Jewish Genetic Diseases

In every ethnic, demographic, or racial group, there are certain inherited disorders that occur more frequently than in the general population. Such is the case for Ashkenazi Jewish individuals whose ancestors lived in Central or Eastern Europe. If you or your spouse is of Ashkenazi Jewish descent, you have the opportunity to be screened to determine if you carry a gene change for these inherited diseases that are more prevalent among Ashkenazi Jews.

What Is Genetic Screening?

Genes are the basic units of heredity passed from parent to child. They occur in pairs, and we inherit one member of each pair from our mother and the other from our father. A change in a gene, known as a mutation, can cause that gene not to work properly. This can lead to disease. Certain diseases are caused when both genes of a pair have mutations. These are recessive diseases. In order to have a child with a recessive disease, each parent has a gene that works properly and a gene that does not. The parents are known as carriers and do not have any health problems related to that disease. Genetic screening can identify carriers by a simple blood test to determine if a couple is at risk to have a child affected with a specific disease.

What If We Are Both Carriers?

If both partners of a couple are identified as carriers for the same disease, they have a 25% risk with each pregnancy to have a child affected with that disease. They also have a 50% chance that their child will be a carrier with no symptoms of that disorder, and a 25% chance that the child will not inherit a gene mutation from either parent. If a couple is at risk to have a child with any of the diseases for which we screen, prenatal diagnosis is available to determine whether or not the fetus is affected. This is possible through either chorionic villus sampling (CVS) at 10-12 weeks of pregnancy or amniocentesis in the second trimester of pregnancy. In addition, there are technologies involving *in vitro fertilization* (IVF) that provide other reproductive options. When a carrier couple is identified, our genetic counselors can provide information and support which may be helpful in making important family planning decisions.

The Mount Sinai Center for Jewish Genetic Diseases is the oldest center in the country dedicated to the care of patients with genetic disorders that are prevalent in the Jewish community and to conducting research to improve diagnosis and treatment. The Center conducts a Jewish genetic disease screening program which provides expert screening and genetic counseling to individuals at risk for being carriers of these diseases. All services are provided by board-certified genetic counselors and clinical and molecular geneticists.

For further information,
or to schedule a consultation, please
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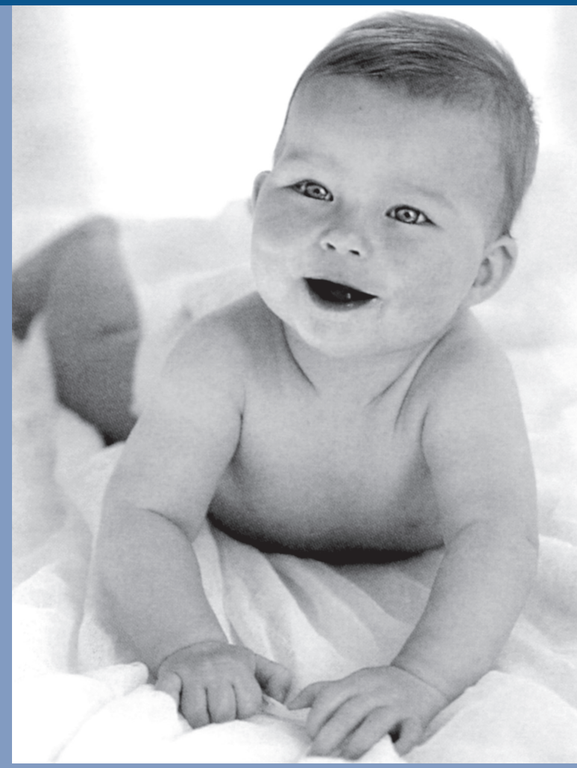
Jewish Genetic Diseases Screening Program



Center of Jewish Genetic Diseases
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Diseases Included In The Ashkenazi Jewish Screening Panel

Ideally, both members of a couple should be screened prior to starting a family, or as soon as you learn of your pregnancy, to allow all available options to be considered. You may decide to be screened for each of the diseases described below or for selected diseases.

Bloom syndrome is a condition in which children grow poorly, have frequent infections and may have learning disabilities. As adolescents and young adults, individuals with Bloom syndrome are predisposed to develop common cancers such as breast cancer, colon cancer and leukemia. The carrier frequency in the Ashkenazi Jewish population is approximately 1 in 134. Testing for one common mutation allows for a carrier detection rate that is approximately 99%.

