Genetics Home Reference

Help Me Understand Genetics

Mutations and Health

Reprinted from https://ghr.nlm.nih.gov/

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services

Published December 21, 2016

Mutations and Health

Table of Contents

What is a gene mutation and how do mutations occur? 3

How can gene mutations affect health and development? 5

Do all gene mutations affect health and development? 6

What kinds of gene mutations are possible? 7

Can a change in the number of genes affect health and development? 13

Can changes in the number of chromosomes affect health and development? 14

Can changes in the structure of chromosomes affect health and development? 21

Can changes in mitochondrial DNA affect health and development? 32

What are complex or multifactorial disorders? 35

What does it mean to have a genetic predisposition to a disease? 36

What information about a genetic condition can statistics provide? 38

How are genetic conditions and genes named? 40

What is a gene mutation and how do mutations occur?

A gene mutation is a permanent alteration in the DNA sequence that makes up a gene, such that the sequence differs from what is found in most people. Mutations range in size; they can affect anywhere from a single DNA building block (base pair) to a large segment of a chromosome that includes multiple genes.

Gene mutations can be classified in two major ways:

- Hereditary mutations are inherited from a parent and are present throughout a person's life in virtually every cell in the body. These mutations are also called germline mutations because they are present in the parent's egg or sperm cells, which are also called germ cells. When an egg and a sperm cell unite, the resulting fertilized egg cell receives DNA from both parents. If this DNA has a mutation, the child that grows from the fertilized egg will have the mutation in each of his or her cells.
- Acquired (or somatic) mutations occur at some time during a person's life and are present only in certain cells, not in every cell in the body. These changes can be caused by environmental factors such as ultraviolet radiation from the sun, or can occur if a mistake is made as DNA copies itself during cell division. Acquired mutations in somatic cells (cells other than sperm and egg cells) cannot be passed on to the next generation.

Genetic changes that are described as de novo (new) mutations can be either hereditary or somatic. In some cases, the mutation occurs in a person's egg or sperm cell but is not present in any of the person's other cells. In other cases, the mutation occurs in the fertilized egg shortly after the egg and sperm cells unite. (It is often impossible to tell exactly when a de novo mutation happened.) As the fertilized egg divides, each resulting cell in the growing embryo will have the mutation. De novo mutations may explain genetic disorders in which an affected child has a mutation in every cell in the body but the parents do not, and there is no family history of the disorder.

Somatic mutations that happen in a single cell early in embryonic development can lead to a situation called mosaicism. These genetic changes are not present in a parent's egg or sperm cells, or in the fertilized egg, but happen a bit later when the embryo includes several cells. As all the cells divide during growth and development, cells that arise from the cell with the altered gene will have the mutation, while other cells will not. Depending on the mutation and how many cells are affected, mosaicism may or may not cause health problems.

Most disease-causing gene mutations are uncommon in the general population. However, other genetic changes occur more frequently. Genetic alterations that occur in more than 1 percent of the population are called polymorphisms. They are common enough to be considered a normal variation in the DNA. Polymorphisms are responsible for many of the normal differences between people such as eye color, hair color, and blood type. Although many polymorphisms have no negative effects on a person’s health, some of these variations may influence the risk of developing certain disorders.

For more information about mutations:

The Centre for Genetics Education provides a fact sheet discussing variations in the genetic code (http://www.genetics.edu.au/Publications-and-Resources/Genetics-Fact-Sheets/FactSheetVariationsinCode).

More basic information about genetic mutations (https://geneed.nlm.nih.gov/topic_subtopic.php?tid=142&sid=145) is available from GeneEd.

Additional information about genetic alterations is available from the University of Utah fact sheet "What is Mutation?" (http://learn.genetics.utah.edu/content/basics/mutation/)

How can gene mutations affect health and development?

To function correctly, each cell depends on thousands of proteins to do their jobs in the right places at the right times. Sometimes, gene mutations prevent one or more of these proteins from working properly. By changing a gene's instructions for making a protein, a mutation can cause the protein to malfunction or to be missing entirely. When a mutation alters a protein that plays a critical role in the body, it can disrupt normal development or cause a medical condition. A condition caused by mutations in one or more genes is called a genetic disorder.

In some cases, gene mutations are so severe that they prevent an embryo from surviving until birth. These changes occur in genes that are essential for development, and often disrupt the development of an embryo in its earliest stages. Because these mutations have very serious effects, they are incompatible with life.

