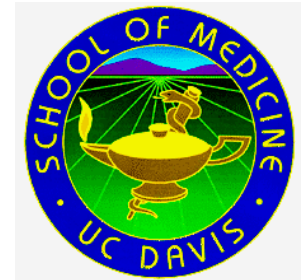




Introduction to Huntington's Disease



Huntington's Disease Society of America
Center of Excellence at UC Davis
August 2016



Welcome!

HDSA Center of Excellence UC Davis Medical Center

Vicki Wheelock MD, Neurologist

Sasha Duffy MD, Neurologist

Lorin Scher MD, Psychiatrist

Lisa Kjer-Mooney LCSW, Social Worker

Rosy Chow LPT, Physical Therapist

Mara Sifry-Platt MS, Genetic Counselor

Amanda Martin BS, Research Coordinator

David Swadell, Research Support Administrator

Care, Outreach, and Reach for a Cure

Our COE Mission:

- *To provide excellent, comprehensive and compassionate care and outreach to HD families*
- *To provide expert education about HD to families, researchers and health care providers*
- *To advance HD research*

Established 2001



39 HDSA Centers of Excellence



The HDSA Centers of Excellence provide an elite multidisciplinary approach to Huntington's disease care and research. HDSA currently has 39 Centers of Excellence across the United States. At these world-class facilities, patients benefit from expert neurologists, psychiatrists, therapists, counselors and other professionals who have deep experience working with families affected by HD and who work collaboratively to help families plan the best HD care program throughout the course of the disease.

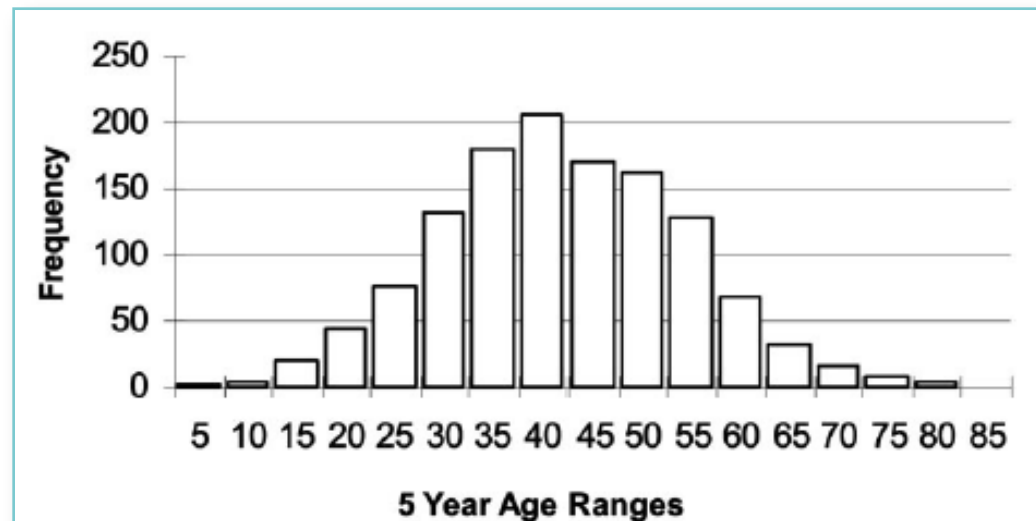
<http://hdsa.org/about-hdsa/centers-of-excellence/>

Huntington's Disease Definitions

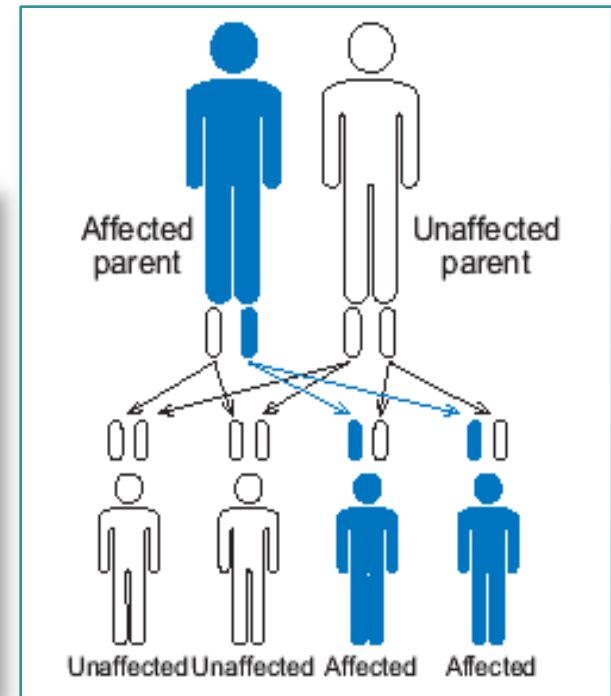
- Slowly progressive, hereditary brain disease that causes changes in movement, thinking and behavior
- Diagnosis is made at the onset of the movement disorder, typically with chorea and impaired voluntary movement.
 - Cognitive and behavioral symptoms often precede the onset of motor symptoms
- Autosomal dominant inheritance
 - High penetrance: everyone with the HD gene expansion will get HD
 - Anticipation: earlier onset in children of fathers with HD
- 30,000 people with HD in US
 - 150,000 at-risk in US
 - About 2000 people are diagnosed each year
- World-wide occurrence in all populations

