Huntington's Disease Society of America

Benefits of Staying Connected with your HDSA Center of Excellence

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Huntington's Disease Society of America

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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

Vicki Wheelock MD

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

No relationships to disclose
or list

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Goals of this session

Connecting with a Center can benefit everyone in the HD family. This workshop will highlight Center services offered to:

- HD patients
- Family members caring for someone with HD
- Those at-risk or who have undergone predictive testing

This interactive workshop will address challenges in predictive testing, the HD prodrome, diagnosis and care for HD and JHD, and focus on support available for families

HDSA Center of Excellence Definition

- 43 elite centers throughout the US
- Selected for multidisciplinary care and expertise in HD
- Goals: to provide state-of-the-art care, support, resources and opportunities for research participation to people and families affected by HD

Mission

To provide help for today …..

…….through access to clinical care, outreach and education

And hope for tomorrow……

……through access to research

History

- HDSA Centers of Excellence (COE) began in 1999
  - Pilot Center: Emory University
- Next phase: 2000-2002
  - 20 additional Centers
- Program revision 2014 with new COE levels
  - Expansion to 41 Centers and 6 COE partners
  - Program expansion 2018: 43 Centers

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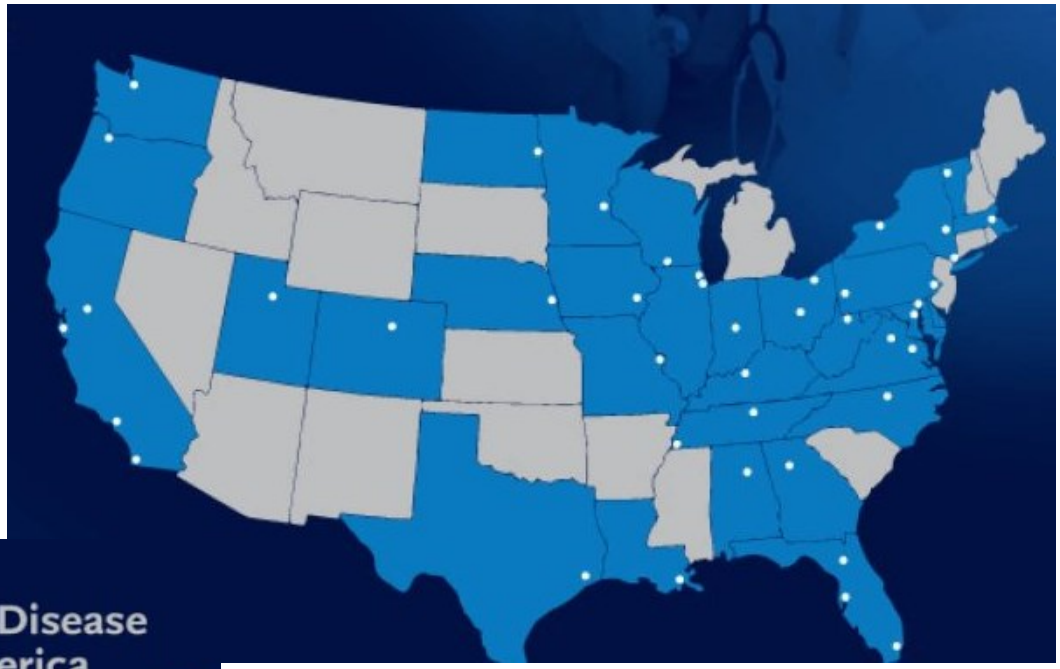
Benefits of the HDSA COEs

- **Increased access to** care and services
- Provides **both clinical** and **social** services
- Promotes **professional** and **lay education**
- Offers **HD clinical research** opportunities
- **Works with HDSA locally and nationally** to continually improve the lives of those affected by HD

Multidisciplinary Care for HD

- *Neurologist*
- *Geneticist*
- *Genetic counselor*
- *Psychiatrist*
- *Social Worker*
- *Neuropsychologist*



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Centers of Excellence

- *Physical therapy*
- *Speech therapy*
- *Occupational therapy*
- *Palliative care*
- *Hospice*

