Huntington's Disease Society of America

The information provided by speakers in workshops, forums, sharing/networking sessions and any other educational presentation made as part of the 2008 HDSA convention program is for informational use only.

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.

The Neuroscience Institute
University Hospital • Cincinnati, Ohio
University of Cincinnati College of Medicine

Huntington's Disease: Juvenile Onset

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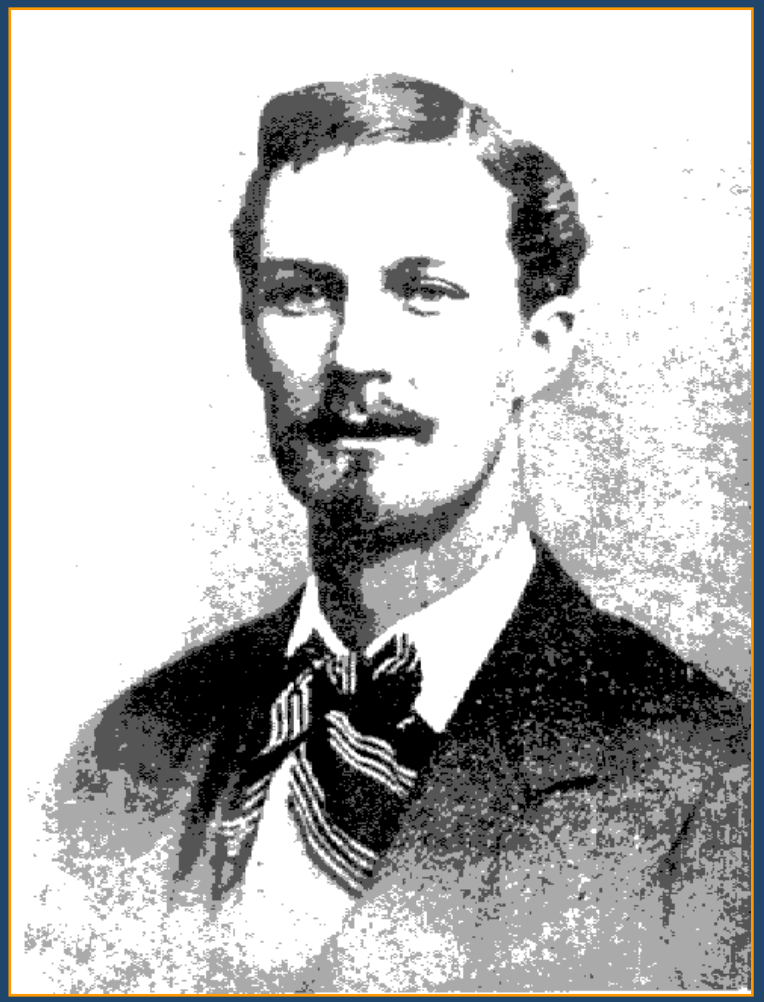
HDSA Convention
Pittsburgh, PA: June 5th, 2008

History

- Described in 1872
- George Huntington



“if by chance these children go through life without it, the thread is broken and the children and grand-children of the original shakers may rest assured that they are free from the disease”

- George Huntington

Lay Organizations

HD COMMITTEE TO COMBAT HUNTINGTON'S DISEASE, INC.
Suite 1804 · 250 West 57 Street · New York, N.Y. 10019

NEWSLETTER

NUMBER 1 — ©1968, Committee to Combat Huntington's Disease, Inc. — SPRING 1968

Purposes of the Committee to Combat Huntington's Disease, Inc.

The Committee's Charter contains a statement of the purposes for which the Committee was organized. Briefly, these purposes are:

Educational. To collect information about all aspects of Huntington's disease and distribute it to professionals, individuals, and the general public for the purpose of increasing public awareness."

Assistance. "To assist those afflicted with Huntington's disease and their families in meeting the social, economic, and emotional problems resulting from such affliction."

Research. The Committee will raise funds to help support the advancement of the day-to-day work of the Committee to Combat Huntington's Disease, Inc. is carried out by six operating committees working within the framework of the larger organization. Any member who wishes to join the operating committee whose work interests him most. These committees are:

Financial Committee. Responsible for fund-raising activities and for disposition of the funds that are raised.

