Genetics Home Reference

Your Guide to Understanding Genetic Conditions

Handbook

Help Me Understand Genetics

Inheriting Genetic Conditions

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Chapter 3

Inheriting Genetic Conditions

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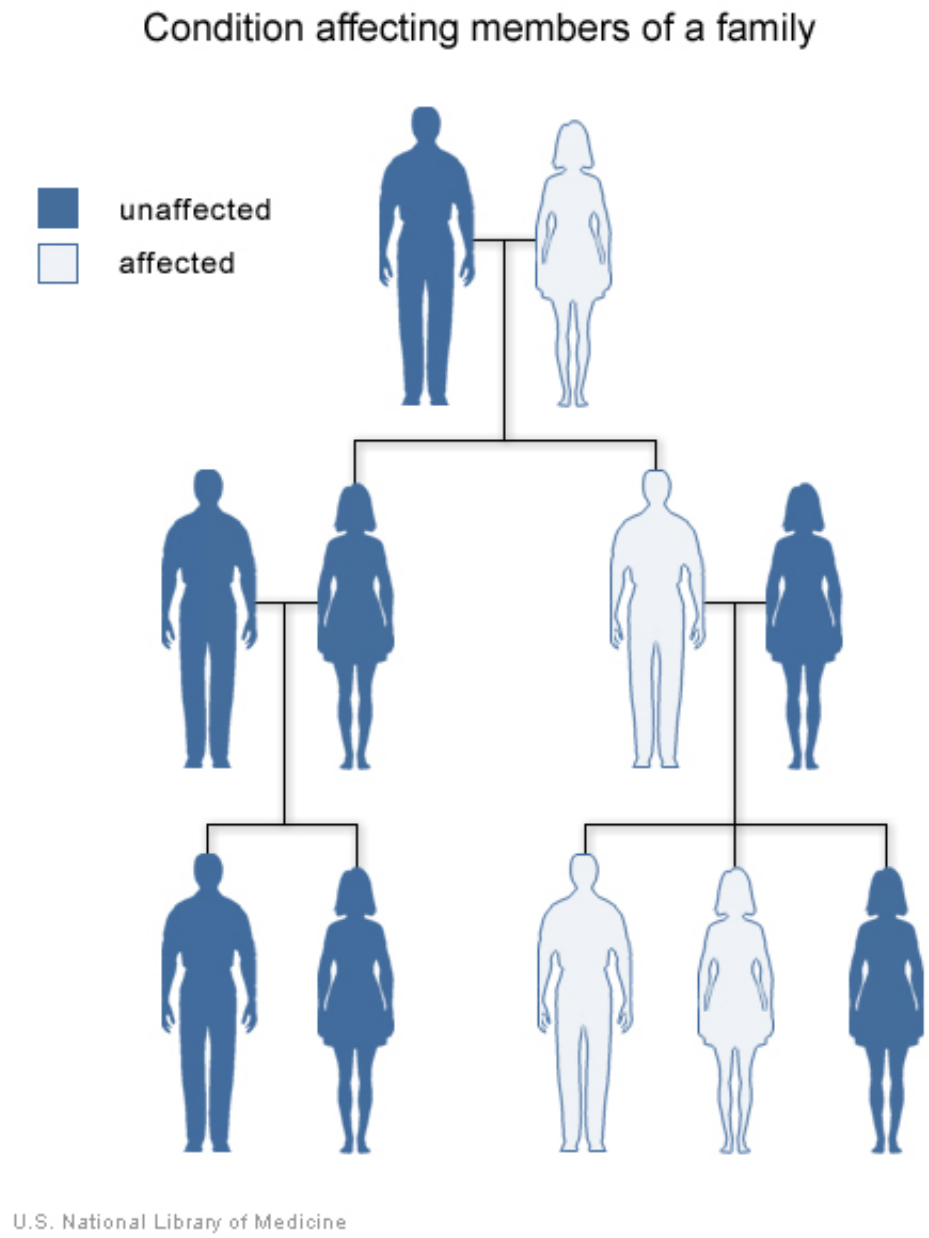
What does it mean if a disorder seems to run in my family?

A particular disorder might be described as “running in a family” if more than one person in the family has the condition. Some disorders that affect multiple family members are caused by gene mutations, which can be inherited (passed down from parent to child). Other conditions that appear to run in families are not inherited. Instead, environmental factors such as dietary habits or a combination of genetic and environmental factors are responsible for these disorders.