Scope of Care

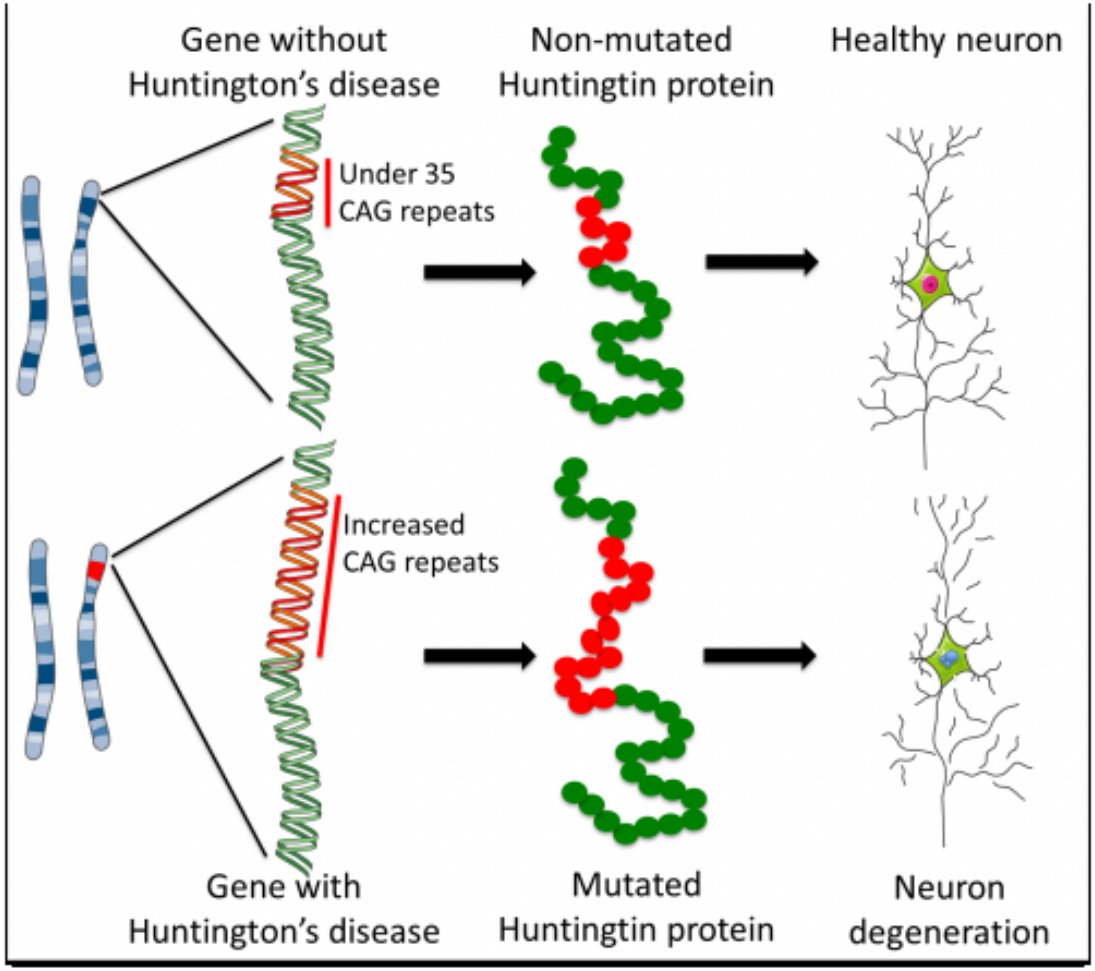
- Access to expert advice
- Genetic testing and predictive testing for HD
- Management of the HD prodrome
- Diagnosis of Huntington's disease
- Regular follow-up to monitor HD symptoms and plan for future needs
- Assistance with disability application
- Family support
- Potential enrollment in HD studies

Before we start our interactive scenarios, let's review some background about HD

HD is caused by an expansion in the number of CAG repeats in the huntingtin (HTT) gene.

Huntingtin gene (HTT) → huntingtin protein

CAG repeat length	
NORMAL	< 26
Unstable	27 – 35
Reduced penetrance	36 - 38
Huntington's disease	>38
Juvenile HD	>60, but sometimes less