Membership Committee. Solicits all members of the Committee; eventually, this committee will be instrumental in encouraging other groups interested in Huntington's disease to form with which to initiate local organizations.

Administrative Committee. Works with the Executive Secretary to coordinate various daily activities of the Committee.

Family Counseling Committee. Helps to determine the needs of families involved in Huntington's disease, and plans action to aid these families and individuals.

Publications and Publicity Committee. Prepares the newsletter and other publications; makes sure that the work of the Committee receives coverage in newspapers, magazines, etc.

Program Committee. Plans general meetings of interest; makes arrangements such as speakers, etc.

Woody Guthrie

Maracaibo, Venezuela

US Venezuela Project

Huntington's Disease - Symptoms

- Motor abnormalities (movement disorder)
- Dementia
- Psychiatric disorder/Personality change

Motor Abnormalities

- Chorea
- Dystonia
- Parkinsonism
  - Bradykinesia
  - Rigidity
  - Postural instability

Clinical Manifestations

- Dysarthria/Dysphagia
- Oculomotor abnormalities
  - Blink to break fixation
  - Slowed volitional saccades
  - Jerky smooth pursuits

Cognitive Problems

- Bradyphrenia
- Dementia
- Executive functioning abnormalities
  - Planning
  - Sequencing problems

Behavioral Problems

- Depression
  - 30 - 50%
  - Increased suicide risk
- Psychosis
  - 10% lifetime risk
- Personality changes
  - Irritability, apathy, etc

Natural History of HD

- Onset
  - Mean age at onset: 39 yrs
  - Range: 2 - 80 yrs
- Duration
  - Mean survival: 19 yrs
  - Typical range: 15 - 25 yrs

Juvenile Onset

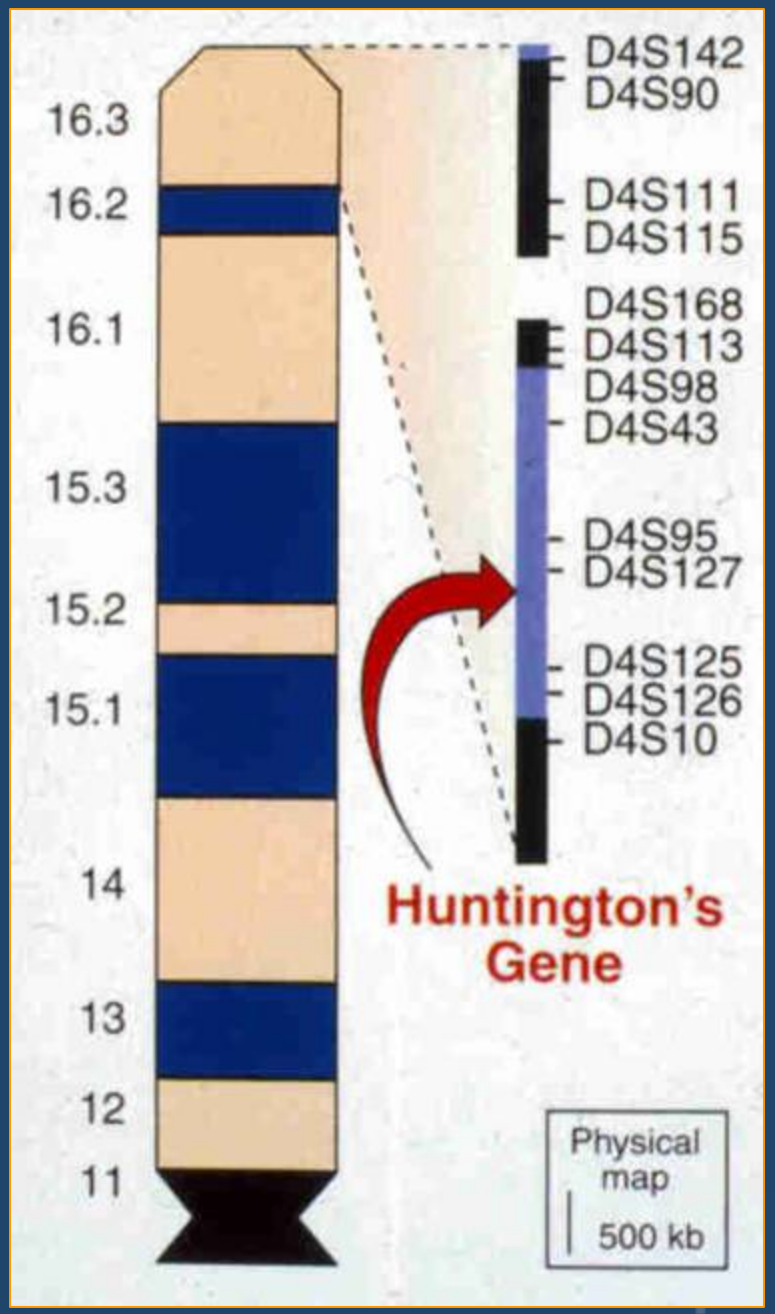
- Definition
  - Age at onset 20 y/o or earlier
- Frequency: 5 to 7% of HD cases
- Inheritance
  - 80% - 90% paternal inheritance
  - Usually >60 CAG repeats
- Clinical Manifestations
  - Dystonia
  - Bradykinesia
  - Rigidity

