



# Juvenile Huntington's Disease

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# Presenter Disclosures

**Alexandra Duffy**

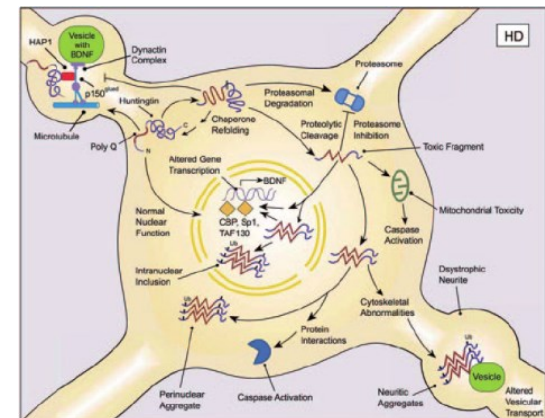
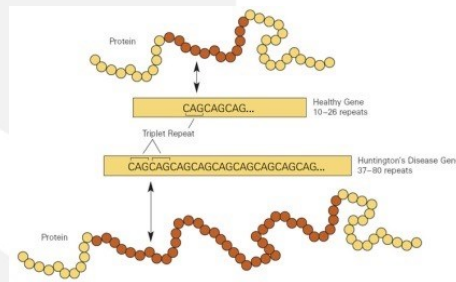
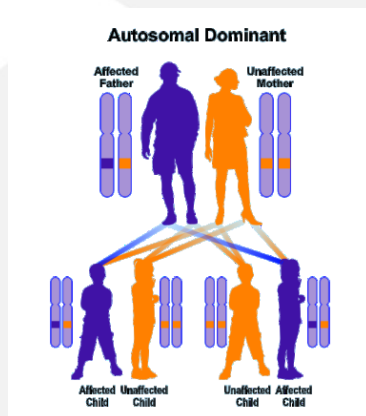
