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Service information: Huntington disease

Gene/Locus: *HTT (huntingtin)*, 4p16.3 **OMIM:** #143100 (*613004 – *HTT* gene)

Referrals: Clinical Geneticists, Neurologists, Specialists in Care of the Elderly, Psychiatrists. (referrals are not accepted from GPs or from other specialities).
Testing: Diagnostic testing offered in clinically affected patients, presymptomatic testing in patients at risk of developing HD (presymptomatic referrals and diagnostic referrals from patients under the age of 16 are accepted from Clinical Genetics only)
Target Reporting Times:

- Routine diagnostic 28 calendar days
- Presymptomatic testing 14 calendar days from Clinical Genetics only
- Exclusion testing workup 28 calendar days from Clinical Genetics only
- Urgent testing* 3 calendar days

***Please contact the laboratory for urgent testing, e.g. prenatal diagnosis, prenatal exclusion testing or diagnostic testing in pregnant women.**

Test Details:

- **PCR across the expandable *HTT* CAG repeat region**, using two sets of primers, to detect CAG repeat expansions.
- **Triplet-Primed PCR (TP-PCR)** of the *HTT* CAG repeat region to detect large pathogenic expansions of the *HTT* CAG repeat region if required.
- PCR analysis of **microsatellite markers** can be offered for exclusion testing in cases where an individual at risk of Huntington disease does not wish to know whether they have inherited the familial *HTT* expansion.

Service Details:

Molecular genetic testing using two PCR primer sets together with TP-PCR is predicted to detect pathological expansions of the *HTT* CAG repeat region with high sensitivity in Huntington disease (HD). The following allele size ranges are used:

Repeat size range	Range	Comments
<27 CAGs	Normal	Not associated with disease.
27-35 CAGs	Intermediate	Not associated with disease, but repeats can show instability.
36-39 CAGs	Incomplete penetrance	Likely to be affected, but shows incomplete penetrance.
>39 CAGs	Affected	Likely to be affected.

In the case of a normal HD test result when disease symptoms are clearly present, testing for HD-like disease, such as HDL1 (*PRNP* gene), HDL2 (*JPH3* gene), DRPLA (*ATN1* gene) or SCA17, could be considered. However, the funding for this testing will need to be provided by your department.

Sample Requirements:

- **EDTA** blood sample (1-4 ml), labelled with patient's **full name**, **date of birth** and **NHS number**, or genomic DNA (≥20 µl at ≥50 ng/µl). Please send two separate blood samples for presymptomatic testing.
- Samples should be accompanied by a **fully** completed referral card which should include the patient's full name, date of birth and NHS number.
- Please also include details of the test, relevant clinical details and full details of the referring clinician/centre
- Appropriate familial samples are required in the case of exclusion testing.
- Maternal samples are required in cases of prenatal diagnosis to exclude maternal cell contamination.

Consent:

Please note that in submitting a sample, it is the responsibility of the clinician to ensure that consent has been taken i) for testing, ii) for storage, and iii) for the use of this sample and the information generated to be shared with the patient's relatives and their health professionals. Following testing, a sample of the patient's DNA may also be used anonymously to validate new tests and for internal quality control purposes.