A Parent's Guide to Genetics & Hearing Loss

Centers for Disease Control and Prevention
National Center on Birth Defects and Developmental Disabilities

About 1 in 500 infants is born with or develops hearing loss during early childhood. Hearing loss has many causes: some are genetic (that is, caused by a baby's genes) or non-genetic (such as certain infections the mother has during pregnancy, or infections the newborn baby has). A combination of genetic and non-genetic factors also can cause hearing loss. For many babies, the cause of hearing loss is unknown.

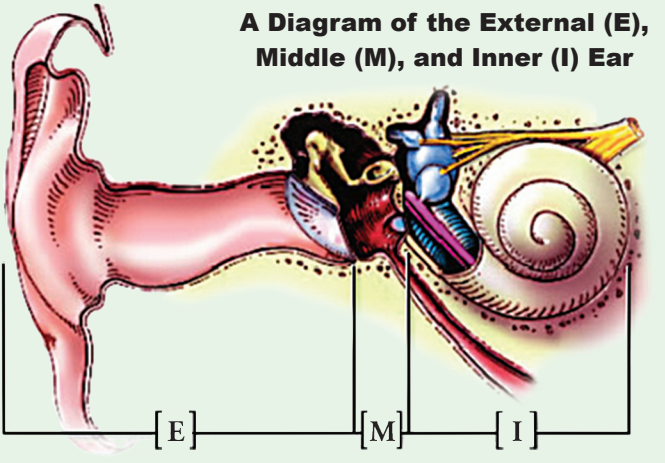
This booklet answers many of the questions that families have about the causes of hearing loss, including genetic causes. For some of the topics, more extensive details are given in the shaded boxes.

About The Causes of Hearing Loss

What are the types of hearing loss? There are many different ways to talk about the different types of hearing loss.

- ❏ One way is based on whether or not a baby is born with hearing loss. If the baby is born with hearing loss it is called congenital. If the hearing loss occurs after the baby is born it is called acquired.
- ❏ Another way depends on whether or not the hearing loss gets worse over time. Hearing loss that gets worse over time is called progressive. Hearing loss that does not change is called non-progressive.
- ❏ A third way depends on whether or not other symptoms are present; that is, is it syndromic or non-syndromic.
- ❏ A fourth way depends on whether or not hearing loss runs in the family. If it does, it is called familial; if it does not it is sporadic
- ❏ A fifth way is based on where in the ear the hearing loss occurs. If the loss occurs in the outer or middle ear it is conductive. If it occurs in the inner ear it is sensorineural. If the loss occurs in both areas it is mixed.

A Diagram of the External (E), Middle (M), and Inner (I) Ear



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www.iurc.montp.inserm.fr/cric/audition/english/ear/fear.htm

One way to describe hearing loss is as “congenital” or “acquired”. Congenital means that a person was born with the hearing loss. Babies born with hearing loss can be identified through a newborn hearing screening test. The test often is done before a baby leaves the hospital in which he or she was born. The screening test does not tell the cause of the baby’s hearing loss. It can tell only whether the baby might have a hearing loss. Acquired hearing loss means that a person could hear when he or she was born, but developed hearing loss later in life. Acquired hearing loss also can be described by the age at which it starts. If hearing loss starts before the age when children usually begin talking, it is called “*pre*lingual”, which means “before speaking”. If hearing loss starts after the age when children begin talking, it is called “*post*lingual”, which means “after speaking”.

If the hearing loss gets worse over time, it is called “progressive”. If the hearing loss does not change over time, it is “nonprogressive” or stable.

“Syndromic” means that a person has other symptoms besides hearing loss. For example, some people with hearing loss also are blind. There are many different syndromes that have hearing loss as one of the symptoms. “Nonsyndromic” means that the person does not have any other symptoms.

If more than one person in a family has hearing loss, it is said to be “familial”. That is, it runs in the family. If only one person in the family has hearing loss, it is called “sporadic”. That is, it does not run in the family.