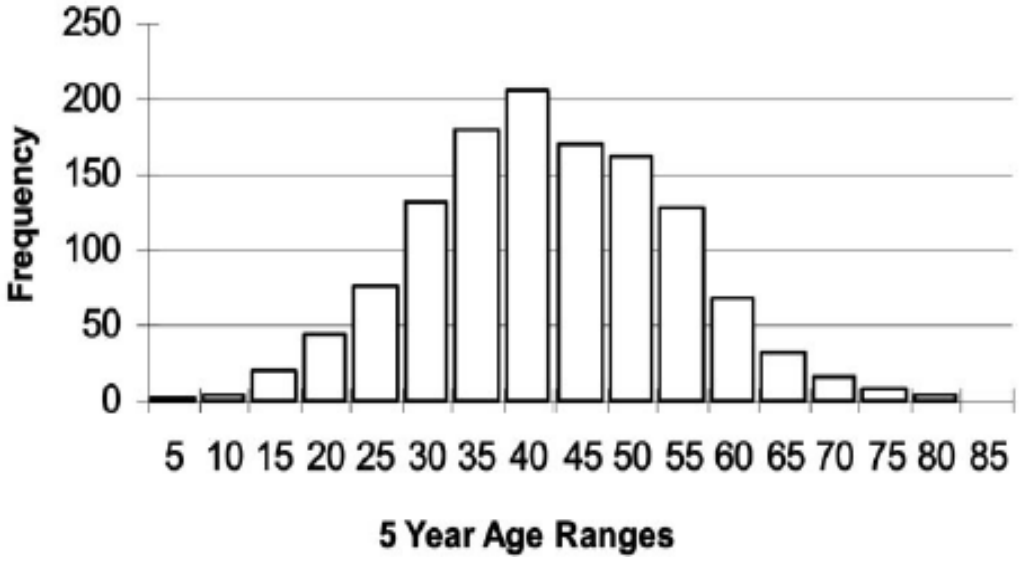


HD Collaborative Research Group *Cell* 72:971–983

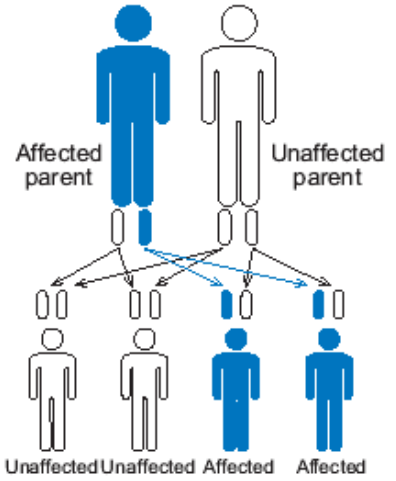
How common is HD?

When do people get HD?

HD is seen in 1/2500 – 1/10,000 people worldwide.

