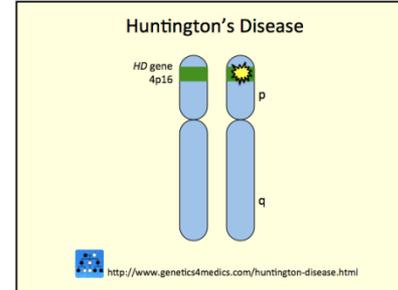




Juvenile Huntington's Disease

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What is JHD?



- Huntington's disease (HD) is an inherited neuropsychiatric degenerative disease, caused by a mutation in the Huntingtin gene on chromosome 4
- Juvenile Huntington's disease (JHD) is defined as onset of symptoms of HD before age 21
- It is uncommon, as only 5-10% of HD cases have juvenile onset

CAG repeat length correlates with age of onset of HD

- CAG repeat > 40 – adult-onset HD (onset > 21 years of age)
- CAG repeat > 55-60 – JHD (onset < 21 years of age)
- CAG repeat > 80 – childhood-onset (< 10 years of age)
- These numbers are not definite, however, and just a general trend
 - Some individuals with onset > 21 years have had CAG > 60, and some individuals with onset < 21 years have had CAG repeat length in the 40s

Anticipation in HD

- “Anticipation” refers to the potential for onset of an inherited disease to occur at an earlier age with each generation
- In HD, when this occurs it is usually associated with an increase in CAG repeat length between generations
- CAG repeat length is more “mutable” in spermatozoa, so paternal inheritance is more likely to result in CAG expansion between generations
 - This leads to an increased incidence of JHD with paternal inheritance (75% of cases)



Clinical Features of JHD

- The same triad of motor, psychiatric, and cognitive features seen in adult HD affects those with JHD
 - But with some differences

Motor Symptoms of JHD

- Those with adolescent-onset JHD can present with chorea like adult-onset HD, but younger onset typically involves more “parkinsonian” motor features – slowness and stiffness
- Dystonia, which is involuntary sustained muscle contraction, is often seen earlier in the course for JHD patients than in their adult counterparts



Cognitive Symptoms of JHD

- Decline in school performance can be an early sign
 - Impaired memory, impaired concentration, and slowness of thinking can contribute to this

Psychiatric Symptoms of JHD

- Irritability, mood changes, inattention, obsessiveness, and apathy can also occur early in the disease
 - Also commonly occur in children/adolescents without JHD, and likely more commonly in children of HD families

Seizures in JHD



- Seizures, which are episodes of transient neurologic symptoms caused by uncontrolled electrical activity in the brain, are much more common in JHD patients than in adult HD patients
 - Noted in 38% of JHD patients in one study by Cloud et al, in which younger age of onset was associated with higher incidence of seizures
- Multiple seizures types are possible in JHD – simple partial seizures (symptoms without loss of awareness, such as a sensation), complex partial seizures (symptoms with loss of awareness, often with one side shaking but also can be with a sensation, or staring spells), generalized seizures (whole body shaking with loss of awareness)

Issues in the Diagnosis of JHD

- A review by Ribai et al of 29 JHD cases at Salpêtrière Hospital in Paris published in 2007 showed a mean delay in diagnosis of 9 years
 - Motor symptoms at onset were noted in only 34.5%, and surprisingly none had rigidity at onset
 - Psychiatric and behavioral difficulties were the first sign in the remaining 65.5%
- Possible contributors to delay in diagnosis included attribution of initial symptoms to other conditions (such as depression, etc) despite a family history of HD, and also lack of clear family history in some cases (transmitting parent had not yet developed symptoms)

When to Test

- “The greatest challenge to the clinician is the 10- to 20-year-old patient presenting with behavioral symptoms or cognitive changes, ***as attentional difficulties, depression, and anxiety are common disorders in the general population.***”

Lehman and Nance, *Neurology* 2013; 80: 976-977.

When to Test

- Presymptomatic testing of minors at risk for HD is not advised
- Sometimes children and teens in HD families have school issues, symptoms of ADHD, mood symptoms, and/or behavioral issues that may raise the question of possible JHD
- Testing should be considered when there is evidence of cognitive decline and/or motor features suggestive of HD

Difficult Diagnosis of JHD

- “In order to avoid both a failure to diagnose HD in a teenager with predominantly behavioral symptoms and a premature or incorrect attribution of symptoms to HD, we advocate an intermediate approach to children who present with atypical or nonspecific symptoms: a brief period of watchful waiting, roughly a year in duration, to confirm a progressive course.”
- “This observation period need not be a time of sitting by idly, rather it can be used to document the patient’s cognitive baseline through neuropsychological testing, treat the motor and behavioral symptoms, and optimize psychosocial factors.”

Lehman and Nance, *Neurology* 2013; 80: 976-977.

Diagnosis of JHD

- It is important to **seek evaluation by a child neurologist or movement disorders neurologist.**
 - It is sometimes advisable to have cognitive testing (neuropsychological testing) and a movement disorders exam to establish a baseline.
 - Assessments can be repeated in 6-12 months to look for changes

If in doubt, get checked out...

- Symptoms in a child or teen that worry patients may be due to psychological factors such as stress, adjustment reaction, or mood disorders.
- Seek support from pediatrician, counselors, school personnel, support groups





If in doubt, get checked out...

- If these or other symptoms raise concern, early evaluation is not just ok, it is encouraged!
 - If these symptoms prove to be part of a condition other than JHD (as in those listed on the previous slide), addressing the symptoms can help improve quality of life and function.
 - If these symptoms occur with decline in academic performance and/or possible motor symptoms -> seek out a neurology referral

If in doubt, get checked out...

