Lesson 287: PreAnesthetic Assessment of the Patient With Huntington’s Disease

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TIME TO COMPLETE ACTIVITY: 2 hours
REVIEW DATE: August, 2010
TERMINATION DATE: August 31, 2011

TARGET AUDIENCE: Anesthesiologists

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Needs statement

Huntington’s disease (HD) is a genetically linked neurodegenerative disorder. When patients with HD receive anesthetic care, the disease presents challenges for the anesthesiologist; it is thus important that, perioperatively, patients with HD are appropriately managed. Rarely encountered disease states have been identified as important topics for clinical anesthesiologists.

Learning Objectives

At the end of this activity, the participant should be able to:
1. Cite the prevalence of HD.
2. Summarize the clinical symptoms and signs of HD.
3. Describe treatment modalities and their possible effects on anesthetic care of patients with HD.
4. Review the pathophysiology of HD.
5. Present a differential diagnosis.
6. Accurately diagnose HD.
7. List possible fatal complications with HD.
8. Choose common pharmacotherapies used in treating patients with HD.
9. Present an appropriate perioperative plan.
10. Recognize that patients with HD may be more sensitive to certain medications, compared with the general population.

Case History

A 38-year-old woman with long-standing HD was admitted for placement of a percutaneous endoscopic gastrostomy tube as a result of advancing dysphagia and weight loss. She had a history of seizures and neurodegenerative symptoms. Laboratory values, review of systems, and physical examination findings were normal, except for signs of slightly decreased mentation, hyperreflexia, slow motor responses, and Parkinson-like behavior.

Huntington’s disease (HD) is a devastating, progressive, autosomal dominant, neurodegenerative disorder characterized by chorea, cognitive impairment, and disturbances of personality, mood, and behavior.¹

Before the 19th century, those with HD were thought to be possessed by spirits, and were treated as witches and shunned by society. The first definite mention of the disease was by a medical student Charles Waters in the first edition of Robley Dunglison’s textbook The Practice of Medicine in 1842. Mr. Waters noted the characteristic choreiform movements and strong hereditary pattern associated with the condition.²

Although partially described by others, George Huntington, MD, accurately and succinctly described the disease that would come to bear his name in 1872 as a triad of features consisting of movement disorder, dementia, and a tendency toward a variety of psychiatric disorders. Unknowingly, Dr. Huntington described the exact pattern of inheritance of autosomal dominant disease years before the discovery of Mendelian genetics.² The disease went largely unrecognized by popular media until American singer-songwriter Woody Guthrie was diagnosed with HD in 1952, eventually succumbing to complications in 1967. His death led to the formation of the Committee to Combat Huntington’s Disease.³

Background

The estimated prevalence of HD is approximately 5 per 100,000, with a slightly decreased prevalence among those of non-European ancestry. The mean age at onset is between 35 and 45 years.⁴ The disease progresses inexorably with death occurring in 15 to 20 years, usually from pneumonia or heart disease.⁵
HD is a trinucleotide repeat disorder caused by an abnormal increase in the number of cytosine-adenine-guanine repeats in the HD gene located on chromosome 4. The number of trinucleotide repeats correlates with the penetrance and age of onset of HD, with a large number of repeats corresponding to greater penetrance and earlier onset.6

The huntingtin protein (htt) associated with HD is expressed in all human and mammalian cells; the highest concentrations occur in the brain and testes, with moderate amounts in the liver, heart, and lungs.4 The exact function of the wild-type 3144 amino acid htt is unknown but appears to be involved in scaffolding multiple proteins for signaling processes and intracellular transport, as well as transcription of messenger RNA.7 Htt also seems to be essential for development and tissue maintenance because in knockout murine models, embryonic death occurs by day 7.5,7

The basal ganglia atrophy gradually, beginning years before the onset of symptoms, and ultimately manifest as the main phenotypic alteration—generalized involuntary movements.4 Multiple pathologic mechanisms have been proposed by which mutant htt causes neuronal dysfunction, but an exact comprehensive mechanism still is unknown.8

A presymptomatic genetic test is available for HD; however, because of the implications of a positive result, genetic counseling is usually recommended before proceeding. Preimplantation testing of susceptible embryos recently has become available for in vitro fertilization procedures.