It is not always easy to determine whether a condition in a family is inherited. A genetics professional can use a person's family history (a record of health information about a person's immediate and extended family) to help determine whether a disorder has a genetic component.



Some disorders are seen in more than one generation of a family.

For general information about disorders that run in families:

Genetics Home Reference provides consumer-friendly summaries of genetic conditions (http://ghr.nlm.nih.gov/ghr/conditionsByName). Each summary includes a brief description of the condition, an explanation of its genetic cause, and information about the condition's frequency and pattern of inheritance.

The National Human Genome Research Institute fact sheet Frequently Asked Questions About Genetics (http://www.genome.gov/10001191) offers a general description of genetic disorders. Please refer to the first two questions, “What are genetic disorders?” and “How do I find more information about a specific disorder or learn whether a particular disease has a genetic component?”

The Department of Energy offers a fact sheet called Genetic Disease Information—Pronto! (http://www.ornl.gov/TechResources/Human_Genome/medicine/assist.html)

What are the different ways in which a genetic condition can be inherited?

Some genetic conditions are caused by mutations in a single gene. These conditions are usually inherited in one of several straightforward patterns, depending on the gene involved:

Inheritance pattern	Description	Examples
Autosomal dominant	Only one mutated copy of the gene is needed for a person to be affected by an autosomal dominant disorder. Each affected person usually has one affected parent (illustration on page 8).	Huntington disease, neurofibromatosis 1
Autosomal recessive	Two copies of the gene must be mutated for a person to be affected by an autosomal recessive disorder. An affected person usually has unaffected parents who each carry a single copy of the mutated gene (and are referred to as carriers) (illustration on page 9).	cystic fibrosis, sickle cell anemia
X-linked dominant	X-linked dominant disorders are caused by mutations in genes on the X chromosome. Only a few disorders have this inheritance pattern. Females are more frequently affected than males, and the chance of passing on an X-linked dominant disorder differs between men (illustration on page 10) and women (illustration on page 11).	X-linked hypophosphatemia
X-linked recessive	X-linked recessive disorders are also caused by mutations in genes on the X chromosome. Males are more frequently affected than females, and the chance of passing on the disorder differs between men (illustration on page 12) and women (illustration on page 13).	hemophilia A, Duchenne muscular dystrophy

Inheritance pattern	Description	Examples
Mitochondrial	This type of inheritance, also known as maternal inheritance, applies to genes in mitochondrial DNA. (Mitochondria, which are structures in each cell that convert molecules into energy, each contain a small amount of DNA.) Because only egg cells contribute mitochondria to the developing embryo, only females can pass on mitochondrial conditions to their children (illustration on page 14).	Leber's hereditary optic neuropathy (LHON)

Many other disorders are caused by a combination of the effects of multiple genes or by interactions between genes and the environment. Such disorders are more difficult to analyze because their genetic causes are often unclear, and they do not follow the patterns of inheritance described above. Examples of conditions caused by multiple genes or gene/environment interactions include heart disease, diabetes, schizophrenia, and certain types of cancer. For more information, please see "What are complex or multifactorial disorders?" in the "Mutations and Genetic Disorders" chapter.

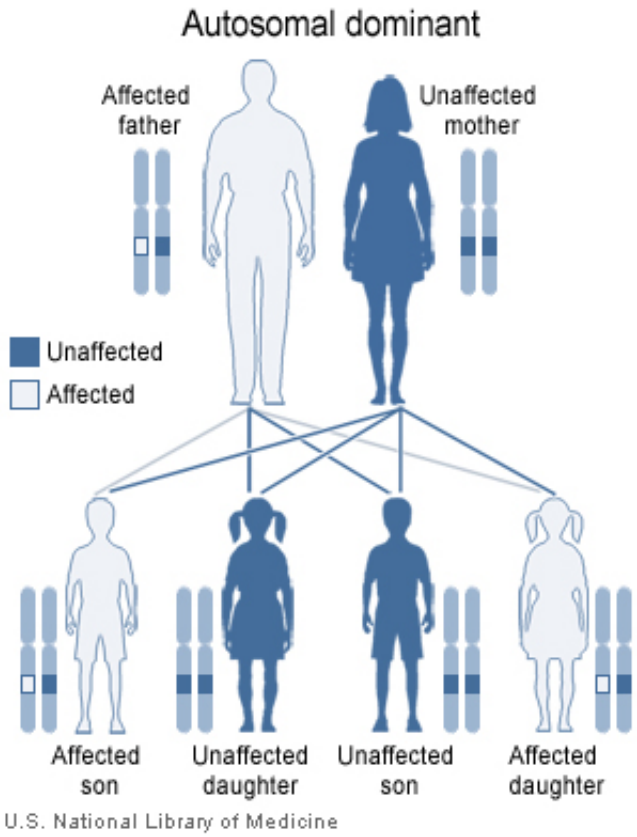
Disorders caused by changes in the number or structure of chromosomes do not follow the straightforward patterns of inheritance listed above. To read about how chromosomal conditions occur, please see "Are chromosomal disorders inherited?" on page 19.