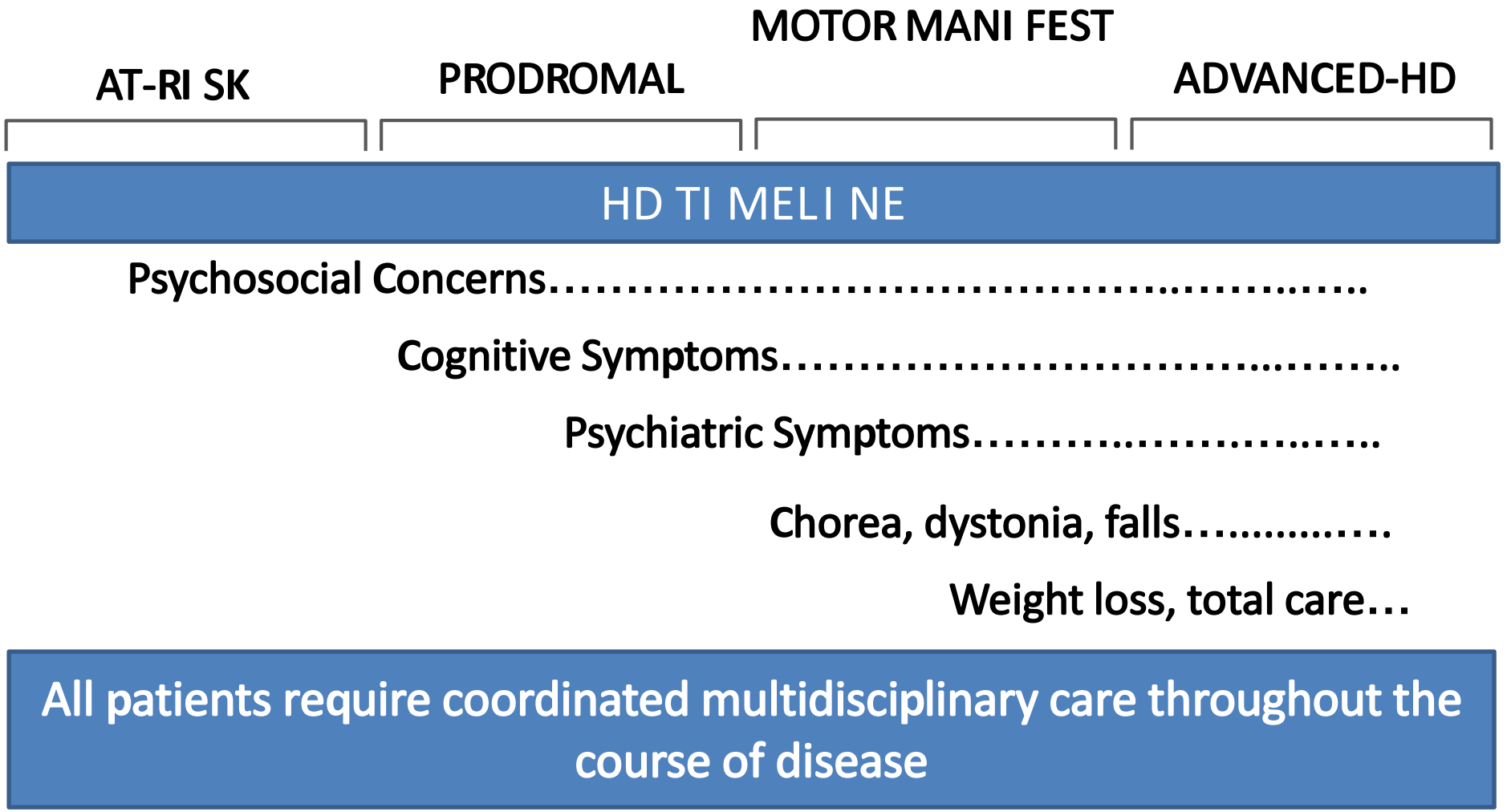


Myers RH. *J Am Soc Exper Ther* 2004;255-262



- Each child with a parent with HD has a **50% chance of inheriting the disease.**
- **May arise e**arlier in those who inherit HD from their father
- **10% of cases arise in families without hx of HD.**

HD over the Life Cycle



Courtesy Mary Edmondson, MD

HD scenarios 1 - 5

Note: these scenarios and the names used are fictitious and not based on any specific patients or families.

The scenarios illustrate issues commonly seen within HD families and are designed to stimulate thoughtful discussion.

Scenario 1: Ron' s story

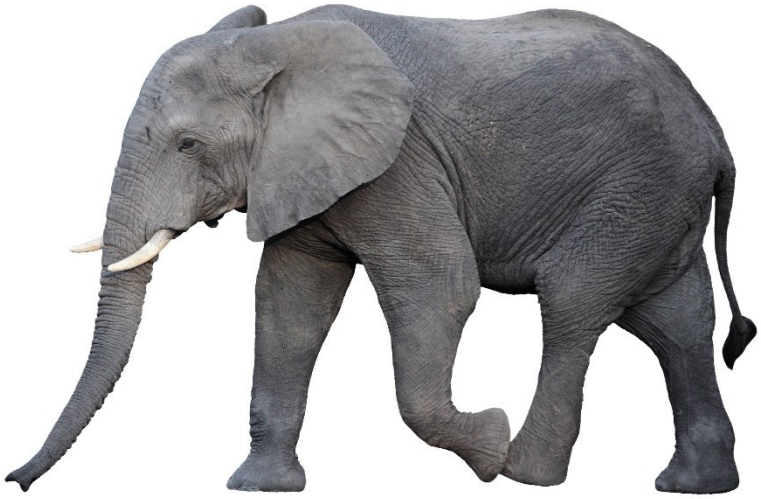
- Denise, 41, is worried about her husband Ron, 42. They've been married for 18 years and have two teenagers. Ron's mother was diagnosed with HD when he was in college. Very much in love, they understood that HD was a possibility for Ron and hoped that he would not inherit the disease. Ron decided that he would not want to test for the HD gene expansion, and Denise supported his decision.
- For the last year or two Ron has been more irritable and moody. He seems more withdrawn and doesn't initiate conversations. He's had some difficulty at work and angrily complains that his supervisor has written him up twice for minor errors. He sometimes forgets to shave or brush his teeth before leaving for work, and he is angered when Denise reminds him about this.
- Denise notices that Ron fidgets when he's watching TV, and he's become very restless in bed. He's had two falls in recent months.

Ron’s story, continued

- When Denise tries to discuss her concerns with Ron, he dismisses her and tells her she’s been more moody.
- She suggests that Ron see his primary care physician, but he angrily tells her that she’s the one who needs help.

- What concerns do you have about Ron and Denise?

- Are there any steps that she can take?



Sometimes HD is the elephant in the room.