A major area of research that pertains to the treatment of patients with HD has centered on cell therapy strategies—for protecting vulnerable neuronal cell populations or replacing dysfunctional or dying cells. HD cell therapy comprises 3 underlying approaches: the potential for self-repair by manipulating endogenous stem cells and/or neurogenesis, the use of fetal or stem cell transplantation as a cell replacement strategy, and the administration of neurotrophic factors to protect susceptible neuronal populations. These approaches have delivered some promising results in certain animal models for HD that are fairly well established.9

**Clinical Presentation**

HD is characterized by problems with motor, cognitive, and behavioral functioning for which there is currently no effective definitive treatment.10 The clinical presentation of HD varies depending on the stage of its progression. The earliest findings in patients, as they transition from an asymptomatic to a symptomatic phase, are mild chorea, impairment of fine motor coordination, and the slowing of ocular saccade.11

The motor problems associated with HD often begin with generalized restlessness, hyperreflexia, and fidgety movements of the fingers, hands, and toes during stress, and progress to the more obvious extrapyramidal signs of chorea.10 Ninety percent of adult-onset patients present with varying degrees of dystonia, parkinsonism, and bradykinesia.10 Although the chorea is progressive, it tends to wane later in the course of the disease as other features accumulate.10 Voluntary motor function also is affected—particularly motor termination and motor impersistence (inability to sustain motor actions or gestures, such as eye closure and tongue protrusion).10 Gait problems are common in patients with HD and mainly characterized by a timing disorder that leads to an increased risk for falls.10

Manifestations of HD on the peripheral nervous system include dysarthria, dysphagia, altered appetite, malnutrition, pancreatic dysfunction, and impaired energy metabolism.7,10 Juvenile onset of HD, which
occurs in 8% of patients, typically does not include chorea, but predominantly rigidity and bradykinesia in addition to seizures and ataxia.12

Deep brain stimulation of the posteroverentral globus pallidus internus may offer a treatment option for patients with predominantly choreiform movements and minimal cognitive impairment, but its role in the management of HD remains unclear.13

Among a range of clinical scoring systems that have been described, the Unified Huntington’s Disease Rating Scale (Table 1) provides a reliable and consistent assessment of the full range of motor, cognitive, and psychiatric symptoms associated with the progression of HD.14 Another scale, the Behavior Observation Scale Huntington (BOSH; Table 2) was designed for the rapid, longitudinal assessment of functional abilities of nursing home residents with HD.15

Dysphagia is a common symptom in patients with HD.16 Patients with chorea often demonstrate rapid lingual chorea, swallow incoordination, repetitive swallowing, prolonged laryngeal elevation, inability to stop respiration, and frequent eructations.16 In contrast, patients with HD with rigidity frequently have mandibular rigidity, slow lingual chorea, coughing on foods, and choking on liquids.16

Table 1. Motor Areas of the Unified Huntington’s Disease Rating Scale

<table>
<thead>
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<th>Area</th>
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<tr>
<td>Ocular pursuit (vertical and horizontal)</td>
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<tr>
<td>Saccade initiation (vertical and horizontal)</td>
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<tr>
<td>Saccade velocity (vertical and horizontal)</td>
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<tr>
<td>Dysarthria</td>
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<tr>
<td>Tongue protrusion</td>
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<tr>
<td>Finger taps (right and left)</td>
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<tr>
<td>Pronate/supinate</td>
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<tr>
<td>Fish-hand-palm sequence</td>
</tr>
<tr>
<td>Rigidity–arms</td>
</tr>
<tr>
<td>Bradykinesia</td>
</tr>
<tr>
<td>Maximal dystonia (trunk, face, extremities)</td>
</tr>
<tr>
<td>Maximal chorea (trunk, face, extremities)</td>
</tr>
<tr>
<td>Gait</td>
</tr>
<tr>
<td>Tandem walking</td>
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</tbody>
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The scale is divided into multiple subsections: motor, cognitive, behavioral, and functional. Scores are calculated by assigning a grade of 0 to 4 for each question of each section, and summing the totals.