Who Gets HD?

Each child with a parent with HD has a 50% chance of inheriting the disease.



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

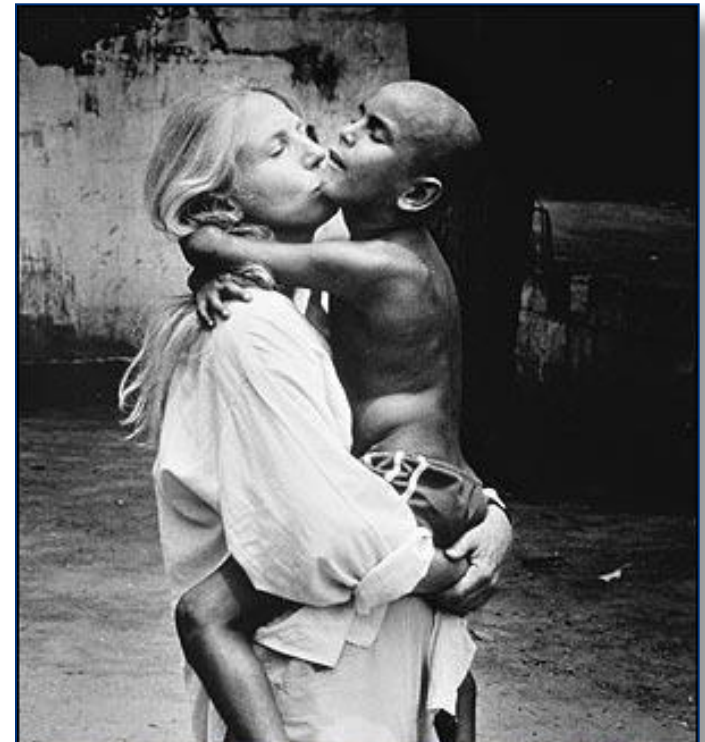


The Search for the HD Gene



Dr. Ramon Avila-Giron, student of Dr. Americo Negrette, showed films of HD patients at HD Centennial Meeting to a skeptical audience, 1972.

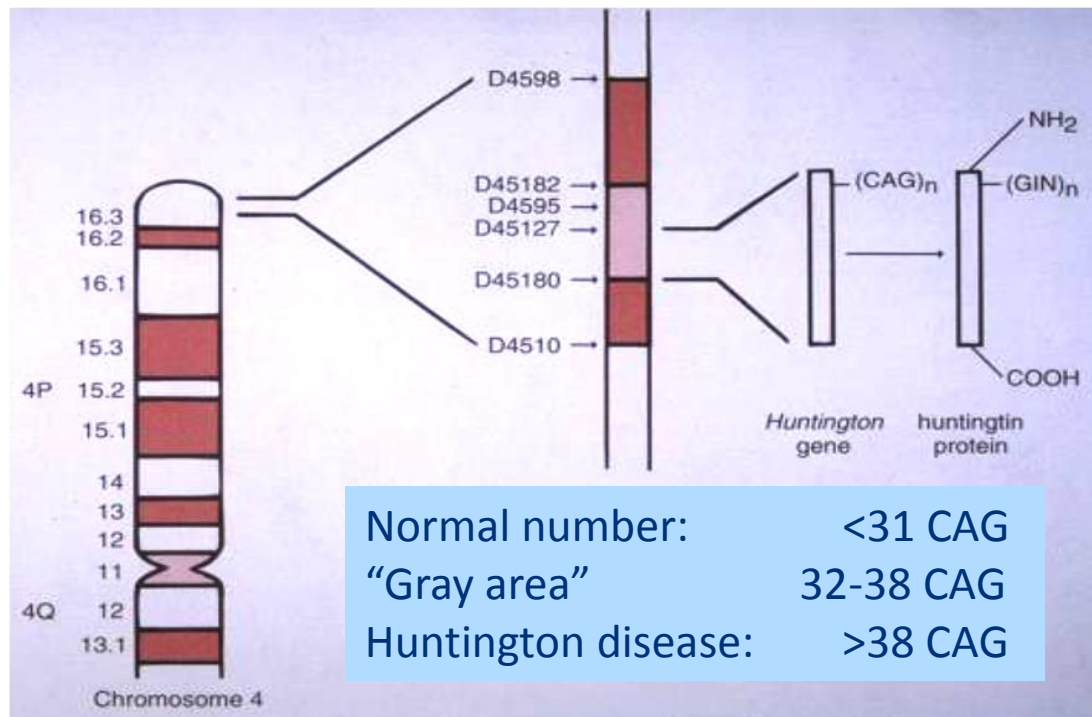
Dr. Nancy Wexler's team visited Lake Maracaibo annually starting in 1979, identifying 18,149 individuals from HD families spanning 10 generations.