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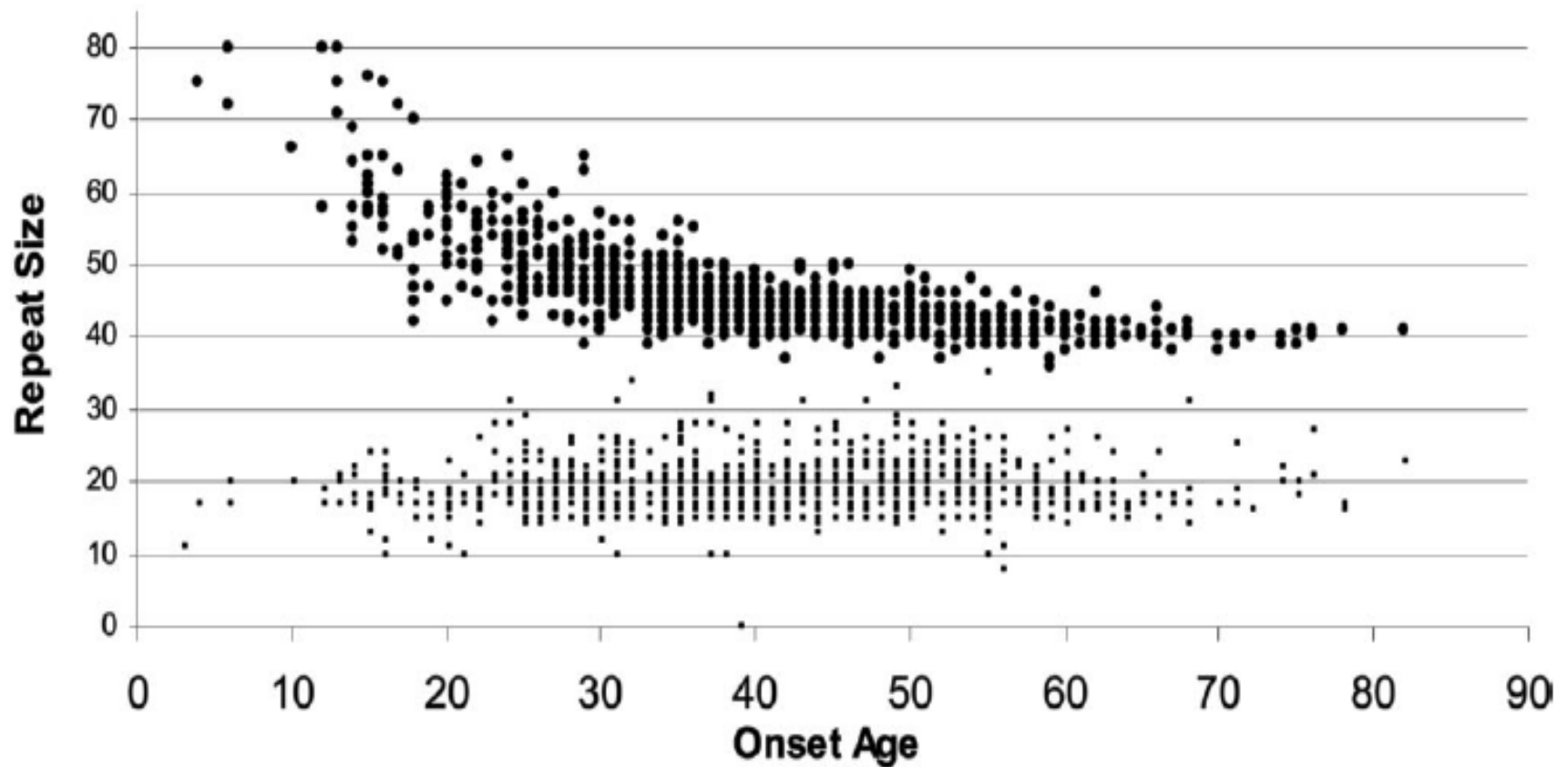
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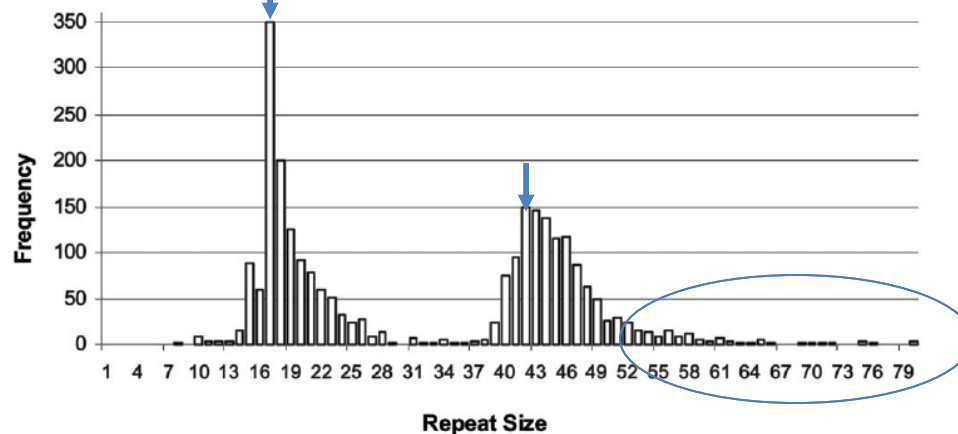
# Juvenile Huntington's Disease