Other genetic factors can also influence how a disorder is inherited: "What are genomic imprinting and uniparental disomy?" on page 17

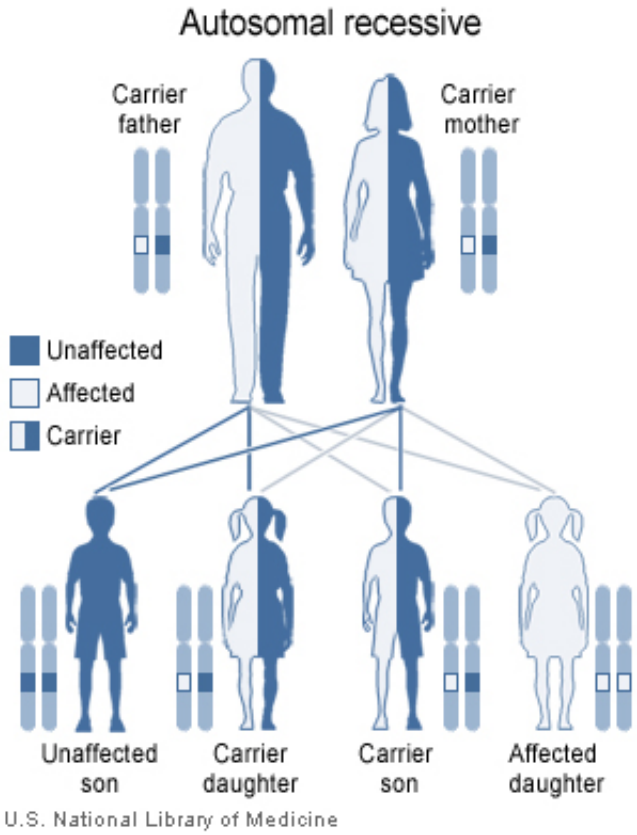
For more information about inheritance patterns:

The Genetics and Public Policy Center provides an introduction to hereditary mutations (http://www.dnapolicy.org/genetics/geneticsAndDisease.jhtml#hered), including their patterns of inheritance.

