R42 Leber Hereditary Optic Neuropathy (LHON) – OMIM 535000

Background

Leber hereditary optic neuropathy (LHON) typically presents as bilateral painless subacute visual failure. The typical age of onset with LHON is 20 to 30 and often starts in one eye followed a few weeks or months later by development of visual failure in the other eye. Visual acuity is severely reduced and eventually results in lifelong blindness. Very rarely additional extraocular findings are observed including neurological abnormalities, nonspecific myopathy and cardiac arrhythmias. The prevalence of LHON is approximately 1:50,000. Males with a pathogenic LHON variant are 4-5 times more likely to be affected than females.

LHON is caused by genetic variants in the mitochondria DNA. Approximately 90% of cases are caused by the following variants, *MT-ND1* m.3460G>A, *MT-ND4* m.11778G>A and *MT-ND6* m.14484T>C. The remaining 10% of cases are caused by other mitochondrial variants. *MT-ND4* m.11778G>A is the most common variant identified in 60-70% of affected individuals of northern European ancestry and 90% of affected patients of Asian ancestry. Variants are variably penetrant and asymptomatic males with a pathogenic LHON variant have a 30-50% risk of developing LHON, whilst females have around a 10% risk of developing LHON. Heteroplasmy is present is 10-15% of individuals with a LHON variant. Those patients with low heteroplasmy (<60%) have a reduced risk of developing LHON.

Idebenone (Raxone®) can be used to treat patients with LHON and is most effective for those in the first year of disease onset.

Recommended Clinical Referral Criteria

- Bilateral loss of central vision in early adulthood
- Family history through the maternal line

Referrals are accepted from the following specialities: Clinical Genetics, Neurology, Ophthalmology.

Molecular Analysis

Diagnostic screen: **LHON –** Pyrosequencing analysis for the following common mitochondrial DNA variants – *ND-4* m.11778G>A, *ND-1* m.3460G>A, *ND-6* m.14484T>C; clinical sensitivity is >90%
Family follow-up: Testing for known familial mitochondrial variants – *ND-4* m.11778G>A, *ND-1* m.3460G>A, *ND-6* m.14484T>C

Test (Price available on request)	**TAT (calendar days)**
Diagnostic test for three common mitochondrial mutations (LHON)	42
Predictive testing for LHON	28

Sample Requirements

Blood – 5ml in EDTA

Mouthwash/buccal cells; other tissue

Please label samples with three identifiers and date of collection.

All samples must be accompanied by request form

Consent for testing & DNA storage is assumed when request for test received

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Accredited to ISO 15189:2012
(8988)

Links

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