

Medications for Huntington's Disease



Vicki Wheelock, M.D.

Director, HDSA Center of Excellence at UC Davis

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Outline

- Introduction and disclaimers
- Medications for cognitive symptoms
- Medications for psychiatric symptoms
- Medications for sleep difficulties
- Medications for juvenile HD
- Medications for chorea and dystonia
- Conclusions

Introduction

- HD symptoms include cognitive impairment, chorea and movement difficulties, and psychiatric challenges. This session will review the indications, benefits and side effects of medications which are commonly used to manage these symptoms.
- It is *extremely important* to recognize that behavioral techniques, counseling, speech, occupational and physical therapies and adaptive equipment are the primary forms of treatment for many HD symptoms.

There is only one medication that is FDA approved for HD

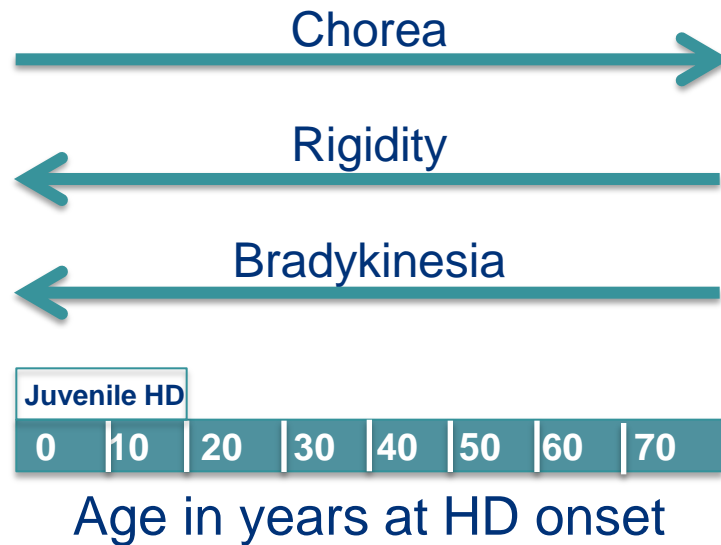
- That drug is tetrabenazine (Xenazine).
- Many other drugs approved for other indications (depression, psychosis, Parkinson's disease, Alzheimer's disease) have been tried and may be used for HD. This is called off-label prescribing.
 - In some cases, there are research studies that support use of these medications in HD.
 - As with all medications, HD patients must be monitored for side effects.
 - There is a great need for additional drugs and more studies.

Please refer to *A Physician's Guide to the Management of HD, 3rd edition* for guidance.

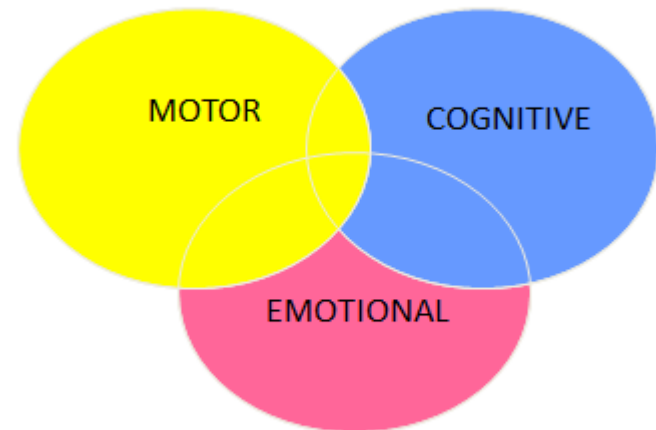
The relationship between HD symptoms and age

From: Harper, PS. *Huntington's disease*

Presenting motor findings



Symptoms in HD



Cognitive Impairments in HD

- Learning and memory
- Perceptual skills
- Unawareness
- Language difficulties

- Executive dysfunction
 - Speed of processing
 - Attention and concentration
 - Planning and organization
 - Lack of initiation
 - Perseveration: getting stuck
 - Impulsivity

Medications for Cognitive Difficulties

- We sometimes prescribe drugs for from Alzheimer's disease.
- Those are best for memory and perhaps perceptual skills.
 - No benefit for executive dysfunction.
- Donepezil, 5-10 mg daily may be tried – not effective in one randomized trial .
- Rivastigmine 6 mg per day studied in open-label trial in Europe; showed possible benefit. Needs additional study.
- Memantine: Pilot trial in 2009 showed no benefit for cognition.
- Latrepirdine (Dimebon) looked promising in Phase 2 trial, but failed in Phase 3 trial to improve cognition.