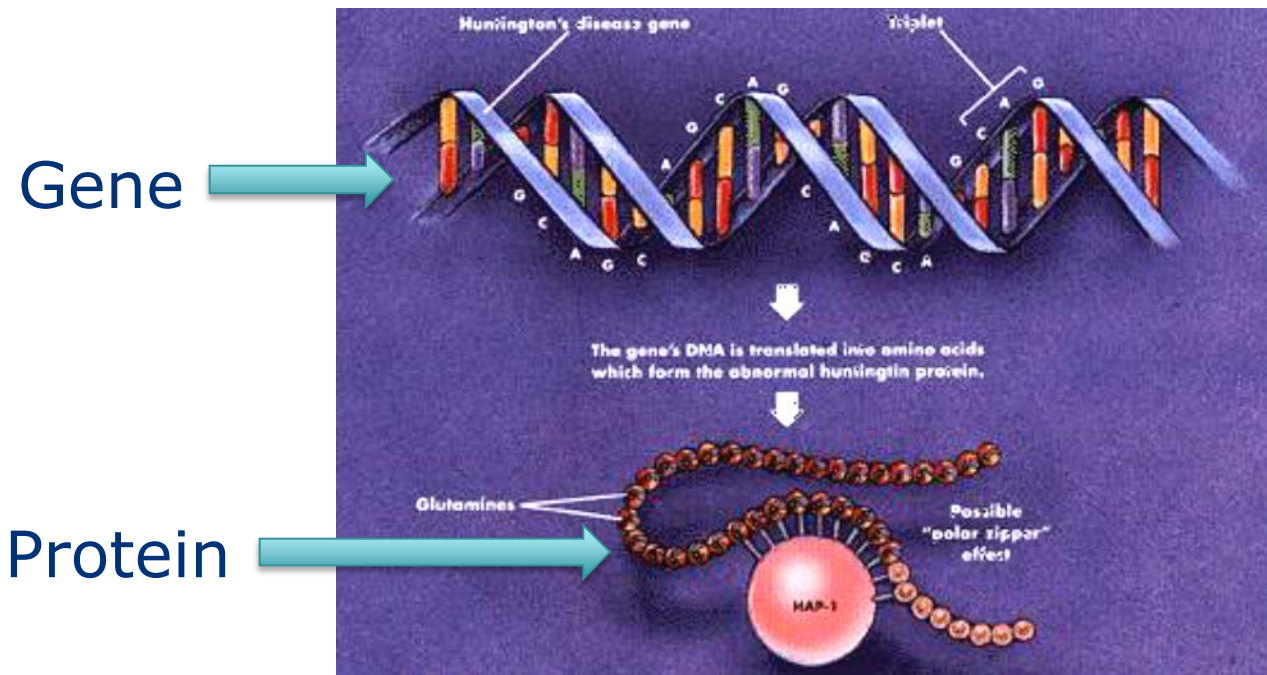
A new study from Nancy Wexler, in Venezuela in the 1990s with a boy with Huntington's disease, suggests there may be ways to delay the onset of the disease.

1993: The HD Gene Is Discovered

Huntington gene → huntingtin protein



The Huntington Disease Mutation



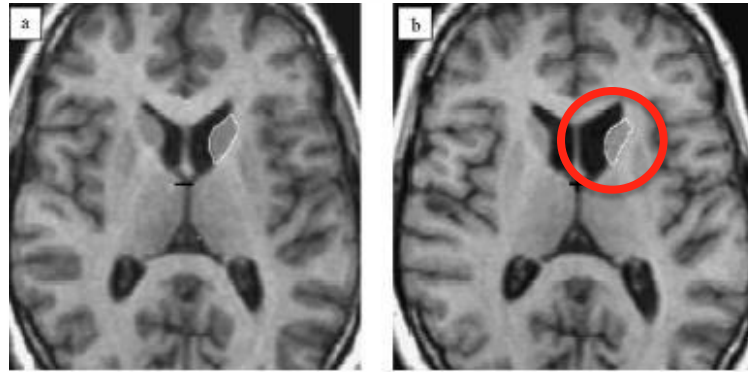
Normal number:	<31 CAG
"Gray area":	32-38 CAG
Huntington disease:	>38 CAG