The middle ear contains small bones that help send sound from the air to the inner ear. The inner ear changes these sounds into nerve signals that go to the brain. “Conductive” hearing loss is caused by problems in the outer or middle ear. “Sensorineural” hearing loss is caused by problems in the inner ear or in the hearing nerve, or both. “Mixed” hearing loss is a result of both kinds of problems.

What Causes Hearing Loss?

Hearing loss can be caused by changes in genes or by outside factors (like injuries, illness or certain medications), or both. For many children with hearing loss, the cause is unknown.

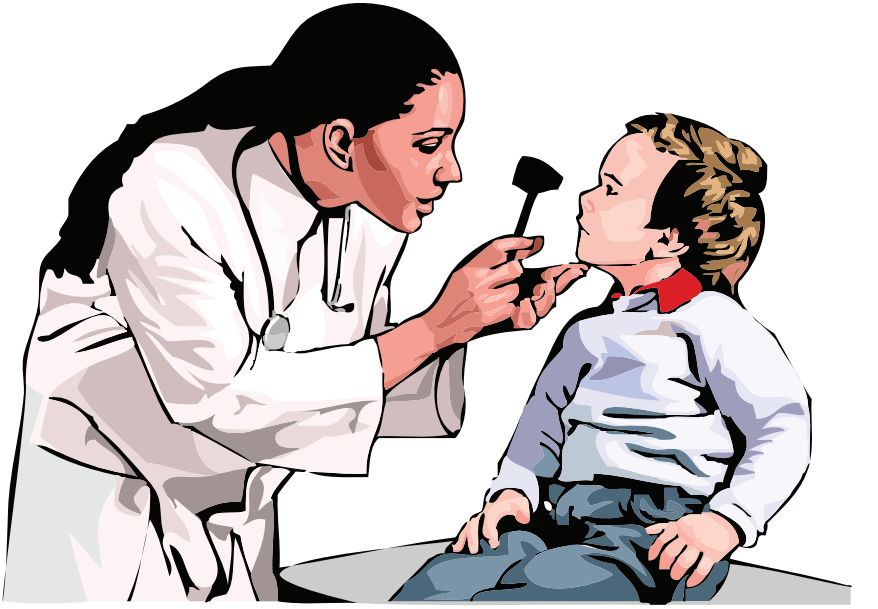
Genes are passed from parents to children and cause things to run in families. There are many genes that are involved in hearing. Sometimes, a gene does not form in the way it should. When this happens, it is called a mutation. Some mutations cause syndromic hearing loss and others cause nonsyndromic hearing loss. Even among some families with genetic hearing loss, a loss is not due to mutations in any of the known genes. Scientists are working to find all of the genes involved in hearing loss. Genes are described in more detail in the next section.

There are also a number of things that are not genetic that can cause hearing loss. For example, babies who are born too early and babies who need help breathing (for example, using a ventilator) are more likely to develop hearing loss than are other babies. Some infections (such as cytomegalovirus) the mother has during her pregnancy can cause the baby to have hearing loss. Also, some infections (such as meningitis) that babies and children have can cause hearing loss.

Sometimes, both genes and environment work together to cause hearing loss. For example, there are some medicines that can cause hearing loss, but only among people who have certain mutations in their genes.

How Do Doctors Figure Out What Caused a Person's Hearing Loss?

Doctors begin by looking at a person's physical features, medical history, and family history. Based on this, they classify the hearing loss in the ways described earlier (congenital or acquired, prelingual or postlingual, progressive or nonprogressive, conductive or sensorineural, syndromic or nonsyndromic, and familial or sporadic). The classifications often point to certain causes. The doctors might ask for more medical tests to look for signs of syndromic hearing loss, and they might ask for genetic tests.



About Genes & Mutations

What Are Genes?

Genes tell the cells of people's bodies how to grow and work. For example, the instructions in certain genes control what color a person's eyes will be. Each person gets half of his or her genes from each parent, and that is why a person tends to look like his or her parents.