Genetics

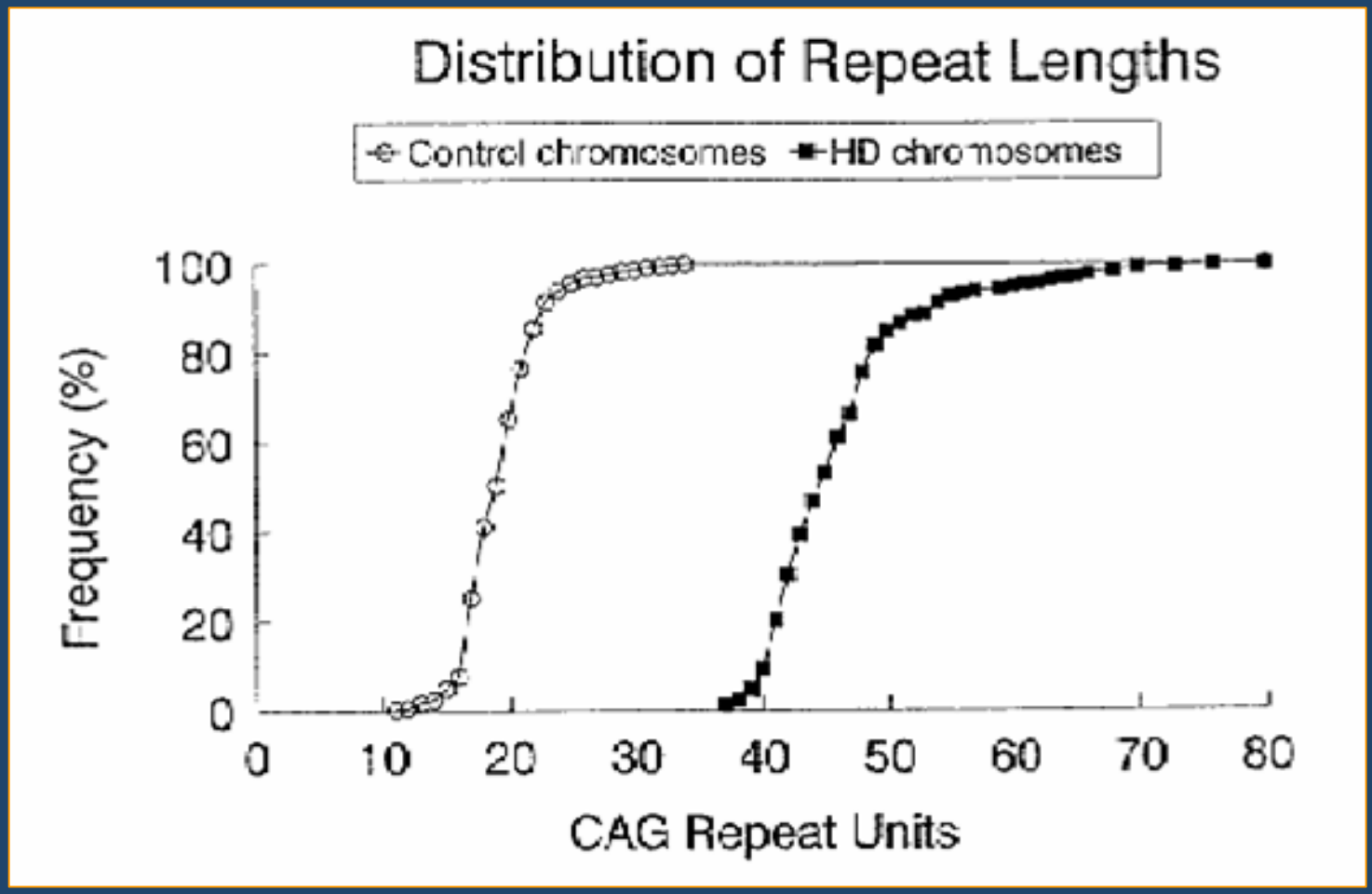
- Autosomal dominant
- Complete penetrance
- Anticipation

