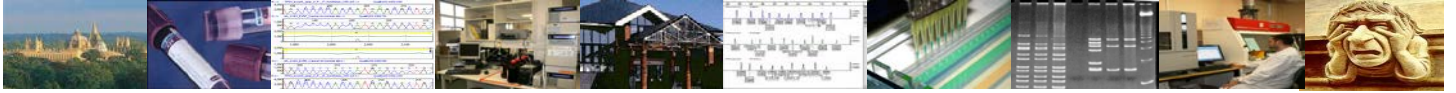


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SPINAL MUSCULAR ATROPHY (SMA) OMIM #600354, 253300, 253550, 253400, 271150.

INTRODUCTION

Spinal muscular atrophy (SMA) is characterised by progressive muscle weakness resulting from degeneration and loss of the lower motor neurons of the spinal cord and the brain stem nuclei. Onset ranges from before birth to adolescence or young adulthood. Poor weight gain, sleep difficulties, pneumonia, scoliosis, and joint contractures are often observed. The phenotype of SMA is associated with disease-causing mutations of the *SMN1* gene and spans a continuum without clear delineation of subtypes. However classifications have been made: prenatal onset and severe joint contractures, facial diplegia, and respiratory failure; onset before six months of age (SMA I); onset between six and 18 months (SMA II); onset in childhood after 12 months (SMA III); and adult onset (SMA IV).

SMA is inherited in an autosomal recessive manner and has a prevalence of approximately 1 in 10 000, with a carrier frequency of 1/40 -1/60 in the European population.

Homozygous loss of the *SMN1* gene on 5q12.2-q13.3 by deletion or gene conversion to *SMN2* accounts for around 96% of cases of SMA.

TESTING

- Diagnostic: For individuals suspected of having SMA
- Carrier: Individuals at increased risk of having an affected child, for example, due to having a family history of SMA, having an affected or carrier partner, or first cousin partnerships. In order to complete this analysis, full information regarding the family relationships is required.
- Prenatal: Prenatal testing must be discussed with the laboratory and arranged in advance

REFERRALS

- Diagnostic: From Clinical Genetics, Clinical Neurology, Paediatrics or Paediatric Neurology only
- Carrier: From Clinical Genetics only
- Prenatal: From Clinical Genetics and Prenatal Diagnosis Departments only

STRATEGY AND TECHNICAL INFORMATION

- MLPA (multiplex ligation-dependant probe amplification) dosage analysis of the *SMN* genes
 - Limitations of test: ~4% of normal chromosomes have 2 copies of *SMN1* per chromosome
SMN1 point mutations will not be detected
- PCR and restriction digest of exons 7 and 8 of the *SMN1* and *SMN2* genes
 - Provides a second independent test for prenatal diagnosis
- Linked marker analysis
 - Provides a second independent test for prenatal diagnosis, also enables exclusion of maternal contamination

TARGET REPORTING TIMES

Diagnostic test:	10 days
Carrier test:	10 days
Prenatal test (includes maternal contamination check):	3 days

N.B. Details are correct for the date of printing only – last updated 01/09/2015