



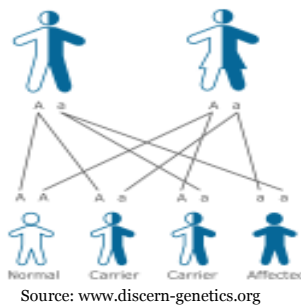
ASHKENAZI JEWISH CARRIER SCREENING

What is carrier screening?

The American College of Obstetricians and Gynecologists recommends that couples planning a pregnancy, or those already pregnant, be informed about genetic carrier screening. Specific ethnic groups are known to have an increased risk for certain genetic conditions, and carrier screening is available to find out if a couple is at risk for having a child with one of these conditions. If both members of a couple are carriers for the same condition, there is a 25% chance that the pregnancy will inherit the condition. *It is important to note that these conditions often occur in families with no previous history of the condition.*

How are these conditions inherited?

The conditions included in most carrier screening tests are inherited in an “autosomal recessive” manner. This means that both parents must be “carriers” for a condition in order to be at risk for a pregnancy to be affected with that condition. If both parents are carriers for the same condition, the chance of having an affected pregnancy is 1 in 4 (or 25%) for *each* pregnancy, as illustrated in the diagram below.



A "carrier" is an individual with no symptoms of a particular disease, but who possesses both a normal gene (inherited from one parent) and a non-working gene (inherited from the other parent) for that condition.

A "non-carrier" is a individual who inherits two normal genes, one from each parent.

An "affected" person has inherited two non-working genes, or mutations, one from each parent.

Who should be screened?

Carrier screening is based on an individual's ethnicity and/or country of origin. With every ethnicity there are certain genetic disorders that are more common. Genetic carrier screening is available for many conditions that are more common in certain populations.

We offer the Ashkenazi Jewish carrier screening panel to all couples with any family history of Ashkenazi Jewish heritage. The carrier frequency of each of the conditions is listed in the table below.

When should carrier screening be performed?

It is strongly recommended that you and your partner undergo genetic carrier screening prior to pregnancy, or as early in pregnancy as possible.

What is the carrier screening process?

- In our office, genetic counseling is provided before carrier screening is ordered. This ensures that you are offered the most appropriate carrier screening options.
- Carrier screening is performed through a simple blood test; no preparation is necessary.
- Test results are provided to you and your physician within 2-3 weeks.
- If both partners are determined to be carriers for the same condition, additional genetic counseling will be available to discuss the nature of the specific disorder as well as prenatal testing options.

CONDITIONS INCLUDED IN OUR ASHKENAZI JEWISH CARRIER SCREENING PANEL

Alpha-1-antitrypsin: Alpha-1 antitrypsin deficiency can cause lung disease in adults and liver disease in adults and children. Three in four adults with a severe deficiency will get emphysema, some when they are younger than 40.

Cystic fibrosis (CF): CF is a chronic disease that affects lung and digestive functions, with onset in childhood.

Tay-Sachs disease: Tay-Sachs disease is a fatal neurodegenerative disease characterized by progressive weakness, loss of motor skills, and blindness.

Canavan disease: Canavan disease is usually fatal in childhood and is characterized by developmental delays, sleep disturbances, seizures, and feeding difficulties.

Familial dysautonomia: Familial dysautonomia is characterized by altered sensitivity to pain and temperature, feeding difficulties and vomiting, absence of tears, and cardiovascular instability.

Bloom syndrome: Bloom syndrome is characterized by short stature, immunological dysfunction, and increased risk of childhood cancers.

Fanconi anemia: Fanconi anemia is characterized by short stature, birth defects (such as malformations of the kidneys, limbs, thumbs), anemia, and an increased risk for leukemia.

Factor XI deficiency: Factor XI deficiency is associated with abnormal bleeding episodes that occurs with surgery, tooth extraction, and major injuries; the frequency of bleeding may vary from once a year to once every ten years.

Familial hyperinsulinemia: Symptoms of this condition include hypoglycemia as well as risks for seizures, hypotonia, poor feeding, and apnea.

Familial hypercholesterolemia: Familial hypercholesterolemia presents with premature atherosclerotic coronary heart disease. Carriers for this condition may be at increased risk for developing high cholesterol.

Familial Mediterranean fever: This condition is more common in the Sephardic Jewish population and is characterized by recurrent inflammation and fevers associated with abdominal pain, pleuritis, or arthritis.

Gaucher disease: Gaucher disease is the most common disorder among the Ashkenazi Jewish population. Symptoms range from mild to severe but generally involve liver and spleen enlargement, low blood count, and bone pain and fracture. Treatment is available using enzyme replacement therapy.

