





## Chapter 25

# Screening and Diagnostic Testing for Genetic Disorders

Although most babies are born healthy, parents-to-be often worry about the possibility that their baby will be born with a medical condition or physical disability. A **birth defect** is a physical problem or intellectual disability that is present at birth, although some birth defects may not be noticed until the child is older. About 3 in 100 babies in the United States are born with a major birth defect.

Many birth defects are caused by problems with a person's **chromosomes** or **genes**. These types of disorders are called **genetic disorders**. Genetic disorders can range from mild, such as **color blindness**, to severe, such as some forms of **hemophilia** or **Tay-Sachs** disease. Some genetic disorders are not harmful and no special treatment is needed. For many genetic disorders, medical treatment and specialized care can greatly improve a child's quality of life. However, for some genetic disorders, there is no effective treatment. Table 25-1 lists some of the more common genetic disorders.

There are many ways to assess the risk of having a child with certain disorders. These tests are called **screening tests**. Other tests are available that can find out for sure if there are specific problems in the baby. These tests are called **diagnostic tests**. Both screening and diagnostic testing are offered to all pregnant women. You don't have to be a certain age or have a family history of a disorder to have these tests.

Whether you want to be tested is a personal choice. Some couples would rather not know if they are at risk or whether their child will have a disorder, but others want to know in advance. Knowing beforehand gives you and your family time to learn about a particular disorder and organize any special care that your child may need. For a very small number of disorders, it may be

**Table 25-1 Common Genetic Disorders**

Disorder	What It Means	Who Is at Highest Risk?
<b>Dominant Disorders</b>		
Neurofibromatosis	Disorder that causes growth of tumors in the nervous system	Those with a family history of the disorder
Isolated polydactyly	Having extra fingers or toes	Those with a family history of the disorder, African Americans; commonly occurs without risk factors
<b>Recessive Disorders</b>		
Thalassemia	Causes anemia; there are different types of the disorder, and some are more severe than others.	Depends on the type of disorder; Mediterranean (especially Greek or Italian), Middle Eastern, African, or Asian descent
Sickle cell anemia	A blood disorder in which the red blood cells have a crescent, or “sickle,” shape rather than the normal doughnut shape. Because of their odd shape, these cells get caught in the blood vessels. This prevents oxygen from reaching organs and tissues, which causes pain.	African Americans
Tay–Sachs disease	A disease in which harmful amounts of a fatty substance called ganglioside GM2 collect in the nerve cells in the brain. It causes severe intellectual disability, blindness, and seizures. Symptoms first occur at about 6 months of age.	Ashkenazi Jews, French Canadians

possible to treat the condition during pregnancy (with fetal surgery, for example). You also may have the option of not continuing the pregnancy. Your health care provider or a **genetic counselor** can discuss all of the testing options with you and help you decide.

## Genes and Chromosomes

Genes are the coded instructions that direct every process that takes place in your body and provide the “blueprints” for all of your physical traits. A gene is a short segment of a chemical called **DNA**. DNA consists of two strands of four different kinds of building blocks called nucleotides. The order in which

**Table 25-1 Common Genetic Disorders, continued**

Disorder	What It Means	Who Is at Highest Risk?
Cystic fibrosis	Causes problems with digestion and breathing. Symptoms appear in childhood—sometimes right after birth. Some individuals have milder symptoms than others. Over time, the problems tend to become worse and harder to treat.	White individuals of Northern European descent
<b>X-Linked Disorders</b>		
Duchenne muscular dystrophy	Causes progressive muscle weakness, loss of muscle tissue, and abnormal bone development. The muscle problems cause problems with movement, especially walking, and breathing problems. Heart defects usually are present. Most affected individuals do not live beyond age 30 years.	Males
Color blindness	A condition in which a person cannot see certain colors	Males
Hemophilia	A disorder caused by the lack of a substance in the blood that helps it clot. Affected individuals are at risk of bleeding to death if they are injured.	Males

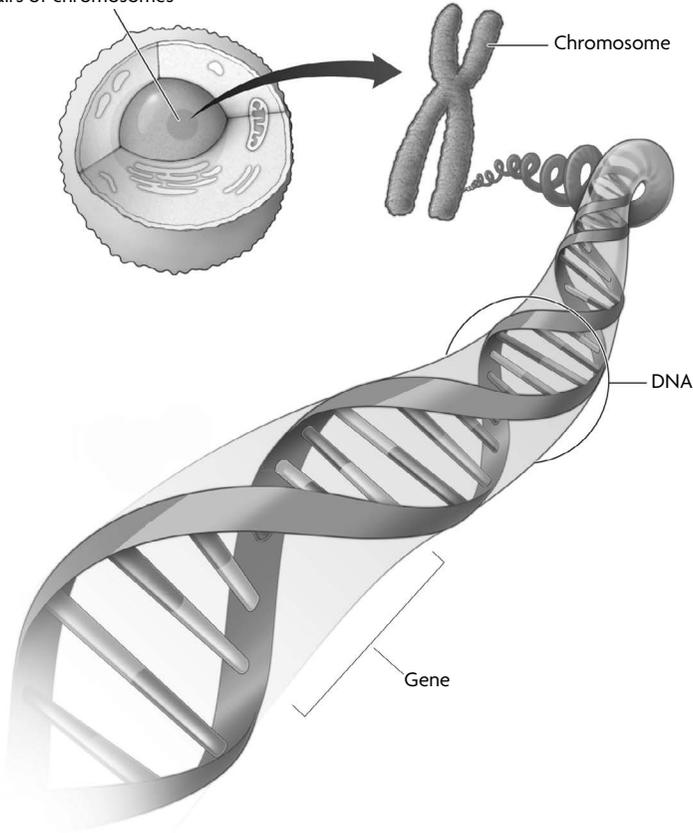
these building blocks occur along the strands of DNA is the genetic code that tells cells how to function.

Genes usually come in pairs. Each member of a gene pair is called an **allele**. Some traits, such as blood type, are determined by a single gene pair. Other traits, including skin color, hair color, and height, are the result of many genes working together.