Genes are stored in a chemical called deoxyribonucleic acid (DNA). DNA is a chemical chain made up of "bases". There are four bases: A, C, T and G. The specific order, or sequence, of these bases determines the exact information carried in each gene, like the way that a specific pattern of letters makes up the words in a sentence.

The DNA is packaged into small units called chromosomes. Each cell in a person's body contains a set of chromosomes, and thus a set of genetic instructions. Every person should have 23 pairs of chromosomes. One chromosome from each pair is from the person's mother and one chromosome of each pair is from the father.

The first 22 pairs of chromosomes are a matching pair in everybody. The 23rd pair is called the sex chromosomes, and they help determine if a person is male or female. A female has two X chromosomes, and a male has one X and one Y chromosome. A mother will give one of her two X chromosomes to each of her children. A father will give either his X or his Y chromosome. A child who gets the father's Y chromosome will be a boy. A child who gets the father's X chromosome will be a girl.

Figure 2

The Relationship Between Cells, Chromosomes, DNA, Bases, and Genes

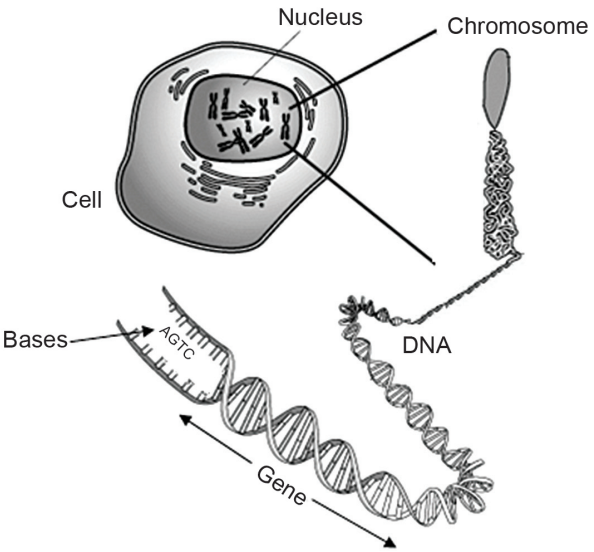


Figure 3

An Example of How Chromosomes Are Passed From Parents To Children

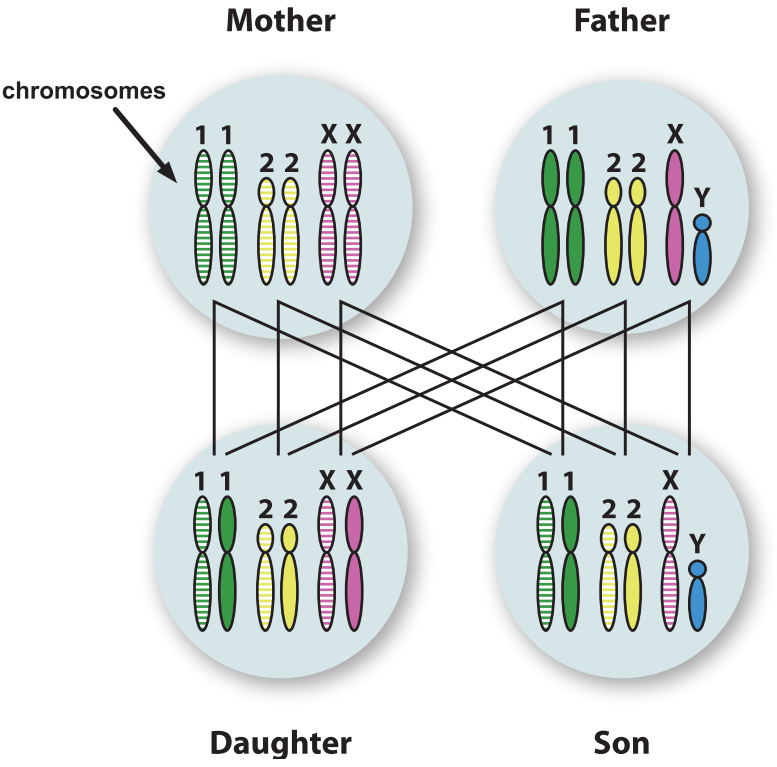


Figure 3 shows how children get their chromosomes and, therefore, their genes from their parents. In this figure, three pairs of chromosomes are shown: pair #1 (green), pair #2 (yellow), and the sex chromosomes (pink and blue). The father's chromosomes are shown in solid color, and the mother's are striped. Children randomly get one of each pair of chromosomes from their mother (striped) and one of each pair from their father (solid). Each daughter gets an X from her mother (striped) and an X from her father (solid). Each son gets an X from his mother (striped) and a Y from his father (solid).

What are Mutations?