Canavan disease is a progressive disease of the central nervous system for which there is no treatment. Symptoms begin in infancy including poor head control, generalized weakness, and enlarged head size. Affected infants also develop seizures, regression of early developmental milestones, and severe mental retardation. Canavan disease is typically fatal in childhood. The carrier frequency in the Ashkenazi Jewish population is about 1 in 40 to 1 in 60. Testing for common mutations in this gene detects about 97% of carriers.

Cystic fibrosis (CF) is a progressive, lifelong condition in which the glands that produce mucus sweat, and intestinal secretions do not function properly. This results in thick mucus accumulation in the lungs, leading to breathing difficulty and infection. CF also causes poor digestion, and males with this disease are usually infertile. There is no cure for CF. Supportive treatments are available to help improve quality of life, and average life expectancy has increased over the years. While some babies with CF still die in infancy, many patients with CF live into their 20s and 30s.

CF is found in all ethnic groups. It is most common among Caucasians, Jewish and non-Jewish alike, with a carrier frequency of about 1 in 25. By testing for some of the more common mutations, at least 94% of Ashkenazi Jewish CF carriers can be identified, as can approximately 90% of non-Jewish, Northern European CF carriers.

Familial Dysautonomia (FD) is a severe disease of the autonomic nervous system. Autonomic nerves control functions such as swallowing, sweating, the ability to cry with tears and to sense pain. Individuals with FD may have severe gastrointestinal problems and pulmonary complications such as pneumonia. The carrier frequency in the Ashkenazi population is approximately 1 in 31. Testing for the common mutations provides a carrier detection rate of 99.5%

Familial Hyperinsulinism is a disease that results in the inability to stop insulin production even in the presence of very low blood sugar. For individuals with this disorder, low blood sugar in the newborn period or during childhood results in seizures, poor muscle tone, poor feeding and breathing difficulty. Although the onset and presentation of the disease is variable, it is fatal when untreated. The treatments include glucose infusions and drugs that reduce insulin release. In some cases, it is necessary to surgically remove most of the pancreas. The carrier frequency of familial hyperinsulinism in the Ashkenazi Jewish population is approximately 1 in 68. Screening for two mutations will detect about 90% of carriers in this population*.

Fanconi Anemia (Type C) is a chronic disease associated with short stature, bone marrow failure, congenital malformations and a predisposition to leukemia. For some children, the condition may also involve learning disabilities or mental retardation. The carrier frequency in the Ashkenazi Jewish population is about 1 in 100. Testing for common mutations provides a carrier detection rate of approximately 99%.

Gaucher disease (Type I) is characterized by enlargement of the spleen and liver as well as blood abnormalities, including anemia, easy bruising, and impaired clotting. In addition, there are orthopedic problems, such as bone and joint pain, and an increased susceptibility to bone fracture. The age of onset of symptoms is variable, with some individuals showing symptoms in childhood and others remaining relatively symptom free into their 50s or 60s. In addition, the severity of symptoms varies among patients. Enzyme replacement therapy has been developed in recent years and has been highly effective in reversing some symptoms and reducing the severity of others. Type I Gaucher disease is the most common genetic disorder in the Ashkenazi Jewish population, with a carrier frequency of about 1 in 15. Testing for common mutations provides a carrier detection rate of approximately 95%.

Glycogen storage disease Ia (GSD Ia) usually presents in infancy. Individuals with GSD Ia have difficulty controlling their glucose metabolism. As a result, their glucose levels can drop dangerously low. Individuals with the condition also experience a variety of biochemical abnormalities, as well as delayed growth and development. Other characteristics of the condition include enlargement of the spleen, gastrointestinal problems, recurrent infection and pancreatitis. Dietary restriction has proven to be effective in the management of GSD 1a. The carrier frequency in the Ashkenazi Jewish population is approximately 1 in 64. Testing for two mutations provides a carrier detection rate of at least 95%.

Joubert syndrome 2 is a neurological disorder associated with a specific brain malformation. Symptoms include developmental delay and, often, mental retardation, breathing difficulties, ataxia, failure to thrive, retinal degeneration and renal dysfunction. The carrier frequency in the Ashkenazi population is approximately 1 in 110. Testing for one common mutation provides a carrier detection rate of at least 95% in this population.

Lipoamide dehydrogenase deficiency (E3) is a highly variable disease in its age of onset and clinical presentation. Age of onset can vary from infancy to adulthood. The symptoms can vary from fatigue following mild exertion to, in some cases, episodes of decompensation followed by severe neurological decline and, occasionally, death. Individuals with this disease are managed with dietary supplements. Dietary management and prompt medical attention during periods of decompensation can prevent the more severe symptoms. The carrier frequency of this condition in the Ashkenazi Jewish population is approximately 1 in 107. Screening for two mutations will detect greater than 95% of carriers in this population.