- Genetically inherited neuropsychiatric degenerative disease
- Autosomal dominant inheritance pattern
  - 50/50 chance of inheriting the gene from an affected parent
- Caused by abnormal CAG expansion of the HD gene leading to a mutated huntingtin protein which causes cellular disturbances and dysfunction

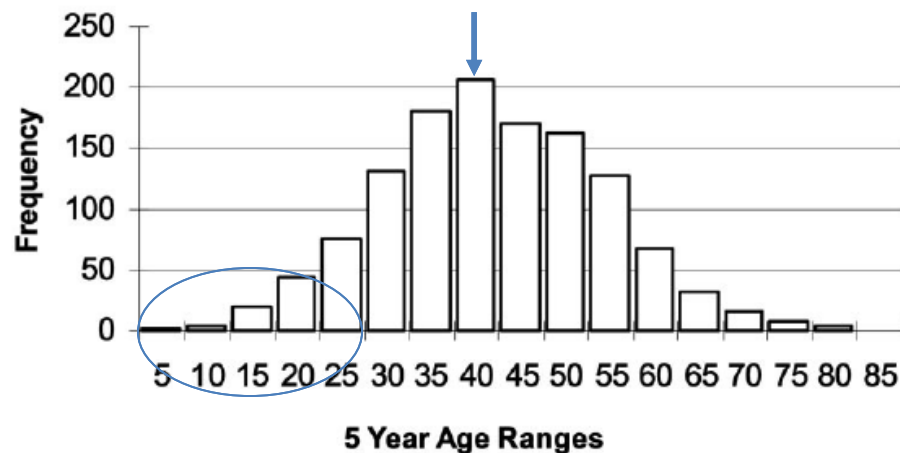




**FIG. 3.** HD repeat size and onset age. The relationship between the repeat size and the age at onset is presented. Persons with repeats of 60 or larger commonly have very young onset, before the age of 20, and among these large repeats there is a clear relationship between repeat size and onset age. For persons with 55 repeats or fewer, the relationship between repeat size and onset age is much weaker and the repeat size is not predictive of onset age.



**FIG. 2.** Normal and expanded HD repeat sizes. The distribution of repeats for Huntington's disease may be divided into four categories. Repeats of 26 or fewer are normal. Repeats between 27 and 35 are rare and are not associated with the expression of the disease, but occasionally fathers with repeats in this range will transmit a repeat to descendants that is expanded to the range for expression of the illness. Repeats between 36 and 39 are associated with reduced penetrance whereby some individuals will develop HD and others will not. Repeats of 40 or larger are associated with the expression of HD. Persons carrying repeats in this range will develop HD, assuming they do not die of other causes before onset.



**FIG. 1.** Huntington's disease onset ages. The age at onset distribution in Huntington's disease is very broad and may vary from as young as 3 or 4 years of age to as old as 85. Onset presented here represents initial signs of motor impairment.

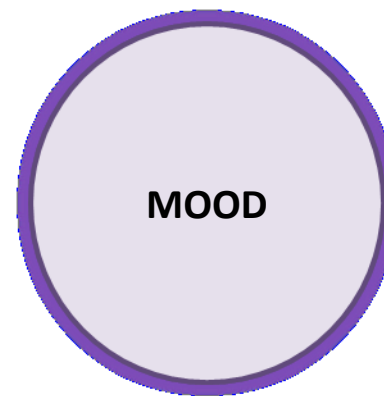
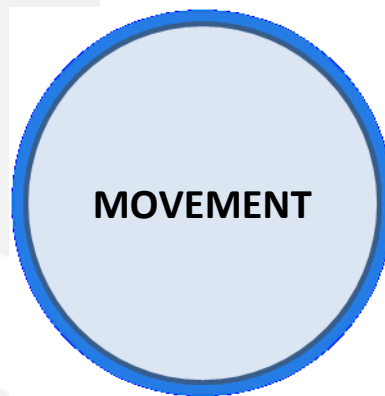
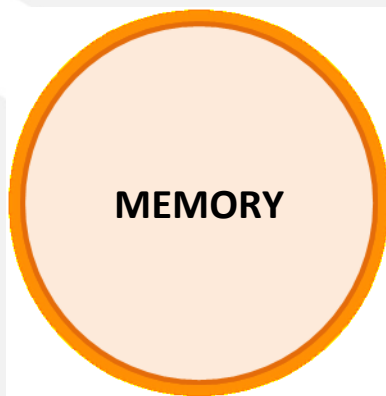
## How do we get from 40 to 60 repeats?