For more detailed information, see the presenting about Genetics entitled, " _____ "

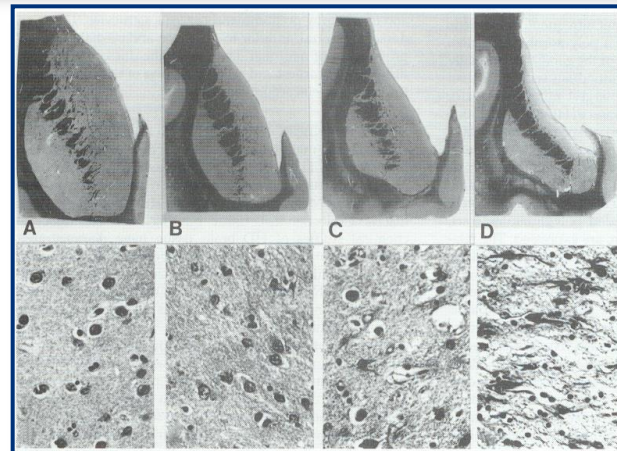
Brain changes in HD

Aylward EH. Brain Research Bulletin 2003;62:137-141

MRI scan



Microscopic view



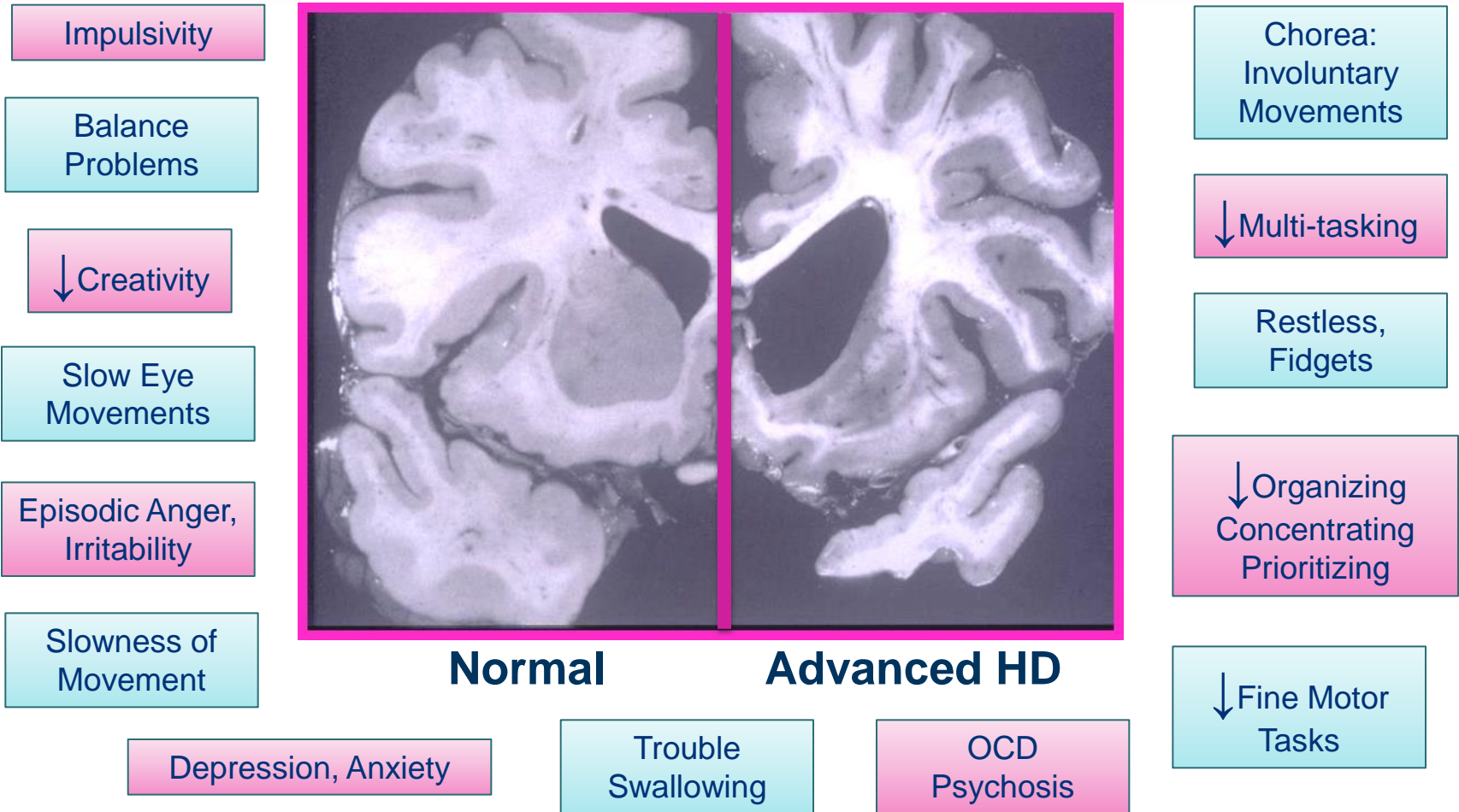
Thinking

Movement

Behavior

Introduction to HD

Symptoms in Huntington's disease



Motor symptoms

- Chorea: involuntary movements, often sudden, irregular and purposeless
 - Nearly all adults with HD experience chorea
 - Examples: blinking, grimacing, neck, shoulder, trunk, hand and leg movements
- Slowness of movement, muscle and joint rigidity
- Dystonia: repetitive, abnormal patterns of muscle contraction frequently associated with a twisting quality
- Poor balance and falls
- Exercise, physical therapy, medications can help

Differential HD motor features with age

- **Juvenile onset** motor features:
 - Rigidity, slowness, muscle spasms
- **Adult onset** motor features:
 - Chorea
 - Rigid-dystonic (about 10%)
- **Effect of disease progression**
 - Slowness of movement, loss of voluntary motor control, rigidity, dystonia



Nance M et al. *Ment Retard Dev Disab Res Rev*2001;7(3):153-7.

Louis ED et al. s. *Arch Neurol* 2000 Sep;57(9):1326-30

Psychiatric symptoms in HD

- Depression 40 - 80%
- Anxiety 30 - 40%
- Obsessions/compulsions 10 - 20%
- Irritability common
- Apathy 20%
- Episodic anger common
- Psychosis 5%

Depression in HD

- Very common. May occur:
 - before diagnosis
 - at the time of diagnosis
 - later in the disease
- Thoughts of suicide may occur
 - Most commonly occurs around the time of diagnosis
 - Over 25% of patients with HD attempt suicide at some point in the illness.
 - Reported rates of completed suicide among individuals with Huntington's disease range from 3-13%
 - **Treatment** of depression with counseling, medications, and family and community support prevents suicide

Cognitive impairment in HD

- Starts early – even before motor symptoms, and is slowly progressive
- First symptoms may include decrease in work performance or ability to carry out home activities
- The type of cognitive impairment is called “frontal-executive” disorder
