Condition: Down syndrome (Trisomy 21)

Inheritance:

Chromosomal

Genetic etiology:

Presence of three copies (trisomy) of chromosome 21 material. Most often this is due to having 47 chromosomes, with three copies of #21, due to nondisjunction. In about 5% of cases it is due to translocation between chromosome 21 and another chromosome, usually 14. Approximately 2% of affected individuals are mosaic for a trisomy 21 cell line.

Frequency:

Approximately 1:800 livebirths.

Clinical features:

Children are hypotonic at birth and may have congenital anomalies, especially cardiac and gastrointestinal. Facial features include flat occiput, up-slanting palpebral fissures, furrowed tongue, short fingers and toes, incurved fifth finger (clinodactyly), and a wide space between the first and second toes. Cognitive development tends to be delayed, though is variable. There is an increased risk of respiratory infection during childhood and a higher risk of leukemia and transient leukemoid reactions in infancy than the general population. Adults are at risk of early onset Alzheimer disease.

Management:

Although there is no definitive treatment, affected individuals benefit from surveillance for treatable complications and participation in early intervention and educational programs to stimulate development. Congenital anomalies, when they occur, usually can be treated surgically.

Genetic counseling:

Recurrence risk to a couple with an affected child is approximately 1%. Instances where a parent carries a balanced Robertsonian translocation are associated with an increased recurrence risk. Pregnancies can be screened for carrying fetuses with Down syndrome by biochemical testing and ultrasound, and trisomy 21 can be readily detected by prenatal chromosomal analysis. Advanced maternal age is the best documented risk factor other than having a previously affected child.

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

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