

Huntington's Disease DNA Screen

Background

Huntington's disease (HD) is an autosomal dominant genetic disorder. Expansion of a CAG trinucleotide repeat in the *HD* gene occurs in 98-99% of Huntington's disease cases, and is essentially absent in normal controls (Kremer et al., 1994). Alleles with ≥ 40 CAG repeats are abnormal; alleles with 36-39 repeats are abnormal with reduced penetrance; alleles with 27-35 repeats are normal but potentially mutable upon transmission to offspring; and alleles with ≤ 26 repeats are normal. The number of CAG repeats does not reliably predict the age of onset, the rate of disease progression, or the severity of symptoms for an individual patient.

Indications for Testing

- Confirm clinical diagnosis of Huntington's disease
- Presymptomatic testing for Huntington's disease

Restrictions/Exclusions from Testing

- Presymptomatic testing of minors (< age 18) (including evaluations for adoptions)
- Anonymous testing

Genetic Counseling

Genetic counseling can be useful to patients and families considering genetic testing. The laboratory can provide referrals to genetics clinics in the patient's locale or a listing can be found at www.genetests.org

Ordering

1. Obtain blood samples:
 - from the patient
 - from an affected relative, if possible - to establish that the mutation is detectable
2. Fill out a Clinical Lab Request - Genetics for each patient.
(Available at <http://depts.washington.edu/labweb/Divisions/MolDiag/MolDiagGen/index.htm>).
 - Request: "Huntington's Disease"
 - If a specimen is being submitted from an affected relative for confirmatory testing, please indicate "Relative of (patient name)" on the relative's requisition.
3. Provide items needed for test interpretation:
 - Reason for ordering test (e.g. confirm diagnosis; R/O HD; presymptomatic)
 - Clinical history (chorea; dementia; psychiatric symptoms)
 - Family history/pedigree (relatives with HD or possible HD)
4. Call Laboratory Medicine Community Services at (206)598-6066 to arrange the best method of shipment.

Sample Requirements and Specimen Handling

Whole blood - EDTA (purple top) - 5 mL.
Samples should be received within 72 hours of collection.
Samples may be refrigerated until shipped.
For prenatal diagnosis specimens, consult laboratory.
Heparin (green top) tubes are not acceptable.

Test Frequency and Reporting

Test results usually within 1-2 weeks of specimen receipt. A written interpretative report is provided.

References

- Mahbubul H, Hayden MR. Huntington Disease. In: GeneReviews at GeneTests: Medical Genetics Information Resource (database online). Copyright, University of Washington, Seattle. 1997-2003. Available at <http://www.genetests.org>
- Kremer B, Goldberg P, Andrew SE et al. A worldwide study of the Huntington's disease mutation. The sensitivity and specificity of measuring CAG repeats. *New Engl J Med* 1994; 330:1401-1406.
- Margolis RL, Ross CA. Diagnosis of Huntington Disease. *Clin Chem* 49 (10):1726-1732, 2003.

Huntington's Disease DNA Testing Recommended Clinical Protocols

A. Diagnostic Testing of Symptomatic Patients

The following clinical protocol is recommended:

1. Pre-test counselling:
Patients should understand the meaning and limitations of a positive, negative or indeterminate test result (the laboratory can supply a patient information booklet for this process).
If there is a significant history of depression or other psychiatric disorder, it is advisable for the patient to have an established relationship with a psychiatrist, psychologist, or therapist.
2. Clinical evaluation by a neurologist.
3. Laboratory testing.
4. Post-test counselling.
5. If the patient has the mutation causing Huntington's Disease (HD), it may be appropriate to refer relatives for genetic counselling (we can provide a list of available medical genetics clinics).
Relatives requesting presymptomatic testing should follow the protocol below.

B. Presymptomatic/Predictive Testing of Patients at Risk for Huntington's Disease

The DNA test can determine whether most patients at risk for HD have inherited the mutation causing the disease. **Given the likely impact of presymptomatic testing on life plans and insurability, patients should be adequately informed and counselled before the test is ordered and the results given.**

The following clinical protocol is recommended:

1. Clinical evaluation by a physician. If the patient has signs or symptoms suggestive of HD, he/she should be referred to a neurologist.
2. Pre-test counselling:
 - Patients should evaluate their reasons for undergoing predictive testing, and consider what they will do with the results of the study (whether positive, negative, or indeterminate).
 - Patients should be made aware of the meaning and limitations of a positive, negative, or indeterminate test result (the laboratory can supply a patient information booklet for this process).
 - Patients should identify a support person to help them cope with results.
 - If there is a significant history of depression or other psychiatric disorder, it is advisable for the patient to have an established relationship with a psychiatrist, psychologist, or therapist.
3. Laboratory testing.
4. Post-test counselling. Results of test should be given in person, preferably with a support person present.
5. For individuals given an abnormal result, a follow-up phone call within 1-2 days and an in-person follow-up visit within 1-2 months are recommended. Subsequent follow-up visits are recommended at least annually. For individuals given a normal result, a follow-up phone call within 1-2 months and a followup visit or telephone call within 6 months are recommended.

C. Other Indications for Testing

Prenatal testing may be appropriate in some circumstances. This is usually best handled by referral to a clinic specializing in medical genetics or prenatal genetic testing.

Presymptomatic testing for patients at 25% risk poses ethical difficulties, because a positive result in the consultand automatically indicates that the at-risk parent also has the disease-causing gene. These issues should be resolved with the family before testing is initiated. Referral to a genetics clinic with experience in HD counselling may be appropriate.

Testing of asymptomatic minors (individuals under 18) is generally not appropriate, except as part of an evaluation for possible juvenile HD. This includes testing a child to be placed for adoption.

The laboratory does not perform anonymous testing. For patients who have special concerns about confidentiality, please contact the laboratory to discuss the procedures in place to maintain a high standard of confidentiality for test results.

For Further Information or Referrals

This protocol is based on the experience of the Medical Genetics Clinic at the University of Washington Medical Center, as well as recommendations in the literature. For further information, or to discuss referral of patients, please contact:

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