THE GENETICS OF CYSTIC FIBROSIS

Cystic fibrosis* **(CF*)** is a **genetic*** or **inherited*** disease that occurs when both parents pass a CF **gene*** on to their child. Cystic Fibrosis can be found in all races and ethnic groups. Cystic Fibrosis is, however, most often seen in people who are white and who are not of Hispanic ethnicity. At present, about 30,000 children and adults in the United States have CF (about 70,000 worldwide).

Each person has a set of blueprints or instructions found in his or her genes. Genes contain the instructions for how the body develops and works. For example, genes control eye, hair, and skin color. Genes tell the body how tall to grow. Genes determine what blood type a person has. Genes can also cause people to have certain health problems. In all of our body **cells*** we have two sets of **chromosomes*** one from our mother and one from our father. Chromosomes are made up of many genes—they are the holders for genes in the cells. Each cell has 23 pairs of chromosomes that contain thousands of genes. Chromosomes and genes are made of special chemical structures called **DNA*** (deoxyribonucleic acids). The pattern of DNA is what makes up the instruction code in each gene. Genetic testing to look for CF is sometimes called CF **DNA testing**.*

Cystic fibrosis is a disease that is caused by an abnormal gene. An abnormal gene is called a **genetic mutation**.* The gene that causes problems in CF is found on the seventh chromosome. There are many **mutations*** (abnormal genes) that have been shown to cause CF disease. Over 1000 mutations have been discovered, but there are about 30 that are common. The most common gene mutation is called **deltaF508**.* When a person receives two abnormal CF gene mutations, the person will have CF disease. The cells in the body will follow the instructions from the CF genes and will not work properly. For more on what happens to cells in a person with CF, see "What Causes Problems in Cystic Fibrosis?" in Appendix 2.

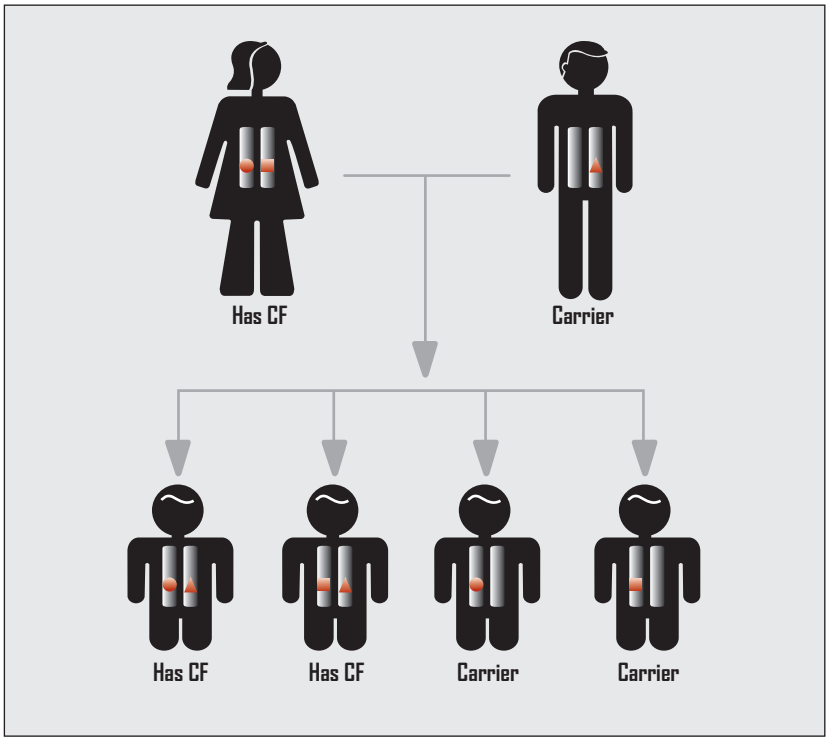
HOW CF IS INHERITED

A person must inherit two CF genes to have CF disease. When your child was **conceived*** he or she received a CF gene from both you and your partner. A child can inherit CF only if both parents carry a CF gene (that is, each parent either has CF or is a **carrier***) and both parents pass the CF gene on to their child.

There is nothing that parents do to cause CF in their child and usually they do not know that they are carriers of a CF gene.

A carrier is a person who has one abnormal CF gene and one normal gene. Remember, each cell in a person has two of each chromosome, one from the mother and one from

INHERITING CF: PARENT WITH CF AND PARENT CARRYING CF GENE



*See CF Words to Know Glossary.

the father. If one of the seventh chromosomes has a CF gene and one does not, the person is a carrier and does not have any **symptoms*** or disease problems. This is the way the CF gene is passed on for many generations.

If your child received one CF gene and one non-CF (normal) gene, he or she would not have CF disease—your child would be a CF carrier instead. The normal gene, not the CF gene, would control what the body's cells do and would help make sure they work well enough to prevent CF disease. About 1 out of every 25 white Americans is a CF carrier. There are more CF carriers in the white non-Hispanic race than in any other race.

