APERT SYNDROME – HSS Service
OMIM 101200

INTRODUCTION
The craniofacial service covers a diverse range of disorders characterised by craniosynostosis (premature fusion of one or more of the cranial sutures) resulting in facial deformity. Apert syndrome is a severe phenotype characterised by coronal or multiple suture craniosynostosis and syndactyly of at least three digits in the hands and feet. This severe phenotype may be identified on an ultrasound scan after ~18-20 weeks. Almost all cases are caused by one of two dominant activating mutations of the \textit{FGFR2} gene (p.S252W or p.P253R). These mutations are recurrent \textit{de novo} mutations that arise exclusively from the father, often associated with increased paternal age. No confirmed case of germinal mosaicism has been reported, so a recurrence risk of <1% is quoted for a \textit{de novo} \textit{FGFR2} mutation. Mutation analysis therefore enables clarification of the clinical diagnosis and determination of recurrence risks.

The service is funded by the National Commissioning Group for Highly Specialised Services (HSS) for referrals from England, Scotland, Wales and Northern Ireland.

TESTING
All diagnostic samples should be accompanied by a completed clinical questionnaire & consent form (click here)
The aim is to provide a joint Molecular and Clinical service, and Professor Andrew Wilkie (+44 (0)1865 222619) is available for advice. We test:
- Clinically affected patients
- Relatives of clinically affected patients in whom a mutation has been identified
- Prenatal testing is available in cases where a mutation has been identified, or where a diagnosis is suspected on ultrasound scan. These must be discussed with the laboratory and arranged in advance, where possible.

REFERRALS
- From Clinical Genetics, Paediatrics, Craniofacial clinics and Dysmorphologists.
- Prenatal testing is only accepted from Clinical Genetics and / or Prenatal Diagnosis.

STRATEGY & TECHNICAL INFORMATION
- For new diagnostic cases: Fluorescent sequencing of \textit{FGFR2} exon 8 (IIla) to detect the p.S252W (c.755C>G) and p.P253R (c.758C>G) mutations
  - The p.S252W mutation accounts for 66.5% of Apert cases, p.P253R for 32.5%, and other \textit{FGFR2} mutations for 1%.
  - The p.S252W mutation is generally associated with more severe craniofacial deformity, but less severe syndactyly, compared with the p.P253R mutation.
- Family tests: When a mutation has been identified in a family the individual is tested only for the familial mutation.

TARGET REPORTING TIMES: Supraregionally funded by HSS for referrals from the UK
Diagnostic test: 8 weeks
Familial Mutation test: 10 days
Prenatal testing (includes maternal contamination check): 3 days

N.B. Details are correct for the date of printing only – last updated 11/06/2015