- Mutable normal allele (27-35) and reduced penetrance
- “Mutable” gene is unstable and may undergo anticipation in that it may increase from one generation from the next
- Maternal transmission: +/- 2
- Paternal transmission: -2 to + 20 or more
- Paternal cases for most JHD cases, 90% (case reports from maternal inheritance)

HD Status	Predictive Test Result	CAG Repeat Length
Unaffected	Normal	10-26
	Intermediate	27-35
Affected	Reduced Penetrance	36-39
	Full Penetrance	40-Above

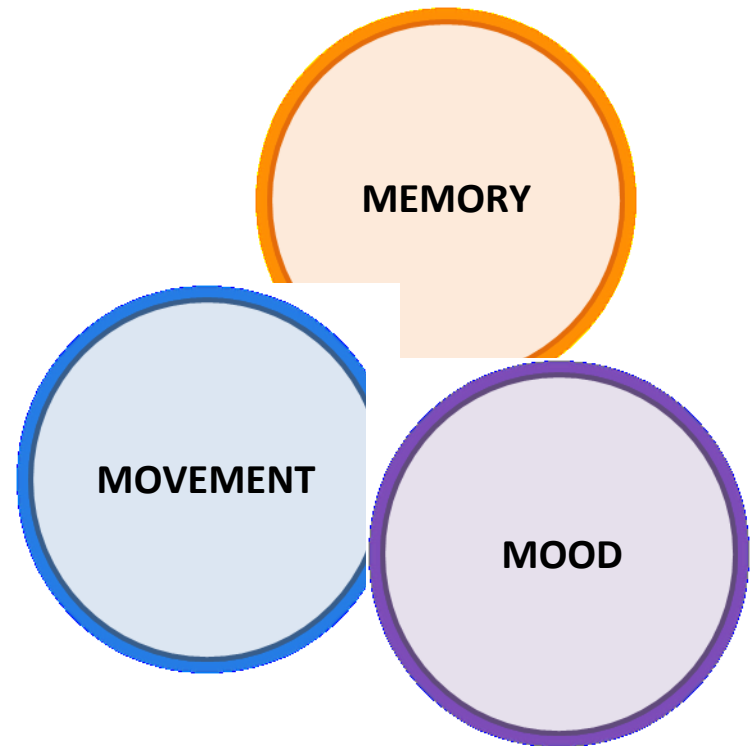
# Juvenile Huntington's Disease

- Affects memory, movement and mood
- Leading to changes in thinking, difficulties with movements and psychiatric and behavioral disturbances
- Different from typical adult-onset HD, particularly a child under 10 years of age
- Unique challenges



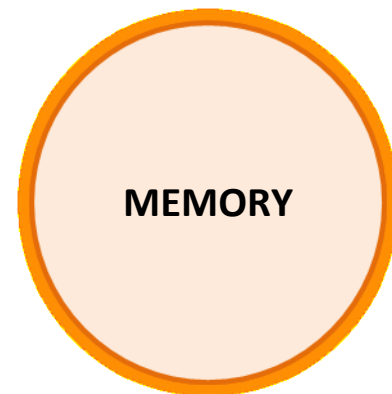
## Typical Initial Symptoms of JHD

- + family history, usually in the father
- Stiffness in the legs
- Clumsiness in the arm and legs
- Decline in cognitive function
- Changes in behavior
- Seizures
- Changes in oral motor function
- Chorea in adolescent
- Behavioral disturbances



# Juvenile Huntington's Disease

- Decline in cognitive function (thinking and reasoning)
- Initially subtle following by progression
- May appear distracted, easily be overwhelmed and/or having difficulty completing tasks
- Loss of skills previously gain (milestones) and difficulty learning new skills
- Decline in school performance
- Attention and concentration difficulties
- Problems with multitasking and decision making



# Juvenile Huntington's Disease

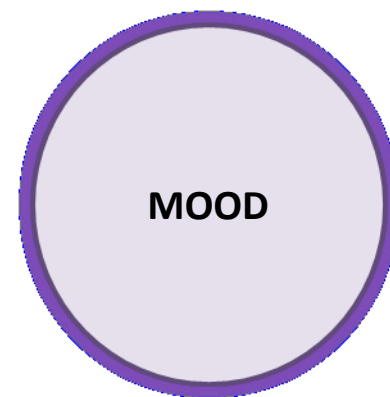
- Worsening of motor skills
- Changes in speech, riding a bicycle, or throwing a ball
- Rigidity or stiffness
- Dystonia (abnormal tightness and posturing)
- Difficulty walking
- Clumsiness
- Poor oral control with drooling and difficulty swallowing
- Chorea is rare but can be seen in adolescent onset



