

Hereditary Angioedema [HAE]

C1INH-HAE: [SERPING1] & normal-C1INH-HAE [FXII-HAE (F12); PLG-HAE; ANGPT1-HAE]

Background

HAE is a rare, life threatening primary immunodeficiency that causes spontaneous oedema of the submucosal layers. The majority of cases are caused by pathogenic variants in the gene encoding C1INH (*SERPING1*) that alter either its synthesis (C1INH-HAE: type I) or function (C1INH-HAE type II). It affects approximately 1:50000 of the population. Rarely, HAE can present with normal C1INH (nl-C1INH-HAE) and is caused by variants in the *F12* gene (FXII-HAE c.983C>A or C>G, c.971_1018+24del and c.892_909dup) or due to a single variant in plasminogen (PLG-HAE, c.9886A>G; p.(Lys330Glu) or angiopoietin1 (ANGPT1-HAE, c.355G>T; p.(Ala119Ser).

Inheritance: Autosomal dominant

Recommended Clinical Referral Criteria

- Initial diagnoses made by biochemical complement testing (C1INH concentration and functional, C3 and C4).
- FXII-HAE, PLG-HAE and ANGPT1-HAE testing can be used to exclude the diagnosis of unclassified HAE (U-HAE), or acquired angioedema (InH-AAE or ACEI-AAE).
- Diagnosis of the disease in newborns and children or in asymptomatic relatives.

Referring specialisms

- Referrals for diagnostic testing must come from an immunology or clinical genetics specialist
- Referrals for asymptomatic testing must come from a clinical genetics specialist

Molecular Analyses

C1INH-HAE:

Bi-directional sequence and MLPA dosage analysis of the coding region of *SERPING1*

nl-C1INH-HAE

FXII-HAE: Bi-directional sequence of *F12* Ex9

PLG-HAE: Bi-directional sequence *PLG* Ex9

ANGPT1: Bi-directional sequence *ANGPT1* Ex2

Test	TAT (calendar days)
Mutation screening and dosage analysis (<i>SERPING1</i>)	42
Targeted analysis (<i>F12</i> , Ex9; <i>PLG</i> , Ex9; <i>ANGPT1</i> , Ex2)	42
Testing for known familial mutations (<i>SERPING1</i>)	42



Contact Details

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Sample Requirements

Blood – 5ml in EDTA (1ml neonates/infants);
Please contact lab prior to sending a prenatal
sample.
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

Links

Orphanet

<http://www.orpha.net/>

OMIM

<http://www.omim.org/>

Genetic Test Registry

<http://www.ncbi.nlm.nih.gov/gtr/>

Support

<http://www.immunodeficiencyuk.org/>