Genetics

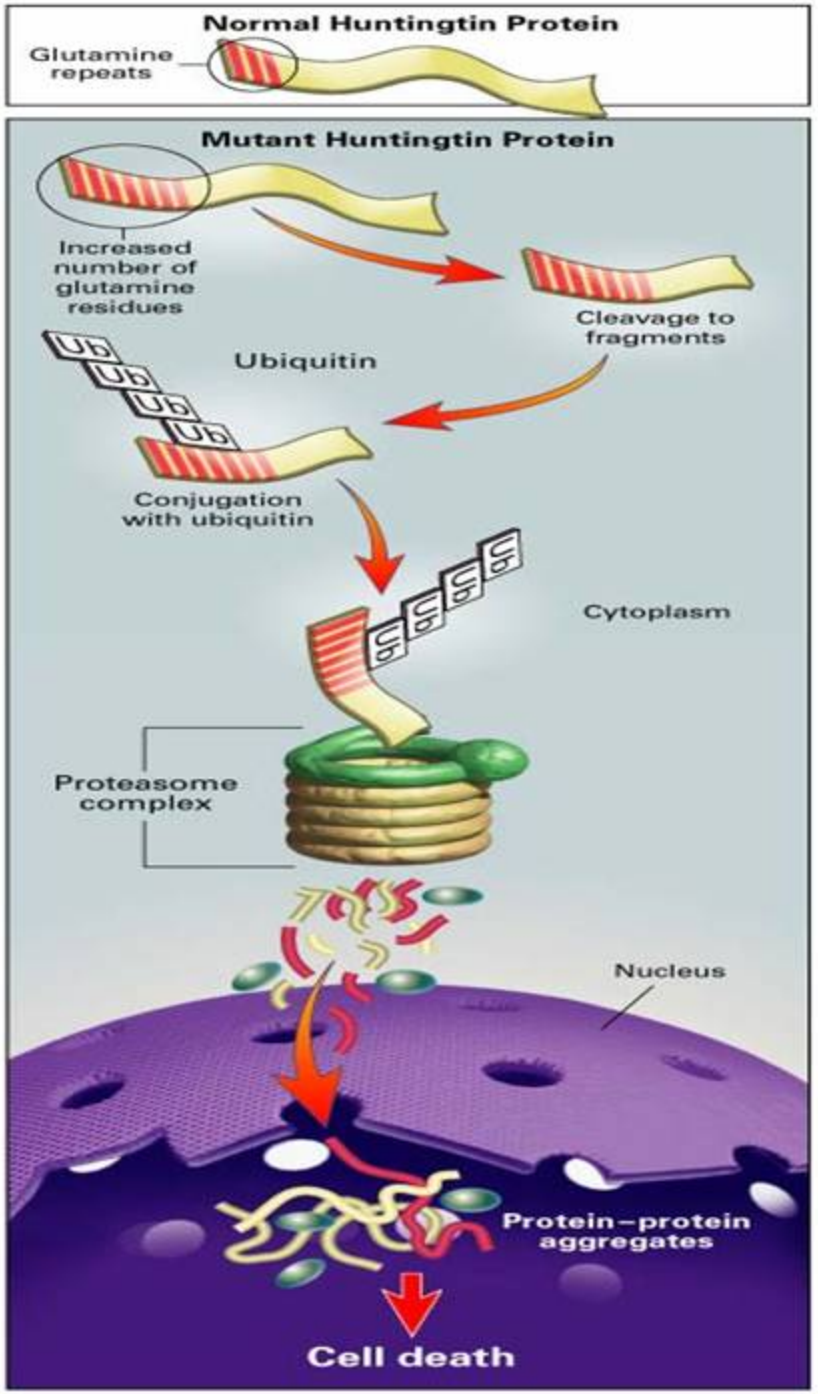
- Chromosome 4p16.3
- IT15 gene
- Expanded CAG repeat (polyglutamine)
- Huntingtin