Table 2. The Behavior Observation Scale Huntington Comprises 32 Items in 3 Subscales

<table>
<thead>
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<th>Subscale</th>
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<tr>
<td>1) Activities of daily living</td>
</tr>
<tr>
<td>2) Mental rigidity and aggression</td>
</tr>
<tr>
<td>3) Sociocognitive functioning</td>
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Modified from reference 15.
Anesthetic Management of The Patient With HD

General Considerations

When patients with HD undergo anesthesia, multiple possible complications must be considered, including a difficult airway, sleep disturbances (which can be related to a mood disorder—either depression or, less commonly, mania), increased risk for pulmonary aspiration, and altered reactions to certain drugs.

Moreover, the patient may be elderly, frail, unable to cooperate, or suffering from malnutrition, so that a preoperative evaluation and obtaining consent become difficult. Patients with advanced disease may be incapable of providing informed consent. Consent for elective cases should then be deferred to a responsible family member or guardian.

In patients with HD undergoing elective surgery, ongoing aspiration pneumonitis and pneumonia should be ruled out by physical examination, room air oxygen saturation, and chest radiography. An indication of the patient’s nutritional status and gross pancreatic function can be attained by ordering an electrolyte panel including serum magnesium, calcium, and phosphorous levels, in addition to liver function tests and a complete blood count.

Preoperative Considerations

Preoperatively, patients with advanced choreiform movements and dementia may require chemical sedation before interventions such as positioning and placement of IV lines. Nandita et al reported a case of a 45-year-old man with advanced HD undergoing elective cataract surgery who required oral premedication with haloperidol and lorazepam. Butyrophenones and phenothiazines are used clinically to potentially reduce choreiform movements.

Specific Considerations: Anesthetic Technique/Drugs

The clinical anesthesiologist administering anesthesia to the patient with HD encounters challenges involving the choice of drugs and techniques. Both regional and general anesthesia techniques have been used. Successful rapid sequence and inhalational induction techniques have been described.

Neither depolarizing nor nondepolarizing muscle relaxants are contraindicated. Decreased pseudocholinesterase activity may be observed in patients with poor nutritional status. It should be noted that only one case of delayed recovery from succinylcholine has been reported—thought to be consistent with pseudocholinesterase deficiency independent of HD. Additionally, although cases have been reported of increased sensitivity to the lesser-used thiopental (IV induction agent) and the frequently used midazolam (anxiolytic agent), these 3 anesthetics have been administered successfully to patients with HD.

Ideally, the anesthetic management of patients with HD allows rapid recovery of pharyngeal reflexes to reduce the likelihood of aspiration. In general, rapid-sequence or modified rapid-sequence induction is recommended for induction. The use of total IV anesthesia (TIVA) with propofol is suitable because it allows precise titration, easy induction, early emergence, and rapid restoration of airway reflexes that ultimately reduce the risk for pulmonary aspiration. Successful TIVA with propofol and
remifentanil has been reported, in which the patient achieved stable oxygen saturation, heart rate, and blood pressure, and recovered fully without incident.\textsuperscript{21}

Inhalational agents are easy to titrate and have been administered successfully.\textsuperscript{22} Nagele and Hammerle\textsuperscript{19} described a case report in which rapid-sequence induction with 400 mg of thiopental and 100 mg of succinylcholine was successful. After the patient was intubated, anesthesia was maintained with 250 mcg of fentanyl and 1.5\% to 2\% inspired sevoflurane. After the 70-minute procedure, muscle function recovered, and sevoflurane was discontinued. The patient regained consciousness and recovered without incident. Ondansetron (8 mg) and ranitidine (50 mg IV) were administered to prevent postoperative nausea and vomiting and ultimately reduce the risk for aspiration. Postoperatively, the patient experienced a short episode of shivering and was treated with meperidine.\textsuperscript{19}

Rocuronium has been shown to be a suitable alternative when rapid-sequence induction becomes necessary.\textsuperscript{22} According to Kulemeka and Mendonca,\textsuperscript{23} rocuronium produced a predictable duration of muscle relaxation that provided a suitable alternative for rapid-sequence induction.