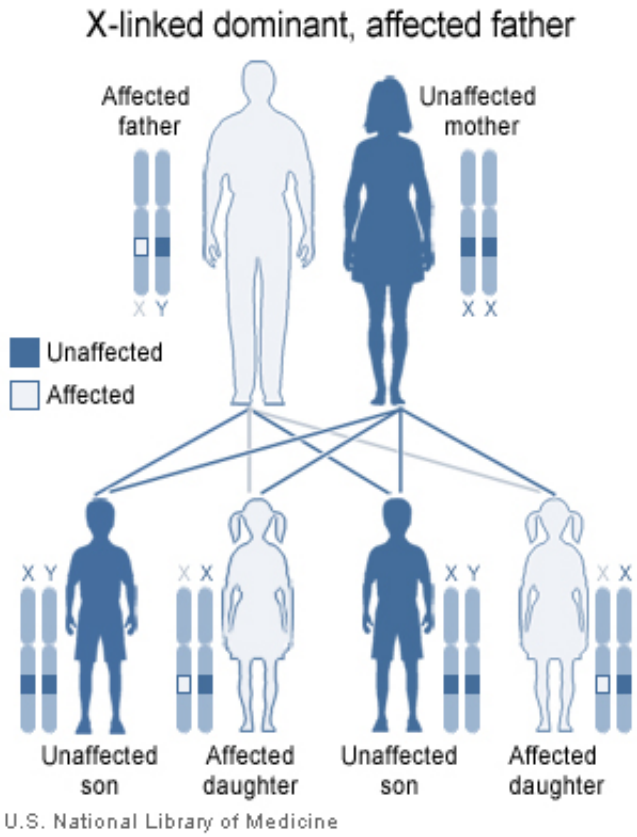
Illustrations: Inheritance patterns



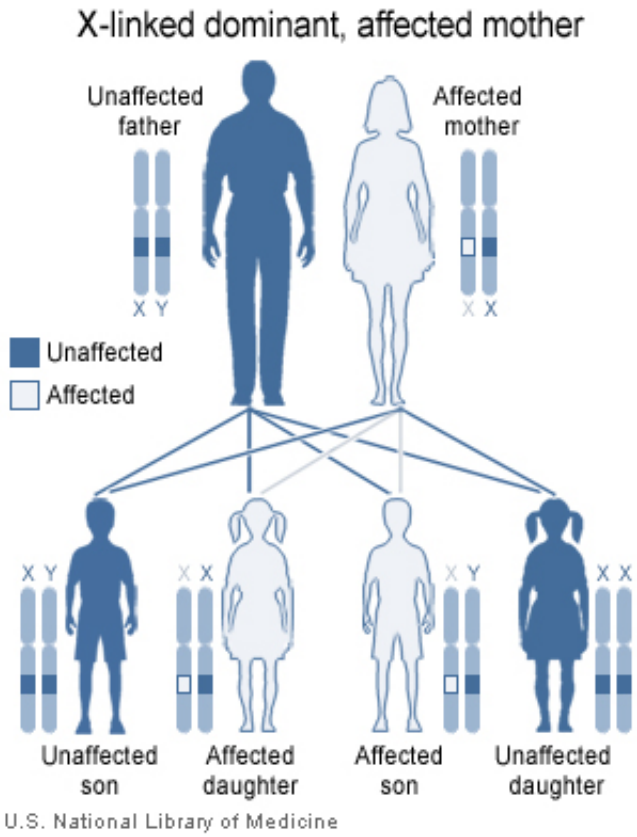
In this example, a man with an autosomal dominant disorder has two affected children and two unaffected children.



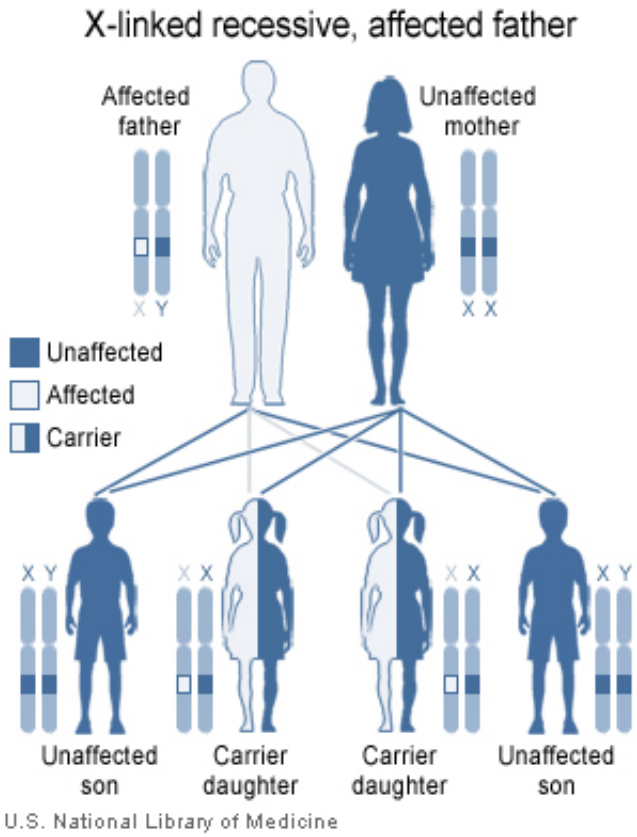
In this example, two unaffected parents each carry one copy of a gene mutation for an autosomal recessive disorder. They have one affected child and three unaffected children, two of which carry one copy of the gene mutation.