- If the symptoms are part of JHD, early assessment and early initiation of treatments can yield better symptom management than a delayed diagnosis
 - This may be especially true for psychiatric and behavioral symptoms, where delayed treatment may be less effective

Management

- As in adult-onset HD, treatment is aimed at control of symptoms – cognitive, behavioral, psychiatric, and motor with the goal of maintaining/improving overall function
- A multi-disciplinary approach (like what is employed at HDSA CoEs) can be very helpful in addressing multiple symptoms in a collaborative fashion – anecdotally, this can ensure that issues are not overlooked and can optimize medication regimens and overall care
 - Our model includes a neurologist (sometimes multiple), psychiatrist, nurse practitioner, LCSW, genetic counselor, and physical therapist
- Caregivers and school must be involved in the treatment plan
- Local Regional Center – eligible if diagnosed before age 18



Cognitive Symptom Management

- Neuropsychological testing is sometimes useful in detecting which cognitive areas are affected
- Caregivers and the patient's school must collaborate and development of an IEP (individualized education program) is common
- Continued involvement in school activities is important for mental and social stimulation
- In specific cases involving ADHD symptoms, medications can be considered

Psychiatric Symptom Management

- Irritability, mood changes, inattention, obsessiveness, and apathy can occur early in the disease
 - Again: Seek support from pediatrician, counselors, school personnel, support groups
 - If pervasive, persistent, and/or severe enough to affect function, warrant evaluation from a psychiatrist



Psychiatric Symptom Management

- Psychiatric care may be needed with medications and/or counseling
 - Anti-depressant, anti-anxiety medications are sometimes used, as well as mood stabilizers.
 - Dopamine receptor blocking medications sometimes need to be avoided because they can worsen motor symptoms

Motor Symptom Management

- Rigidity and slowness of movement (parkinsonism) can sometimes improve with dopaminergic medications (as used in Parkinson's disease)
- Dystonia is the most common movement disorder for JHD patients – can respond to muscle relaxants and anticholinergic medications, though these are often limited by side effects (sedation, cognitive side effects especially)
 - Targeted botulinum toxin injections can be helpful by weakening the overactive muscles affected by dystonia



Motor Symptom Management

- Physical and occupational therapy can be very helpful in assessing gait and improving daily function
- Speech therapy can be helpful in assessing swallowing and clarity of speech

Seizure Management

- Again, not present in all JHD cases (38% in one study), but it is useful to know about seizure safety – ask your clinician about this
- Treatment depends upon the type of seizure as to which anti-epileptic medication is chosen. There is no specific medication for JHD-related seizures.
 - Sometimes EEG and MRI of the brain can be helpful in determining the type of seizure, and referral to an epileptologist is sometimes necessary
 - EEG monitoring at a tertiary center is sometimes needed to distinguish involuntary movements from seizures
- In some individuals, seizures can subside during the course of JHD

Seizure or Dystonia?

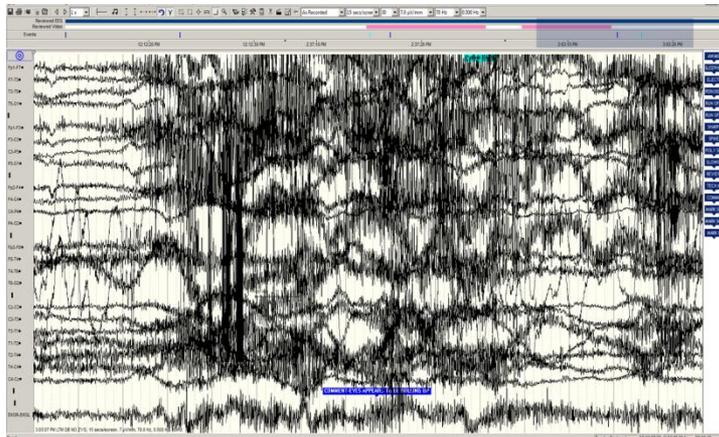


Figure 4-133: Onset of a Generalized Tonic-Clonic Seizure.

- Recurrent seizures and recurrent dystonia can be difficult to distinguish from one another, as both conditions can appear similar with repetitive movements, as in this case
- Additional workup such as continuous monitoring of the brain's electrical activity with EEG during the episodes in question can help to distinguish one condition from the other, which is important because the treatment of dystonia and treatment of seizures can be different

On the horizon...



- Research in HD has typically been restricted to individuals older than 16 years
- Recently, some studies have allowed younger subjects to participate as long as they have parental/guardian consent
 - ENROLL-HD
- Kids-HD/JHD are studies involving brain imaging being conducted by Dr. Peg Nopolous at the HDSA CoE at the University of Iowa, with Kids-HD for those from HD families and Kids-JHD for those with HD symptoms
 - Contact Sonia Slevinski (toll-free: 866-514-0858) or kids-hd@uiowa.edu

On the horizon...

- At the UCDMC, we have a planned study involving JHD patients and their families in which we will obtain skin samples that can then be used to create a “bank” of cells for future gene editing studies
- And of course, so many promising and hope-inspiring studies in the adult-HD population with the goal of a disease-modifying treatment!
- HDYO (Huntington’s Disease Youth Organization) is a great resource to find information about local support and activities and about JHD in general
- Help for JHD: <http://help4jhd.org/>
<http://www.blogtalkradio.com/help4hd/2016/05/19/help-4-jhd-live>



Who to contact?



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 - Dr. David Witt
 - Taryn Rosenthal, Genetic Counselor



Thank You!

- Thank you to HD patients and families for allowing us here at UCDCMC to be part of your lives – your courage, hope, and tirelessly giving nature is truly inspiring