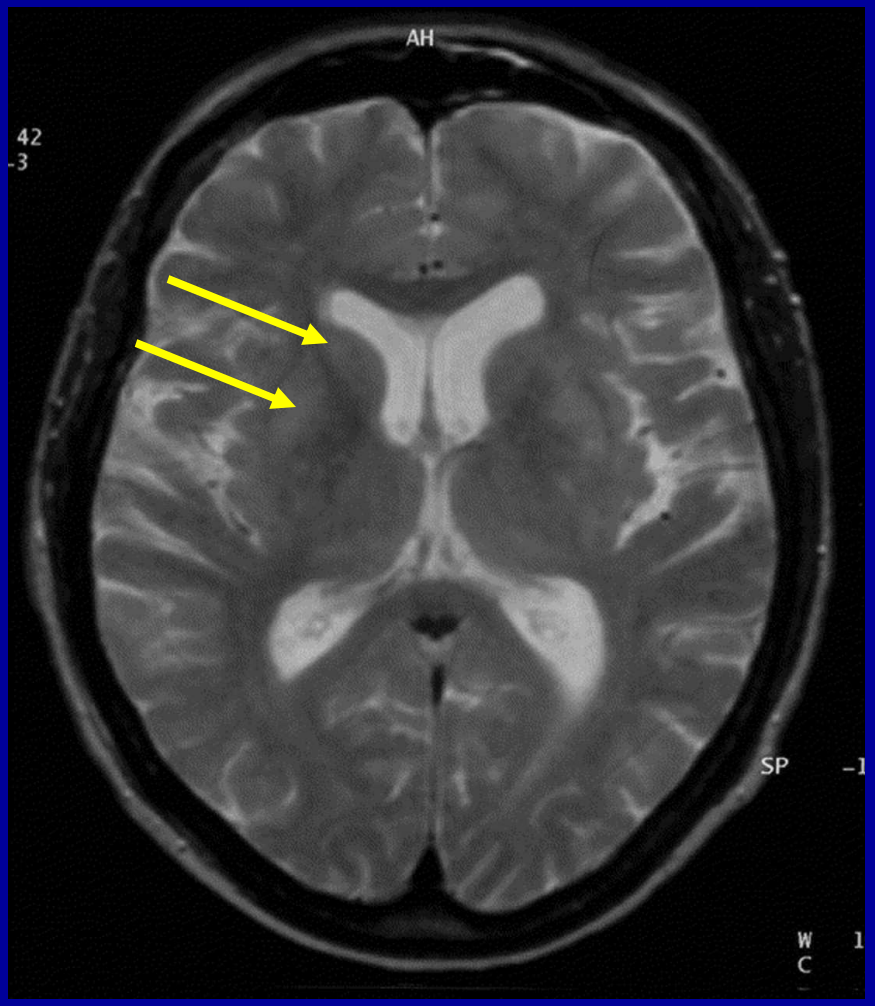
- Autosomal dominant
- Each child has 50% chance inheritance
- CAG repeat or expansion
- Excessive glutamine in Huntington protein
- Normal CAG 10-35
- Borderline CAG 27-35
  - may expand if passed by male
- Low abnormal CAG 35-39
  - may develop disease
- Abnormal CAG >40
  - will develop disease

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

Ability	Huntington's Disease	Alzheimer Disease
Speed of processing	Slow, but relatively accurate	Slow, often inaccurate
Speech output	Slurred and slow, but accurate	Normal in clarity and rate; often the incorrect word
Learning new information	Disorganized and slow, but can learn	Rapid forgetting, defective storage of information
Free recall of memory	Impaired: cannot find the right word;...can recognize with choices, benefits from cues	Impaired: memory store is defective; ....cannot recognize, cues don't help
Motor memory	Impaired: cannot learn or recall motor memories	Intact: can learn and retain motor memories

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 obessiveness can be seen
- Psychosis
  - Hallucination rare
  - Delusion more common but still rare

Depression

- Depression
  - Studies suggest about 40%
  - 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, rosaglitazone
  - Specific mitochondrial agents

Living with HD

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

Thanks!

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