- What would happen if we didn't try so hard to ignore it?
- **Commonly, HD patients avoid and delay seeking diagnosis and treatment.**
- What are the issues that prevent people at risk who may be symptomatic, their families, friends and loved ones from discussing a possible diagnosis of HD?
- Are there any other medical diagnoses that we try so hard to avoid?

Benef its of HD Diagnosis

- Permits **early symptom management**: evaluation, education, treatment and anticipatory guidance
- **Relieves uncertainty**
- Allows patients to decide how they would like to be cared for **while still able to make informed decisions**
- May **open doors** for those who choose to:
  - Participate in research
  - Become more fully involved in the HD family community
  - Find spiritual meaning in illness
  - Clarify life's priorities

Ron's story, continued

- Ron agrees to be seen at the HDSA Center of Excellence. He's seen by the neurologist, the social worker and the genetic counselor. His neurological exam shows clear signs of early-stage HD and he agrees to have a blood draw for genetic testing.
- The COE team provides Ron and Denise with information about HD. They discuss his job performance issues and whether and when he might qualify for disability. The neurologist recommends that he start taking a medication for depression, undergo formal cognitive testing, regulate his sleep-wake cycle, follow a heart-healthy diet and increase his exercise.
- Ron returns a month later and learns that his genetic testing is positive for HD, with 42 and 17 CAG repeats. His mood has improved since starting medication, and he is coming to terms with his diagnosis of HD. Ron and Denise join the local HD support group.
- Ron decides to volunteer for an HD research study.

Scenario 2: Ben's story

- Ben is married, age 58, with 3 young adult children, and works full time in a financial services job. He receives a call from his first cousin Barbara telling him that her father (his 74 year old uncle) was recently diagnosed with Huntington's disease several years after the onset of memory difficulties and involuntary movements. There is no other family history of HD in their grandparents or extended family.

- Barbara tells Ben that HD is a genetic disorder, and his mother is at 50% risk of having inherited the gene for HD. She has been notifying the other relatives in the family about this new diagnosis. She asks him to relay the news on to his 3 children and his two younger brothers.

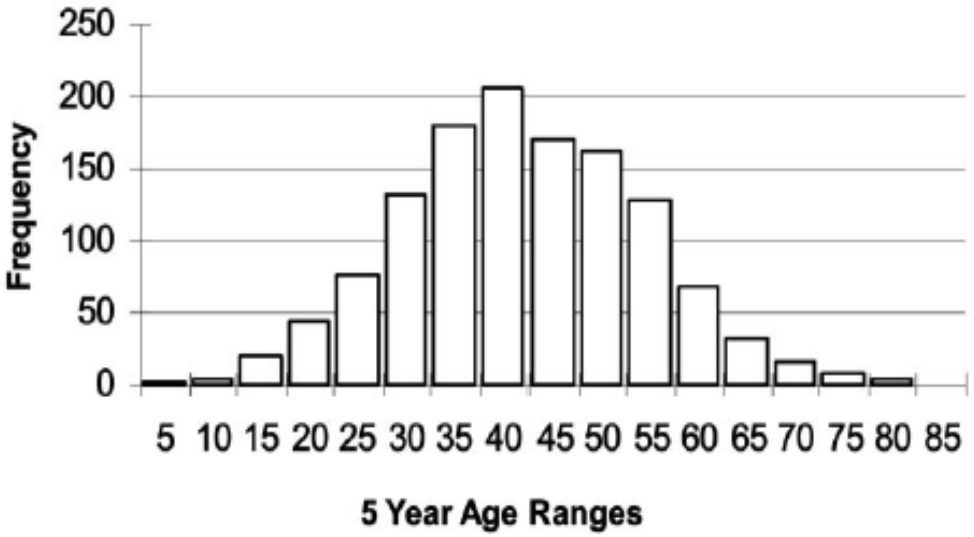
Scenario 2: Ben's story

- Ben is shocked to learn about this. He immediately realizes that some of the changes he's been noticing in his 80 year old mother may be due to HD, not just old age. She has been forgetful, seems clumsy, sometimes imagines that people are trying to break into her home, and seems restless and fidgety all the time.

- What other concerns may Ben have?

Who gets HD?

- **The HD gene is highly mutable. Extra CAGs may appear across generations.** ***10% of cases arise in families without hx of HD.***
- A CAG repeat length in the unstable (27 – 35) or reduced penetrance (26-38) range can expand to a disease-associated CAG repeat length of >38.
- This may result in the first diagnosis of HD in an older family member.
- This occurs more commonly with paternal (father-to-child) inheritance.
- Higher CAG repeats lengths lead to earlier onset of symptoms.