A mutation is any change in a gene that makes it different from what it should be; that is, a usual copy (the copy that most people have). If the change causes a difference in the way that the gene works, the person with the mutation might have a particular condition (such as hearing loss) that can run in the family. Different changes run in families in different ways. These different changes, or mutations, are described on the next few pages.

A mutation is any change in the usual DNA sequence. For example, suppose part of a gene usually has the sequence GTAC. A mutation can change the sequence to GTTC in some people. This change in sequence can change the way that the gene works so that people with this mutation can have a particular condition. Not all mutations affect the person who has them.

Genetic conditions often are described in terms of the chromosome that contains the gene. If the gene is on one of the first 22 pairs of chromosomes, called autosomes, the genetic condition is called an "autosomal" condition. If the gene is on the X chromosome, the condition is called "X-linked", or "sex-linked".

Genetic conditions also are grouped by how they run in families. Different mutations cause conditions to run in families in different patterns. Mutations are called "dominant" or "recessive" depending on how they cause conditions and how they run in families.

Autosomal Dominant Conditions

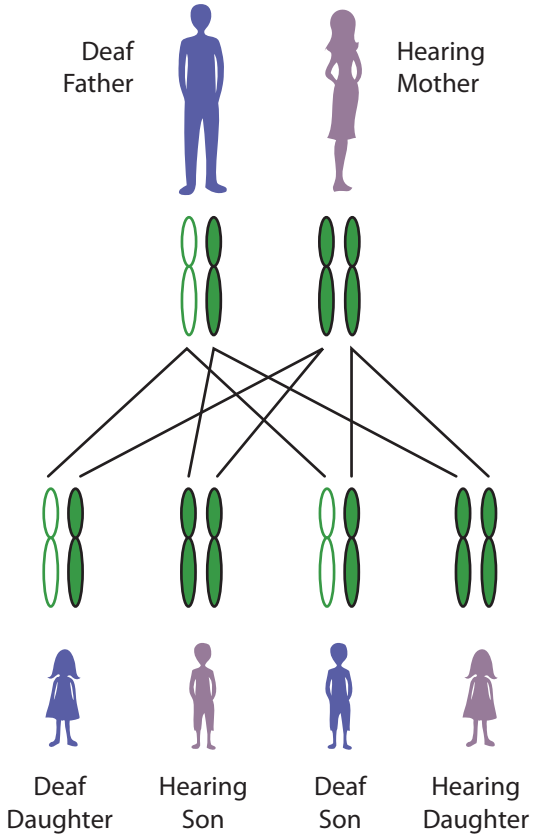
“Autosomal” conditions affect both males and females equally. In “dominant” conditions, the condition is passed from parent to child. If one parent has the condition, each child has a 50% (1 in 2) chance of having it as well.

“Autosomal” genes are genes that are found on one of the first 22 pairs of chromosomes, the pairs that are the same for both males and females. In the case of “dominant” conditions, a child will have the condition if he or she has one copy of the gene with the dominant mutation. It takes only one copy of a dominant mutation to cause the condition.