Genetics


Distribution of Repeat Lengths
Control chromosomes
HD chromosomes
Frequency (%)
100
80
60
40
20
0
0
10
20
30
40
50
60
70
80
CAG Repeat Units

Neuronal Intranuclear Inclusions (NIIs)



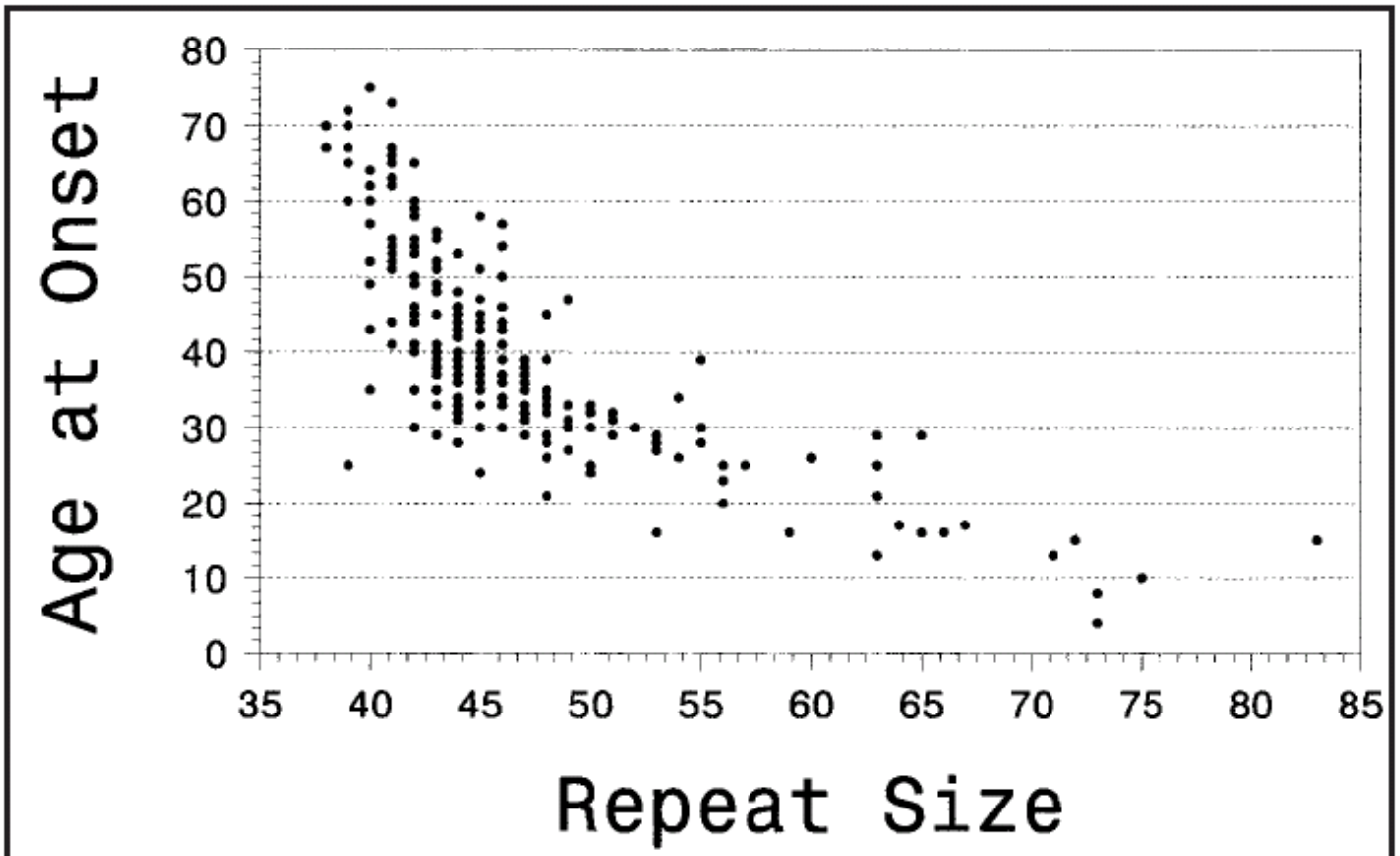


Fig. 1: The CAG repeat sizes for 220 persons HD diagnosed through the New England Huntington's Disease Research Center are presented in relationship to the age at onset of motor impairment. Repeat size is strongly related to age at onset. Onset age before age 20 is usually associated with a repeat size of more than 60 CAG units. Among persons with adult onset, the range in onset age for a given repeat is large and may vary by 30 years or more and thus repeat size is not a good predictor of age at onset.

Nance MA and Myers RH: Ment Retard Dev Disabil Res Rev: 7(3):153-7, 2001

Diagnostic Considerations in Juvenile HD

- Premature or inappropriate diagnosis should be avoided
- Avoid attributing minor symptoms to onset of HD
- Isolated behavioral disturbances, without motor or cognitive dysfunction, should be followed carefully (but are not diagnostic)
- Children in HD families are not exempt from other genetic or acquired disorders

Nance MA and Myers RH: Ment Retard Dev Disabil Res Rev: 7(3):153-7, 2001

Diagnostic Considerations in Juvenile HD:
When child's symptoms are inappropriately attributed to HD (gene positive)

- Failure to make a correct diagnosis
- Alterations in self-image or self-esteem
- Effects on employability
- Effects on insurability