It is important to note that genes themselves do not cause disease—genetic disorders are caused by mutations that make a gene function improperly. For example, when people say that someone has "the cystic fibrosis gene," they are usually referring to a mutated version of the *CFTR* gene, which causes the disease. All people, including those without cystic fibrosis, have a version of the *CFTR* gene.

For more information about mutations and genetic disorders:

The Centre for Genetics Education offers a fact sheet about genetic changes that lead to disorders (http://www.genetics.edu.au/Publications-and-Resources/Genetics-Fact-Sheets/FactSheetMutations).

The Tech Museum of Innovation offers a brief overview of genetic mutations and disease (http://genetics.thetech.org/about-genetics/mutations-and-disease).

Do all gene mutations affect health and development?

No; only a small percentage of mutations cause genetic disorders—most have no impact on health or development. For example, some mutations alter a gene's DNA sequence but do not change the function of the protein made by the gene.

Often, gene mutations that could cause a genetic disorder are repaired by certain enzymes before the gene is expressed and an altered protein is produced. Each cell has a number of pathways through which enzymes recognize and repair mistakes in DNA. Because DNA can be damaged or mutated in many ways, DNA repair is an important process by which the body protects itself from disease.

A very small percentage of all mutations actually have a positive effect. These mutations lead to new versions of proteins that help an individual better adapt to changes in his or her environment. For example, a beneficial mutation could result in a protein that protects an individual and future generations from a new strain of bacteria.

Because a person's genetic code can have a large number of mutations with no effect on health, diagnosing genetic conditions can be difficult. Sometimes, genes thought to be related to a particular genetic condition have mutations, but whether these changes are involved in development of the condition has not been determined; these genetic changes are known as variants of unknown significance (VOUS). Sometimes, no mutations are found in suspected disease-related genes, but mutations are found in other genes whose relationship to a particular genetic condition is unknown. It is difficult to know whether these variants are involved in the disease.

For more information about DNA repair and the health effects of gene mutations:

The University of Utah Genetic Science Learning Center provides information about genetic disorders (http://learn.genetics.utah.edu/content/disorders/) that explains why some mutations cause disorders but others do not.

The National Coalition for Health Professional Education in Genetics explains how mutations can be harmful, neutral, or beneficial (http://www.nchpeg.org/dentistry/index.php?option=com_content&view=article&id=22&Itemid=55&limitstart=3).

What kinds of gene mutations are possible?

The DNA sequence of a gene can be altered in a number of ways. Gene mutations have varying effects on health, depending on where they occur and whether they alter the function of essential proteins. The types of mutations include:

Missense mutation (image on page 9)

This type of mutation is a change in one DNA base pair that results in the substitution of one amino acid for another in the protein made by a gene.

Nonsense mutation (image on page 9)

A nonsense mutation is also a change in one DNA base pair. Instead of substituting one amino acid for another, however, the altered DNA sequence prematurely signals the cell to stop building a protein. This type of mutation results in a shortened protein that may function improperly or not at all.

Insertion (image on page 10)

An insertion changes the number of DNA bases in a gene by adding a piece of DNA. As a result, the protein made by the gene may not function properly.

Deletion (image on page 10)

A deletion changes the number of DNA bases by removing a piece of DNA. Small deletions may remove one or a few base pairs within a gene, while larger deletions can remove an entire gene or several neighboring genes. The deleted DNA may alter the function of the resulting protein(s).

Duplication (image on page 11)

A duplication consists of a piece of DNA that is abnormally copied one or more times. This type of mutation may alter the function of the resulting protein.

Frameshift mutation (image on page 11)

This type of mutation occurs when the addition or loss of DNA bases changes a gene's reading frame. A reading frame consists of groups of 3 bases that each code for one amino acid. A frameshift mutation shifts the grouping of these bases and changes the code for amino acids. The resulting protein is usually nonfunctional. Insertions, deletions, and duplications can all be frameshift mutations.