DNA is packaged into structures called **chromosomes**. Chromosomes also come in pairs. One allele of a gene pair is located on one chromosome in a pair, and the other allele of the gene pair is located on the other chromosome in the pair. Every **cell** in your body except **eggs** and **sperm** contains 23 pairs of chromosomes (46 chromosomes). The egg and the sperm each contain half that amount—23 chromosomes (not pairs). Chromosome pairs 1–22 are called **autosomes**. The 23rd pair of chromosomes are the **sex chromosomes**, which are called X and Y.

Genes are inherited—they are passed down from parents to children. During fertilization, when an egg and sperm join, the cell that is formed contains the full set of 46 chromosomes (or 23 pairs of chromosomes). In this way, a baby receives one half of its genes from the mother and one half from the father.

Cell nucleus containing  
23 pairs of chromosomes



**Chromosomes and genes.** Chromosomes are the structures inside cells that carry a person's genes. Each person has 22 pairs of autosomes and one pair of sex chromosomes. A single gene is a segment of a large molecule called DNA.

A baby's sex is determined by the sex chromosomes it receives. The egg always has an X chromosome, but the sperm can have either an X or a Y chromosome. A combination of XX results in a female and XY results in a male.

## Inherited Disorders

Some genetic disorders are caused by a change in a gene. These changes are called **mutations**. Most mutations are harmless. Some mutations, however, can cause disease or can affect a child's appearance or physical function. Mutations can be passed down from parents to their children, or they can

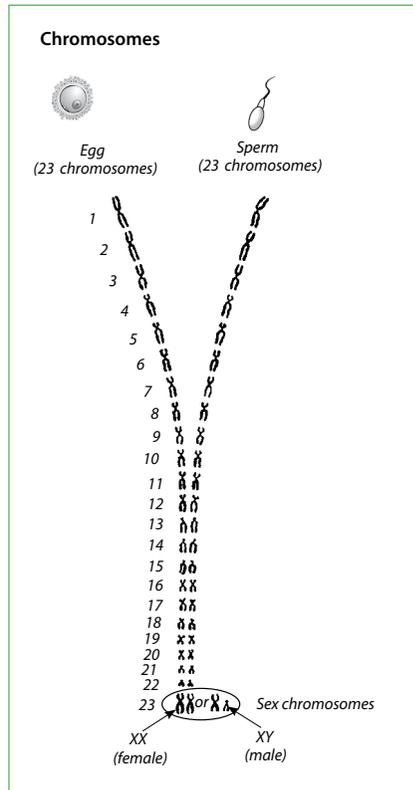
appear for the first time in a child. If a parent has a mutation, there is a chance that his or her child will receive the mutation and inherit the disease or disability. The chance of a child inheriting a mutation depends on whether the gene is dominant or recessive (see Table 25-1).

### Autosomal Dominant Disorders

With a dominant gene disorder, just one gene inherited from either parent can cause the disorder. A disorder is called **autosomal dominant** when the mutation is located on any of the 44 chromosomes that are not the sex chromosomes. If one parent has the gene that causes an autosomal dominant condition, each child of the couple has a 50% chance of inheriting the disorder. An example of an autosomal dominant disorder is **neurofibromatosis**. This is a group of disorders that causes growth of tumors in the nervous system.

### Autosomal Recessive Disorders

With an **autosomal recessive** gene disorder, two genes inherited from both parents are needed to cause the disorder. If only one parent has the gene, then the child cannot have the recessive disorder. If a child inherits a recessive gene for a disorder, he or she is known as a **carrier** of the disorder. Carriers often do not know that they have a recessive gene for a disorder. They usually do not have any symptoms of the disorder, but they are able to pass the gene to their children. If both parents are carriers, there is a 25% chance that the child will get the gene from each parent and will have the disorder. There is a 50% chance that the child will be a carrier of the disorder—just like the



**How genes are inherited.** Every cell in the body, except for eggs and sperm, has 46 chromosomes. The chromosomes carry all of a person's genes. During fertilization, when an egg and sperm join, the cell that is formed contains the full set of 46 chromosomes (or, 23 pairs of chromosomes). In this way, a baby receives one half of its genes from the mother and one half from the father. A baby's sex is determined by the sex chromosomes it receives. The egg always has an X chromosome, but the sperm can have either an X or a Y chromosome. A combination of XX results in a female and XY results in a male.

carrier parents. If only one parent is a carrier, there is a 50% chance that the child will be a carrier of the disorder.

Some recessive disorders are known to occur more often in certain races and ethnic groups. The following are examples of recessive disorders:

- **Sickle cell disease**—In this disorder, red blood cells have a crescent shape that causes them to block the blood vessels. This cuts off the flow of **oxygen** to organs, causing variable episodes of severe pain and organ damage. It occurs most often in African Americans.
- **Tay–Sachs disease**—This disorder causes blindness, seizures, and death, usually by age 5 years. It occurs most often in people of Eastern European Jewish descent (Ashkenazi Jews) and among French Canadians and Cajuns.
- **Cystic fibrosis**—This disorder causes severe problems with breathing and digestion and can lead to early death. It is most common in non-Hispanic white individuals.

### **Sex-Linked Disorders**

Disorders that are caused by genes on the sex chromosomes (the X chromosome or Y chromosome) are called **sex-linked disorders**. An example of a sex-linked disorder is color blindness. In this condition, a gene that controls how the eye sees color does not function properly. The gene is located on the X chromosome. Boys can be affected by color blindness if they inherit one of the mutations. Girls usually are not affected if they inherit one of the mutations because the other X chromosome has a normal gene. This normal gene “cancels out” the abnormal gene.

### **Multifactorial Disorders**

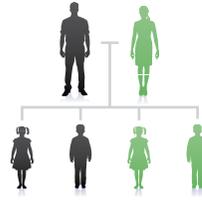
Multifactorial disorders are caused by a number of different factors working together. Some factors are genetic, whereas others are environmental. These disorders can run in families, but the way they are inherited is not completely understood. **Neural tube defects**, heart defects, and cleft palate are examples of multifactorial disorders. Many people are born with genes that give them a higher chance of developing cancer or **diabetes mellitus** but never develop these diseases. This may be because an environmental factor, such as exposure to a cancer-causing chemical, smoking, a high-fat diet, or being overweight, is needed to trigger the disease.