- Limitation of academic, career, or social goals

Nance MA and Myers RH: Ment Retard Dev Disabil Res Rev: 7(3):153-7, 2001

Diagnostic Considerations in Juvenile HD: Differential Diagnosis

- Mental retardation (multiple causes)
- Tourette syndrome
- Juvenile parkinsonism
- Stimulant drugs
- Hereditary ataxias
- DRPLA
- Pelizaeus-Merzbacher disease
- Metabolic disorders

Nance MA and Myers RH: Ment Retard Dev Disabil Res Rev: 7(3):153-7, 2001

Diagnostic Considerations in Juvenile HD: Potential problems in at-risk children

- Disrupted social and home environment in some HD families
- Mild to severe depression
- Sleep disturbance
- Poor school performance or attendance

Nance MA and Myers RH: Ment Retard Dev Disabil Res Rev: 7(3):153-7, 2001

Features of HD in the first decade of life

- Positive family history of HD (usually father)
- Declining cognitive function
- Behavioral disturbance
- Rigidity of limbs or trunk
- Oral motor dysfunction (dyarthria, dysphagia, drooling)
- Seizures: generalized or myoclonic (25%)
- Dystonia, ataxia, cerebellar signs, tremor
- Chorea uncommon

Nance MA and Myers RH: Ment Retard Dev Disabil Res Rev: 7(3):153-7, 2001

Features of HD in adolescents

- Movement disorder: variable
- Severe behavioral disturbance may be the presenting symptom in adolescents
- Behaviors requiring medical or legal intervention:
  - Arson
  - Suicidal ideation or attempts
  - Sexually aggressive or inappropriate behavior
  - Incapacitating drug or alcohol abuse