1. *Neurology* 2006;67:1268–1271

2. *Parkinsonism and Rel Disord* 13 (2007) 453–454

3. *Arch Neurol.* 2010;67(2):154-160

Medications for Cognitive Difficulties

- Dysexecutive function: Trial of atomoxetine failed to help with attention and executive function (J Paulson, 2009)
- Apathy and lack of initiation may respond to stimulant drugs such as methylphenidate, pemoline, or dextro-amphetamine (see Rosenblatt, *A Physician's Guide to the Management of HD, 3rd edition*).
 - Apathy may worsen with sedating drugs such as anti-psychotics or benzodiazepines

Medications for Depression

Class	Trade Name®	Generic Name
Selective Serotonin Reuptake Inhibitors (SSRIs)		
	Zoloft	Sertaline
	Celexa	Citalopram
	Lexapro	Escitalopram
	Paxil	Paroxetine
	Prozac	Fluoxetine
Non-selective Serotonin Reuptake Inhibitors (NSRIs)		
	Welbutrin	Bupropion
	Effexor	Venlafaxine
Other	Remeron	Mirtazepine

Side effects: well-tolerated. Occasional stomach upset, dizziness, sleepiness, sexual dysfunction; withdrawal syndrome for Paroxetine.

Medications for Anxiety

Class	Trade Name®	Generic Name
Selective Serotonin Reuptake Inhibitors (SSRIs)		
	Zoloft	Sertaline
	Celexa	Citalopram
	Lexapro	Escitalopram
	Paxil	Paroxetine
	Prozac	Fluoxetine
Benzodiazepines	Klonopin	Clonazepam
Non-benzodiazepine anxiolytic	Buspar	Buspirone

Side effects: well-tolerated. Occasional stomach upset, dizziness, sleepiness, sexual dysfunction; withdrawal syndrome for Paroxetine.

Medications for Psychosis

Class	Trade Name®	Generic Name	Side Effects
Atypical neuroleptics (newer agents)			
	Zyprexa	Olanzapine	Weight gain, sedation, metabolic syndrome, possible parkinsonism
	Seroquel	Quetiapine	
	Geodon	Ziprasidone	
	Abilify	Aripiprazole	
Typical neuroleptics (older agents)			
	Haldol	Haloperidol	Parkinsonism, tardive dyskinesia, sedation
	Prolixin	Fluphenzine	
	Risperdal	Risperidone	

Medications for Mania

Class	Trade Name®	Generic Name	Side Effects
Anti-epileptic drugs			
	Depakote	Divalproex sodium	Weight gain, liver toxicity
	Lamictal	Lamotrigine	Skin rash, possibly fatal
	Topamax	Topiramate	Memory impairment, kidney stones
	Tegretol	Carbamazepine	Bone marrow suppression, skin rash
Neuroleptic drugs			
	Many; depends on severity of symptoms. May need injectable medication.		Major sedation, parkinsonism

Medications for Obsessive-Compulsive Disorder

- SSRI antidepressants (see slide 9)
- For severe cases, neuroleptics may be necessary (see slide 11)

Medications for Irritability

- Behavioral strategies are always first-line
- Medications can be considered if behavioral strategies are not adequate
 - SSRI drugs such as sertraline, fluoxetine, paroxetine
 - Benzodiazepines (clonazepam)
 - Anti-epileptic drugs such as Depakote
 - Rarely, neuroleptics

Insomnia in HD

- First, try “sleep hygiene”
 - Go to bed at night, get up in the morning
 - Limit caffeine to no more than 1-2 cups before noontime
 - Limit or eliminate alcohol
 - Regular exercise, early in the day
 - Quiet night-time activities before bed – no computer
- If this fails,
 - Avoid sedatives like Ambien, Lunesta, benzodiazepines, etc: use only on occasion.
 - Melatonin may help people get to sleep and is safe
 - Antidepressants: trazodone ,mirtazepine
 - Occasional use of neuroleptic quetiapine

Treating Juvenile HD

- Medications for cognition and school performance – not recommended
- Medications for psychiatric symptoms may occasionally be needed. Consult a Child Psychiatrist.
- Movement-related problems are usually different than in adults: slowness, rigidity and dystonia are most common
 - Some may have chorea
- Seizures may occur in JHD

