

HD Irritability Treatment Algorithm: Patient and Family Summary

Irritability is a major symptom of Huntington's disease causing much distress and relationship problems for patients and families. HD causes damage to parts of the brain that control or "put the brakes" on unwanted behaviors. The HD person can become cranky and more quickly irritated and angry over small things, and it takes longer for the angry thought or action to resolve. In its extreme, irritable behaviors escalate to aggression. It is important to remember that this symptom is not a personal character attribute of the HD person, but is caused by the disease. This symptom is treatable: The earlier the better -- because this symptom may occur well before onset of motor symptoms.

Although education and drug treatment can help manage this symptom, irritability often goes untreated because general doctors may not ask questions about it, and patients and families may find it embarrassing and hard to talk about.

If irritability symptoms are a part of your HD, you and your care-partner, who may be more aware of this symptom, should talk about it before the doctor's visit. Also try to identify situations that trigger irritable behaviors --- so they can be avoided as much as possible. Hunger, fatigue, emotional stressors, noise, new situations or events can set off irritability behaviors. Others may be unique to you.

Tell your story, and if after discussion with your doctor, a drug trial for irritability is appropriate:

Step 1 (For severe symptoms): The experts agree that the "best" drug treatment for very severe irritability behaviors that are aggressive and threatening is an antipsychotic drug. The experts preferred olanzapine (Zyprexa), risperidone (Risperdal), and quetiapine (Seroquel) most commonly. Haloperidol (Haldol), an older antipsychotic was less preferred.

Step 1 (For less severe symptoms): If the irritability behaviors are not threatening, more experts choose a selective serotonin reuptake inhibitor (SSRI) drug as first treatment, though some experts use an antipsychotic drug first in this situation also. Experts report the SSRI choice as causing fewer side effects, but not giving as much effective control as the antipsychotic. The most highly preferred SSRI drugs are citalopram (Celexa) and sertraline (Zoloft). This type of drug is often used for treatment of depression, anxiety, and obsessive compulsive symptoms too. So SSRI treatment for irritability symptoms may help other HD symptoms.

Step 2: Finding the best dosage will take several visits. Don't skip any. Most experts use a 2 to 4 week time interval between the visits to give sufficient time for the benefits of treatment to develop". Be patient because it can take up to 6 or more weeks for the full effect at any dose to emerge, so be patient. Don't get disappointed and stop the drug too soon because the symptom isn't better immediately. Many experts believe that a low dose of SSRI drug may not be as helpful as a higher one.

Step 3: If the first choice initial drug did not give sufficient control, the experts most often combined an SSRI and an antipsychotic. Another alternative was the addition of antiepileptic mood stabilizer drug. This type of drug is also used to treat seizures, post- traumatic stress and manic depression. The most common ones chosen are valproic acid (Depakote) and carbamazepine (Tegretol).

Step 4: If the first try of combinations are not sufficient, they try others. It may take several tries to get best result. Experts also use mirtazapine (Remeron), a drug that is helpful for depression and insomnia can be helpful for irritability too. Experts who have used propranolol (Inderal) for irritability symptoms have found it beneficial.

Don't stop trying to bring this symptom under control. Because each HD person is unique, experts say it may take several trials of drugs or drug combinations to control this symptom. Don't expect any drug to be good enough to eliminate irritability completely, but with treatment you can be an HD irritability survivor.

Summary by LaVonne Goodman M.D. based on Groves M, van Duijn E, Anderson K, Craufurd D, Edmondson MC, Goodman N, van Kammen DP, Goodman L. An International Survey-based Algorithm for the Pharmacologic Treatment of Irritability in Huntington's Disease. PLoS Curr 2011;3():RRN1259.

Algorithm for the treatment of irritability in Huntington's disease

Serotonin reuptake inhibitor (SSRI)

First choice drug for:

- non-emergent irritability
- comorbid depression
- comorbid anxiety
- comorbid obsessive-compulsive behaviors

Step 1. Start with low dose

citalopram	(20 mg)
sertaline	(50 mg)
paroxetine	(20 mg)
fluoxetine	(20 mg)
escitalopram	(10 mg)

Though many survey experts chose 4 weeks or more, the authors suggest a shorter 2-4 week dosing interval
Check for adherence

Step 2. Dose optimization

Symptom control often requires mid to high level dosing

citalopram	(20-40 mg)
sertaline	(50-200 mg)
paroxetine	(20-60 mg)
fluoxetine	(20-60 mg)
escitalopram	(10-20 mg)

Reassess response and side effects at each dosage increment
Check for adherence

Step 3. Alternate mono- or combination therapy

If inadequate response to SSRI, experts chose the following alternatives (listed in order of preference):

- add APD
- add AED
- switch to another SSRI
- switch to APD
- switch to AED
- add BZD
- switch to BZD

Authors suggest trial of propranolol

If response remains inadequate, authors suggest second trial of switching drugs within class

Check for adherence

Antipsychotic (APD)

First choice drug for:

- severe aggressive behaviors
- comorbid psychosis
- comorbid impulsivity

Alternative choice drug for:

- less severe irritability

Step 1. Start with low dose

olanzapine	(2.5-10 mg)
risperidone	(0.5-2 mg)
haloperidol	(0.5-2 mg)
quetiapine	(25-200 mg)
tiapride*	(50-200 mg)
sulpiride*	(100-600 mg)

*tiapride, sulpiride available in Europe

Check for adherence

Step 2. Dose optimization

- urgent as outpatient: 2-3 days - weekly
- less severe: 2-4 weeks

Reassess response and side effects at each dose increment

Check for adherence

Step 3. Alternate mono- or combination therapy

If inadequate response to APD, experts chose the following alternatives (listed in order of preference):

- switch to another APD
- add SSRI
- add AED
- add BZD
- switch to AED
- switch to SSRI

If response remains inadequate, authors suggest second trial of switching drugs within class

Check for adherence

Abbreviations

AED	mood stabilizing anti epileptic drug
APD	antipsychotic
BZD	benzodiazepine
SSRI	selective serotonin reuptake inhibitor

