What is Carrier Screening?

Carrier screening is performed by a simple blood test to determine if an individual or a couple is at risk to have a child with a specific genetic disease.

Genes are basic units of hereditary information that code for all of the body’s traits and functions. Genes are carried on larger structures called chromosomes. Most individuals have 46 chromosomes or 23 pairs. Those pairs are numbered 1 through 22 and the 23rd pair (called the sex chromosomes) determines whether a person is male or female. Typically, a male has one X and one Y chromosome and a female has two X chromosomes. One copy of each pair of chromosomes and each pair of genes is inherited from the mother and the other copy is inherited from the father. For the sex chromosomes, an X chromosome is always inherited from the mother and an X or a Y chromosome is inherited from the father. A change, known as a mutation, in a gene can cause that gene not to function properly. This can lead to disease. There are multiple modes of inheritance by which a genetic disease can be inherited.

Autosomal recessive conditions, like CF and SMA, occur when mutations are present in both copies of the same gene. Each parent has one copy of a gene that works properly and one copy that does not. The parents are unaffected and are considered “carriers” of the disease.

X-linked conditions, like Fragile X syndrome, occur when there is a mutation on the X chromosome. An X-linked condition is usually inherited from a woman who is a carrier of the condition. Carrier females have a working copy of a gene on one X chromosome and a copy with a mutation on the other X chromosome. Women pass on one of their X chromosomes in each egg. When the X chromosome with the mutation is passed on in an egg and a Y chromosome is passed on in a sperm, the resulting male fetus will have the X-linked condition. Males with X-linked inheritance are generally affected and females are usually unaffected carriers.*

If both partners of a couple are identified as carriers of the same recessive condition, such as CF or SMA, the couple has a 25% risk with each pregnancy to have a child affected with that disease. The couple also has a 50% chance with each pregnancy to have a child who is a carrier with no symptoms of the disease, and a 25% chance to have a child who does not inherit a gene mutation from either parent and is not a carrier.

If a woman is identified as a carrier of an X-linked condition, such as Fragile X syndrome, she has a 50% chance with each pregnancy to pass on the X chromosome with the mutation and an increased risk to have an affected son or mildly affected daughter.

If a couple is at risk to have a child with any of these genetic disorders, prenatal diagnosis is available to determine whether or not a fetus is affected. Prenatal diagnostic testing is available through chorionic villus sampling (CVS) at 10-12 weeks of pregnancy and amnioncentesis after 15 weeks of pregnancy. Prenatal diagnostic testing for autosomal recessive conditions, such as CF and SMA, is available when both partners are carriers. Prenatal diagnostic testing for Fragile X syndrome is recommended for a woman who is a premutation or full mutation carrier. In addition, there are other reproductive options, such as in vitro fertilization (IVF) with preimplantation genetic diagnosis (PGD). When an at-risk couple is identified, our genetic counselors can provide information and support which may be helpful in making important family planning decisions.

ARRANGING CARRIER SCREENING

For further information, or to schedule a genetic counseling appointment please call (212) 241-6947.

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* Sometimes carrier females may be mildly affected. This is disease and/or mutation specific.

What options are available after carrier screening?

What is Carrier Screening?

Certain genetic disorders occur more frequently in the general population, regardless of ethnic background. Three common inherited genetic diseases are cystic fibrosis (CF), Fragile X syndrome, and spinal muscular atrophy (SMA). Carrier screening to determine if you or your partner are at risk to have a child with one of these conditions is available. This brochure provides information about each of these diseases and how they are inherited.
Cystic Fibrosis

Cystic fibrosis (CF) is an autosomal recessive disease that primarily affects the lungs and digestive system. CF is caused by mutations in the CFTR gene, which can result in the production of unusually thick mucus. Mucus accumulates in the lungs, leading to breathing difficulties and infection, and obstructs the pancreas, preventing proper secretion of enzymes needed for digestion of food. Also, men with CF are generally infertile.

CF is a chronic and progressive disease. There is no cure for CF. Treatments are available to help improve the quality of life, and the average life expectancy continues to increase. While some babies with CF still die in infancy, many patients with CF live into their 20s and 30s, or beyond.