Nance MA and Myers RH: Ment Retard Dev Disabil Res Rev: 7(3):153-7, 2001

Diagnostic Considerations in Juvenile HD: When family history of HD is absent

- Non-paternity
- Adoption
- Early death of an at-risk parent
- Onset of symptoms in the child before the parent's onset

Nance MA and Myers RH: Ment Retard Dev Disabil Res Rev: 7(3):153-7, 2001

Clin Genet 2006: 69: 486–496
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CLINICAL GENETICS
doi: 10.1111/j.1399-0004.2006.00624.x

Social and Behavioural Research in Clinical Genetics

Section Editor:
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The personal experience of juvenile Huntington's disease: an interpretative phenomenological analysis of parents' accounts of the primary features of a rare genetic condition

Smith JA, Brewer HM, Eatough V, Stanley CA, Glendinning NW, Quarrell OWJ. The personal experience of juvenile Huntington's disease: an interpretative phenomenological analysis of parents' accounts of the primary features of a rare genetic condition. Clin Genet 2006: 69: 486–496. © Blackwell Munksgaard, 2006

There has been a paucity of research into the psychosocial impact of juvenile Huntington's disease (JHD) on the child and the family. The study reported here is part of larger project that aimed to address this

JA Smith[a], HM Brewer[a,b], V Eatough[a], CA Stanley[b], NW Glendinning[b] and OWJ Quarrell[b,c]

[a]Birkbeck University of London, [b]Huntington's Disease Association, London, and [c]Sheffield Children's Hospital, Sheffield, UK

Smith JA et al: Clin Genet: 69: 486-496, 2006

Parents' perceptions of the main problems associated with JHD

- First becoming aware that something is wrong
- Physical symptoms
- Speech and communication difficulties
- Behavioral problems
- A slow but relentless process

Smith JA et al: Clin Genet: 69: 486-496, 2006

Genetic testing of children at risk for HD

- 44 symptomatic children tested for HD
- 33 positive; 11 negative
- Incomplete or atypical symptoms profiles in children with negative results
- All children with positive results had a positive family history for HD

Nance MA; US Huntington Disease Genetic Testing Group: Neurology: 49 (4): 1048-1053, 1997

Genetic testing of children at risk for HD

- HD in first decade of life: >80 CAG repeats
  - Declining school performance
  - Seizures
  - Oral motor dysfunction
  - Rigidity
  - Gait disorder
- HD in second decade of life
  - Symptoms were more varied
  - Usually behavioral and motor symptoms
- Caution with “diagnostic” testing in incomplete or atypical symptom profiles or no family history

Nance MA; US Huntington Disease Genetic Testing Group: Neurology: 49 (4): 1048-1053, 1997

Treatment

- Supportive
- Symptomatic

Treatment: Supportive (role of social worker is very important)

- Education
- Genetic counseling
- Psychosocial support
- Legal services
- Disability review support
- Lay support groups
- Physical, occupational, speech therapy

Treatment: Symptomatic

- Antidepressants
- Mood stabilizers
- Antipsychotics
- Antianxiety medications
- Dopamine-blocking agents (limited in children)
- Anti-Parkinsonian medications
- Anti-spasticity medications
- Botulinum toxin injections

