Chicago Center for Jewish Genetic Disorders

Physicians Guide to Jewish Genetic Disorders & Screening

About Genetic Screening

Individuals of Ashkenazi Jewish ancestry carry genes for the disorders listed in this guide more frequently than Sephardic Jews and non-Jews. Although a "carrier" of one of these genes is not affected by the disorder, he or she is at increased risk for having a child with the disorder. Couples in which one or both partners are of Ashkenazi Jewish descent should be advised of the increased risk. Carrier screening is now available for all of the disorders, and prospective parents should be given this information.

Genetic counseling should also be provided for couples at risk for Jewish genetic disorders. Genetic counselors are available at a number of hospitals in the Chicago area. Contact information is available through the Chicago Center for Jewish Genetic Disorders.

Negative genetic screening results for any of these disorders may lower the risk for a couple but do not eliminate the risk completely. Different ethnic backgrounds may have lower detection rates due to decreased test sensitivities.

The Chicago Center for Jewish Genetic Disorders is a cooperative effort of the Jewish United Fund/Jewish Federation of Metropolitan Chicago, Children's Memorial Hospital and the Illinois Jewish Genetic Disorders Committee.

Jewish Federation of Metropolitan Chicago

Children's Memorial Hospital

MICHAEL REESE HEALTH TRUST

The Center is supported by the Michael Reese Health Trust

Vital Statistics: Eastern European Jewish Genetic Disorders

Disease	Inheritence Pattern	Outlook	Carrier Frequency	Carrier Screening	Prenatal Testing	Testing Method	Detection Rate[1]	Non-Jewish Testing Rate[2]	Disease Incidence	Treatment
Bloom Syndrome	Recessive	Individuals can be functional	1 in 110	Yes	Yes	DNA	95-97%	Unknown	1 in 40,000	For symptoms
Canavan Disease	Recessive	Fatal, from early childhood through early teens	1 in 38	Yes	Yes	DNA	98%	60%	1 in 6,400	None
Dystonia	Dominant	Individuals can be functional	1 in 900	Yes	Yes	DNA	98%	50%	Unknown	For symptoms
Familial Dysautonomia	Recessive	50% live to 30 years of age	1 in 30	Yes	Yes	DNA	99%	Unknown	1 in 3,700	For symptoms
Fanconi Anemia (Type C)	Recessive	Onset ranges from 17 months to 22 years–increased risk for cancer	1 in 89	Yes	Yes	DNA	99%	Unknown	1 in 32,000	For symptoms
Gaucher Disease (Type 1)	Recessive	Varies from mild to debilitating	1 in 10	Yes	Yes	DNA	95%	70%	1 in 900	Effective treatment (Enzyme replacement)
Mucolipidosis IV	Recessive	Developmental delays may be progressive from mild to severe	1 in 100	Yes	Yes	DNA	95%	Unknown	Unknown	For symptoms
Niemann-Pick Disease (Type A)	Recessive	Fatal by 3-5 years of age	1 in 70	Yes	Yes	DNA	95%	Unknown	1 in 32,000	None
Tay-Sachs Disease	Recessive	Fatal in early childhood	1 in 26-30	Yes	Yes	Hex A enzyme/ DNA test[3]	94-98%[4]	97-98% enzyme only[5]	1 in 3,000	None
Cystic Fibrosis	Recessive	On average, fatal by age 30	1 in 25-29	Yes	Yes	DNA	97%	75-90%	1 in 2,500	For symptoms
DFNB1 (Congenital Deafness)	Recessive	Profoundly deaf	1 in 20	Yes	Yes	DNA	95%	>99%[1]	6 in 10,000	None
Non-Classical Adrenal Hyperplasia	Recessive	With early treatment symptoms are reversed	1 in 3	Yes	Yes	DNA	95%	95%	1 in 27	Effective postnatal treatment

[1] Sequencing of the entire gene

[2] Sequencing of the entire gene should be done due to genetic heterogeneity

[3] Both Enzyme testing and DNA testing should be done for Tay-Sachs. Tay-Sachs carrier testing by enzyme analysis on pregnant woman and those taking oral contraceptives must be done on leukocytes.

[4] 98% by Hex A enzyme, 94% by DNA-based test

[5] DNA detection rate unknown

About the Disorders

Bloom syndrome results in poor growth and poor resistance to infection. There is a high rate of cancer from which individuals usually die before age 30.

Canavan disease is characterized by progressive loss of white matter in the brain. Infants appear to be normal at birth but are later found to be hypotonic (floppy), fail to achieve head control and become developmentally delayed by 5-8 months. Features include an enlarged head, mental retardation, seizures and feeding difficulties. Death usually occurs by age 20 years.