Juvenile Onset HD: Rigidity

Class	Trade Name®	Generic Name	Side Effects
Benzodiazepines			
	Valium	Diazepam	Sedation
	Klonopin	Clonazepam	Sedation
Anti-spasticity			
	Lioresal	Baclofen	Sedation
	Zanaflex	Tizanidine	Sedation
Anti-parkinson agents			
	Symmetrel	Amantadine	Hallucinations
	Sinemet	Carbidopa-levodopa	Hallucinations

Juvenile Onset HD: Anti-seizure Medications

Trade Name®	Generic Name	Side Effects
Keppra	Levetiracetam	Sedation
Depakote	Divalproex sodium	Stomach upset, liver toxicity
Tegretol	Carbamazepine	Bone marrow depression, skin rash
Dilantin	Phenytoin	Sedation, gum disease
Klonopin	Clonazepam	Sedation
Many others ... will depend on seizure type		

Adult-onset HD: Chorea is a difficult symptom

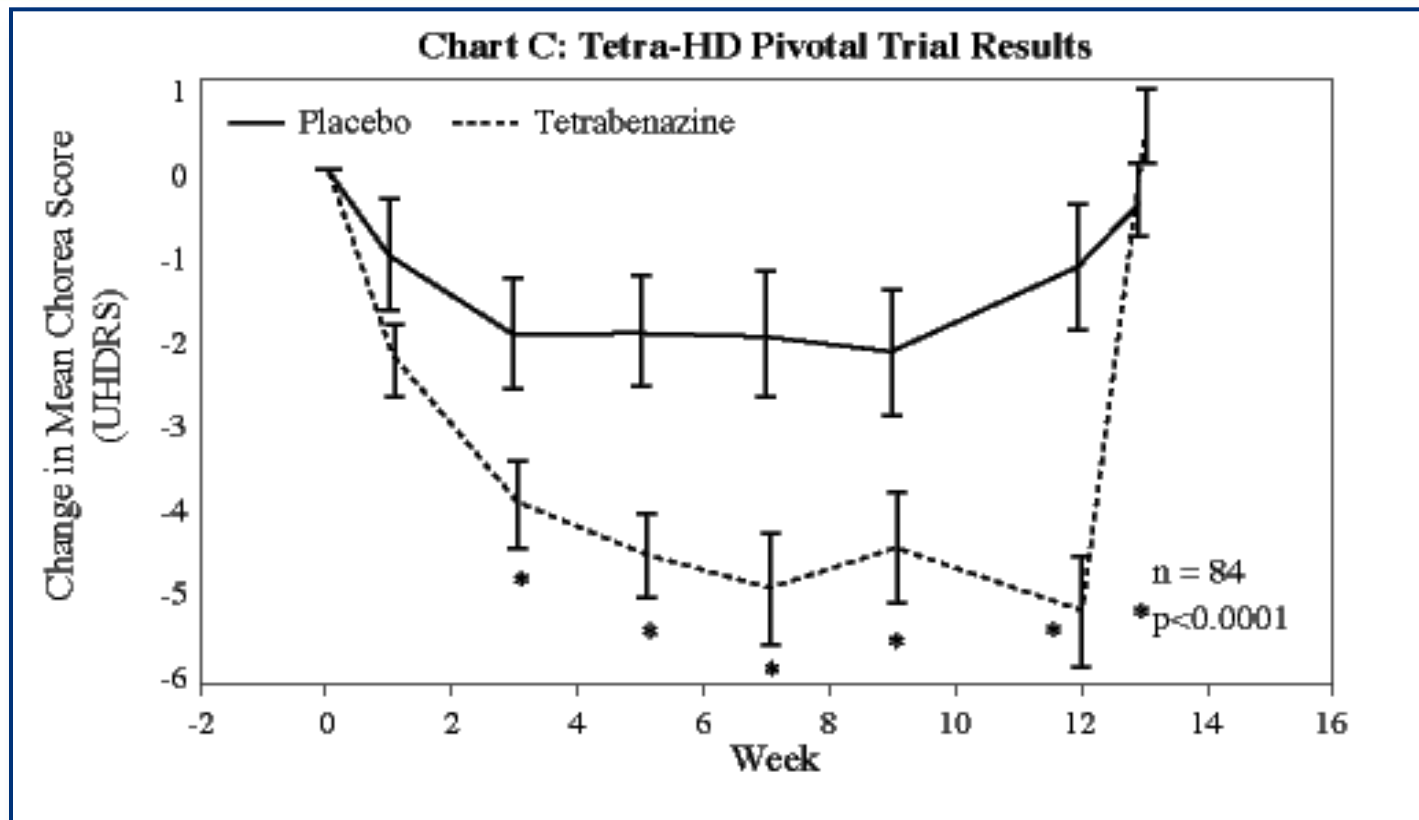
- Affects nearly all adult HD patients (progressively disabling)
- Reduces employability
- Contributes to social isolation and stigmatization
- Presents an increased safety risk (falling, worsened gait, need for supervision)
- Contributes to weight loss
- Can lead to injury and make caregiving difficult, especially in late-stage HD