**MOVEMENT**

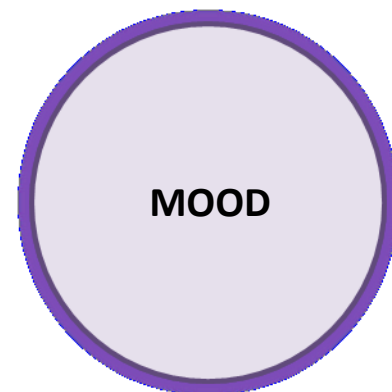
# Juvenile Huntington's Disease

- Psychiatric and behavioral changes
- Depression: sadness, tearful, feeling hopeless, changes in sleep, appetite, energy, and overall performance
- Attention difficulties or hyperactivity
- Hypersexuality
- Aggressiveness, impulsivity, explosive behavior
- Obsessive thinking



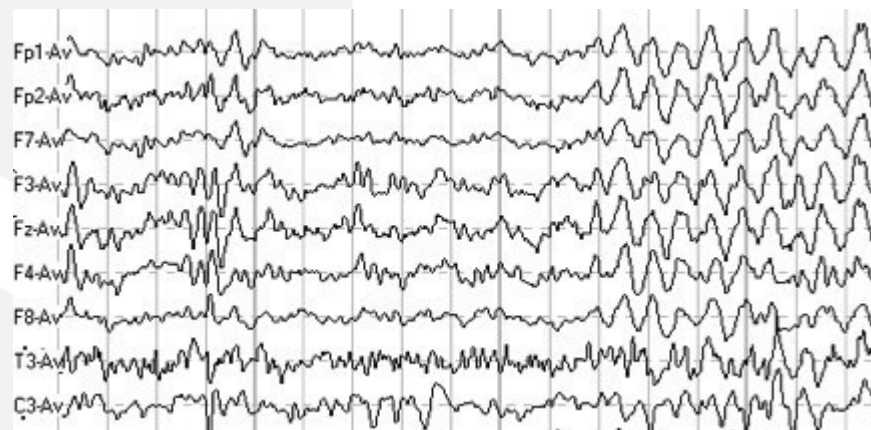
# Juvenile Huntington's Disease

- Affect of disease on the brain verses psychological stress of the disease
- Behaviors can be unpredictable and difficult to manage (disease verses normal changes and urges of being a teenager)
- Can lead to substance abuse (drugs or alcohol)
- Causes disruptions in family or social life



# Seizures

- Can be the presenting symptom
- About 30 – 50 % of children with JHD (38%)
- May be any type and differ in severity
- Babies and children can have seizures due to many other causes not related to JHD



# A survey-based study identifies common but unrecognized symptoms in a large series of juvenile Huntington's disease

Amelia D Moser<sup>1</sup>, Eric Epping<sup>1</sup>, Patricia Espe-Pfeifer<sup>2</sup>, Erin Martin<sup>1</sup>, Leah Zhorne<sup>3</sup>, Katherine Mathews<sup>3</sup>, Martha Nance<sup>4</sup>, Denise Hudgell<sup>5</sup>, Oliver Quarrell<sup>6</sup> & Peg Nopoulos<sup>\*,7</sup>

## Summary points

- Juvenile onset Huntington's disease (JHD) is ultra-rare which results in gaps in knowledge of the phenomenology of symptoms.
- Adult onset HD (AOHD) and JHD have, in general, overlapping typical symptoms with motor, cognitive and psychiatric problems.
- Yet there are some unique features of JHD such as motor manifestation that are the opposite of those seen in AOHD (hyperkinesia in AOHD and hypokinesia in JHD).
- There may be additional symptoms that are common but unrecognized in JHD.
- Social media has provided a format in which families of children with rare diseases such as JHD can communicate on a regular basis regarding their children.
- A web-based survey was created assessing the phenomenology of a set of five symptoms felt by families to be common but under-recognized: pain, itching, sleeping difficulties, psychosis and tics.
- This survey was distributed to caretakers of JHD patients to evaluate the phenomenology of these symptoms.
- Disrupted sleep was the most prevalent symptom (87%), followed by tics (78%), pain (69%), itching (60%) and psychosis (39%).
- There are symptoms in the JHD population that are not considered classic, however, are common and cause significant issues for both patients and caregivers.