Researchers have been able to identify some of the environmental factors that trigger a few of these disorders. Neural tube defects are a group of

## Types of Genetic Disorders

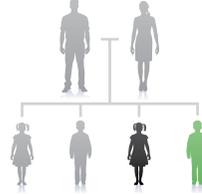
### Dominant Disorder

If one parent has a dominant gene disorder, there is a 50% chance that it will be passed to each child.



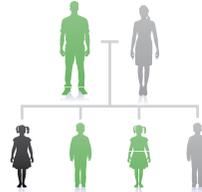
### Recessive Disorder

If both parents carry the recessive gene for a disorder, there is a 25% chance that a child they have will have the disorder, a 50% chance that a child will be a carrier, and a 25% chance that a child will not get the gene at all.



### X-linked Disorder

If a woman is a carrier of an X-linked disorder and she has a son, there is a 50% chance that he will have the disorder. If she has a daughter, there is a 50% chance the daughter will be a carrier. If the father has an X-linked disorder, all the daughters will be carriers and none of the sons will be affected.



 Affected person

 Carrier

 Unaffected person

disorders that can happen when the fetal spine does not form correctly. They have been linked in some cases to a woman not getting enough **folic acid**, a B vitamin, in the weeks before pregnancy and during early pregnancy. For this reason, it is recommended that all women of childbearing age take a vitamin supplement containing 400 micrograms of folic acid daily to help prevent neural tube defects if a pregnancy should occur (see the section “Take Folic Acid” in Chapter 1, “Getting Ready for Pregnancy”). However, for most multifactorial disorders, the causes are not known.

## Chromosomal Disorders

Some genetic disorders are caused by having too many or too few chromosomes. Having an abnormal number of chromosomes is called **aneuploidy**. Another type of genetic disorder is caused by problems with the structure of chromosomes. These disorders sometimes are called “structural chromosomal disorders.”

## ***Aneuploidy***

Most children with aneuploidy have physical defects and intellectual disabilities. The most common aneuploidy is a **trisomy**, in which there is an extra chromosome. Examples of trisomies include **trisomy 13 (Patau syndrome)**, **trisomy 18 (Edwards syndrome)**, and **trisomy 21 (Down syndrome)**. Down syndrome is the most common trisomy in the United States. It occurs in about 1 in 700 births, and it is estimated that there are about 6,000 new cases each year. A **monosomy** is a condition in which there is a missing chromosome. Monosomies are much rarer than trisomies. An example of a monosomy is **Turner syndrome**, in which a female has a missing X chromosome.

Aneuploidy usually occurs because the mother's egg or father's sperm contains an abnormal number of chromosomes. These errors occur when the egg or sperm are formed and usually happen by chance. However, the chance of these errors occurring in a woman's eggs increases as she ages. The chance of aneuploidy therefore increases as well. For example, the risk of having a baby with Down syndrome calculated according to the mother's age when the baby is born is as follows:

- 1 in 1,250 at age 25 years
- 1 in 1,000 at age 30 years
- 1 in 400 at age 35 years
- 1 in 100 at age 40 years
- 1 in 30 at age 45 years

It's important to keep in mind that although women older than 35 years are considered most likely to have a baby with Down syndrome, about 80% of babies with Down syndrome are born to women who are younger than 35 years simply because younger women have far more babies.

## ***Structural Chromosomal Disorders***

In these types of disorders, a part of a chromosome may be missing (deletion), a part of a chromosome may be duplicated (duplication), or a piece of a chromosome can break off and relocate to another chromosome (translocation). Some structural chromosomal disorders are inherited due to the presence of abnormal chromosomes in the eggs or sperm. Others occur during prenatal development or even later in life.

Translocations do not always cause a disease or physical disability. A translocation is called unbalanced when genetic material is lost or gained. A balanced translocation does not result in any gain or loss of genetic material. People who have a balanced translocation usually have no medical effects. However, a person with a balanced translocation can have a child with an

unbalanced translocation. Unbalanced translocations also have been linked to repeated *miscarriages*.

Structural chromosomal disorders are named according to the chromosome number that is affected and sometimes by the location where the deletion, insertion, or translocation occurs. Examples of structural chromosomal disorders include the following:

- 5p deletion syndrome—Also known as cri du chat syndrome, this disorder is caused by a deletion from chromosome 5. It causes severe intellectual and physical disabilities, poor growth, and weak muscle tone. Babies with this syndrome have a high-pitched cry that has been compared to that of a cat.
- 22q11.2 deletion syndrome—Also known as DiGeorge syndrome, this disorder is caused by a deletion from chromosome 22 at a specific location called 11.2. It causes a variety of signs and symptoms. Children with this syndrome have developmental delays and learning disabilities as well as heart defects, problems with some endocrine glands, and characteristic facial features.
- 4p deletion syndrome—This condition, also known as Wolf-Hirschhorn syndrome, is caused by deletion of genetic material near the end of one of the arms of chromosome 4. It causes characteristic facial features of wide-set eyes, small head, and misshapen ears. Children with this syndrome may have intellectual and developmental disabilities as well as physical problems, including seizures, weak muscles, and dental problems.

## Assessing Your Risk

All women are offered the option of having screening and diagnostic testing during pregnancy regardless of whether they have risk factors. In the past, if the mother was aged 35 years or older at the time of delivery, she was automatically considered at high risk of having a child with Down syndrome and offered diagnostic testing. However, any woman of any age can give birth to a child with Down syndrome or another trisomy, although the risk increases with increasing age of the mother. For this reason, a woman's age is no longer used to determine whether she should have screening or invasive diagnostic testing.