Repeat expansion (image on page 12)

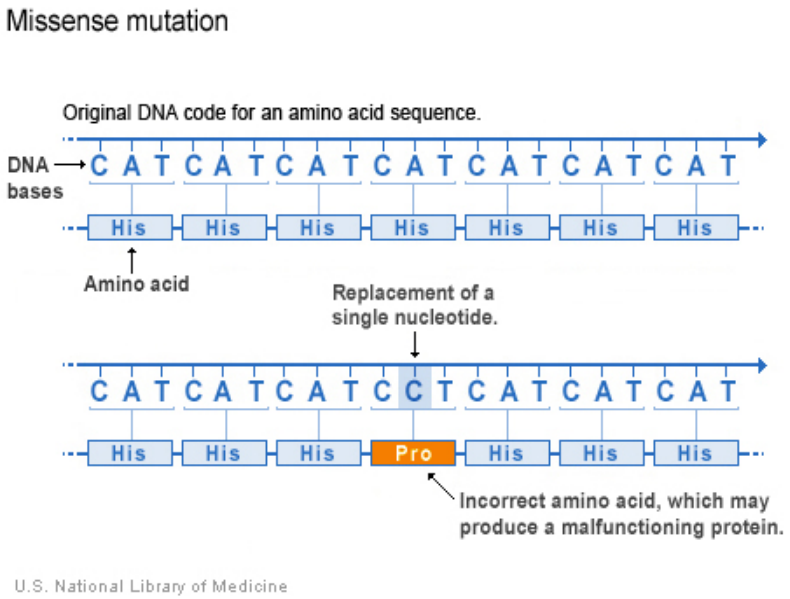
Nucleotide repeats are short DNA sequences that are repeated a number of times in a row. For example, a trinucleotide repeat is made up of 3-base-pair sequences, and a tetranucleotide repeat is made up of 4-base-pair sequences. A repeat expansion is a mutation that increases the number of times that the short DNA sequence is repeated. This type of mutation can cause the resulting protein to function improperly.

For more information about the types of gene mutations:

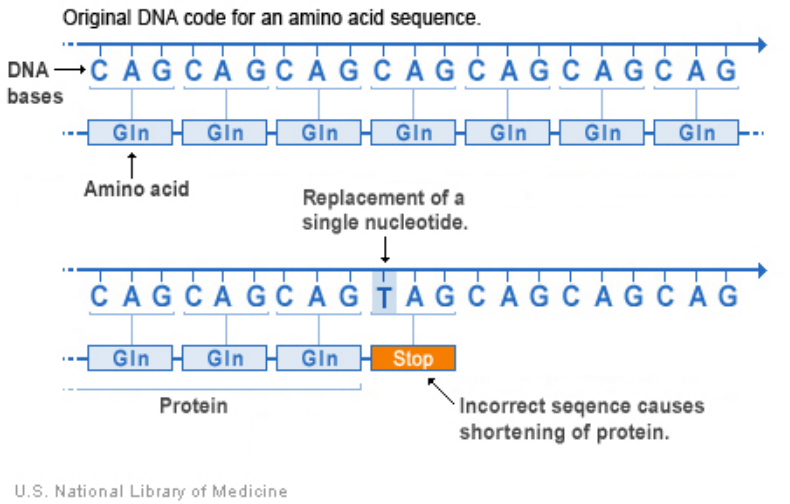
The National Human Genome Research Institute offers a Talking Glossary of Genetic Terms (https://www.genome.gov/glossary/). This resource includes definitions, diagrams, and detailed audio descriptions of several of the gene mutations listed above.

A brief explanation of different mutation types (http://www.yourgenome.org/facts/what-types-of-mutation-are-there) is available from yourgenome.org.