Figure 4 shows how children get dominant conditions from their parents. In this example shown, the usual copy is symbolized by and the copy with the dominant mutation is symbolized by . When one parent has the dominant condition, he or she has a usual copy ( ) and a copy with the dominant mutation ( ). He or she will give each child one or the other. Therefore each child has a 50% (1 in 2) chance of getting the gene with the dominant mutation and of having the condition. If the other parent has two usual copies, and therefore does not have the condition, he or she will give each child one of the two usual copies ( ). Even though a child gets one of the usual copies from the parent who does not have the condition, if he or she gets a dominant copy from the parent with the condition, the child also will have the condition.

Figure 4

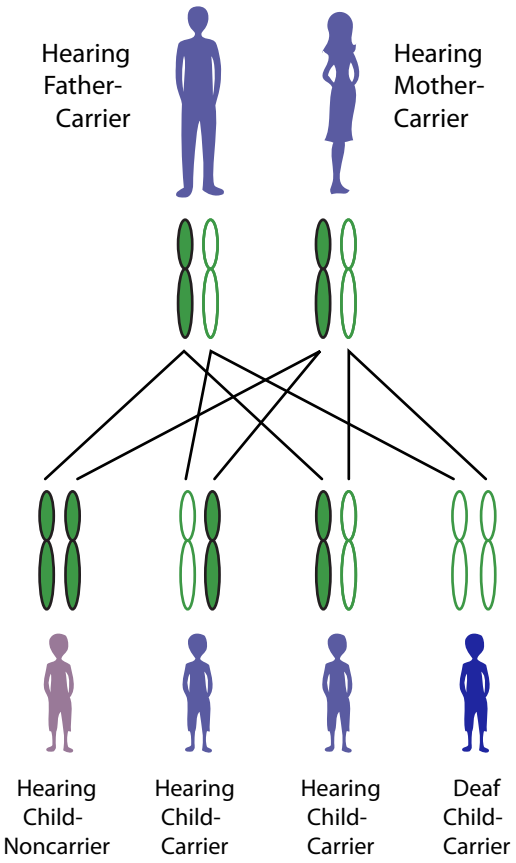
An Example of Autosomal Dominant Inheritance



In this figure, is a usual copy and is a copy with a dominant mutation.

Figure 5

An Example of Autosomal Recessive Inheritance



In this figure, is a usual copy and is a copy with a recessive mutation

Autosomal Recessive Conditions

“Autosomal” conditions affect males and females equally. “Recessive” conditions also are due to changes in genes, but they run in families in a different way than dominant conditions. This is because people who have one copy of a recessive mutation do not have the condition. They are called “carriers”. If two carriers have a child together, there is a 25% (1 in 4) chance that the child will get two copies of the mutation and, therefore, have the condition.

“Autosomal” genes are genes that are found on one of the first 22 pairs of chromosomes, the pairs that are the same for both males and females. In the case of “recessive” conditions, a child will have the condition only if he or she does not have a usual copy of the gene.

Figure 5 shows how recessive conditions run in families. In this example, each parent is a carrier and has one usual copy (symbolized by) and one copy with a recessive mutation (symbolized by). Each parent will give the child either the usual copy ( ) or the copy with the recessive mutation ( ). Each has a 50% (1 in 2) chance of happening. If the child gets one usual copy ( ) from one parent and one copy with the recessive mutation ( ) from the other parent, the child will be a carrier like both parents. If the child gets the copy with the recessive mutation ( ) from both parents, and therefore doesn’t have a usual copy, the child will have the condition. When both parents are carriers, there is a 25% (1 in 4) chance that each child will get a copy with a recessive mutation from both parents and, therefore, have the condition.

X-Linked Recessive Conditions

X-linked conditions usually affect only males. In such instances, a mutation is passed in the family through female carriers who do not have the condition. However, each son of a female carrier has a 50% chance of inheriting the mutation and, therefore, of having the condition.