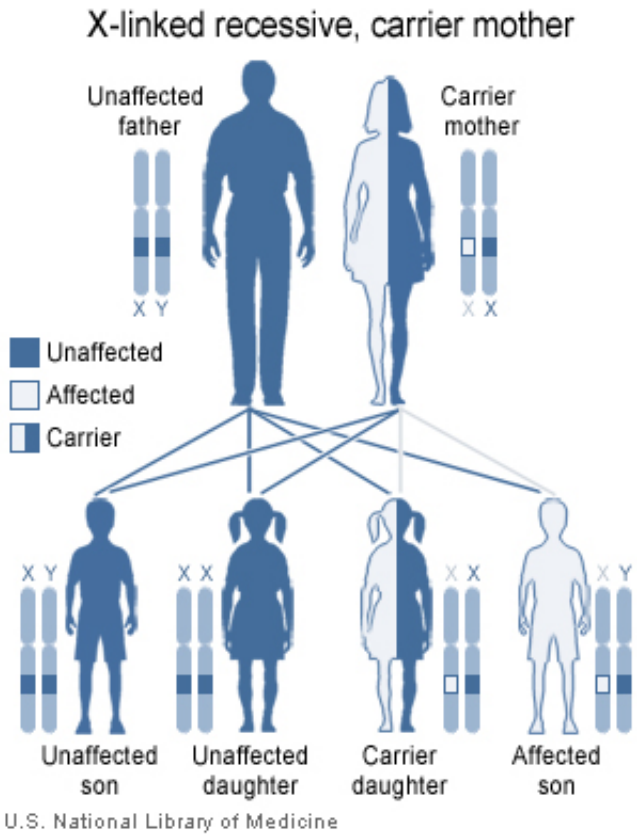
In this example, a man with an X-linked dominant condition has two affected daughters and two unaffected sons.



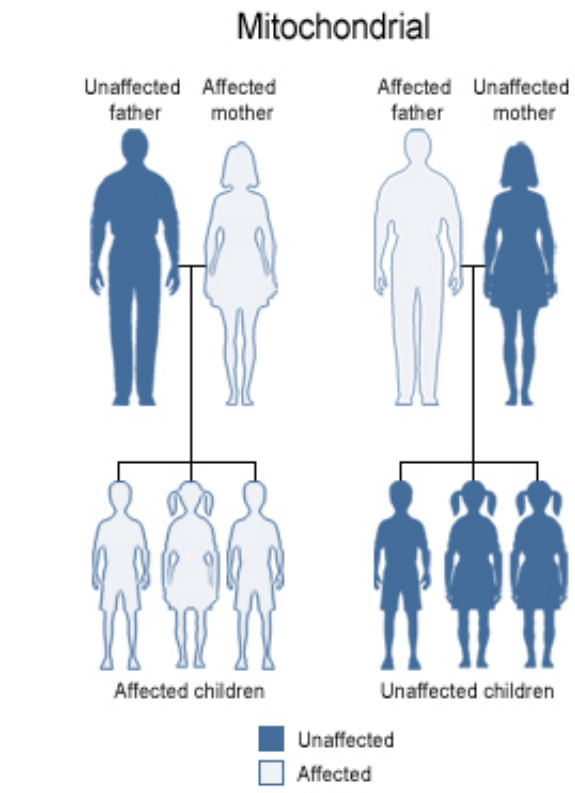
In this example, a woman with an X-linked dominant condition has an affected daughter, an affected son, an unaffected daughter, and an unaffected son.



In this example, a man with an X-linked recessive condition has two unaffected daughters who each carry one copy of the gene mutation, and two unaffected sons who do not have the mutation.



In this example, an unaffected woman carries one copy of a gene mutation for an X-linked recessive disorder. She has an affected son, an unaffected daughter who carries one copy of the mutation, and two unaffected children who do not have the mutation.



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In one family, a woman with a mitochondrial disorder and her unaffected husband have only affected children. In another family, a man with a mitochondrial condition and his unaffected wife have no affected children.

If a genetic disorder runs in my family, what are the chances that my children will have the condition?