*Neurodegener. Dis. Manag.* (2017) 7(5), 307–315

# Young Adult Huntington's Disease

- The young adult with features of JHD and HD
- Not everyone fits perfectly into JHD and adult onset HD
- Special attention to an individuals' presentation and particular needs
- You can be a part of both JHD and HD



## Challenges in diagnosing JHD

- Many symptoms found in other conditions
  - What else could it be?
- + HD genetic testing does not necessarily mean that the symptoms are due to JHD
- Complicated family history
  - Parent not affected yet
  - Early death of a parent (before they were affected)
  - Misdiagnosis or lack of diagnosis in affected parent
  - Non-paternity
  - Adoption



## Box 1

### Diagnostic criteria for childhood-onset Huntington's disease ( $\leq 10$ years)

- A family history of Huntington's disease (usually in the father) and two or more of:
  - Declining school performance
  - Seizures
  - Oral motor dysfunction
  - Rigidity
  - Gait disturbance

Reproduced with permission from [13].



Quarrell, OWJ et al. *Managing juvenile Huntington's disease*. Neurodegenerative Disorders Management 2013.

## Evaluation for possible JHD

- Talk to your health care provider
- Seek referral or reach out to a HD Center
- What to expect:
  - Medical and neurological history
  - Family history
  - Developmental history
  - Neurological exam
  - Discussion about impression and plan
  - Do not be afraid to ask questions
  - *A diagnosis of JHD takes time*
  - Routine follow-up



## Genetic testing?

- If the history and examination are strongly suggestive of HD then may proceed with confirmatory genetic testing
- If symptoms are not typical or exam is not clear then genetic testing should not necessarily be pursued at that time
- **GOAL:** make an appropriate and timely diagnosis while avoiding the potential risks of testing a child inappropriately or prematurely



## Why do we not just test minors?

- In the vast majority, it is an adult onset disease
- We do not have a disease modifying agent or cure
- Issues of informed consent
- In adults, fewer than 10% of individuals chose to undergo predictive genetic testing



## Potential risks of premature genetic testing

- Incorrect attribution of symptoms to HD
- Failure to make the correct diagnosis
- Stigmatizing the child
- Insurability
- Employability
- Psychological effects on the child
- Social effects on the child

## Your medical team

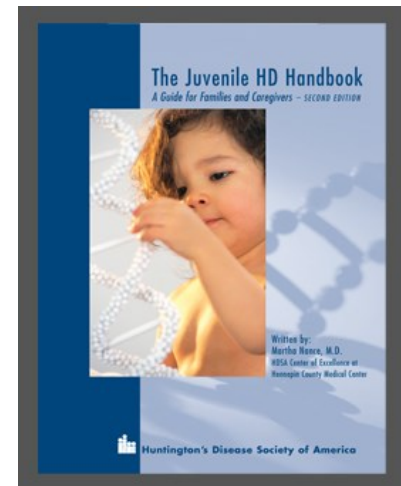
- HD COE: Neurologist, Psychiatrist, Social Worker, Genetic Counselor, Therapist, Research Coordinator
- Therapy: Physical, occupational and speech
- Dietician
- Primary care physician
- Dental care



## Your medical care

- Each person has their own individual course with medical care tailored to their needs
- You are not alone on this journey
- Treatment focuses on
  - Education
  - Movement disorders
  - Cognitive disorders
  - Behavioral and Psychiatric issues
  - Seizures
  - Psychosocial dynamics

**The Juvenile Huntington's Disease Handbook**  
**A Guide for Physicians , Neurologists and Other Professionals**  
*Martha Nance, MD*  
HDSA Publications



