Condition: Angelman syndrome

Inheritance:
Chromosomal

Genetic etiology:
Angelman syndrome is associated with defects based on genomic imprinting. Approximately 68% have a deletion of the maternal 15q11.2-q13 region. About 7% have uniparental disomy, with two paternal copies of chromosome 15. About 3% have small deletions in the region that lead to abnormal imprinting. About 11% have a mutation in the *UBE3A* gene, which resides in this region of chromosome 15 and is imprinted. The balance of patients cannot be diagnosed at the molecular level, and either have mutations undetectable with current technology or may be misdiagnosed.

Frequency:
1/12,000 – 1/20,000

Clinical features:
Affected individuals have severe developmental delay. Most have seizures, and hyperactivity is common. Walking is delayed, or may not occur at all, and for those who do walk, gait is stiff and clumsy.

Management:
Management is focused on supportive care and treatment of seizures.

Genetic counseling:
Recurrence of microdeletion or uniparental disomy in siblings of a proband are rare. Imprinting center or *UBE3A* mutations can be transmitted as dominant traits. Genetic testing is available, including analysis of patterns of methylation in the critical region on chromosome 15, as well as FISH or CGH analysis for deletion and use of polymorphisms to determine uniparental disomy. Detection of imprinting center or *UBE3A* mutations requires sequence analysis.

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