To help guide the decision about which tests to have or not to have, your health care provider may ask you certain questions about your health and your family history (see box “Risk Factors for Genetic Disorders”). These questions are designed to find out whether you have risk factors that increase your chances of having a baby with a genetic disorder. Even if you have risk factors, it does not mean that your baby will have a disorder. In fact, most

## Risk Factors for Genetic Disorders

It's a good idea to review your risk factors before you see your health care provider to discuss prenatal screening and diagnostic testing. It may be helpful for you to talk with your and your partner's family members for information about diseases or conditions that run in your families.

- \_\_\_ What is your age?
- \_\_\_ What is the baby's father's age?
- \_\_\_ If you or the baby's father is of Mediterranean or Asian descent, do either of you or anyone in your families have thalassemia?
- \_\_\_ Is there a family history of neural tube defects?
- \_\_\_ Have you or the baby's father ever had a child with a neural tube defect?
- \_\_\_ Is there a family history of congenital heart defects?
- \_\_\_ Is there a family history of Down syndrome?
- \_\_\_ Have you or the baby's father ever had a child with Down syndrome?
- \_\_\_ If you or the baby's father is of Eastern European Jewish, French Canadian, or Cajun descent, is there a family history of Tay–Sachs disease?
- \_\_\_ If you or your partner is of Eastern European Jewish descent, is there a family history of Canavan disease or any other genetic disorders?
- \_\_\_ If you or your partner is African American, is there a family history of sickle cell disease or sickle cell trait?
- \_\_\_ Is there a family history of hemophilia?
- \_\_\_ Is there a family history of muscular dystrophy?
- \_\_\_ Is there a family history of Huntington disease?
- \_\_\_ Does anyone in your family or the family of the baby's father have cystic fibrosis?
- \_\_\_ Does anyone in your family or the baby's father's family have an intellectual disability? Or have they had early menopause or tremors at an early age?
- \_\_\_ If so, was that person tested for fragile X syndrome?
- \_\_\_ Do you, the baby's father, anyone in your families, or any of your children have any other genetic diseases, chromosomal disorders, or birth defects?
- \_\_\_ Do you have a metabolic disorder such as diabetes mellitus or phenylketonuria?
- \_\_\_ Do you have a history of pregnancy issues (miscarriage or *stillbirth*)?

babies with a birth defect are born to couples who have no known risk factors. Risk factors that may increase the risk of having a child with a genetic disorder include the following:

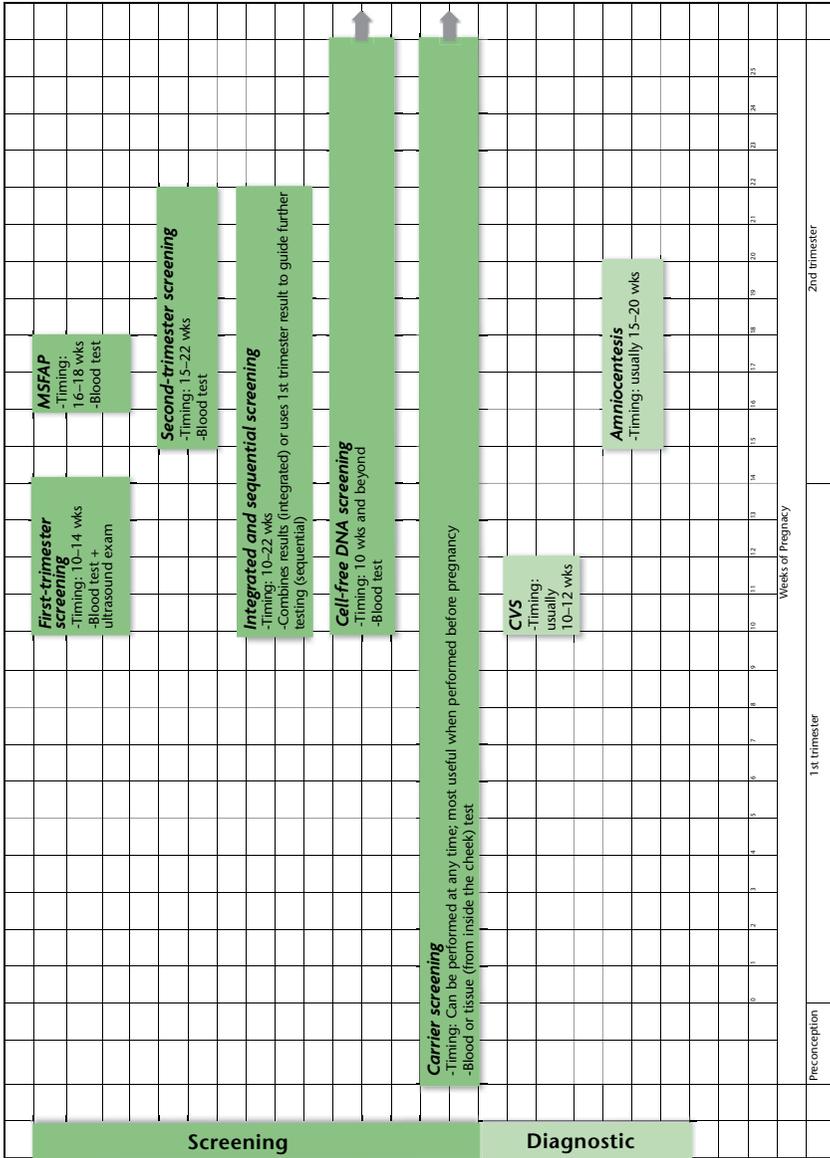
- Older age in either the father or mother
- One or both parents have a genetic disorder.
- A couple already has a child with a genetic disorder.
- There is a family history of a genetic disorder.
- One or both parents belong to an ethnic group that has a high rate of carriers of certain genetic disorders.

A genetic counselor or other health care provider with expertise in genetics can be useful in some situations. A genetic counselor can study your family health history and make recommendations about which tests are most appropriate for you. He or she also can interpret test results, provide counseling about your options, and talk about any concerns you may have.

