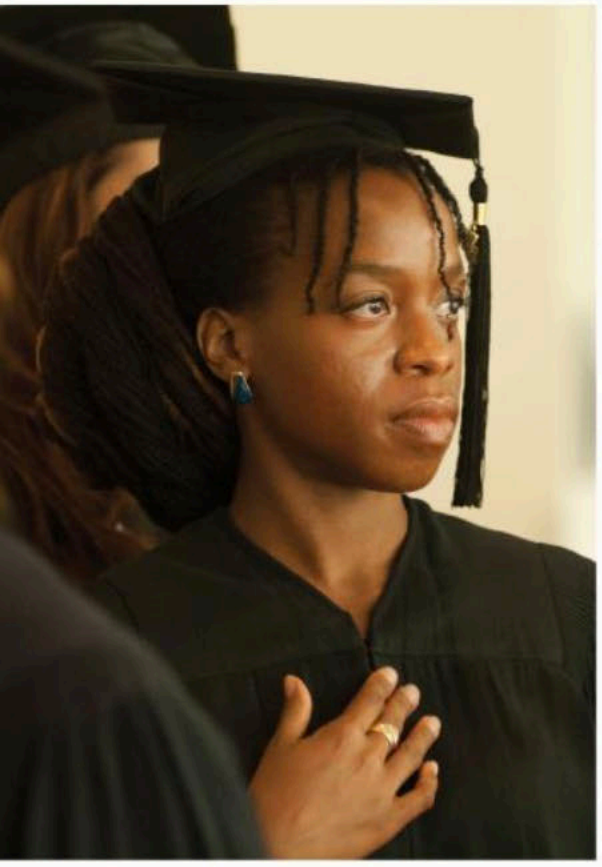

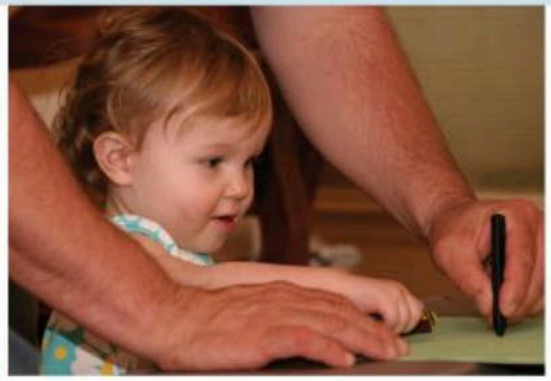

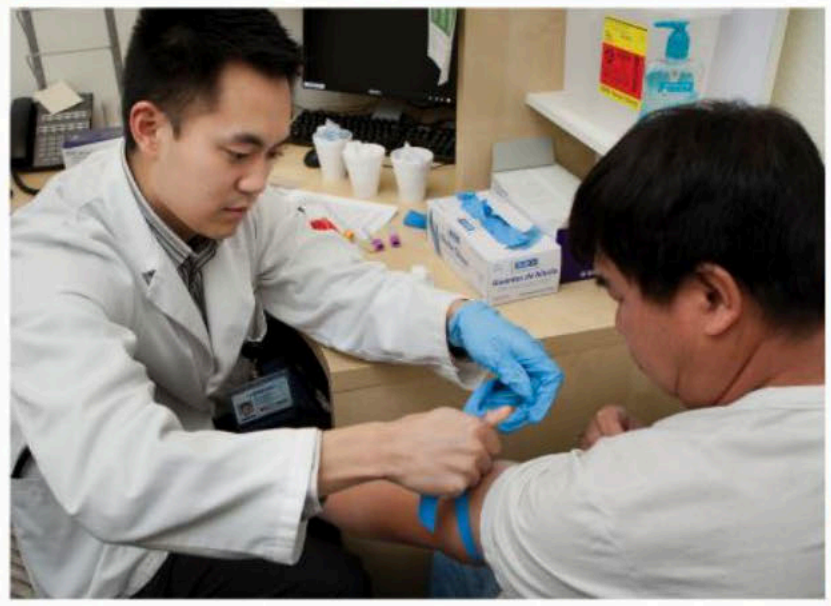

UC DAVIS HEALTH SYSTEM

Juvenile Huntington's Disease

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Huntington's Disease Society of America Center of Excellence

HDYO

JHD genetics

- Typically, CAG repeats are > 60
- More likely to occur with inheritance from father (75%)
  - The CAG repeat length is “mutable” in spermatozoa and may increase from one generation to the next
  - This can also occur with maternal inheritance, but is less likely
- The range can be as low as 45 repeats, and can overlap the range seen in adult HD
- The longest CAG repeat length reported is >250, associated with JHD in a child with onset during their second year of life

How common is JHD?

- Review of JHD from Salpetrière Hospital in Paris
  - 29/1452 referrals had JHD, or 2%
  - Symptom onset 14.5 yr (range 5-20)
  - Mean delay in diagnosis: 9 years
  - Initial symptoms: psychiatric or behavioral in 65%
  - CAGn 62 $\pm$ 11 (range 45-89)
  - All cases with onset < age 10 had paternal inheritance
- Review of HD prevalence by UK group showed ranges of 1-15% of all HD case series world-wide, but with average of 5% overall.