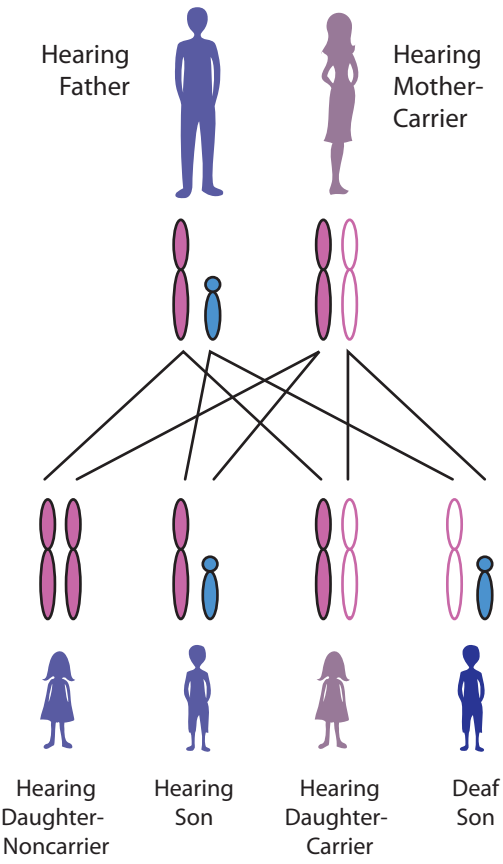
"X-linked" genes are genes that are found on the X chromosome. "Recessive" means that a person has the condition only if he or she does not have at least one usual copy of the gene.

A female has two X chromosomes and, therefore, two copies of each X-linked gene. A woman who has one usual copy and one copy with a recessive mutation is called a carrier. A carrier does not have the condition, but can pass the copy with the recessive mutation on to her children.

A male has only one copy of the X chromosome, which he has gotten from his mother. His other chromosome is a Y chromosome that he has gotten from his father. Therefore, a male has only one copy of each X-linked gene. If the male gets his mother's X chromosome that has the recessive mutation, he will have the condition. If he gets his mother's X chromosome that has the usual copy of the gene, he will not have the condition. Therefore, a son of a carrier mother has a 50% chance of having the condition. Because a male has only one X chromosome and, therefore, must pass that X chromosome to each of his daughters, each daughter will be a carrier. Because a male has only one Y chromosome, he will pass that Y chromosome (and not the X chromosome) to each of his sons, so none of his sons will have the condition or be carriers.

Figure 6

An Example of X-linked Recessive Inheritance



In this figure, is an X chromosome with a usual copy of the gene, and is an X chromosome with a copy with a recessive mutation. is a Y chromosome.

What are GJB2 and Connexin 26?

The *GJB2* gene contains the instructions for a protein called Connexin 26; this protein plays an important role in the functioning of a part of the ear called the cochlea. The cochlea is a very complex and specialized part of the body that needs many instructions to guide its development and functioning. These instructions come from genes such as the *GJB2*, *GJB3*, and *GJB6*. Changes in any one of these genes can result in hearing loss.

Among some populations, about 40% of newborns with a genetic hearing loss who do not have a syndrome have a mutation in the *GJB2* gene. There are many different mutations in this gene that can cause hearing loss. Most of these mutations are recessive, meaning that a person can have one usual copy of the gene and one copy of the mutation and will have full hearing function. (Everyone has two copies of the *GJB2* gene, one from each parent). However, a person who has two copies of a gene with a mutation, one mutation inherited from each parent, will have hearing loss. This means that if both parents have a copy of the gene with a mutation, they can have a child with hearing loss, even though both parents can hear. In fact, most babies with hearing loss are born to parents who can hear.

