Condition: Hereditary dystonia

Inheritance:
Genetically heterogeneous.

Genetic etiology:
A large number of genes have been identified that are associated with dystonia, either occurring in isolation or along with other neurological features. Two of particular importance are Dopa-responsive dystonia (DYT5) and primary dystonia (DYT1). DYT5 is due to mutation in the GCH1 gene that encodes the enzyme GTP-cyclohydrolase I. DYT1 results from mutation of *TOR1A,* which encodes the protein torsin A. The most common mutation is a three base deletion of GAG in exon 5.

Frequency:
DYT5 occurs in approximately 1/2 million individuals; DYT1 most common in Ashkenazi Jews, where the frequency is 1/3,000 – 1/9,000.

Clinical features:
Dystonia is defined as an involuntary sustained muscle contraction. It may occur focally, or may involve multiple muscle groups. Dopa-responsive dystonia (DYT5) begins in childhood and manifests as a gait disorder that tends to display diurnal variation, worsening later in the day. The disorder is due to mutation in gene involved in DOPA synthesis, and therefore symptoms improved markedly upon treatment with DOPA. DYT1 has onset in the first two decades. Dystonia may present focally, but commonly evolves to multifocal.

Management:
Treatment of DYT5 with DOPA; dystonia treated with various medications, including muscle relaxants, anticholinergics, dopa, botulinum toxin injection, and surgery (stimulation of basal ganglia); physical therapy.

Genetic counseling:
Related to mode of inheritance; DYT1 and DYT5 are autosomal dominant. Genetic testing is possible.

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