JHD Symptoms

- Usually, one parent has HD
  - In childhood-onset HD, sometimes the child may develop symptoms before their affected parent
- Cognitive decline, reduced school performance
- Behavioral disturbances
- Rigidity of limbs and trunk
- Oral motor dysfunction: difficulty with speech, swallow or drooling
- Seizures in 25%
- There is slow progression of symptoms over time

Relationship between CAG repeat length and age at onset

Nance and Meyers, MRDD Research Reviews 2001;7:153–157.

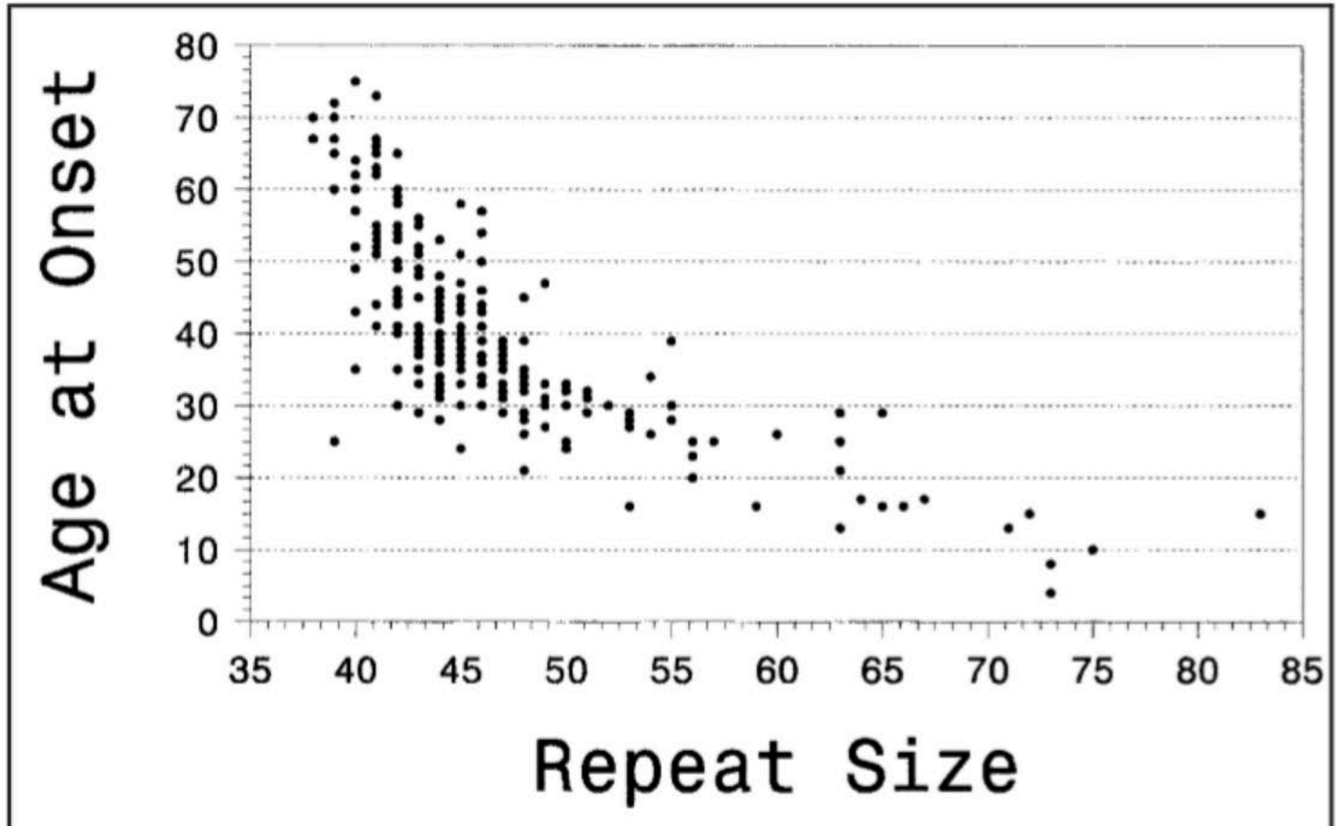

Fig. 1: The CAG repeat sizes for 220 persons HD diagnosed through the New England Huntington's Disease Research Center are presented in relationship to the age at onset of motor impairment. Repeat size is strongly related to age at onset. Onset age before age 20 is usually associated with a repeat size 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.

Diagnosis: when to test

- Diagnosis is made when there is evidence of cognitive decline and/or motor features suggestive of HD
- Presymptomatic testing of minors at risk for HD is not advised
- Sometimes children and teens in HD families have school issues, symptoms of ADHD, and/or behavioral difficulties that may raise the question of possible JHD.
- "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***."
- Symptoms that do NOT suggest JHD: Tics, tremors and spasticity

Lehman and Nance, Neurology® 2013;80:976–977