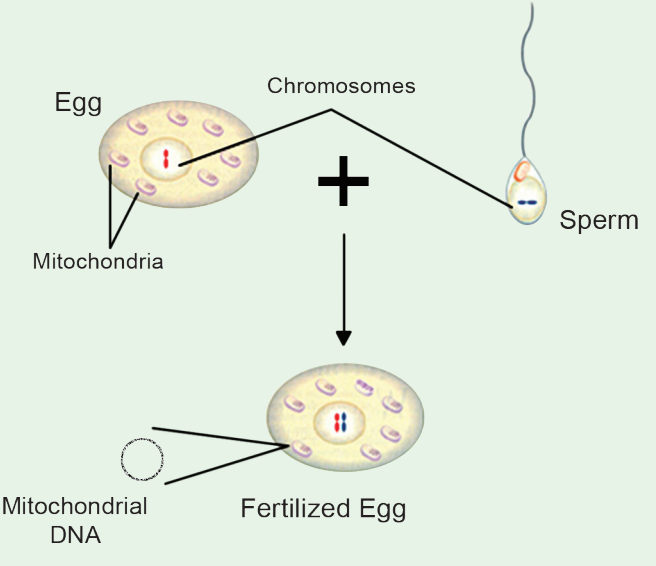
Multifactorial Conditions

Sometimes conditions such as hearing loss are caused by a combination of genetic mutations and non-genetic factors. These conditions are said to be “multifactorial”. If their first child has a multifactorial condition, the parents’ chance of having a second child with the condition depends on the specific condition, and is usually about 3% to 5%.

People who have multifactorial conditions often are born into families with no other affected members. Parents of a child with any such condition have a greater chance of having another child with the same condition than parents who do not have a child with the condition.

Figure 7

The Relationship Between Chromosomes, Mitochondria, and Mitochondrial DNA



Mitochondrial Conditions

"Mitochondrial" conditions are different from most other genetic conditions because only the mother can pass them to her children. If a woman has a mitochondrial condition, the chance that she will pass it on to her children depends on the particular condition and on how severely she is affected. Fathers with a mitocondrial condition do not pass it on to their children.

Not all of a person's genes can be found on their chromosomes. A few genes are found on small, circular pieces of DNA in the mitochondria, tiny parts of cells that make energy. These genes are called "mitochondrial" genes. Each cell has many mitochondria and, therefore, many copies of each mitochondrial gene. The chance that a person will have a mitochodrial condition depends on the number of his or her mitochondria that carry a mutation. Mitochondrial genes are passed on to children differently from the way that genes on chromosomes are passed on because each person gets his or her mitochondrial genes only from his or her mother. Therefore, if a woman carries a variation in one of her mitochondrial genes, each child has a chance of having the condition or of being an unaffected carrier. The exact chance depends on the number of copies with mutations that the mother is carrying. A male with a mitochondrial condition will not pass the condition to his children, because males do not pass their mitochondrial genes to their children.

Figure 8 shows how a fertilized egg (which will grow into a baby) gets chromosomes from the mother's egg and the father's sperm (shown as red and blue chromosomes), but gets mitochondrial DNA only from the mother's egg.

About Genetic Testing

What Is Genetic Testing?

A genetic test involves looking at a person's DNA to see if certain mutations are present. A person's DNA sample usually is gotten from one of two different sources: (1) a small sample of a person's blood, or (2) cheek cells from a person's mouth. To get the cheek cells, a small, toothbrush-like swab is rubbed inside a person's mouth. The cheek swab is easy and painless, but the DNA obtained from this method is sometimes unstable and might not be usable.

Once a person's DNA sample is obtained, there are two different ways to look for mutations. The first way looks only for certain mutations. This "mutation-specific testing" will detect that one type of mutation if it is present, but it will not detect other mutations that also might be present. This type of testing is used when most of the people who have a genetic condition have the same mutation.

The other type of genetic testing is called "sequencing". In this method, the DNA sequence is determined for the entire gene or for a certain part of it. This method will detect any mutation that is present in the part of the gene looked at. This type of testing is harder and costs more. It usually is used when any one of several mutations in a gene could cause a condition.

What Are the Benefits of Genetic Testing?

If a mutation is found, it might explain why the person has a condition such as hearing loss. In some cases, knowing what mutation a person has will allow doctors to predict how severe the condition might become and what other symptoms can be expected. Then, the person can get any other medical care that might be needed. Also, knowing the cause of a person's condition will let him or her know what the chances are of passing the condition on to his or her children. It also lets other family members know the chances that they might have a child with the same condition.

What Are the Limits of Genetic Testing?