## Types of Tests for Genetic Disorders

Many types of tests are available to help address concerns about genetic disorders:

- **Carrier screening**—Carrier screening is done on parents (or potential parents). It can show if you or your partner carries a gene for a disorder that could be passed to your children. Carrier screening can be done before pregnancy (**preconception**) or during pregnancy and involves a simple blood test. Cystic fibrosis carrier screening is offered to all women of reproductive age because it is one of the most common genetic disorders.
- Screening tests for aneuploidy and neural tube defects—These prenatal screening tests assess the risk that a baby will have Down syndrome and other trisomies as well as neural tube defects. They are done at different times during pregnancy. These tests do not tell whether the baby actually has these disorders, only the risk that the baby has the disorders. There are no risks to the unborn baby with having these screening tests.
- Diagnostic tests—Diagnostic tests can provide information about whether the baby has a genetic condition. These tests are done on cells obtained through **amniocentesis**, **chorionic villus sampling (CVS)**, or, rarely, **fetal blood sampling**. The cells can be analyzed using different techniques.



**Prenatal testing.** This chart shows the various types of prenatal testing that are available to assess the risk of having a child with a genetic disorder (screening tests) or detecting a genetic disorder in the baby (diagnostic tests). Abbreviations: CVS, chorionic villus sampling; MSFAP, maternal serum alpha fetoprotein.

## Deciding Whether to Be Tested

If you or your partner is at an increased risk of being a carrier of a genetic disorder, you may want to consider preconception carrier screening. For most disorders, carrier screening of people who are not at increased risk is not recommended. However, you still can request carrier screening for some disorders even if you do not have a family history of the disorder.

Screening tests for birth defects are offered to all pregnant women, but it is your choice whether you want to have them done. Diagnostic tests, such as amniocentesis, also are available as a first choice for all pregnant women, even for those who do not have risk factors. A first step in deciding whether to have genetic testing and what kind of testing to have is to learn the medical facts about the different kinds of testing:

- **Types of results**—Screening tests only give you the probability of your baby being born with a disorder. Results of prenatal screening tests often are given as a number such as 1 in 800, meaning that there is a 1 in 800 chance that your baby will have a defect. These results then are further described as being “high risk” or “low risk.” Diagnostic testing tells you whether or not the baby will be born with a chromosome disorder or a specific inherited disorder.
- **Risks**—Diagnostic tests are invasive. A sample of tissue needs to be taken using a needle. This can pose some risks to the pregnancy, although these complications are rare. There are no risks with having screening tests, which involve a blood test and an *ultrasound exam*.
- **Accuracy**—If you decide to have screening tests, there is a possibility of false-positive and false-negative results. A test result that shows there is a problem when one does not exist is called a false-positive result. A test result that shows there is not a problem when one does exist is called a false-negative result. A false-positive result can cause anxiety and may lead to unnecessary testing or treatment. A false-negative result can mean that you do not get the recommended counseling or preparation for having a child who has a medical condition or disability. With diagnostic testing, false-positive results and false-negative results are rare. Information about the rates of false-positive and false-negative results for each screening test that is offered should be made available to you.
- **Timing**—Screening tests for birth defects can be performed in the first trimester or in the second trimester, but the accuracy of results is higher when first-trimester results and second-trimester results are combined.

Diagnostic tests also are performed in the first trimester (generally between 10 weeks and 12 weeks of pregnancy for CVS) and in the second trimester (usually between 15 weeks and 20 weeks of pregnancy for amniocentesis). Having earlier results with CVS gives greater reassurance and allows time to get more information from a health care provider or genetic counselor if a disorder is diagnosed. Also, if you want to end the pregnancy, it is generally considered safer during the first trimester rather than later in the pregnancy, and first-trimester pregnancy termination procedures are often easier to obtain than second-trimester procedures.

- **Cost**—You also may want to check with your insurance carrier to make sure that the tests that you and your health care provider choose are covered by your insurance carrier. Some insurance carriers cover diagnostic testing only if you have risk factors for having a baby with a genetic disorder or if you have a positive screening test result.

Once you know the medical facts, you also need to consider how you will use the information gained from having these tests. Your answers to these questions depend on your personal beliefs, health history, and the specific disorders you are testing for. Your decision may not be clear right away and may change as you go through the testing process. These decisions often are difficult to make. Parent support networks (such as the National Down Syndrome Society, March of Dimes, and the Cystic Fibrosis Foundation), counselors, social workers, and clergy may be able to provide additional information and support.

Your health care provider or a genetic counselor can discuss all of the options with you and recommend which tests may be best for your individual situation. There also is the option of not having any testing. If you do decide to have testing, you should understand the advantages, disadvantages, and limitations of each test.

## Carrier Screening

Carrier screening detects if a person carries a gene for many, but not all, recessive disorders. If you are a carrier, it means that you can pass the gene to your children. For this test, a sample of blood or saliva is taken and sent to a lab for study. Tests performed on the sample can determine whether the person carries the specific genes.

Carrier screening has traditionally been recommended for people who are at higher risk of certain genetic disorders because of their family history,

ethnicity, or race. Individuals of Eastern European (Ashkenazi) Jewish ancestry may be offered carrier screening for Tay–Sachs disease, **Canavan disease**, cystic fibrosis, and **familial dysautonomia** and may want to have tests for other diseases, including **mucoylipidosis IV**, **Niemann–Pick disease type A**, **Fanconi anemia group C**, **Bloom syndrome**, and **Gaucher disease**. Individuals of African, African American, and African Caribbean descent are offered carrier screening for sickle cell disease and for the blood disorders beta-**thalassemia** and alpha-thalassemia. Specific carrier screening tests also are offered to individuals of Southeast Asian (alpha-thalassemia), French Canadian and Cajun (Tay-Sachs disease), and Mediterranean (beta-thalassemia) descent.

However, scientists are beginning to recognize the growing difficulty of assigning a person to just one particular race or ethnicity. Many people are of mixed races and come from multiple ethnic backgrounds. For this reason, all women are offered screening for cystic fibrosis, which is a common disorder affecting many different races and ethnic groups. Screening for cystic fibrosis is most effective in populations that have a high rate of carriers, such as non-Hispanic white and Ashkenazi Jewish populations.

