

TESTING FOR GENETIC DISEASE AT NEW YORK UNIVERSITY SCHOOL OF MEDICINE

Bloom disease, Canavan disease, Cystic fibrosis, familial dysautonomia, familial hyperinsulinism Fanconi anemia, Fragile X, Gaucher disease, glycogen storage disease 1A, maple syrup urine disease, mucopolidosis IV (ML4), Niemann-Pick disease, Spinal Muscular Atrophy, and Tay-Sachs disease, are hereditary disorders that are more common in certain ethnic groups. In the past, people learned about their risk for having affected children only after the child was born. Through genetic testing, it is possible to identify people whose children may be at increased risk. At New York University School of Medicine, genetic testing is offered for all of these conditions.

WHAT CAUSES GENETIC DISEASE?

For most of the traits in our bodies, we have two genes, one inherited from the mother and one from the father. If there is a change in the gene (mutation), it may not work in the proper way. Some diseases occur when a person has a change in only one gene. Other diseases (called “recessive”) occur when both genes have changed.

WHAT IS A CARRIER?

A carrier is a person who has a change in one of the genes for a recessive disease. Because two changes are required to produce the disease, the person remains well and unaware of his or her carrier status. When two carriers have a child, the child has a 25% chance of having the disorder. When a carrier has a child with a person who is not a carrier, the child is not at risk for the disease. Fragile X is an X-linked disorder. Women who are carriers are at increased risk of having an affected child.

HOW ARE GENETIC TESTS USED TO IDENTIFY CARRIERS?

There are two ways that carrier testing is done. One way is by direct analysis of the genes. The genes are extracted from blood cells. The genes are tested for mutations. The second way is to test for the amount or activity of a gene product that normally prevents disease. Affected individuals have little, if any, of the gene product. Carriers have a 50% reduction in the gene product. The choice of test depends on its ability to detect as many carriers as possible.

HOW DO CARRIERS USE GENETIC INFORMATION?

When carriers decide to have children, the disease status of the baby can be learned before birth by using prenatal diagnosis. Prenatal diagnosis involves collecting a small sample of placenta between 10 to 12 weeks of pregnancy or a sample of the fluid that surrounds the fetus between 15 to 20 weeks of pregnancy. (The length of a pregnancy is usually 40 weeks.) Genetic testing is performed on these samples to learn whether the baby has the disease, is a carrier like the parents, or is not a carrier. Sometimes carriers may decide no to have children with other carriers.

IS GENETIC TESTING ACCURATE?

The tests cannot detect all carriers/mutations – although a negative result will substantially reduce the risk for being a carrier. There is a small chance that an error may occur, despite the fact that the testing laboratory uses procedures to assure a high level of quality. In rare instances a result cannot be determined and it may be necessary to obtain another sample. This testing will be performed at no additional cost.

HOW WILL I LEARN MY TEST RESULT?

The results of carrier testing are usually available within three to four weeks from when the specimen was collected and if you are found to be a carrier, a genetic counselor will call you. Your test results will be sent to you and your physician. If you want to discuss your test result with a genetic counselor, you may do so at any time.

IS GENETIC TESTING REIMBURSABLE?

Generally yes, but you should check with your insurance first.

CONFIDENTIALITY OF TEST RESULTS

The test results are your confidential information. They will not be disclosed to others, including your partner, your physician, or your insurance carrier, without your prior consent.