Remifentanil, an opioid that is degraded by nonspecific blood and tissue esterases, has been administered at high doses for a long duration without accumulation and with rapid recovery. Because patients with HD may have poor nutritional status, plasma protein and cholinesterase levels may be reduced, delaying the degradation of remifentanil and prolonging recovery of spontaneous respiration. Thus, a lower concentration of remifentanil may be required for malnourished patients.\textsuperscript{21}

Perioperatively, chorea generally can be managed with butyrophenones, phenothiazines, benzodiazepines, or the monoamine-depleting agent tetrabenazine. Anticholinergics may worsen the symptoms of chorea; therefore, glycopyrrolate, a quaternary amine with far less penetration of the central nervous system, should be used instead of atropine to avoid central effects that may worsen choreiform movements.\textsuperscript{17} Anti-parkinsonian agents may ameliorate hypokinesia and rigidity, but may increase chorea. Myoclonus in HD responds well to valproic acid.

It should be emphasized that although abnormal responses of patients with HD to anesthetic medications have been reported, prolonged responses to succinylcholine and sodium thiopental and increased sensitivity to midazolam appear to depend directly on the patient’s state of malnutrition rather than the disease process.\textsuperscript{24

When anesthesia must be administered urgently, full-stomach precautions must be observed because of the increased risk for aspiration. In one case of emergency anesthesia, the patient was successfully intubated with a fiber-optic bronchoscope with sedation and spontaneous breathing. Although 10\% lidocaine spray was used as a topical anesthetic in the nasal passages and pharynx during intubation, the cough and swallow reflexes remained intact, which potentially could have posed difficulties during intubation.\textsuperscript{20}

When appropriate, regional techniques—including spinal anesthesia—have been found to be an effective option. Regional anesthesia avoids many of the potential disadvantages of general anesthesia and is associated with a high rate of successful outcomes. Spinal anesthesia is a particularly appealing option in patients with HD undergoing surgery in which cessation of choreiform movement is required. Esen et al\textsuperscript{25} described successful spinal anesthesia in a 44-year-old woman with a 15-year history of HD who underwent elective foot surgery to correct a hallux valgus deformity. The patient was treated with
oral famotidine 40 mg and diazepam 5 mg at 1 hour before surgery, and sedated with IV midazolam 2.5 mg, which slightly decreased the chorea. Spinal anesthesia was accomplished on the first attempt with 3.5 mL of hyperbaric bupivacaine 0.5% with the patient in the lateral decubitus position. The patient was then positioned supine, and a spinal block level of T7 was reached after 10 minutes. The block eliminated all choreiform movements in the lower extremities for the duration of the surgery, which would not have been possible with an ankle or selective foot block. After the 90-minute procedure, the patient recovered full motor and sensory function within 2 hours without complications.²⁵

In summary, providing anesthesia to patients with HD poses unique challenges; such difficulties can be overcome, however, by having a proper understanding of the disease and its implications for anesthetic management. Based on a review of the literature by Gilli and colleagues,²⁰ the majority of perioperative complications reported in patients with HD seem to be attributed to general medical conditions rather than to the disease itself. The major complications associated with HD appear to be increased risks for aspiration and a difficult airway.

Although abnormal responses to some medications have been reported, the majority of anesthetic drugs can be administered without complications in these patients. It is imperative to obtain a thorough medical history from the patient’s family or old medical records to ascertain the extent and progression of the disease.

**Management of the Case Presented**

Options for the procedure were discussed with the patient, her family, and the surgeon, after which the patient was given general anesthesia using TIVA. A rapid-sequence induction was performed with propofol, rocuronium, and remifentanil. The procedure lasted 40 minutes, and included an infusion of propofol through full completion of the procedure. After full reversal of anesthesia, the patient was extubated successfully and brought to the recovery room. There were no significant issues and she was discharged home later that day.