CF occurs in all ethnic groups; however, its incidence varies with ethnicity. Many mutations have been identified in the CFTR gene. Carrier screening is performed by testing for the most common of these mutations. Although this testing can detect the majority of disease-causing mutations, a negative result does not eliminate the possibility that an individual is a carrier of a rare mutation. The carrier frequency and detection rate of testing in specific ethnic groups is provided in the table below.

Cystic Fibrosis Carrier Frequency and Detection Rate

<table>
<thead>
<tr>
<th>Ethnic Group</th>
<th>Carrier Frequency</th>
<th>Detection Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ashkenazi Jewish</td>
<td>1 in 20</td>
<td>91%</td>
</tr>
<tr>
<td>Non-Hispanic Caucasian</td>
<td>1 in 25</td>
<td>91%</td>
</tr>
<tr>
<td>Hispanic</td>
<td>1 in 58</td>
<td>81%</td>
</tr>
<tr>
<td>African American</td>
<td>1 in 61</td>
<td>73%</td>
</tr>
<tr>
<td>Asian</td>
<td>1 in 98</td>
<td>54%</td>
</tr>
</tbody>
</table>

Fragile X Syndrome

Fragile X syndrome is the most common inherited form of mental retardation. Fragile X syndrome is inherited in an X-linked manner. Individuals with Fragile X syndrome have varying degrees of mental retardation, behavioral and/or emotional problems (including autistic-like features), and some males may have subtle physical findings. Fragile X syndrome is caused by a change in the FMR1 gene on the X chromosome. Within the FMR1 gene, there is a region of repeating DNA bases referred to by the letters CGG. The number of CGG repeats present within the FMR1 gene determines if an individual has Fragile X syndrome or is at risk to have a child with Fragile X syndrome. Individuals with Fragile X syndrome have a full mutation, which contains 200 or more repeats. All males with a full mutation are affected, meaning they have mental retardation and other associated features. About half of females with a full mutation are affected, often less severely than males with a full mutation.

Fragile X syndrome is inherited from a mother who is a “carrier” of this condition. Approximately 1 in 100 to 250 women in the general population are Fragile X carriers. A woman is considered to be a carrier if she has either a premutation (55-199 repeats) or a full mutation. Female premutation carriers and full mutation carriers are at risk of having a child with Fragile X syndrome. A premutation, if passed on in an egg, may stay as a premutation, or increase in size to a full mutation resulting in a male with Fragile X syndrome or a possibly affected female. This event of repeat expansion in the FMR1 gene tends not to occur in sperm. Hence, males with a premutation do not have the same risk as female premutation carriers to have a child with Fragile X syndrome. For this reason, Fragile X carrier testing is not routinely offered to men.

Individuals with a premutation are not expected to have symptoms of Fragile X syndrome and are of normal intelligence and appearance. However, female premutation carriers may be at increased risk for premature ovarian failure usually occurring before age 40. In addition, some males** with a premutation may develop neurological problems involving tremor and balance in later adult life.

Spinal Muscular Atrophy

Spinal Muscular Atrophy (SMA) is an autosomal recessive disease that results in severe and progressive weakness of the voluntary muscles. Breathing, swallowing, head and neck control, walking, and crawling are affected. There are four types of SMA: classified as Types I, II, III, and IV, which range from severe (onset in early infancy) to mild (onset in young adulthood), respectively. Approximately 60% of individuals with SMA are severely affected and die in early childhood. SMA is caused by a deletion and/or mutation of both copies of the SMN1 gene. Affected individuals have no functional copy of the SMN1 gene. Whereas most individuals have two copies of the SMN1 gene, SMA carriers usually have only one copy of the SMN1 gene. Approximately 1 in 40 individuals within the general population is a carrier of SMA.

Carrier testing for SMA is performed by determining the number of SMN1 gene copies present in an individual. This method can detect approximately 90-94% of SMA carriers.** The remaining 6-10% of SMA carriers cannot be detected, due to a duplication (or 2 copies) of the SMN1 gene on one chromosome and a deletion (or no copies) of the SMN1 gene on the other chromosome, or because they carry a gene change not detectable by this test. Carrier screening of both partners provides the most accurate assessment of a couple’s risk for having an affected child. Prenatal diagnostic testing for SMA is available for couples where both partners have been identified as SMA carriers. Prenatal testing cannot predict the severity of the disease, or SMA type.

* Detection rate of SMA carriers can vary with ethnicity.

** Less is known about female premutation carriers.

** Carrier rate can vary with ethnicity.