When a genetic disorder is diagnosed in a family, family members often want to know the likelihood that they or their children will develop the condition. This can be difficult to predict in some cases because many factors influence a person's chances. One important factor is how the condition is inherited. For example:

- A person affected by an autosomal dominant disorder has a 50-percent chance of passing the mutated gene to each child. There is also a 50-percent chance that a child will not inherit the mutated gene (illustration on page 8).
- For an autosomal recessive disorder, two unaffected people who each carry one copy of the mutated gene (carriers) have a 25-percent chance with each pregnancy of having a child affected by the disorder. There is a 75-percent chance with each pregnancy that a child will be unaffected (illustration on page 9).
- The chance of passing on an X-linked dominant condition differs between men and women because men have one X and one Y chromosome, while women have two X chromosomes. A man passes on his Y chromosome to all of his sons and his X chromosome to all of his daughters. Therefore, the sons of a man with an X-linked dominant disorder will not be affected, and his daughters will all inherit the condition (illustration on page 10). A woman passes on one or the other of her X chromosomes to each child. Therefore, a woman with an X-linked dominant disorder has a 50-percent chance of having an affected daughter or son with each pregnancy (illustration on page 11).
- Because of the difference in sex chromosomes, the probability of passing on an X-linked recessive disorder also differs between men and women. The sons of a man with an X-linked recessive disorder will not be affected, and his daughters will carry one copy of the mutated gene (illustration on page 12). With each pregnancy, a woman who carries an X-linked recessive disorder has a 50-percent chance of having sons who are affected and a 50-percent chance of having daughters who carry one copy of the mutated gene (illustration on page 13).

It is important to note that the chance of passing on a genetic condition applies equally to each pregnancy. For example, if a couple has a child with an autosomal recessive disorder, the chance of having another child with the disorder is still 25 percent (or

1 in 4). Having one child with a disorder does not "protect" future children from inheriting the condition. Conversely, having a child without the condition does not mean that future children will definitely be affected.

Although the chances of inheriting a genetic condition appear straightforward, in some cases factors such as a person's family history and the results of genetic testing can modify those chances. In addition, some people with a disease-causing mutation never develop any health problems or may experience only mild symptoms of the disorder. If a disease that runs in a family does not have a clear-cut inheritance pattern, predicting the likelihood that a person will develop the condition can be particularly difficult.

Because estimating the chance of developing or passing on a genetic disorder can be complex, genetics professionals can help people understand these chances and make informed decisions about their health.

For more information about passing on a genetic disorder in a family:

The National Library of Medicine MedlinePlus web site offers information about the chance of developing a genetic disorder on the basis of its inheritance pattern. Scroll down to the section "Statistical Chances of Inheriting a Trait" for each of the following inheritance patterns:

Autosomal dominant (http://www.nlm.nih.gov/medlineplus/ency/article/002049.htm)

Autosomal recessive (http://www.nlm.nih.gov/medlineplus/ency/article/002052.htm)

X-linked dominant (http://www.nlm.nih.gov/medlineplus/ency/article/002050.htm)

X-linked recessive (http://www.nlm.nih.gov/medlineplus/ency/article/002051.htm)

What are genomic imprinting and uniparental disomy?

Genomic imprinting and uniparental disomy are factors that influence how some genetic conditions are inherited.

Genomic imprinting

People inherit two copies of their genes—one from their mother and one from their father. Usually both copies of each gene are active, or "turned on," in cells. In some cases, however, only one of the two copies is normally turned on. Which copy is active depends on the parent of origin: some genes are normally active only when they are inherited from a person's father; others are active only when inherited from a person's mother. This phenomenon is known as genomic imprinting.

In genes that undergo genomic imprinting, the parent of origin is often marked, or "stamped," on the gene during the formation of egg and sperm cells. This stamping process, called methylation, is a chemical reaction that attaches small molecules called methyl groups to certain segments of DNA. These molecules identify which copy of a gene was inherited from the mother and which was inherited from the father. The addition and removal of methyl groups can be used to control the activity of genes.

Only a small percentage of all human genes undergo genomic imprinting. Researchers are not yet certain why some genes are imprinted and others are not. They do know that imprinted genes tend to cluster together in the same regions of chromosomes. Two major clusters of imprinted genes have been identified in humans, one on the short (p) arm of chromosome 11 (at position 11p15) and another on the long (q) arm of chromosome 15 (in the region 15q11 to 15q13).

Uniparental disomy

Uniparental disomy (UPD) occurs when a person receives two copies of a chromosome, or part of a chromosome, from one parent and no copies from the other parent. UPD can occur as a random event during the formation of egg or sperm cells or may happen in early fetal development.

