Condition: Spinal muscular atrophy

Inheritance:

Spinal muscular atrophy.

Genetic etiology:

Mutation in *SMN1* gene, encoding the protein survival motor neuron. The region on chromosome 5 surrounding this gene has a complex structure, with an inverted duplication that includes the *SMN2* gene. *SMN2* differs from SMN1 by eight nucleotides, one of which results in skipping of exon 7 in SMN2 mRNA processing. The most common *SMN1* mutation is deletion, but other mutations, including gene conversion of *SMN1* to *SMN2*, may occur. Increased copy number of the *SMN2* gene tends to ameliorate the phenotype. The survival motor neuron protein is involved in synthesis and trafficking of small nuclear ribonucleoproteins required for mRNA processing.

Frequency:

Approximately 1/10,000 – 1/25,000.

Clinical features:

The major pathology in SMA is loss of spinal motor neurons, leading to progressive muscle weakness and atrophy. There are different allelic variants with different ages of onset. Classical SMA (Werdnig-Hoffman disease) presents in infancy with hypotonia, fasciculations, absent reflexes, and weakness. Other forms may be associated with later onset and slower progression.

Management:

Supportive care. Children with the infantile form usually die within the first two years. Later onset forms may be compatible with long term survival.

Genetic counseling:

Parents of an affected child face a 25% risk of recurrence. Genetic testing is available.

Human Genetics and Genomics, Fourth Edition. Bruce R. Korf and Mira B. Irons.