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Scenario 2: Ben's story

- Ben contacts the local HDSA Center of Excellence. He's worried that his mother may have HD. He wonders if he and his two brothers should immediately come in for HD testing. He isn't sure how to discuss HD with his three children. His daughter Maria married last year and is planning to start her family.
- Ben speaks with the HD nurse. She explains that the decision to undergo testing for the HD gene is very personal and that he and his brothers should take time to consider their options.
- The nurse helps him make an appointment for his mother to be seen. Ben's mother is confirmed to have HD with 40 and 17 CAG repeats.
- Ben helps his mother move into assisted living. He decides that, at this time, he does not want to test for the HD gene.
- Ben and his wife have a family meeting to discuss HD with their children. They share resources provided by the Center of Excellence.

Scenario 3: Maria's story

- Ben's daughter Maria is 28 years old. She has completed college and is works for a high tech start-up company. She is married to her college boyfriend Mike. They hope to have start a family soon.
- Ben told Maria and her siblings that their grandmother has HD. He explained that he is at 50% risk of having inherited the HD gene. Maria and her siblings are each at 25% risk. Maria goes on line and learns that when the HD gene is inherited from a father the onset might be earlier in the next generation.
- Maria and Mike decide that they would want to know if HD is a possibility for their children before they have children.
- What options does Maria have?

Predictive Genetic Testing for HD

HD Predictive Testing Centers

- 2015 update of HDSA Genetic Testing Guidelines
- Concerns about stigma and genetic discrimination
  - Insurance, employment, education, other
  - Genetic Information Non-discrimination Act (GINA) - 2009
- Counseling by neurologist, geneticist, or genetic counselor, mental health provider
  - **Explore reasons for and against testing for that individual**
  - Concept of “genetic biopsy” - risk of suicide
  - Results given **in person** with follow-up counseling
- Available to those 18 and older
- Only 5 - 10% of people at risk chose to test – but this may be increasing

Resources

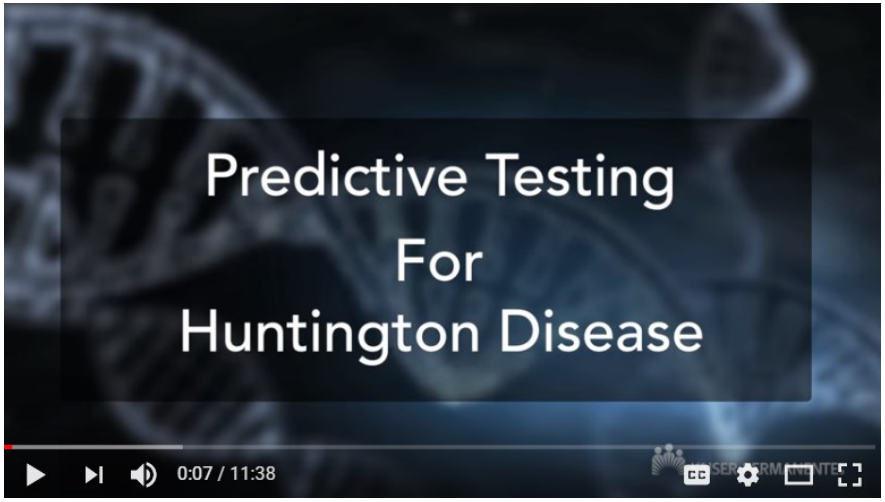
HDSA Website:

http://hdsa.org/wp-content/uploads/2015/02/HDSA-Gen-Testing-Protocol-for-HD.pdf

See HD Predictive testing video with

Mara Sifry-Platt, MS, LCGC

https://www.youtube.com/watch?v=4HW5YdgM4zs



One reproductive choice: Pre- implantation diagnosis (PGD)

- Uses in vitro fertilization techniques
- PGD is a way to test an embryo before implantation into a woman's uterus.
- The early-stage embryo is tested for markers of expanded or normal HD gene.
- Only embryos that are gene negative are implanted.
- Non-disclosure PGD can be performed in a way that doesn't disclose the at-risk parent's status if the couple desires.
- I ssues: Cost , medical burden to mother, high-risk pregnancy

See www.hdfreewithpgd

See also https://www.ucdmc.ucdavis.edu/huntingtons/genetics-prenatal.html

Scenario 4: Ron and Denise's son Justin

- Denise and Ron have 2 teen-aged sons, Justin (17) and Derek (15). They have talked about HD with Justin and Derek a few times over the years. When Denise tells them that their father was diagnosed with HD the boys are very concerned.