Glycogen storage disease type Ia: This disorder, also called von Gierke disease, is characterized by low blood sugar, short stature, and accumulation of glycogen and fat in the liver and kidneys.

Glycogen storage disease type IIIa: This condition presents with low blood sugar, enlarged liver, increased lipids in the blood, and skeletal myopathy.

Lipoamide dehydrogenase deficiency: This condition presents in infancy with severe psychomotor retardation and results in death during childhood.

Maple syrup urine disease (MSUD): Individuals with MSUD often have a maple syrup odor in the urine and ear wax. Without diagnosis and treatment, amino acids accumulate in the body. Symptoms include central nervous system anomalies, feeding difficulties, coma, and death.

Mucopolidosis type IV: This disorder affects the brain and nervous system beginning in the first year of life, and results in mental and physical retardation and impaired vision.

Nemaline myopathy: This disorder presents with severe muscle weakness in the face, neck and limbs; a severe form is associated with respiratory disease, contractures, and death in the first year of life.

Niemann-Pick disease (type A): This disorder presents with progressive physical and mental disability with death occurring by 4 years of age.

Connexin 26 gene mutations: Individuals with two connexin 26 gene mutations are expected to develop non-syndromic severe to profound sensorineural hearing loss in childhood.

Torsion dystonia: Torsion dystonia causes dystonic muscle contractions resulting in repetitive twisting or directional movements. Posturing of a foot, leg, or arm are the most common presenting symptoms.

Usher syndrome: Usher syndrome is characterized by congenital sensorineural hearing loss and adolescent-onset of retinitis pigmentosa (loss of vision).

CARRIER FREQUENCY AND DETECTION

DISEASE	CARRIER FREQUENCY	DETECTION RATE
Alpha-1-antitrypsin	~1 in 30	~ 95%
Cystic fibrosis ^{cau}	~1 in 25	~ 95%
Tay-Sachs disease ^{AJ}	~1 in 28	>93%
Canavan disease ^{AJ}	~1 in 57	>99%
Familial dysautonomia ^{AJ}	~1 in 30	>99.5%
Bloom syndrome ^{AJ}	~1 in 100	>97%
Fanconi anemia ^{AJ}	~1 in 89	>99%
Factor XI deficiency ^{AJ}	~1 in 23	>96%
Familial hyperinsulinemia ^{AJ}	~ 1 in 89	~90%
Familial hypercholesterolemia ^{AJ}	~ 1 in 56	>90%
Familial Mediterranean fever ^{SH}	~1 in 5	~90%
Gaucher disease ^{AJ}	~1 in 13	90%
Glycogen storage disease type Ia ^{AJ}	~1 in 71	94%
Glycogen storage disease type IIIa ^{SH}	~1 in 35	
Lipoamide dehydrogenase deficiency ^{AJ}	~ 1 in 94`	~ 90%
Maple syrup urine disease ^{AJ}	~1 in 80	~99%
Mucopolidosis type IV ^{AJ}	~1 in 100	>95%
Nemaline myopathy ^{AJ}	~1 in 108	>95%
Niemann-Pick type A ^{AJ}	~1 in 80	~95%
Connexin 26 gene mutations ^J	~1 in 25	~ 60%
Torsion dystonia ^{AJ}	~1 in 900	>95%
Usher syndrome, type 1 ^{AJ}	~1 in 70	

KEY:

cau: Increased risk in the Caucasian population
 AJ: Increased risk in the Ashkenazi Jewish population
 SH: Increased risk in the Sephardic Jewish population

UNDERSTANDING YOUR RESULTS

What does a “screen negative” result mean?

A “screen negative” carrier screen result means that your chance of being a carrier for the conditions included in the screening panel has been greatly reduced. A negative result significantly lowers, but does not completely eliminate, the chance of being a carrier. Only the most common mutations in a particular gene are analyzed in carrier screening. The percentage of carriers detected by each carrier screen is listed in the table above.

When your carrier screen is “screen negative”, we generally do not recommend that your partner pursue carrier screening, as the chance for an affected pregnancy is greatly reduced.

What does a “screen positive” result mean?

A “screen positive” carrier screen result means that you were found to be a carrier for one or more conditions included in the screening panel. When the test determines that you are a carrier, the next step is for your partner to have carrier screening performed. Both parents must be carriers for the pregnancy to be at risk for the condition. If testing determines that a couple is at risk, prenatal testing using chorionic villus sampling (CVS) or amniocentesis can be performed to determine whether the pregnancy has inherited the condition.

QUESTIONS?

If you have any questions concerning the above information, please do not hesitate to contact us at 312-981-4400.