

CARRIER SCREENING IN THE ASHKENAZI JEWISH POPULATION

WHY DOES MY JEWISH BACKGROUND PUT ME AT AN INCREASED RISK?

While there are many genetic conditions that occur in persons of all ethnic backgrounds, there are several conditions that occur more frequently in people of Ashkenazi, or Eastern European, Jewish ancestry. These genetic conditions are called autosomal recessive conditions based on the way they are inherited. In order for an individual to be affected by an autosomal recessive condition, they must have two genes or traits for that condition, one inherited from their mother and one inherited from their father. Each of us carries a few recessive genes that do not work properly. Because there are thousands of genes, the likelihood that we would meet and have children with another person who carries the same recessive gene that we do is small. However, that chance increases if we come from the same ethnic group as our partner because people from the same ethnic group share common ancestors, and therefore, common genes.

In large ethnic groups it is difficult to pinpoint which genetic conditions occur more frequently, but some are known. For example, individuals who have African ancestry are at increased risk to carry Sickle Cell trait and individuals who are from Mediterranean countries (Greece, Italy, Turkey) are at increased risk to carry β -thalassemia trait. Because the Ashkenazi Jewish community is more close-knit, researchers have been able to identify more of the autosomal recessive genetic conditions in this population, so more extensive carrier screening is available.

Carrier screening for genetic conditions more common in the Ashkenazi Jewish population is recommended for every couple where at least one member of the couple is Ashkenazi Jewish. Genetic counseling may be helpful to couples considering carrier screening. During a genetics consultation, many questions can be answered, such as explaining the inheritance of these conditions, teaching more about the diseases, and helping a couple understand their risks and reproductive options.

WHAT CONDITIONS AM I AT RISK FOR?

The first genetic condition that was shown to have an increased carrier rate in the Ashkenazi Jewish population was Tay Sachs disease. Currently, screening is offered for a number of genetic conditions that vary in frequency. The carrier frequency of cystic fibrosis in the Ashkenazi Jewish population is the same as in the European Caucasian population. Please refer to the list of the nine genetic conditions and their descriptions at the end of this fact sheet.

WHAT IF I HAVE A FAMILY HISTORY OF ONE OF THESE CONDITIONS?

If you have a family history of one of these conditions, such as a brother, sister or cousin, then you may have a higher chance of being a carrier. Your specific chance to be a carrier is determined based on how you are related to the person in your family with the condition. If the changes in the gene, or traits, are known for your family member, then the testing can look for those specific traits and rule out whether or not you have inherited them. Genetic counseling is recommended prior to testing people who have a family history of an autosomal recessive genetic condition.

HOW DOES THE TESTING WORK?

A blood sample is taken and the DNA that codes the genes being tested is analyzed for the most common changes. Please note that enzyme analysis is often performed for Tay Sachs disease instead of, or in conjunction with, DNA analysis. The detection rate, or chance of finding a change when someone really is a carrier, varies for each condition. Only the common mutations can be tested for so not everyone who is a carrier will have a "positive" carrier screen.

For most of these conditions, the detection rate is very good if you are Ashkenazi Jewish. However, if you are not Ashkenazi Jewish the detection rate may be poor. This means that sometimes a couple who is at risk to have a child with one of these genetic conditions will not be detected using current carrier screening technology. Please refer to the chart below for specific information.

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Genetic Condition	Chance to have a child with the condition if both Ashkenazi Jewish	Chance to be a carrier if Ashkenazi Jewish	Chance an Ashkenazi Jewish Carrier will be detected by screening	Chance to have a child with the condition if one person is Ashkenazi Jewish and one person is from the general Caucasian population	Chance to be a carrier if from the general Caucasian population	Chance a person from the general Caucasian population will be detected by screening
Tay Sachs Disease	1 / 3,600	1/30	98% by enzyme; 94% by DNA	1/ 36,000	~1/300 (1/30 in French Canadians)	98% by enzyme, small by DNA
Cystic Fibrosis	1 / 3,300	1/ 29	97%	1/ 3,300	1/ 29	90% if Northern European Caucasian
Canavan disease	1 / 6,400-1/13,456	1/40-58	98%	unknown	unknown	Low, unless family mutation is known
Familial Dysautonomia	1 in 3,700	1 in 36	99%	1/21,000~	Less than 1/150	
Gaucher Disease	1/1,000	1 /10	90-98%	unknown	unknown	
Niemann Pick, Type A	1/ 32,000	1 /90	95%	unknown	unknown	
Mucopolipidosis IV	1 in 100,000	1 in 100	95%	unknown	unknown	
Fanconi Anemia	1 /32,000	1 / 89	99%	~1/56,000	~1/158	
Bloom Syndrome	1/ 40,000	1 /100	95-97%	unknown	unknown	

WHAT HAPPENS IF I AM A CARRIER?