 - Difficulty with organizing, prioritizing, decision-making, creativity, multi-tasking, ability to start and end activities
 - Memory difficulties are milder
 - Rate of decline can be variable
- Leads to need for workplace accommodations and eventually for disability

Huntington Disease Stages

- **Stage 0:** Presymptomatic
- **Stage 1:** Slightly lower performance at work; independent at home with only slight assistance in managing finances, chores and self-care
- **Stage 2:** May still work (lower level), mostly independent at home; may need help with financial management or chores
- **Stage 3:** No longer able to work; needs help with financial, home activities and personal care
- **Stage 4:** Needs 24 hour caregiving for major assistance with care
- **Stage 5:** Largely bedbound; full-time nursing care required

How do we diagnose HD?

- HD symptoms do not usually start until adulthood – 30's and 40's is most common.
 - Onset can be earlier for those with a higher CAG number
 - Onset can be much later for those with a lower CAG number
- Some people with the HD gene expansion develop mood or cognitive changes first, and then later develop chorea and movement symptoms.
- Currently, HD is diagnosed at the onset at movement symptoms and changes in the neurologic exam.
 - There are situations when we diagnose HD if there is documented cognitive decline.
- At the time of diagnosis, your physician may order a blood test for genetic testing for the HD gene expansion in order to confirm the diagnosis.

More about HD diagnosis

- Being diagnosed with HD can be very difficult and emotionally charged, similar to being diagnosed with cancer or another serious illness.
- Although there is no cure yet available, it's important to start HD management **early**.
- We are hopeful that research will lead to meaningful treatments in the next few years. Much progress has been made!
- Until that time, there are important things patients can do to help manage this illness.
- Starting management early can provide a smoother course in the future.

Are there any advantages to early diagnosis?