- ❏ Not all of the genes that cause conditions are known. So, even if a condition runs in a family, it might not be possible to find the mutation that causes it.
- ❏ Some tests are hard to do. For example, the bigger a gene is, the harder it is to study the whole gene.
- ❏ Sometimes, it is not possible to tell if a mutation is the cause of a condition, or just a coincidence.

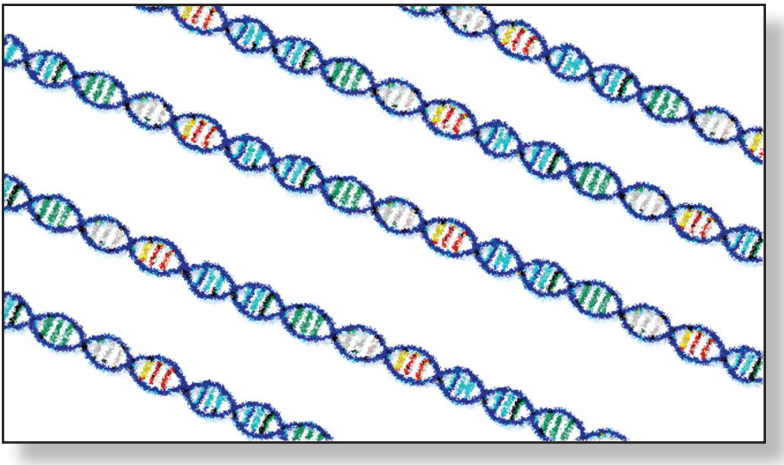
Some mutations cause conditions among most people, but not among all people who carry them. For each such mutation, a positive result (that is, a result showing that a person has one or more copies of a mutation) might not mean that the person will get the associated condition. Likewise, a negative result (that is, a result showing that a person does not carry a copy with that mutation) does not guarantee that the person will not get the associated condition. This is because the person might have a different mutation that was not detectable by the test used, or the person might have a mutation in a different gene that also causes the same condition.

What Are the Risks of Genetic Testing?

Some people have strong feelings when they get the results of a genetic test. Some people feel angry, sad, or guilty if they find out that they or their child has a mutation. It is important to remember that everyone carries mutations of some kind, and that a person's genes are no one's "fault."

Genetic tests are different from other medical tests in that the results provide information about other members of the family, and not just the person being tested. Some family members do not want to know that a mutation runs in their family. Also, because children get their genes from their parents, genetic tests that involve several family members can reveal personal information, such as a child having been adopted or having a different biological father.

Sometimes, people are concerned about keeping the results of their genetic tests private. For example, they do not want their friends, relatives, or coworkers to find out. Companies that offer genetic testing are very careful to make sure that test results are kept private. Test results cannot be seen by anyone who is not involved in the testing, unless the person tested or his or her parents or guardians give permission.



Where Can I Find More Information?

For more information about genes related to hearing loss and about genetic testing, contact a genetic counselor in your area.

For more information about hearing and hearing loss, see the National Institute on Deafness and Other Communication Disorders at http://www.nidcd.nih.gov/health/hearing/

The U.S. Department of Health and Human Services has a guide that explains about genes and genetic testing at http://www.accessexcellence.org/AE/AEPC/NIH/index.html

The Genetic Science Learning Center has some information about basic genetics, genetic conditions and genetic counseling at http://learn.genetics.utah.edu/

Cold Spring Harbor Labs has a tutorial about genetics that is a little more in-depth than those at some of the other sites. It can be found at http://www.dnaftb.org/dnaftb/

This GeneTest site has a clinic directory to help find a genetics center in your area. This site can be found at http://www.ncbi.nlm.nih.gov/sites/GeneTests/?db=GeneTests

The Hereditary Hearing loss Homepage gives an up-to-date overview of the genetics of hereditary hearing loss for researchers and clinicians working in the field. This site can be found at: http://hereditaryhearingloss.org/

For more information on Early Hearing Detection and Intervention, see http://www.cdc.gov/ncbddd/hearingloss/index.html

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