When a person tests positive as a carrier for one of these conditions, we recommend screening the partner to determine if there will be a chance for the couple to have a child affected with the condition. If BOTH members of the couple are carriers for the SAME condition, then that couple has a 25% risk (1 in 4) with each pregnancy to have a child with that condition. This couple may consider prenatal diagnosis by CVS or amniocentesis to learn a fetus' status, may test a child at birth, or may consider alternative parenting options such as adoption, egg or sperm donation, or preimplantation genetic diagnosis. Specific testing options may vary based on the condition involved.

When one member of the couple is a carrier for a specific condition, but the other member of the couple has a negative carrier screen for the same condition, the chance for the couple to have a child with the condition is small. In some cases, additional testing may be considered. Each couple's specific risk will be determined by their ethnic background and corresponding carrier detection rate. In some cases, additional testing may be available. A genetic counselor can review the results, benefits, limitations and options for further testing with the patient/couple.

SHOULD I HAVE CARRIER SCREENING FOR ANY OR ALL OF THESE CONDITIONS?

The decision to pursue screening is a personal one. Some women/couples want to know if their chance to have a child with these conditions is increased prior to or during pregnancy. Other women/couples do not feel like the chance of these conditions is high enough for them to consider screening. Some people may choose screening for the conditions with higher carrier frequencies (such as Tay Sachs Disease, CF, Canavan Disease and Familial Dysautonomia), but not for the less common conditions. Some couples may pursue screening if both members are of Jewish ancestry, while others may chose screening when only one member is of Jewish ancestry. Talk with your doctor and/or arrange to speak with a genetic counselor for more information.

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Tay Sachs disease -A degenerative, neurological disease where children usually develop normally until about 6 months of age and then begin to lose skills they had gained. Sometimes a “cherry-red spot” will be seen on an eye exam. Most individuals with Tay Sachs disease will pass away in early childhood. Carrier testing is done by enzyme analysis and DNA analysis. The chance to be a Tay Sachs carrier is also increased in certain French Canadian populations.

Cystic Fibrosis (CF)- Individuals with CF typically have a buildup of mucus in the lungs and other organ linings, leading to respiratory failure, frequent infections, pancreatic problems, and male infertility. People with CF typically have normal intelligence, but their lifespan is often shortened due to complications of the disease. However, there is a wide range of clinical symptoms for people with CF, from very mild symptoms and infertility to life threatening problems. Treatments are available to improve life expectancy, but currently the only cure for the respiratory failure associated with CF is lung transplantation. The chance to be a carrier of CF is also increased in the general Caucasian population. See “Carrier Screening for Cystic Fibrosis” on the USC Genetic Counseling website for additional information.

Canavan disease-Another severe neurological disorder of the central nervous that is characterized by developmental delay, poor muscle tone, large head, seizures, blindness and gastrointestinal reflux with death in the first several years of life. No effective treatment is currently available.

Familial dysautonomia- A neurological disorder that is characterized by poor suck and feeding difficulties, episodes of vomiting, abnormal sweating, pain and temperature insensitivity, fluctuating blood pressures, absent tearing and scoliosis. There is currently no cure for familial dysautonomia, but treatments can improve the length and quality of life.

Gaucher disease- Classical Gaucher disease comes to attention in childhood or adolescence with enlargement of the liver and spleen and the increasing brittleness of the bones. Intelligence is usually normal. Genetic enzyme replacement therapy is available. Some people with Gaucher disease may not show any symptoms until late adulthood or many never show symptoms. This wide range in expression of Gaucher disease can make interpreting test results difficult to predict outcome.

Niemann-Pick Type A- Symptoms of this condition usually occur in early childhood and include enlarged liver and spleen, problems gaining weight (also known as “failure to thrive”), a cherry–red spot on eye exam, and loss of physical and mental skills. Children with Niemann-Pick type A usually pass away in early childhood.

Mucopolipidosis Type IV - This is a progressive disorder characterized by poor growth and developmental delays, clouding of the corneas (white part of the eye), progressive vision loss and strabismus. Most affected infants do not progress in speech, walking or development beyond 1-2 years old. Life expectancy may be normal, but there currently is no effective treatment.

Fanconi Anemia (Group C)- This condition is a rare form of severe anemia where children may also have developmental delays, problems gaining weight (failure to thrive) and physical birth defects such as missing bones in the arm, cardiac defects or kidney problems. There is an increased risk for leukemia. Some children have been successfully treated with bone marrow transplantation. Life expectancy is 8-12 years.

Bloom syndrome- Children are often recognized at birth as having a rash on the face and patches of lighter and darker skin on their bodies. They also tend to be smaller than expected for their age. The main concerns with Bloom syndrome are the increased risk for cancers such as leukemia, skin cancer, and digestive cancers, as well as the chance for intellectual disability.

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