



Huntington Disease Service Description

1 Background

OMIM#143100

Huntington disease (HD) is an autosomal dominant progressive neurodegenerative disease, caused by mutation in the HTT gene on chromosome 4p. Typical clinical features include motor symptoms, cognitive deterioration, and psychiatric symptoms.

The nature of the mutation is an increase in the number of CAG repeats within exon 1 of this gene. Patients with HD have an allele with 36 or more repeats. Alleles are classified according to CAG repeat number as follows: (Am J Hum Genet 62, 1243-7, 1998):

CAG repeat no.	Allele description
≤ 26	Normal allele
27 – 35	Mutable normal allele – may occasionally mutate to HD alleles in subsequent generations
36 – 39	HD allele with reduced penetrance
≥ 40	HD allele

Laboratory tests determine the number of CAG repeats in patient samples.

2 Standard service

A Essential referral information

In addition to supplying standard patient identification and referral information (see Section I below), the following should be clearly indicated:

- Patient's symptoms - so that we can be sure this is a diagnostic test
- Any family history, including names, dates of birth and genetics test results if available.
- An indication of informed patient consent for diagnostic testing, which **must** be on an NCMG consent form (see Section I below).

B Samples required

Generally 5-10ml of EDTA blood (FBC bottle) is required. Sample identification policy is detailed at (see Section I below).

Blood specimens must be appropriately packaged (see Section I), and preferably sent by courier to arrive as soon as possible. Do not freeze prior or during postage.

Please note that extracted DNA is stored from patient's samples at the National Centre for Medical Genetics, and kept indefinitely unless a written request for its disposal is received from the patient or their parent/guardian.

C Restrictions on testing

- We would normally only accept diagnostic requests from a Consultant Neurologist, Psychiatrist, Geriatrician or Clinical Geneticist, where full informed consent of the patient has been obtained.

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National Centre for Medical Genetics

Dublin, Ireland

Division of Molecular Genetics

- **Consent is only accepted on NCMG consent forms** (see Section I below).
- Predictive testing is only performed in conjunction with a counselling programme run by the Clinical Genetics Division of the National Centre for Medical Genetics. For further information regarding referrals, please see <http://www.genetics.ie/clinical/> or phone 01-4096739.
- Predictive testing is not normally considered for children under age 16.

D Tests offered

A number of tests are performed on a routine basis. Molecular confirmation of Huntington Disease (HD) is possible using a PCR based assay to detect the number of CAG repeats within exon 1 of the HTT gene. See the table above for the classification of these alleles.

1. Diagnostic tests for patients with clinical symptoms suggestive of Huntington disease (HD). Due to the implications of a positive test result, we recommend that such tests should be performed only with full informed consent of the patient.
2. Predictive tests for asymptomatic individuals who have a family history of HD. Such tests are only performed in conjunction with a counselling programme run by the National Centre for Medical Genetics. Patients should be referred to the Director, Prof. A. Green.
3. Prenatal testing must be arranged in advance with the laboratory through our own Clinical Genetics team.

E Diagnostic Sensitivity of tests

The test is highly sensitive and highly specific. An HD allele is detected in ~100% of affected individuals; HD alleles are detected in ~0% of normal individuals; individuals with a family history of HD and who have an HD allele are ~100% likely to develop the disease within the average lifespan.

F Interpretation:

Following laboratory analysis, a report is prepared which gives results based on the CAG repeat classification system above. This is sent to the referring clinician.

Results are given in the form of a written interpretative report to the referring clinician.

G Target reporting times:

As reporting times are constantly evolving, please refer to www.genetics.ie/molecular, or contact the molecular genetics laboratory, to receive up-to-date information on anticipated reporting times for your referral.

- The following are current target reporting times for each category of test offered (information correct as of 12/01/10):

Routine Query Affected	8-10 wks
Predictive	4 wks after 2 nd sample has been received.
Prenatal diagnosis	2 wks (CVS) 4 wks (amnio)

- Please contact the laboratory if you have not received a report within a week of your patient being due back in clinic.
- Please note it is our policy not to issue verbal results.

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- Request for copies of reports on the day that your patient is in clinic cannot normally be accommodated. We usually require 24 hours notice in which to fax a copy of a report.

H Further tests

Please contact the laboratory to arrange any other related tests, eg prenatal diagnosis, prenatal exclusion testing, or testing for Dentatorubral-Pallidoluysian atrophy (DRPLA) or Spinal Cerebellar Ataxia (SCA) – which may be advised for a query affected patient who has been shown to not have Huntington Disease.

I Web Links to Related Documents

Standard referral information/NCMG request form

http://www.genetics.ie/pir/2006_NCMG_Referral_Form.pdf

Sample/Patient identification policy

<http://www.genetics.ie/pir/SampleIdentificationPolicyWeb.pdf>

Packaging of specimens for transport

http://www.genetics.ie/pir/sending_samples.pdf

NCMG Huntington Disease Consent form

http://www.genetics.ie/pir/HD_consent.pdf

Please note that hard copies of the above documents may be requested from:

Division of Molecular Genetics, National Centre for Medical Genetics, Our Lady's Children's Hospital, Crumlin, Dublin 12. Tel: 01 4096733; Fax: 01 4096971

The NCMG Molecular Genetics laboratory participates in external QA schemes run by the UK NEQAS for Molecular Genetics, the European Molecular Genetics Quality Network (EMQN), and the Cystic Fibrosis European Network. Results of assessments are available for inspection upon request.

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