Another carrier screening option is called **expanded carrier screening**. It is now possible with new technology to screen for a wide variety of disorders with a high degree of accuracy and at a relatively low cost. Many labs now offer expanded carrier screening. There are some concerns about expanded carrier screening, including whether the disorders a lab screens for are appropriate for carrier testing and how the results are communicated. If you are interested in this type of screening, talk to your health care provider or genetic counselor.

Once you know your carrier status for a disorder, you do not need to be tested again in a future pregnancy for that disorder. If new carrier screening tests become available for a disorder that you have not been tested for and for which you may be at risk, you may want to discuss carrier screening for these disorders with your health care provider.

## Results

As an example, let's say that you have decided to have carrier screening for cystic fibrosis. If your test result is negative, no further testing is needed. If your test result is positive, the next step is to test your partner. If results of both tests are positive, a genetic counselor or your health care provider will help you understand your risks of having a child with the disorder, as well as your options.

## **Timing**

Carrier screening can be done either before pregnancy or during the early weeks of your pregnancy. If the screening is done before you are pregnant, you can use the results to decide if you want to get pregnant. If it's done after you are pregnant and you screen positive for being a carrier of a disorder, diagnostic testing may be possible to see if the baby has the disorder or is a carrier of the disorder.

## **Important Considerations**

A negative screening test result does not necessarily mean that you do not have a gene for the disorder being tested for. For example, with cystic fibrosis, the standard test looks only for a limited number of genetic changes. There are other, less common genetic changes that can cause cystic fibrosis. Therefore, a negative carrier test result does not completely rule out the risk that a person is a carrier. Your health care provider or genetic counselor can provide information about the limitations of the screening tests that you decide to have.

## **If You or Your Partner Is a Carrier**

Being a carrier of a disorder doesn't usually affect your own health. It also does not mean that all of your children will be affected. Your health care provider or genetic counselor can calculate the chances that a child will have the disorder or that a child will be a carrier. Once you receive this information, you can think about several options:

- If you have had carrier screening before pregnancy, you may choose to proceed with becoming pregnant with the option of considering prenatal diagnostic testing. You may choose to use *in vitro fertilization* with donor eggs or sperm to achieve pregnancy. **Preimplantation genetic diagnosis** can be used with this option. You also may choose not to become pregnant.
- If you are already pregnant, you may want to have diagnostic testing, if it is available, to see if the baby will be born with the disorder.

You also may want to consider telling other family members if you or your partner is a carrier. They may be at risk of being carriers themselves. However, you are not obligated to do so. Your health care provider or genetic counselor can give you advice about the best way to do this. It cannot be done without your consent.

## Screening Tests for Aneuploidy and Neural Tube Defects

A variety of tests that screen your unborn baby for aneuploidy and neural tube defects are available. Screening tests can be performed in the first trimester or in the second trimester (see Table 25-2). Results of these tests also can be combined in various ways; this type of integrated or sequential screening has higher detection rates than tests performed independently.

The types of screening tests that you will be offered depend on which tests are available in your area, how far along you are in your pregnancy, and your health care provider’s assessment of which tests best fit your needs. Another type of screening test called a **cell-free DNA** test may be offered to women who are at high risk of having a child with aneuploidy (see box “Cell-Free DNA Test”).

**Table 25-2 Screening Tests for Genetic Disorders**

Screening Test	Test Type	What Does it Screen for?	Down Syndrome Detection Rate
Cell-free DNA test	Blood test that analyzes fetal DNA from the placenta that circulates in the mother’s blood	<ul style="list-style-type: none"> <li>• Down syndrome</li> <li>• Trisomy 18</li> <li>• Trisomy 13 (some labs)</li> </ul>	99%
Combined first-trimester screening	Blood test for two proteins in the mother’s blood plus an ultrasound exam	<ul style="list-style-type: none"> <li>• Down syndrome</li> <li>• Trisomy 18</li> </ul>	82–87%
Second-trimester single screen for neural tube defects	Blood test for alpha fetoprotein	<ul style="list-style-type: none"> <li>• Neural tube defects</li> </ul>	80%
Second-trimester quad screen	Blood test for four proteins in the mother’s blood	<ul style="list-style-type: none"> <li>• Down syndrome</li> <li>• Trisomy 18</li> <li>• Neural tube defects</li> </ul>	81%
Integrated screening	Blood test and an ultrasound exam in the first trimester, followed by quad screen in the second trimester	<ul style="list-style-type: none"> <li>• Down syndrome</li> <li>• Trisomy 18</li> <li>• Neural tube defects</li> </ul>	94–96%
Contingent sequential	First-trimester combined screening result: <ul style="list-style-type: none"> <li>• Positive: diagnostic test offered</li> <li>• Negative: no further testing</li> <li>• Intermediate: second-trimester screening test offered</li> </ul>	<ul style="list-style-type: none"> <li>• Down syndrome</li> <li>• Trisomy 18</li> <li>• Neural tube defects</li> </ul>	88–94%

## Cell-Free DNA Test

A screening test called the cell-free DNA test is available for women. A small amount of fetal DNA, which comes mainly from the **placenta**, circulates in the mother's blood. The cell-free DNA in a sample of the mother's blood can be screened for Down syndrome, trisomy 13, trisomy 18, and sex chromosome abnormalities. In women who are at high risk of having a baby with a chromosome disorder, this test is 99% accurate in detecting cases of Down syndrome and has a very low rate of false-positive results. This test can be done as early as the 10th week of pregnancy in some women. Results take about 1 week to process.

The cell-free DNA test works best for women who have an increased risk of having a child with a chromosome disorder, such as women who already have a child with a chromosome disorder. For women at low risk of having a baby with a chromosome disorder, conventional screening remains the most appropriate choice. Cell-free DNA testing is not recommended for women carrying more than one baby.

The cell-free DNA test has certain limitations. It does not screen for neural tube defects. An additional screening test needs to be done to check for these disorders. In addition, although it is highly accurate in detecting chromosome problems in high-risk women, it is not as accurate as diagnostic tests. A positive cell-free DNA test result should be followed by a diagnostic test.

