Condition: Prader-Willi syndrome

Inheritance:
Chromosomal

Genetic etiology:
Prader-Willi syndrome is associated with defects based on genomic imprinting. Approximately 70% have a deletion of the paternal 15q11.2-q13 region. About 25% have uniparental disomy, with two maternal copies of chromosome 15. A small proportion has a mutation of the imprinting center on chromosome 15. The specific dysregulated gene or genes responsible for the phenotype are not known.

Frequency:
1/10,000 – 1/25,000

Clinical features:
At birth, individuals with Prader-Willi syndrome are hypotonic, lethargic, and have difficulty feeding. These signs gradually resolve, and by early childhood an eating disorder emerges. This can lead to obesity, and is accompanied by developmental delay and major disturbances of behavior. There are distinctive facial features and short stature is common.

Management:
In infancy support is required for feeding. Later on, support is required to avoid obesity and manage behavior and cognitive problems. Treatment with growth hormone has been found to be helpful in managing body habitus and normalizing height.

Genetic counseling:
Recurrence of microdeletion or uniparental disomy in siblings of a proband are rare. Imprinting center mutations can be transmitted as dominant traits, though some are do novo mutations. 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 mutations requires sequence analysis of the imprinting region, though not all imprinting center mutations can be identified.

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