Familial Dysautonomia (FD) is a disorder that results from the abnormal development of the nervous system, particularly the sensory and autonomic systems. The autonomic nervous system controls involuntary functions, such as swallowing, temperature, and blood pressure regulation. Individuals with FD cannot regulate these functions. Other common manifestations are indifference to pain, inappropriate perception of heat and taste, excessive sweating, gastrointestinal problems, poor speech and motor problems.

Fanconi anemia (Type C) is a disorder which causes children to have anemia, short stature, learning disabilities or mental retardation. There may also be birth defects of the limbs, heart or kidneys. Risk for leukemia and early death is increased.

Gaucher disease (Type 1) can be very mild or severe. The absence of the enzyme glucocerebrosidase leads to the progressive build up of fatty substances in the liver, spleen and bone marrow. Children and adults may have nosebleeds, anemia, an enlarged liver and spleen, bone pain, and easily broken bones. Because the severity is so variable and very effective treatment is available, decisions about carrier testing are difficult.

Mucolipidosis IV is a disorder where children appear normal at birth but develop signs of central nervous system deterioration during the first year of life. Motor and mental retardation are usually mild to moderate, and are slowly progressive. Individuals with ML IV currently range from 1 to 30 years of age. Prognosis beyond this age and life expectancy are not known.

Niemann-Pick disease (Type A) is a severe neurodegenerative disorder of infancy. Affected babies exhibit an enlarged liver and spleen, poor growth and progressive physical and mental deterioration. Death usually occurs in early childhood (before age 5) due to infection.

Tay-Sachs disease is characterized by the onset of severe mental and developmental retardation during the first 4-8 months of life. An early sign of the disease is the macular cherry-red spot, an unusual abnormality in the retina of the eye. The involvement of the central nervous system progresses rapidly and affected children become totally debilitated. Death usually occurs in early childhood. The Tay-Sachs gene is also more common among French Canadians from eastern Quebec and Cajuns from southern Louisiana.

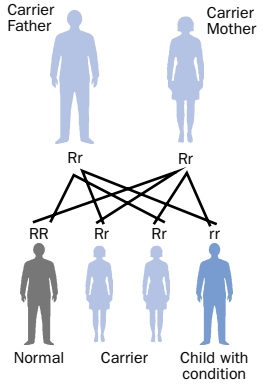
Dystonia is an autosomal dominant disorder (an individual only needs one copy of an abnormal gene to be affected) characterized by sustained, twisting muscle spasms. With time, the frequency and duration of these spasms increase, leading to joint contractures and progressive disability. Children of an individual affected with Dystonia have a 50% chance of inheriting the gene mutation that cause the disease, but symptoms of Dystonia occur in only 30% of the individuals who inherit the gene mutation.

Cystic fibrosis (CF) is common among Caucasians, particularly those of northern European origin. It occurs with the same frequency in the Jewish and non-Jewish populations. The disease causes lung infections, difficulty breathing, and problems with bowel function, weight gain and growth. Children frequently need to be hospitalized, have respiratory therapy and take several medications. The average lifespan is 30 years.

Connexin 26-related hearing loss (DFNB1, GJB2) is an autosomal recessive disorder resulting in congenital, non-progressive, mild-to-profound hearing impairment. There are no other medical findings associated with this condition.

Non-Classical Adrenal Hyperplasia (NCAH) is an autosomal recessive disorder resulting from reduced ability to convert cholesterol to cortisol. This leads to excess production of adrenal androgens. This disorder is related to congenital adrenal hyperplasia but does NOT result in premature death due to salt-wasting or ambiguous genitalia in female infants. Affected individuals can have severe acne, excess facial and body hair, short stature, menstrual irregularities in females, and decreased fertility in both males and females. These effects can be reversed or minimized with postnatal treatment. Because this condition is easily treated, carrier screening and prenatal testing may not be appropriate.

Autosomal Recessive Inheritance



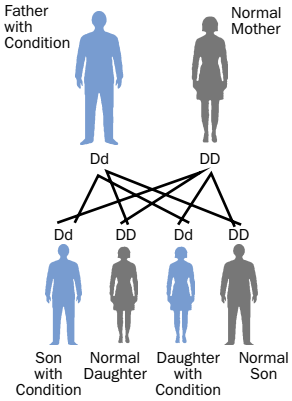
A disorder is considered recessive when a single normal copy of the gene is sufficient to prevent disease.

Carriers are normal and healthy.

Both members of a couple who are carriers have a 25% (1-in-4) chance of having affected children.

Typically a family history is not seen because the condition requires both parents to be carriers and most people are unaware of their carrier status because they are unaffected.

Autosomal Dominant Inheritance



People who possess one mutant copy of a gene for a dominant disorder are usually affected.

A child conceived by an affected individual has a 50% chance of inheriting the abnormal copy of the gene (and thus the disorder).

Dominant disorders do not "skip" generations.

Except when there has been a new mutation causing a dominant disorder, every affected individual has an affected parent.

Chicago Center for Jewish Genetic Disorders

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