DISEASE	SIGNS AND SYMPTOMS	OUTCOME	POSSIBILITY FOR TREATMENT	CARRIER FREQUENCY	TYPE OF TEST
Bloom syndrome	Short stature. Hyperpigmented and sun-sensitive skin. Cancers at a young age. Respiratory infections. Infertility in males.	Progressive due to cancers and lung disease.	Sunlight avoidance. Use of sunscreen. Antibiotics for infection. Surveillance for cancer.	1:80 in Jews of Eastern European descent.	DNA test for most common mutations. Mutations do not predict severity of disease.
Canavan disease	Mental retardation. Seizures. Cerebral palsy.	Rapidly progressive. Fatal by age 9-12.	None.	1:40 in Jews of Eastern European descent. Much lower in other groups.	DNA test for most common mutations. Mutations do not predict severity of disease.
Cystic fibrosis	Frequent respiratory infections leading to lung damage. Digestive abnormalities. Infertility in males. Sometimes bleeding problems and heart failure occur.	Usually progressive, even with treatment. Median survival in the mid to late 20's	Antibiotics for infections. Respiratory inhalation therapies. Enzyme replacement for digestive problems. Heart and lung transplants for advanced disease.	1:20 in Caucasians and Jews of Eastern European descent. Lower in other groups.	DNA test for most common mutations. Mutations do not predict severity of disease.
Familial dysautonomia	Poor feeding. Vomiting crises. Indifferent to pain. Poor blood pressure and temperature control.	Progressive	Symptomatic for feeding, blood pressure, and respiratory problems.	1:30 in Jews of Eastern European descent.	DNA test for most common mutations. Mutations do not predict severity of disease.
Familial hyperinsulinism	Low blood sugar in the newborn period or during childhood, which may result in seizures, poor tone, poor feeding, and breathing difficulty.	Variable. Fatal, if untreated in severe cases	Glucose infusions. Feeding. Drugs to reduce insulin release. Resection of most of the pancreas	1:100 in Jews of Eastern European descent	DNA test for most common mutations. Mutations do not predict severity of disease.
Fanconi anemia	Low blood counts (RBCs, WBCs, platelets). Hyper-pigmented skin. Short stature. Kidney anomalies.	Progressive, average age of onset of anemia at age 7. Median survival until age 13.	Blood transfusions. Testosterone. Bone marrow transplants.	1:80 in Jews of Eastern European descent	DNA test for most common mutations. Mutations do not predict severity of disease.
Fragile X syndrome	Mental retardation. Large ears. Large testes. Prominent jaw.	IQ may deteriorate with age.	None.	1:268 in Caucasians 1:113 in Jews of Eastern European descent. Carriers are at increased risk for premature ovarian failure.	DNA test for CAG repeats. Number of repeats is predictive of risk to offspring.
Gaucher disease	Bone pain. Chest pain with breathing problems. Massive enlargement of spleen and liver causing bleeding and anemia. Age of onset very variable with half the patients not showing symptoms until age 45.	Usually progressive, but can be halted with treatment. Early-onset disease is usually more severe.	Costly enzyme replacement therapy. Bone marrow transplantation. Gene therapy on the horizon.	1:13 in Jews of Eastern European descent. Lower in other groups. Carriers are at increased risk for Parkinson disease.	DNA test for most common mutations. Mutations do not predict severity of disease.
Glycogen storage disease 1A	Low blood sugar, elevated blood lipids.	Poor growth. Increased risk for liver tumors	Frequent feeding	1:100 in Jews of Eastern European descent.	DNA test for most common mutation. Mutation does not predict severity of disease.
Maple syrup urine disease	Acidosis, coma, shock	Early death	Treatment of metabolic abnormalities may provide temporary improvement	1:100 in Jews of Eastern European descent.	DNA test for most common mutation. Mutation does not predict severity of disease.
Mucopolipidosis IV	Profound mental retardation. Visual impairment.	Progressive	None	1:100 in Jews of Eastern European descent.	DNA test for most common mutations. Mutations do not predict severity of disease.
Niemann-Pick	Enlargement of liver and spleen. Failure to thrive. Mental retardation. Cerebral palsy.	Rapidly progressive. Fatal.	None at present.	1:90 in Jews of Eastern European descent.	DNA test for most common mutations. Mutations do not predict severity of disease.
Spinal Muscular Atrophy	Causes the loss of motor nerve cells in the spinal cord and brainstem, causing weakness in muscles.	The earlier the onset of symptoms, the shorter the lifespan. In severe cases, the respiratory system is affected.	None at present. Clinical trials without any documented success.	1:50 in individuals...	DNA test for most common mutations. Mutations do not predict severity of disease.
Tay-Sachs	Blindness. Mental retardation. Seizures. Paralysis.	Rapidly progressive. Fatal by age 4-5.	None.	1:25 in Jews of Eastern European descent and French-Canadians. 1:300 in other groups.	DNA test for most common mutations. Mutations are predictive of severity of disease.