## Treatment options

- Early intervention
- Safety devices and equipment assessment
- Physical therapy and range of motion exercises
- Safety measures and fall prevention
- Rigidity
  - Sinemet, Amantadine, Botulinum toxin therapy
- Spasticity and dystonia
  - Baclofen, Tizanidine, Clonazepam
- Chorea
  - Tetrabenazine (Xenazine)
  - Neuroleptics: Zyprexa, Risperdal, Abilify, Haldol, etc

## Treatment options

- Provide a stable and predictable environment
- Create daily schedule
- Minimize distractions and noise
- Simplify tasks and decisions
- Re-orientation
- Creative reminders
- Modifications at school (Individual Education Plan)



MEMORY

## Treatment options

- Affect of disease on the brain verses psychological stress of the disease
- Depression: sadness, tearful, feeling hopeless, changes in sleep, appetite, energy, and overall performance
  - Anti-depressants (SSRI, SNRI, TCA, other): Zoloft, Celexa, Effexor, Wellbutrin, Remeron, etc



## Treatment options

- Behaviors can be unpredictable and difficult to manage (disease verses normal changes and urges of being a teenager)
- Aggressiveness, impulsivity, explosive behavior
  - Behavioral and environmental modification, safety plan
  - Antipsychotics, mood stabilizers or anti-anxiety Rx
- Obsessive thinking
  - Reassurance and redirection
  - Anti-depressants/ SSRI's



## Addressing sexuality and hypersexuality

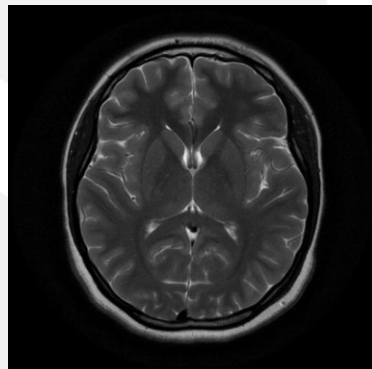
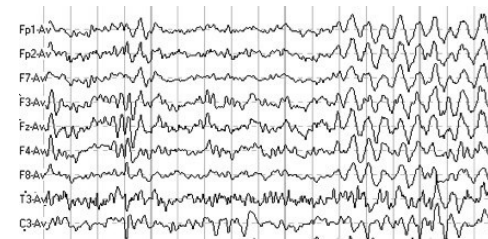
- JHD verses adolescent/teenager(s) changing body and hormonal urges
- Managing menstrual hygiene
- Contraceptive medication
- Education about sex
- Discussing and redirecting inappropriate sexual behavior (touching self in public)
- Possible treatment with medication

# Treatment of seizures

- Appropriate work-up: brain imaging, electroencephalogram, p blood tests
- Many different types of seizures
- Seizure precautions discussed
- Importance of medication compliance
- Medication treatment (depending on seizure type): Keppra, Depakote, Lamictal, Tegretol, Topamax, Zonegran, etc



During an EEG, electrodes are placed on your child's scalp so the electrical activity of the brain can be recorded.



## Other medical issues to address

- Choking (dysphagia)
  - Avoidance of aspiration
  - Use of a straw and modification of food consistency
  - Small and slow
- Nutrition
  - Nutritious high calorie food
  - Frequent snacks (milkshakes, ensure, muscle milk)
- Communication
  - Electronic communication devices
  - Hand gestures



## Late Stage JHD

- Early discussions regarding possibilities and goals of care
- Severe stiffness in limbs leaving some children wheelchair or bed bound
- Treatment of any discomfort
- Attention to possible malnutrition, infections of the urine and lung and skin sores
- In home services and placement outside of the home
- Sensitive issues to discuss: feeding tube, goals of care, palliative care, hospice care
- Advance directive
- *Have someone that can support you, that can speak for you, and act for your loved one in order to carry forward these wishes in a very difficult time.*

