ACHONDROPLASIA AND HYPOCHONDROPLASIA

(ACH OMIM 100800; HCH OMIM 146000)

INTRODUCTION
Achondroplasia (ACH) is the most frequent form of short-limb dwarfism and is characterised by short stature caused by rhizomelic shortening of the limbs, characteristic facies with frontal bossing and midface hypoplasia and lumbar lordosis.

Hypochondroplasia (HCH) has a similar but milder phenotype which can overlap with the normal population at the mild end and achondroplasia at the severe end of the spectrum.

Both are autosomal dominant disorders caused by mutations within the FGFR3 gene which encodes a transmembrane tyrosine kinase receptor and is localised to chromosome 4p16.

~99% of achondroplasia patients have one of 2 mutations within FGFR3 exon 10.
~70% of hypochondroplasia patients have one of 2 mutations within FGFR3 exon 13. Other rare mutations have been found elsewhere in the gene.

TESTING
- Diagnostic: Clinically affected patients
- Familial mutation test: Relatives of clinically affected patients (known mutation)
- Prenatal: At risk of having an affected child (known mutation) / to confirm a suspected diagnosis based on ultrasound examination

REFERRALS
- From Geneticists, Paediatricians, Antenatal Services, Neurologists, Endocrinologists or Dysmorphologists
- Prenatal referrals must be discussed with the laboratory and, where possible, arranged in advance.

STRATEGY AND TECHNICAL INFORMATION
- For new diagnostic cases:
  - ACH - fluorescent sequencing analysis of exon 10 of FGFR3 to detect:
    - ~99% patients with either c.1138G>A or c.1138G>C, both resulting in p.G380R.
    - the rare c.1123G>T (p.G375C) mutation
  - HCH - fluorescent sequencing analysis of exons 7, 10, 13 and 15 of FGFR3
    - 2 mutations in exon 13 account for ~70% of cases, c.1620C>A or c.1620C>G, both resulting in p.N540T
    - In total, the 4 exons cover ~75% of reported mutations

TARGET REPORTING TIMES
- HCH Diagnostic test: 40 days
- ACH Diagnostic test: 10 days
- Familial mutation test: 10 days
- Prenatal test (includes maternal contamination check): 3 days

N.B. Details are correct for the date of printing only - last updated 10/09/2015