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*Dr. Elizabeth A.M. Frost, who is the editor of this continuing medical education series, is clinical professor of anesthesiology at The Mount Sinai School of Medicine in New York City. She is the author of *Clinical Anesthesia in Neurosurgery* (Butterworth-Heinemann, Boston) and numerous articles. Dr. Frost is past president of the Anesthesia History Association and former editor of the journal of the New York State Society of Anesthesiologists, Sphere. She is also editor of the book series based on this CME program, *Preanesthetic Assessment, Volumes 1 through 3* (Birkhäuser, Boston) and 4 through 6 (McMahon Publishing, New York City).*
REFERENCES


26. Image provided courtesy of Steven Finkbeiner, MD, PhD, director of the Taube-Koret Center for Huntington’s Disease Research in San Francisco and associate director of the Gladstone Institute of Neurological Disease at University of California in San Francisco.
Visit [www.mssm.procampus.net](http://www.mssm.procampus.net) today for instant online processing of your CME post-test and evaluation form. There is a registration fee of $15 for this non–industry-supported activity. For assistance with technical problems, including questions about navigating the Web site, call toll-free customer service at (888) 345-6788 or send an e-mail to Customer.Support@ProCEO.com. For inquiries about course content only, send an e-mail to ram.roth@mssm.edu. Ram Roth, MD, is director of PreAnesthetic Assessment Online and assistant professor of anesthesiology at The Mount Sinai School of Medicine, New York, NY.

**Post-test**

1. In which of the following structures does atrophy begin before the onset of symptoms of Huntington’s disease (HD)?
   a. Basal ganglia
   b. Limbic cortex
   c. Corpus callosum
   d. Hippocampus

2. Approximately 90% of patients with HD exhibit all the following signs, except:
   a. bradykinesia
   b. parkinsonism
   c. myoclonus
   d. dystonia

3. In patients with HD undergoing anesthesia, which of the following is a common but potentially fatal symptom?
   a. Dyspnea
   b. Hyperthermia
   c. Dysphagia
   d. Palpitations

4. Increased sensitivity to which drug has been reported in patients with HD?
   a. Fentanyl
   b. Diazepam
   c. Lorazepam
   d. Midazolam

5. Patients with HD who are severely malnourished may require which drug in a lower than normal dose?
   a. Ondansetron
   b. Sufentanil
   c. Alfentanil
   d. Remifentanil
6. Which drug should be avoided in patients with HD to prevent exacerbation of chorea symptoms?
   a. Glycopyrrolate
   b. Atropine
   c. Succinylcholine
   d. Neostigmine

7. Which of the following is a false statement?
   a. HD is a “trinucleotide repeat” disorder caused by an increase in the number of CAG repeats in the HD gene.
   b. HD is characterized by problems with motor, cognitive, and behavioral functioning for which there is currently no effective definitive treatment.
   c. Spinal anesthesia is an absolute contraindication in patients with HD.
   d. Prolonged responses to thiopental and succinylcholine have been reported in patients with HD.

8. Preoperatively, which laboratory study is recommended for patients with HD?
   a. Electrolyte panel
   b. Coagulation profile
   c. Thyroid function tests
   d. Peripheral smear

9. A 38-year-old man with HD presents to the preoperative clinic for an open reduction and internal fixation of the left tibia. He complains of a productive cough. A measurement of SpO2 on room air is 89%; a physical examination including bilateral auscultation reveals marked consolidation in the right lower lobe with crackles. Which of the following is the likely diagnosis?
   a. Pulmonary embolus
   b. Acute exacerbation of asthma
   c. Interstitial lung disease
   d. Aspiration pneumonia

10. Which class of medications should not be used to alleviate symptoms of chorea in patients with HD?
    a. Butyrophenones
    b. Phenothiazines
    c. Benzodiazepines
    d. 5-HT3 inhibitors