## A Functional Scale for Assessing Juvenile-Onset HD

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### A. School attendance

- 3—attends school, no special assistance needed
- 2—attends school, some regular classes, some special or modified classes
- 1—attends school, few or no regular classes
- 0—unable to attend school or work program

### B. Academic/developmental performance

- 3—reading/writing/math skills appropriate to age
- 2—mild decrease in academic performance but still able to take a test or to write
- 1—unable to write legibly but able to communicate orally
- 0—unable to read/write/communicate orally

### C. Chores

- 2—able to assist in age-appropriate manner with household chores
- 1—occasionally assists with chores
- 0—unable to participate in household chores

### D. Activities of daily living

- 3—performs self-cares in an age-appropriate manner
- 2—requires some assistance for bathing, dressing, grooming, or feeding
- 1—assists others who bathe, dress, or feed him/her
- 0—unable to assist in self-cares

### E. Lives

- 2—at home with only family assistance
- 1—at home/group home/foster care with assistance from non-family members
- 0—living in a long-term care facility

**The stage of HD is determined by adding the points, as shown:**

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11-13 points	Stage 1
7-10 points	Stage 2
3-6 points	Stage 3
1-2 points	Stage 4
0 points	Stage 5

## Caregivers

- Handling the emotions of such a diagnosis
- Managing your own feelings
- Practical and emotional support
- Outlets
- Caring for the caregiver
- Support groups
- Knowing your resources
- Respite
- Create your *HD family*

BE KIND TO  
YOURSELF.

You Can Do  
ANYTHING

But Not  
EVERYTHING.

## In the moment...

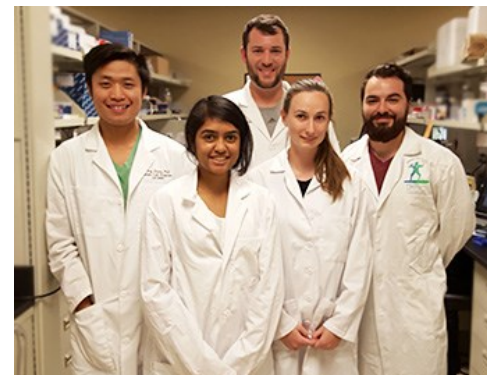
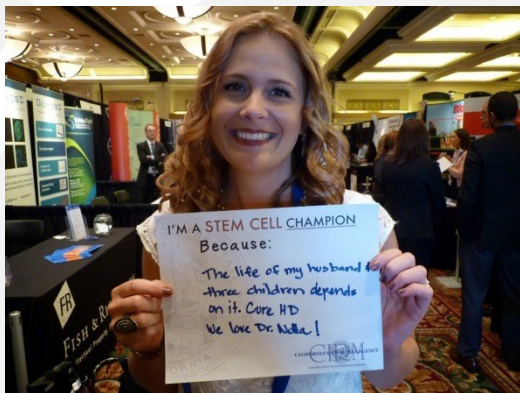
- Attempt to take pause and live in the moment
- Enjoy the simple things in life
- Have the moment be NOT about JHD



**I love  
RIGHT  
NOW**

## Key points

- Education
- Know where to turn for help and support
- Advocate (HD warriors)
- And maintain hope through research!



14 | NEUROLOGY TODAY | NOVEMBER 19, 2015

NEWS FROM THE SOCIETY FOR NEUROSCIENCE ANNUAL MEETING

## Gene Editing Techniques Show Promise in Silencing or Inhibiting the Mutant Huntington's Disease Gene

BY JAMIE TALAN

## JHD Awareness

- Help 4 HD
  - HD H.I.P.E day in Sacramento
  - JHD Walk Sacramento 2015 to fund JHD research
- Documentaries
  - The Warriors: Fighting the Incurable Juvenile Huntington's Disease
- JHD focused research
  - Dr. Kyle Fink at UC Davis working on developing gene editing strategies for JHD
- Kids-HD and Kids JHD at the University of Iowa
  - Looking at brain structure and function in kids at risk or with JHD
- Youth Organizations
  - HDYO
  - National Youth Alliance



*Thank you to our JHD & HD families for your strength, courage, and inspiration!*