- Early diagnosis can:
 - relieve uncertainty. If an at-risk individual is experiencing possible symptoms of HD, the worry and fear can be compounded by not knowing.
 - permit early symptom management: evaluation, treatment, and educational resources can be started right away.
 - allow patients to be proactive in decisions about work, financial and advanced care planning.
 - may open doors to research participation for those who choose it.
- ***If you optimize your physical and mental health at the onset of HD, it can help you and your family more easily manage your symptoms in the future.***

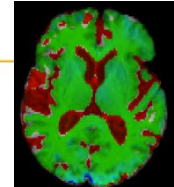
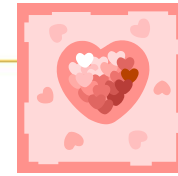
-
- The decision to be seen for possible HD diagnosis is very personal and can be difficult for some people.
 - Being seen by an HD experienced medical provider can be very helpful in establishing a baseline and getting to know the health care team.
 - If you have questions about being seen, please call our social worker Lisa Mooney at (916)734-6277, or call an HD social worker in your area.
 - Listings for HDSA Centers of excellence can be found here:
 - <http://hdsa.org/about-hdsa/centers-of-excellence/>

Management after diagnosis

- Establish with a medical care team: neurologist, primary care physician, mental health provider
 - Consider workplace accommodations or disability planning
 - Future planning: financial, advanced directives
- Establish caregiver support and community resources
 - HD support groups
 - Web-based resources
 - ***You are not alone!***

Neurological and medical care

- General care plan
 - Healthy heart = healthy brain
 - Promote brain health:
 - regular schedules
 - attention to sleep/wake cycles
 - regular exercise program
 - avoidance of brain toxins (tobacco, alcohol, recreational drugs)
- Start the discussion about advanced directives
- Manage any other medical conditions: high blood pressure, thyroid disorders, high cholesterol, and others



Neurologic care plan

- **Physical therapy assessment**
Stretching, strengthening, conditioning, assess for balance, develop home exercise plan
- **Assess need for anti-chorea therapy (see below)**
- **Cognitive screening/neuropsychological testing to establish baseline and assess abilities for work/home**

Behavioral health care plan

- Behavioral and mood symptoms are the most difficult and distressing for HD patients and family members.
- Every HD patient needs a behavioral health plan!

See slide ___ for more details

What kinds of treatments do we have for HD?

- Symptomatic
 - Movement problems
 - Thinking/behavior
 - Mood problems
 - Swallow problems
 - Nutrition
- Neuroprotection:
 - Delay the onset or slow progression
- Research is underway
- Cure: Hope from research

Management of chorea: Behavioral/environmental

- Reduce stress and anxiety
- Seek mood disorders and optimize treatment
- Use routines and schedules
- Allow extra time for ADL tasks
- When chorea is severe, protective padding, helmets and bedding may be necessary.

When might medications be needed?

- *Symptoms bother patient*
- Interference with or interruption of sleep
- Muscle pain
- Frequent dropping (dishware or other items)
- Repetitive injuries (abrasions, bruises, biting the tongue)
- Falls due to trunk and lower limb chorea
- Weight loss

Introduction to HD

Tetrabenazine to reduce chorea: First drug approved for HD in the US

Benefits: Highly effective for chorea

Side effects:

- swallow dysfunction
- ↑depression/suicide
- restlessness

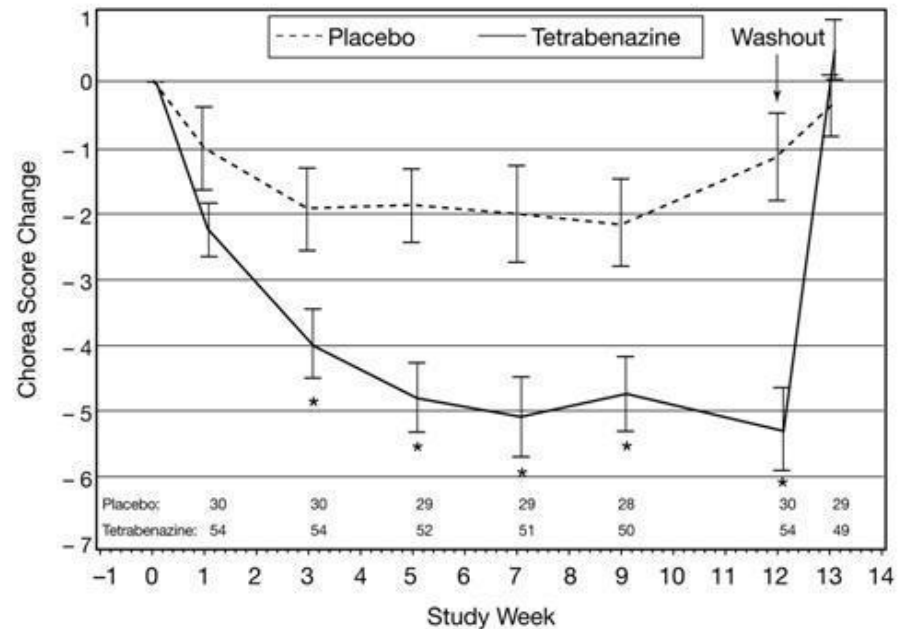
Interactions:

- Some anti-depressants
- Other anti-chorea drugs

Dosing:

- Genetic test
- Monitor EKG

Generic form now available



Safety considerations for tetrabenazine

- There is a Black Box warning from the FDA, because tetrabenazine may cause worsening depression or thoughts of suicide.
- Patients with a history of depression, suicidal thoughts or attempts may not be good candidates for this drug.
- In these cases, we often prescribe antipsychotic medications which are very effective for reducing chorea.
- ***See Medication Management for HD Presentation for more details.***

Other movement disorders

- Myoclonus: quick, brief jerking movements; faster than chorea. Most common in juvenile HD.
- Tremor: Rhythmic oscillations of hands or legs; may be rarely seen in JHD but usually due to anti-chorea medications
- Motor tics: repetitive movements of face or trunk
- Vocal tics: involuntary sounds (throat clearing), sounds (“un-huh”) or words, including repeating words or swearing

Balance Problems



Rosy Chow,
Physical Therapist

May occur early in HD, but more commonly occurs later in the disease.
Physical therapy and exercise help tremendously!

Please see the presentation

**“Coping With Disability
and Muscle Weakness in
Huntington’s Disease”**

for HD - specific exercises.

Physical therapy in HD

- **May help slow progression...and** at a minimum provides physical comfort
 - Your physical therapist can serve as a coach and personal trainer who is medically trained and licensed.
- **Early – mid stage:** Stretching, conditioning, strengthening, gait and balance assessment, home exercise program
- **Later stages:** Assistance with mobility, fall prevention, stretching ,range of motion, caregiver training for transfers and home safety
- Medicare regulations permit long-term PT for to maintain level of function. Renew PT orders at least annually (or more often)

Swallow difficulties and choking



- Patients and families may view choking as one of the most feared consequences of HD.
- Inadequate chewing, delayed transfer of bolus, slow and incomplete swallow are seen
- Choking on liquids is also common
- May contribute to weight loss, dehydration, agitation
- May lead to aspiration pneumonia in advanced HD
- Management: patient and caregiver education, speech therapy referral, revision of food textures and strategies to reduce choking
- Family members should be taught the Heimlich maneuver
- Feeding tubes may be an option for some as a palliative measure

Management of Cognitive impairment in HD

- Testing at the physician's office to assess the degree of difficulty can be done annually
- This may include formal neuropsychological testing for more detailed understanding of abilities
- Work-place accommodations may help: allowing extra time for completion of work, fewer distractions, reduced responsibilities
- At home, we recommend using schedules and routines, reminders, allowing extra time, simplifying responsibilities
- For some patients, medications developed for other neurologic disease may help.

Emotional Symptoms

- Behavioral symptoms are the most difficult and distressing for HD patients and family members.
- Psychiatric symptoms are the most variable feature of HD, but are quite common and include:
 - Depression Anxiety Irritability
 - Obsessive thoughts Compulsive behaviors
 - Apathy Rare: delusions, hallucinations and psychosis
- Suicide is more common in HD, and it can be preventable
- Talk with the physician if patients or family members notice mood symptoms – they are important to diagnose and they are very treatable
- Institute treatment: counseling, medications

Medications for Treatment of Emotional Symptoms

Medications that help depression anxiety, irritability and other mood symptoms in the general population are usually extremely effective in HD.

For more detailed information, Please see slide presentation

“Medications to treat HD”

Other symptoms in HD

Speech difficulties
Seizures (JHD)
Sleep issues
Weight loss
Bowel and bladder changes
Falls and injuries
Pain

Speech Impairment

- The rhythm, intonation and coordination of speech is affected.
- Voice volume may be too soft or suddenly explosive
- Coordination of speaking and breathing affected
- The ability of others to understand the patient's words declines
- Over time, speaking is more delayed, with fewer words, and eventually patients are mute in the late stages of HD
- Cognitive decline further complicates communication
- Recommend: referral to speech therapist for education to employ strategies that take into consideration the cognitive challenges in communication

Seizures

- Common in JHD with onset below age 10
- Rare in adult-onset HD; associated with higher CAGn
- Recent multi-center retrospective review in 90 JHD patients found incidence of seizures was 38%
- Risk correlated with younger age at onset and higher CAGn
 - Seizure types: Multiple different types
- Standard neurological work-up with imaging and EEG is advised
- Medications to prevent seizures are usually effective.