Maple Syrup Urine Disease (MSUD) manifests in the newborn period and can result in severe neurological complications and death. After ingesting dietary protein, affected infants show signs of neurological impairment including poor suck, irritability, lethargy and, if untreated, will ultimately lapse into coma. Patients with MSUD can be effectively managed with dietary restriction of proteins. Early recognition of the disease has been made possible by detection via state newborn screening; however, a significant proportion of treated individuals have impaired intellectual development or neurological complications, particularly as a result of delayed diagnosis, infection, or stress. Although more than one gene has been found to result in MSUD, the primary gene responsible for the condition in the Ashkenazi Jewish population is the E1B gene. The carrier frequency of mutations in the E1B gene in the Ashkenazi Jewish population is approximately 1 in 97. Screening for three mutations provides a carrier detection rate of greater than 95%.

MucolipidosisType IV (MLIV) is a severe neurodegenerative condition that is characterized by a variable degree of growth and psychomotor retardation. In addition, many patients have abnormalities of the cornea and retina. Most patients never develop the ability to speak or walk and remain at a developmental level of 1 to 2 years of age. The carrier frequency in the Ashkenazi population is approximately 1 in 89. Testing for two mutations provides a carrier detection rate of approximately 95%.

Niemann-Pick Type A disease is a severe neurodegenerative condition of infancy which cannot be treated. Symptoms, including loss of brain function and enlargement of the liver and spleen, appear by about 6 months of age. Average life expectancy is about 2–3 years of age. The carrier frequency of Niemann-Pick disease in the Ashkenazi Jewish population is approximately 1 in 115. Testing for the common mutations allows a detection rate for carriers of about 97%.

Nemaline Myopathy is a neuromuscular disorder that most commonly has an infantile onset. This disease has a slowly progressive onset of muscle weakness, particularly involving the tone of muscles in the face, neck, upper limbs, and respiratory tract. In infancy, difficulties with feeding and respiration may lead to death. Affected children also display delayed motor milestones. The carrier frequency of nemaline myopathy in the Ashkenazi Jewish population is approximately 1 in 168. Screening for one mutation will detect at least 95% of carriers in this population.

Tay-Sachs disease is a disorder in which the central nervous system progressively degenerates. This causes loss of coordination, seizures, difficulty swallowing, and poor pulmonary function. Symptoms usually appear at about 6 months of age. Eventually, children with Tay-Sachs disease become blind, severely mentally retarded, paralyzed, and unaware of their surroundings. There is no treatment, and average life expectancy is 3–5 years. Approximately 1 in 27 Ashkenazi Jewish individuals are carriers for Tay-Sachs disease.

Carrier screening involves analysis of the enzyme responsible for Tay-Sachs disease, as well as DNA testing for the most common mutations. The detection rate for carriers is approximately 99% with enzyme analysis, and 98% for DNA.

Usher syndrome is a disease that is associated with deafness and progressive blindness. There are three different types of Usher syndrome which have been associated with mutations in several different genes. In the Ashkenazi Jewish population, mutations for both Usher syndrome Type I and Type III have been identified.

Usher syndrome Type I is associated with profound hearing loss and prepubertal onset of retinitis pigmentosa, a disease that impairs vision because of progressive degeneration of the cells in the retina. The carrier frequency of Type I in the Ashkenazi Jewish population is approximately 1 in 147. Screening for one mutation will detect at least 75% of carriers in this population**.

Usher syndrome Type III is associated with postlingual onset of moderate to severe hearing loss and variable onset and severity of retinitis pigmentosa. The carrier frequency of Type III in the Ashkenazi Jewish population is 1 in 120. Screening for one mutation will detect approximately 95% of carriers in this population.

Walker-Warburg syndrome is a severe disease of the brain, muscle and eyes. It is characterized by muscle weakness, feeding difficulties, seizures, blindness, brain malformations and developmental delay with mental retardation. The average life expectancy for patients is less than 3 years. The carrier frequency for the predominant form of Walker-Warburg in the Ashkenazi population is about 1 in 120. Testing for one Ashkenazi founder mutation detects about 95% of carriers.

* *If only the male partner is identified as a carrier for Familial Hyperinsulinism, prenatal diagnosis is not recommended. However, the child's pediatrician should be made aware of the rare possibility of focal (localized) disease when a mutation is paternally inherited. This may occur in less than 12% of cases.*

** *A carrier detection rate of 75% is lower than that of the other conditions offered on this panel. Please be aware of the limitations of this test.*