A person can be a CF carrier even though CF disease has not occurred in the family for many generations. This is because a person who is a CF carrier must have a child with someone else who is also a CF carrier and both of them have to pass the abnormal gene to the child. Families may have CF carriers who do not have symptoms and have not had a child who received two abnormal CF genes. Most people who have children with CF did not know that CF genes ran in their families. Cystic fibrosis was only recognized as an inherited disease in the 1930s. Many families may not have known about children who had CF and died in past generations.

WHEN BOTH PARENTS CARRY A CF GENE

When a man and a woman who are both CF carriers conceive a child, one of three things happens:

- There is a one in four chance (25% of the time) the child will receive a CF gene from each parent (two abnormal genes total) and will be born with CF disease.
- There is a two in four chance (50% of the time) the child will receive one CF gene from one parent and a non-CF normal gene from the other parent. This child becomes a CF carrier like the parent.
- There is a one in four chance (25% of the time) the child will receive non-CF normal genes from each parent. When this happens, the child cannot have CF disease and is not a CF carrier.

Each time a child is conceived by two CF carriers, the chance that the baby will have CF disease is one in four (25%).

Some parents think that if they have had one child with CF, their other children will be born without the disease. This is not always true. With every pregnancy, parents who both carry the CF gene will always have a one in four (25%) chance of having a child with CF.

For example, the chance of having a girl is one in two or 50%. You might expect a family of four children to have two boys and two girls. But you probably know families who have four girls and no boys. Or four boys and no girls. Likewise, two CF carriers could have four children who all have the CF disease.

WHEN A PERSON WITH CF HAS A CHILD

A person who has CF has two abnormal CF genes. A person with CF will always pass an abnormal gene to his or her child. Every child a person with CF conceives will have at least one CF gene. Whether the child is a carrier or has the CF disease depends on the other parent. If a person with CF conceives a child with another person who is a CF carrier, the chance of having a child with CF is one in two (50%). The risk of the child only being a carrier is one in two (50%). The child will either have CF or be a carrier. If a person with CF conceives a child with a person who is not a CF carrier, the child will always be a CF carrier (100%), but will not have CF.

People with CF have problems with **fertility*** and may not be able to conceive a child naturally. To learn more about fertility and reproduction in CF, see "Puberty and Fertility in CF" in the appendix of the module *Managing Nutrition and Digestive Problems*.

*See CF Words to Know Glossary.

GENETIC TESTING

A person can have a genetic test to see if he or she is a carrier of a CF gene. The genetic test for CF mutations is usually done using a person's blood sample. Sometimes this is done when a woman is considering getting pregnant or early in her pregnancy. There are ways to test a baby before birth to see if the baby has abnormal CF genes. Some tests only look for the most common mutations and might miss a rare CF gene. Other tests can look at the seventh chromosome for every kind of CF gene. This test is usually more expensive and takes longer to get results. If people already know family members who carry the CF gene, they can make sure the CF test is done to find out if they also carry the gene.

Cystic fibrosis carrier testing may be something to think about in a family who has a child with CF. If there are other children who do not have CF, parents may want to know if they are carriers who could pass the CF gene on to their own children. Cousins, aunts, uncles, and other relatives may also want to know if they are CF carriers. A person with CF who is thinking about having a child may want to consider having his or her partner tested to know better what the risk will be of having a child with CF.

A child can be **diagnosed*** with CF from CF genetic testing. If a child is found to have two abnormal CF genes, he or she will have the disease. Even if the child does not have symptoms at the time the test is done, it would be expected that the child will have problems from CF in the future. Cystic fibrosis varies from person to person in the types of problems it causes and when symptoms first appear. Some babies are born with symptoms and most will have some **signs*** of CF disease in the first year of life. But other people with CF may not have problems until later.

If the specific gene mutations for a child are known, the family can use that information to help look at the pattern of genes in the family. This can be most helpful if the child has rare mutations that might not be tested for in a usual genetic screening test.

FUTURE RESEARCH

At this time, knowing the specific gene mutations a person has does not tell us much about how severe a child's disease may be or what treatment will work best. Genetics researchers have found some mutations to be milder. People who have these mutations do not have the digestive problems seen with the more common CF mutations. Even so, there are differences among those with common mutations; the types of problems and when they occur still vary from person to person. Current **research*** on new treatments may benefit some people with CF depending on what CF genes they have. Scientists expect to learn more about this in the future.

Researchers are also looking at other genes that may either help a person who has CF have less severe problems or will make the person's disease more severe. These genes may modify or alter how CF genes work in the body. Scientists are still learning more about how genes work in our bodies.

Scientists are also working on ways to give a person with CF copies of normal genes in the hope that the normal genes will help the cells work normally. Researchers are testing various gene treatments or **therapies*** that could help organs most affected by CF (such as the lungs). In **gene therapy**,* the scientist inserts a normal gene into a cell. But this type of therapy is still very much in the testing phase and it is not clear when it will be available to people with CF.

GETTING MORE INFORMATION

Your CF health care team can tell you more about genetic testing, including carrier and **prenatal*** testing. Many families find it helpful to talk with a **genetic counselor*** about the pattern of inheritance and risks of having another child in the family with CF. This information may help families make a choice about having more children, having genetic testing, or both. Any member of your family, such as a child, niece, nephew, sister, or brother who is considering having a child, can also ask for carrier and prenatal testing and counseling.

*See CF Words to Know Glossary.