Weight loss

- Not seen in early HD, but more common in mid- to late-stages
- There may be many causes:
 - Increased metabolic demands from chorea
 - Cognitive impairment
 - Mood disorders and apathy
 - Swallow dysfunction
 - Poor absorption of food by GI tract has been suggested

Weight loss in HD often leads to worsening of symptoms and functional abilities, and can lead to irritability and agitation

Weight loss management: identify causes

Anti-chorea therapy if indicated

Increase food and calorie intake:

Schedules, structure and reminders to eat

Assistance with meal planning, preparation and feeding

Nutrition/Dietary referrals to help develop plans to increase caloric intake

Appetite stimulants are rarely helpful – not recommended

Discussion about feeding tube placement with health care team

Sleep issues

- Sleep complaints:
 - Difficulty falling asleep or waking up frequently
 - Excessive daytime sleepiness
 - Reversal of sleep-wake cycles
- Management: Behavioral strategies such as setting regular schedules, sleep hygiene, addressing motor issues that may interfere with sleep initiation, melatonin
- Avoid sedative drugs because they can worsen thinking and behavior

Bladder and bowel changes

- Bladder: some patients develop increased frequency of urination, while others may find it difficult to fully empty their bladder.
- Bowel : some patients develop significant constipation, while others may have loose stools or alternating constipation and diarrhea similar to Irritable Bowel Syndrome.
- Sometimes medications used for chorea, mood or behavior can cause bladder or bowel function changes
- Management: schedules, structure, attention to oral intake, bowel program meds, referral to urology or urogynecology specialist

Risk of injuries

- HD patients have a high incidence of accidents, falls, fractures, and brain injuries
 - Risks are related to cognitive and mobility issues
 - Education is vital to prevent injuries
- Those with frequent chorea and/or restricted mobility may develop skin breakdown over the back, buttocks, and limbs which may lead to serious infection
 - Frequent repositioning, padding, treatment of dystonia/chorea, monitoring for skin changes
 - Caregiver education

Pain in HD

- Challenge: HD patients may fail to recognize or report pain, but consider pain if they have sudden changes in behavior or agitation.
- Common causes: hunger, severe chorea, dystonia, occult fractures and sprains, pressure sores, urinary retention and constipation
- Pain is expected in late-stage HD.
 - Pain behaviors: groaning, agitation, screaming
 - Seek to recognize painful conditions and offer adequate pain treatment.
 - Treatments: optimize nutritional support, management of chorea and dystonia, fall prevention, protective padding, frequent repositioning, and analgesics.
 - Start with scheduled analgesics such as acetaminophen.
 - Other prescribed medications can help

Late stage HD: indications for potential referral to hospice

- Significant difficulty with feeding leading to weight loss resistant to medical interventions
- Decline in mobility: wheelchair or bed-confined status
- Severe or repeated infections: pneumonia or urinary tract
- Skin breakdown or bed sores
- Recurrent hospitalizations for other causes
- Pain issues refractory to usual measures

Please see “Challenges in Late Stage HD” Presentation

Is there anything that can slow the progression of HD?

- There is no therapy that's been proven yet to delay the onset of slow the progression
- We recommend:
 - a good, heart-healthy diet
 - regular exercise
 - avoiding smoking and excessive alcohol
- Recent clinical trials of dietary supplements Coenzyme Q10 and Creatine failed to show any benefit.
- Research trials are ongoing, and some show promise for rationale hope of disease-modifying therapy

Research participation

- We have been actively involved in HD research at UC Davis for 18 years.
- Research studies have advanced our knowledge about HD and give hope for developing new treatments.
- Every patient is invited to volunteer for research!
- If you are interested in possible research participation, please see the research page of this website or call research coordinator Amanda Martin at (916)734-3541.

Summary

- Although no disease-modifying treatments yet exist for HD, quality of life-improving treatments do exist.
- Early diagnosis permits starting early management.
 - Early management can improve the course for later stages
- Medical and neurological care should include assessment of chorea and other symptoms.
- Attention to behavioral symptoms is important at all stages
- Regular preventive medical care is recommended.
- Speech, occupational and physical therapy referrals are appropriate at each stage of disease..

Thank you to HD patients and care partners

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

We are grateful to the Joseph P. Roberson Foundation, the Charles and Margaret Pue Charitable Foundation, and many others who have contributed to our HD care and research programs at UC Davis.

