Condition: Huntington disease

Inheritance:

Autosomal dominant.

Genetic etiology:

Triplet repeat expansion mutation in *HD* gene, which encodes the protein huntingtin. The repeat is a CAG encoding a polyglutamine tract within the coding sequence. Presence of 26 or fewer repeats is normal and expansion to 36 or more is associated with disease. Expansions of 36 to 40 repeats are associated with reduced penetrance.

Frequency:

Approximately 1/20,000 in individuals of western European descent.

Clinical features:

Huntington disease affects the nervous system, causing a movement disorder, psychiatric problems, and dementia. Symptoms usually begin in adulthood, though there is a childhood-onset version characterized by rigidity, and generally being inherited from the father. The movement disorder is a chorea, and there are associated problems with gait, coordination, and swallowing. Psychiatric disturbances include behavioral changes, affective disorders, and schizophreniform disorders. Suicide is common, as is death due to progressive neurological disability.

Management:

Supportive management for neurological and psychiatric symptoms.

Genetic counseling:

Affected individuals have a 50% chance of transmitting the gene, and may pass the gene on prior to onset of symptoms. Huntington disease displays age-dependent penetrance and anticipation. The phenomenon of anticipation is due to progressive expansion of the triplet repeat from generation to generation and an association of age of onset and severity with repeat size. Genetic testing is available.

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