## ***First-Trimester Screening***

First-trimester screening consists of a blood test combined with an ultrasound exam. This screening sometimes is called “combined first-trimester screening.” It is done between 10 weeks and 14 weeks of pregnancy to assess the risk of Down syndrome and other aneuploidies. The blood test measures the levels of two different proteins in the mother's blood. An ultrasound exam, called **nuchal translucency screening**, is used to measure the thickness at the back of the neck of the baby. An increase in the thickness of this space may be a sign of Down syndrome, trisomy 18, or other problems.

## ***Second-Trimester Screening***

If you choose to have only combined first-trimester screening for aneuploidy, a blood test that measures a substance called maternal serum

alpha-fetoprotein (MSAFP) can be done to test for neural tube defects. This test generally is done in the second trimester between 16 weeks and 18 weeks of pregnancy.

In the second trimester, a test called a “quadruple” or “quad” screen can be done to detect the presence of four different proteins in the mother’s blood. This test screens for Down syndrome, trisomy 18, and neural tube defects. The quad screen can be done between 15 weeks and 22 weeks of pregnancy. The stage of pregnancy at the time of the test is important because the levels of the substances measured change throughout pregnancy.

### ***Integrated and Sequential Screening***

The results from first- and second-trimester tests can be used together to increase their ability to screen for Down syndrome. The tests can be performed in the following ways:

- **Integrated screening**—Results of the first-trimester and second-trimester tests are analyzed together. The results are given only after the first-trimester and second-trimester screening tests are completed. Integrated screening is highly accurate and has a low rate of false-positive results.
- **Sequential screening**—Results of the first-trimester screening tests are used to determine further testing. If results show that you are at high risk, you can choose to have a diagnostic test. If results show that you are at low or intermediate risk, you can choose whether or not to have second-trimester screening. Compared with integrated screening, the chance of a false-positive result with sequential screening is slightly higher and accuracy is about the same.

### ***Results***

With any type of testing, it is important to be aware of the possibility of false-positive and false-negative results and the consequences of these results. Information about the rates of false-positive and false-negative results can be obtained from your health care provider.

Screening test results are reported as the risk that a specific defect is present and they take your age and other factors into account. For example, the risk in the general population for women aged 31 years having a baby with Down syndrome is 1 in 820. If you are aged 31 years and you have a screening test result for Down syndrome of 1 in 900, it means you have a lower risk of having a baby with Down syndrome than the general population of women the same age as you.

Results also may be described as “screen negative” if the risk is lower than a certain cut-off point and described as “screen positive” if the risk is higher than the cut-off point. Different laboratories have different cut-offs for what is considered screen positive and screen negative.

### ***If Screening Test Results Show an Increased Risk***

In most cases, screening test results are normal. If the results of a screening test raise concerns about your pregnancy, you will need to process the information and decide how to proceed. Your health care provider or genetic counselor can help guide you through your options. Further evaluation, such as diagnostic testing, may be available for the disorder in question and can be done to provide more information. The chances that you will have a positive diagnostic test result following a positive screening test result are low. If you are thinking about having a diagnostic test, you will need to balance the small risk of pregnancy complications that are associated with a diagnostic test against the risk of having a child with the disorder. Your health care provider or genetic counselor can explain these risks to you in detail so that you can make an informed decision.

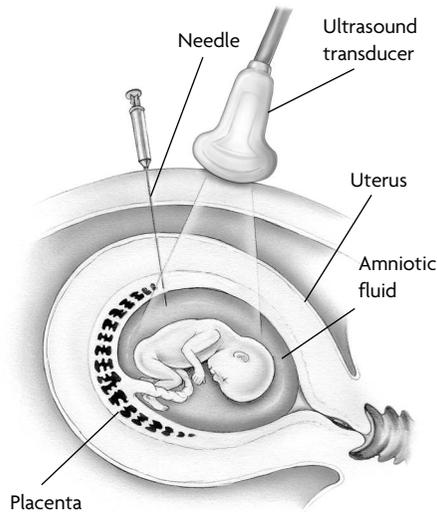
## **Diagnostic Tests**

The fetal cells used in diagnostic testing are obtained using different techniques. Once the cells are obtained, they can be studied in different ways depending on the disorders being tested for. Some tests may not be available in some areas or may need to be done in a special center equipped to perform them.

### ***Amniocentesis***

Amniocentesis usually is done between 15 weeks and 20 weeks of pregnancy. The test generally is not done any earlier than 15 weeks because the risk of complications is higher.

To perform amniocentesis, a thin needle is guided through the woman's abdomen and uterus. A small sample of amniotic fluid is withdrawn. Amniotic fluid contains cells from the baby. These cells are sent to a lab, where they are grown in a special culture. This takes about 10–12 days. When the cells are ready, they are analyzed to find out whether the baby has certain disorders, such as Down syndrome or specific genetic disorders depending on family history and ultrasound exam findings (see “How the Cells Are Analyzed” later in this chapter). The amniotic fluid also can be tested to detect neural tube defects.



**Amniocentesis.** In this procedure, a small sample of amniotic fluid is removed with a needle to be studied.

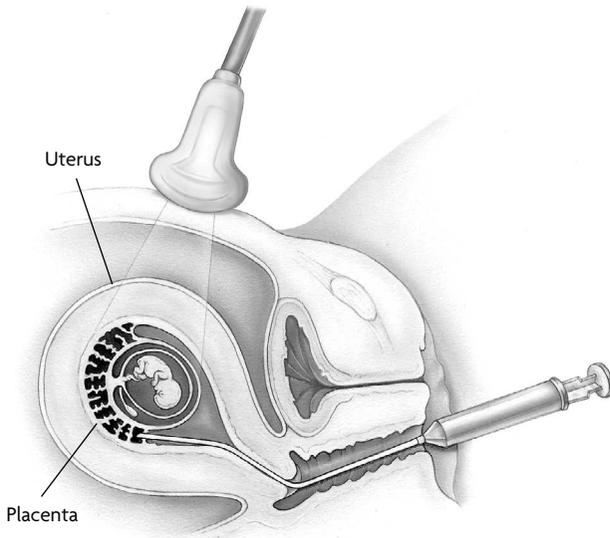
Complications of amniocentesis may include cramping, vaginal bleeding, infection, and leaking amniotic fluid. There is a very small chance of miscarriage (1 in 300–500).