Treatment of JHD features

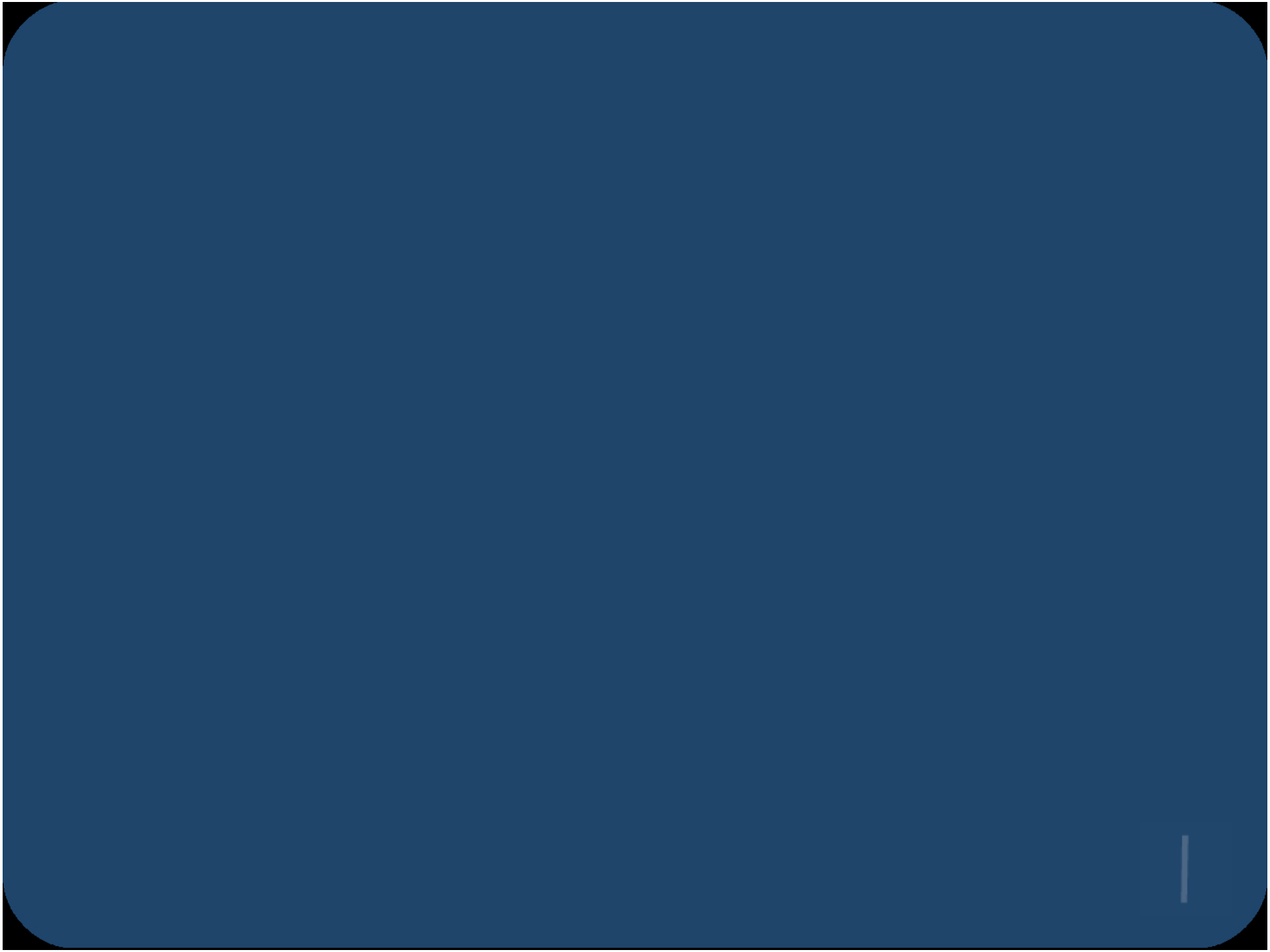
- Parkinsonism (rigidity, bradykinesia)
  - Levodopa (Sinemet)
  - Dopamine agonists
- Dystonia
  - Levodopa (Sinemet)
  - Dopamine agonists
  - Botulinum toxin
  - Baclofen and other muscle relaxants

Treatment

- Depression
  - SSRIs and other antidepressants
- Psychosis
  - Typical and atypical neuroleptics

Future Directions

- New treatments
- Basic research
- Clinical research
- Education
- Active participation
- Cure



HD Clinical Research and Future Directions

- Coenzyme Q10
- Remacemide
- Riluzole (RID-HD)
- Minocycline
- Creatine
- PREDICT-HD, PHAROS
- Fetal Transplants
- Ox-Phos
- SAHA (HDAC)