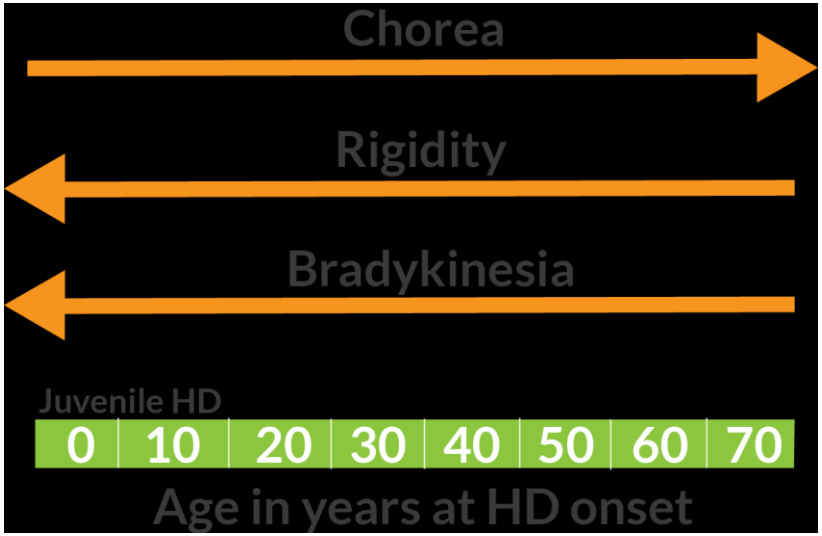
- Justin has been having some difficulties in high school. Previously an excellent student, his grades have dropped from A's in his freshman year to C's in his junior year. He is withdrawn and no longer hangs out with his friends after school, preferring to play video games. His mother notes that Justin rarely smiles.He seems a little clumsy and less coordinated. She hasn't seen any similar changes in Derek.

- What concerns does this raise?

J uvenile Onset HD (J HD)

J uvenile onset HD is defined as symptom onset before age 21

- Only 5-10 %of cases of HD have j uvenile onset
- Only 1-2%of cases have childhood onset, defined as onset before age 10 years



The features of JHD are different than those in adult onset.

- **Instead of chorea**, children/teens have rigidity and stiffness of muscles
- **Cognitive change**s and school/learning issues are prominent
- **Mood changes** also occur

Juvenile HD

- Typically, CAG repeats are > 60
  - The CAG repeat length is mutable in spermatozoa and may increase over generations
  - More likely to occur with inheritance from father (75%) than mother

- Features:
  - Cognitive decline, reduced school performance
  - Behavioral disturbances
  - Rigidity of limbs and trunk
  - Speech and swallow dysfunction
  - Seizures in 25%
  - Rate of progression may be slightly faster than in adult HD

Nance MA. Neurology 1999; 52:392-4.
Cloud LJ et al. Movement Disorders 2012; 27:1797-1800.

J uvenile HD

- **Diagnostic challenges: I s it HD or not?**
  - Behavioral and mood issues are common in children/ teens.
  - Teens may experiment with or become dependent on drugs and alcohol.
  - It's important not to confuse normal behavior issues in kids with J HD.
- **When to consider testing a child or teen for J HD**
  - Movement disorder
  - Cognitive decline with loss of prior learning achievement
  - Decline demonstrated on longitudinal examinations
  - Severe psychiatric manifestations, psychosis

Scenario 4: Ron and Denise's son Justin

- Justin is seen at the Center of Excellence. His neurological exam shows changes consistent with juvenile HD. He and his parents agree to genetic testing, which is positive with 51 and 17 CAG repeats. He is diagnosed with juvenile HD.
- Denise shares Justin's diagnosis with the school counselor. He is evaluated for an Individualized Education Plan (IEP) to help with his learning issues. He starts physical therapy and counseling.
- Justin's brother Derek is very supportive of his older brother. He helps him with his homework and invites him to go out with his friends.
- Justin and Derek get involved with HDSA's National Youth Alliance. They attend the next HDSA National Convention on a scholarship.