Tetrabenazine: First drug for the treatment of Huntington's disease to receive FDA approval (TETRA study)

- Double-blind, placebo-controlled study of tetrabenazine in manifest HD
- 84 people with HD, randomized 2:1 to tetrabenazine or placebo for 12 weeks
- Primary endpoint: chorea score



TETRA Study Results



Tetrabenazine



Benefits: Reduces chorea

Side effects:

Swallow dysfunction

Depression/Suicide

Restlessness

Interactions:

Some anti-depressants

Other anti-chorea drugs

Dosing:

Genetic test

Monitor EKG

Cost: Special program

Tetrabenazine and Depression

- 20% of TETRA participants had new or worsening depression
- Patients, their caregivers, and families are informed of the risks of depression.
 - Monitor the patient for any new or worsening symptoms of depression
 - Seek help immediately if the patient develops thoughts of suicide
 - Sometimes dosage reduction will help
 - If depression or suicidal thoughts don't respond to dose reduction, then tetrabenazine must be discontinued.

Medications for Chorea

- First-line: Tetrabenazine (FDA-approved in 2008 as the first drug in US for HD)
- Second line: benzodiazepines
- Third line: antipsychotic drugs
 - “Typical” (older): haloperidol, fluphenazine
 - “Atypical” (newer): olanzapine, risperidone, others

Anti-Chorea Medications

- In patients with significant psychiatric disturbances (severe depression, mania, anger outbursts or psychosis), neuroleptic drugs made be first-choice because they will treat both the psychiatric symptoms and reduce chorea.
- Atypical neuroleptics work well for both psychiatric symptoms and chorea, except for quetiapine, which doesn't help chorea.

(See slide 11 for details)

Further Recommendations about Treatment of Chorea

- Anti-chorea therapy should be re-evaluated at least annually.
- Some patients will require increasing doses of anti-chorea medications over time. Some may even require the addition of two or more drugs to control chorea.
- Many will eventually develop increasing dystonia and rigidity with HD progression, necessitating reduction or cessation of anti-chorea medications.

Medications for HD

10% of adults have the rigid-dystonic form of HD. Treating rigidity:

Class	Trade Name®	Generic Name
Benzodiazepines		
	Valium	Diazepam
	Klonopin	Clonazepam
Anti-spasticity		
	Lioresal	Baclofen
	Zanaflex	Tizanidine
Anti-parkinson agents		
	Symmetrel	Amantadine
	Sinemet	Carbidopa/Levodopa
	Requip, Mirapex	Ropinirole, pramipexole

Tetrabenazine is not indicated for patients with rigid-dystonic HD.

Treating Dystonia in HD

Class	Trade Name®	Generic Name
Benzodiazepine	Klonopin	Clonazepam
Anti-spasticity	Lioresal	Baclofen
	Zanaflex	Tizanidine
Anticholinergics	Artane, others	Trihexyphenidyl
Chemodeneration	Botox, others	Botulinum toxin
Anti-parkinson agents	Symmetrel	Amantadine
	Sinemet	Carbidopa/Levodopa

Tetrabenazine is not indicated for patients with rigid-dystonic HD.

Concluding Thoughts

- Behavioral strategies, speech therapy, physical therapy, counseling lifestyle changes are important tools in helping to treat HD.
- The only medication for HD that is FDA-approved is tetrabenazine, but many others have been used successfully on an off-label basis.
- All medications have side effects, and selecting the right medication should be individualized for each HD patient.
- All medications should be re-evaluated periodically as HD symptoms change or progress.