### ***Chorionic Villus Sampling***

Chorionic villus sampling is performed earlier than amniocentesis, generally between 10 weeks and 13 weeks of pregnancy. This earlier time frame gives you more time to think about your options and to make decisions. However, CVS is not as commonly performed as amniocentesis and may not be available at all hospitals or centers. It also is important to have CVS performed by an experienced health care provider.

To perform CVS, a small sample of tissue is taken from the placenta. The tissue contains cells with the same genetic makeup as the baby. The sample can be obtained in one of two ways. A small tube can be guided through the woman's vagina and **cervix** (transcervical CVS), or a thin needle can be guided through the abdomen and wall of the uterus (transabdominal CVS). The sample is sent to a lab. The cells are grown in a culture, which takes about 7–14 days. The cells then are analyzed.

Complications from CVS include vaginal bleeding, leakage of amniotic fluid, and infection. When CVS is performed by an experienced health care provider and in a center that performs many of these procedures, the risk of miscarriage with CVS is about the same as the risk with amniocentesis.



**Chorionic villus sampling.** In this procedure, a small sample of cells (chorionic villi) is removed from the placenta for study.

CVS cannot be used to diagnose neural tube defects prenatally. If you have CVS, you may want to have the blood test for MSAFP, a detailed ultrasound exam, or both to detect neural tube defects.

### ***Preimplantation Genetic Diagnosis***

This test may be offered to couples who are using in vitro fertilization to become pregnant and who are at increased risk of having a baby with a genetic or chromosomal disorder. Before an **embryo** is transferred to a woman's uterus, it is tested to determine if it has a specific, known genetic disorder for which the couple is at risk.

### ***How the Cells Are Analyzed***

A number of different technologies are used in prenatal diagnostic testing. Each one is used to detect different kinds of genetic changes. Your health care provider or genetic counselor will assess what information is being sought in the diagnostic test and select the tests that are most appropriate.

Missing, extra, or damaged chromosomes can be detected by taking a picture of the chromosomes and arranging them in order from smallest to largest. This is called a karyotype. A karyotype can show whether

- the number of chromosomes is abnormal

- the shape of one or more chromosomes is abnormal
- a chromosome is broken

A technique called ***fluorescence in situ hybridization*** can be used to detect the most common aneuploidies, which involve chromosomes 13, 18, 21, and the X and Y chromosomes. Results are available more quickly than with traditional karyotyping because the cells do not need to be grown in a lab. A positive test result is confirmed with a karyotype.

***Microarray analysis*** can find chromosomal deletions, insertions, and translocations throughout the entire set of genes. Results may be available more quickly than with karyotyping because the cells do not need to be grown in a lab. This test can tell you a lot of information, but whether everything that is found is a cause for concern is uncertain.

Tests to find specific gene mutations also can be done. A variety of techniques for detecting gene mutations are available. Testing for gene mutations must be specifically requested. There is no one test that can find each and every gene mutation. For example, if you and your partner are carriers of the cystic fibrosis gene, you may want to request prenatal diagnostic testing for this specific mutation.

### ***If Your Baby Has a Disorder***

If diagnostic testing shows that your baby has a disorder, you will need to think about your various options. You may choose to continue the pregnancy, or you may end the pregnancy. There is no right choice in these cases. Your health, values, beliefs, and situation all play a role in the decision.

If you decide to continue with the pregnancy, it's a good idea to learn all that you can about the condition and what it will mean for your baby's health. Some conditions are not serious or life threatening and may require only minimal special health care. With other disorders, it is helpful to prepare for caring for a child with special needs. Neonatologists are doctors who care for infants born with complex medical disorders. There also are pediatric subspecialists with expertise in specific disorders. Your health care provider or hospital staff may be able to help you find this special care. You also can seek out support groups for you and your partner. Ask whether the hospital where you are planning to deliver has pediatric doctors who can provide the best possible care for your infant. If it doesn't, consider requesting a transfer of care so that you can deliver your baby at such a facility.

Remember that educating yourself about your child's condition is crucial. You may find it helpful to find resources in your area that can put you in contact with parents of children with similar disorders (see the "Resources" section in this chapter).

## RESOURCES

The following resources give more information about the science of genetic disorders; the signs, symptoms, and treatment of different types of genetic disorders; and where to find support and counseling if you are at increased risk of having a baby with a genetic disorder or have received a diagnosis of a certain disorder in your child.

### **Cystic Fibrosis Foundation**

[www.cff.org](http://www.cff.org)

*National organization dedicated to research into cystic fibrosis and advocacy for people affected by this disorder.*

### **Genetic Disorders, Genomics and Healthcare**

<http://genome.gov/27527652>

*Information from the National Human Genome Research Institute that covers many aspects of genetics and how it pertains to individuals and their families.*

### **Genetic Science Learning Center**

<http://learn.genetics.utah.edu>

*Site that teaches basic information about genetics through videos, animations, and other learning aids.*

### **March of Dimes**

[www.marchofdimes.com](http://www.marchofdimes.com)

*Comprehensive site that gives information about a wide variety of birth defects, including their causes, diagnosis, and treatment. Also explains the ongoing research being done to improve the outlook for children and adults born with certain disorders.*

### **National Center on Birth Defects and Developmental Disabilities (NCBDDD)**

[www.cdc.gov/ncbddd/index.html](http://www.cdc.gov/ncbddd/index.html)

*Provides information on birth defects, developmental disabilities, and hereditary blood disorders.*

### **National Down Syndrome Society**

[www.ndss.org](http://www.ndss.org)

*National society that advocates for people with Down syndrome. Provides information for new and expecting parents about the health care needs for children with Down syndrome and offers support for individuals and families.*