Scenario 5: Sarah's story

- Sarah is a 37 year old teacher with a family history of HD in her father, paternal grandmother and an aunt. Sarah chose to undergo HD predictive testing 10 years earlier when she was engaged. She learned that she was gene expanded with 46/19 CAG repeats on the HD gene. She and her fiancé later broke up.
- Sarah's mom is worried about her. Two years ago she was terminated from her job, and she then lost 2 other teaching positions within a short time. Sarah hasn't been able to get a job since and no longer tries. She is living with her mom. She has become careless about her appearance. Recently she caused a motor vehicle accident while intoxicated. She sometimes talks about going out with movie actors and other celebrities.
- Sarah's mom tries to convince Sarah to see the neurologist, but she refuses.

Anosognosia: Unawareness in HD

- Unawareness of HD symptoms occurs in more than a third of those with HD. This is caused by disrupted brain circuits.
- Unawareness is often most problematic during the HD prodrome, the transition from healthy (pre-manifest) to clinically diagnosed HD.
  - During the HD prodrome, brain imaging changes are already detectable, as are changes in cognitive test performance
  - HD prodrome symptoms may include changes in mood, decline in thinking skills and slight declines in function. There may be slight neurological changes in coordination and balance, but they are so mild that they are not considered to be diagnostic of definite HD.
- Unawareness is a common and challenging symptom in both prodromal and manifest HD. Convincing the person with HD symptoms to seek care can be very difficult.

Scenario 5: Sarah's story

- Sarah's mom calls the HDSA Center of Excellence social worker. They discuss the steps needed to make an appointment. Since Sarah doesn't want to come in to the HD clinic, the social worker advises bringing Sarah in to see a primary care MD as a first step.

- What type of help does Sarah need?
- Sarah eventually agrees to be seen at the COE. She is diagnosed with Stage 2 HD and started on a mood stabilizer and anti-psychotic medication.
  - Her psychiatric symptoms improve.
  - She agrees to stop using alcohol.
  - Sarah applies for disability benefits on the basis of her diagnosis of HD.
  - She accepts help with setting up a daily schedule and starts physical therapy.

People in the HD prodrome may have difficulties with relationships, home and work function.

We strongly encourage those in the HD prodrome to be seen by a treatment team, ideally a neurologist and a behavioral health specialist such as a social worker and/or psychiatrist.

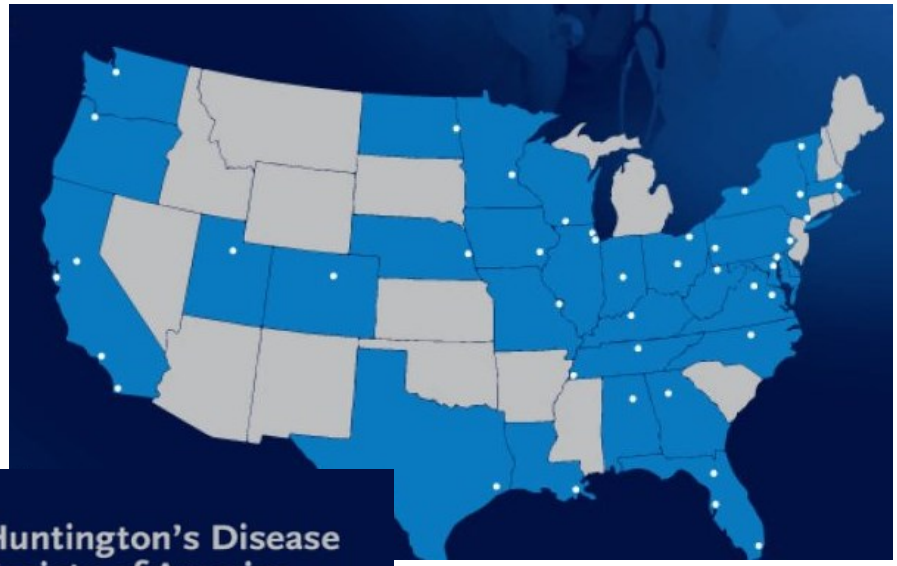
Management includes treatment of mood disorders (depression, anxiety), assessing thinking skills and counseling.

Wrap up: Benefits of staying connected

- **Access** to expert and knowledgeable advic**e**
- **Genetic testing** and **predictive testing** for HD
- **Diagnosis** of Huntington's disease
  - **Helping to navigate the HD prodrome**
  - ***Starting early management is key to helping the person with HD and their family***
  - Applying for **disability benefits**
  - Regular care to **monitor HD symptoms** at all stages and plan for future needs
- **Family support**
- **Potential enrollment in HD studies**

Thank you to HD patients, families and care partners

Our work in HD has been inspired and generously supported by HD patients and family members.



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50 YEARS OF SERVICE
1967-2017

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You have taught us about courage and compassion to help provide help for today and hope for tomorrow