In many cases, UPD likely has no effect on health or development. Because most genes are not imprinted, it doesn't matter if a person inherits both copies from one parent instead of one copy from each parent. In some cases, however, it does make a difference whether a gene is inherited from a person's mother or father. A person with UPD may lack any active copies of essential genes that undergo genomic imprinting. This loss of gene function can lead to delayed development, mental retardation, or other medical problems.

Several genetic disorders can result from UPD or a disruption of normal genomic imprinting. The most well-known conditions include Prader-Willi syndrome, which is characterized by uncontrolled eating and obesity, and Angelman syndrome, which causes mental retardation and impaired speech. Both of these disorders can be caused by UPD or other errors in imprinting involving genes on the long arm of chromosome 15. Other conditions, such as Beckwith-Wiedemann syndrome (a disorder characterized by accelerated growth and an increased risk of cancerous tumors), are associated with abnormalities of imprinted genes on the short arm of chromosome 11.

For more information about genomic imprinting and UPD:

The University of British Columbia's web site about chromosomal mosaicism provides an explanation of UPD and genomic imprinting (http://www.medgen.ubc.ca/wrobinson/mosaic/upd.htm), including diagrams illustrating how UPD can occur.

A fact sheet (http://gucchd.georgetown.edu/hugem/fs16.htm)from Georgetown University's Human Genome Education Model Project II offers a brief discussion of UPD, genomic imprinting, and other forms of nontraditional inheritance.

Genetics Home Reference provides clear, user-friendly information about Prader-Willi syndrome (http://ghr.nlm.nih.gov/condition=praderwillisyndrome) and Angelman syndrome (http://ghr.nlm.nih.gov/condition=angelmansyndrome).

Are chromosomal disorders inherited?

Although it is possible to inherit some types of chromosomal abnormalities, most chromosomal disorders are not passed from one generation to the next.

Some chromosomal conditions are caused by changes in the number of chromosomes. These changes are not inherited, but occur as random events during the formation of reproductive cells (eggs and sperm). An error in cell division called nondisjunction results in reproductive cells with an abnormal number of chromosomes. For example, a reproductive cell may accidentally gain or lose one copy of a chromosome. If one of these atypical reproductive cells contributes to the genetic makeup of a child, the child will have an extra or missing chromosome in each of the body's cells.

Changes in chromosome structure can also cause chromosomal disorders. Some changes in chromosome structure can be inherited, while others occur as random accidents during the formation of reproductive cells or in early fetal development. Because the inheritance of these changes can be complex, people concerned about this type of chromosomal abnormality may want to talk with a genetics professional.

Some cancer cells also have changes in the number or structure of their chromosomes. Because these changes occur in somatic cells (cells other than eggs and sperm), they cannot be passed from one generation to the next.

For more information about how chromosomal changes occur:

As part of its fact sheet on chromosome abnormalities, the National Human Genome Research Institute provides a discussion of how chromosome abnormalities happen (http://www.genome.gov/11508982#6).

The University of British Columbia's web site about chromosomal mosaicism explains chromosomal changes, including a detailed description of how trisomy (the presence of an extra chromosome in each cell) happens.

> Changes to the Chromosomes (http://www.medgen.ubc.ca/wrobinson/mosaic/changes.htm)
>
> How Does Trisomy Arise? (http://www.medgen.ubc.ca/wrobinson/mosaic/tri_how.htm)

The Chromosome Deletion Outreach fact sheet Introduction to Chromosome Abnormalities (http://www.chromodisorder.org/intro.htm) explains how structural changes occur.

Why are some genetic conditions more common in particular ethnic groups?

Some genetic disorders are more likely to occur among people who trace their ancestry to a particular geographic area. People in an ethnic group often share certain versions of their genes, which have been passed down from common ancestors. If one of these shared genes contains a disease-causing mutation, a particular genetic disorder may be more frequently seen in the group.

Examples of genetic conditions that are more common in particular ethnic groups are sickle cell anemia, which is more common in people of African, African-American, or Mediterranean heritage; and Tay-Sachs disease, which is more likely to occur among people of Ashkenazi (eastern and central European) Jewish or French Canadian ancestry. It is important to note, however, that these disorders can occur in any ethnic group.

For more information about genetic disorders that are more common in certain groups:

The National Institute of General Medical Sciences (NIGMS) fact sheet Genes & Populations (http://www.nigms.nih.gov/news/science_ed/genepop/faq.html) offers additional discussion on this topic. Scroll down to the question “Why do researchers sometimes study ethnic and racial groups?”

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