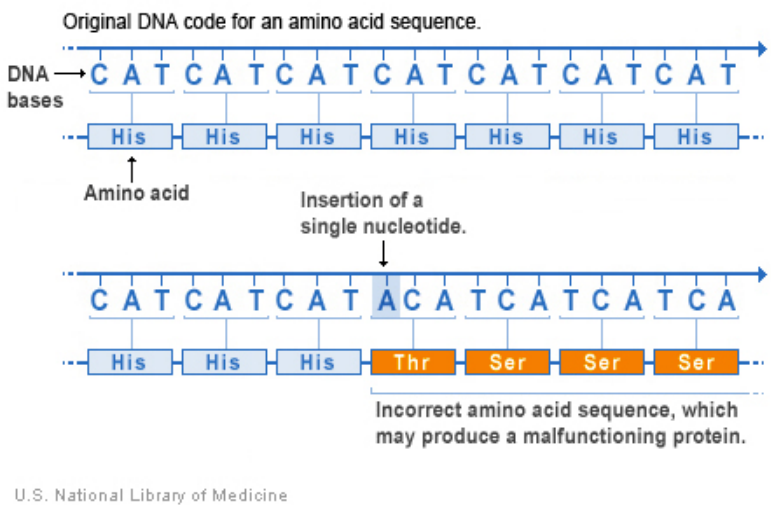
Images



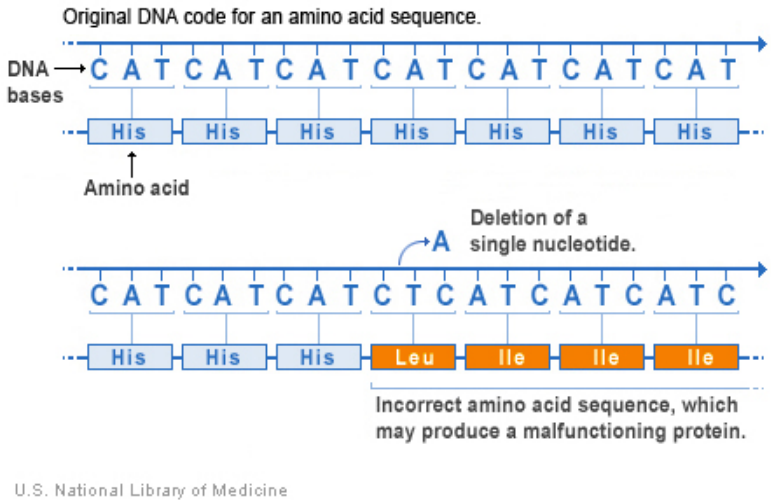
In this example, the nucleotide adenine is replaced by cytosine in the genetic code, introducing an incorrect amino acid into the protein sequence.



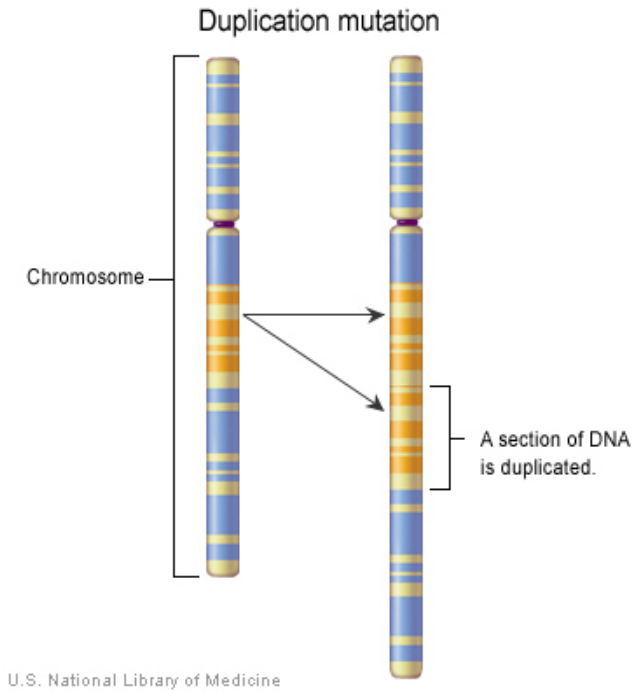
In this example, the nucleotide cytosine is replaced by thymine in the DNA code, signaling the cell to shorten the protein.



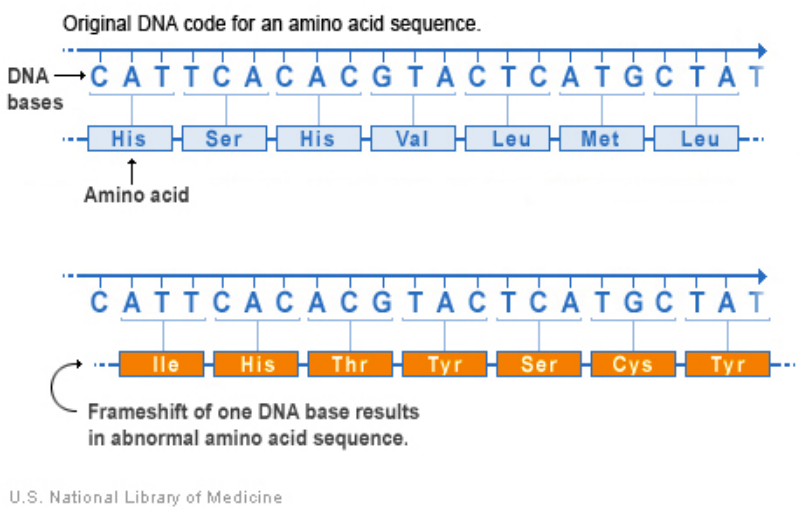
In this example, one nucleotide (adenine) is added in the DNA code, changing the amino acid sequence that follows.



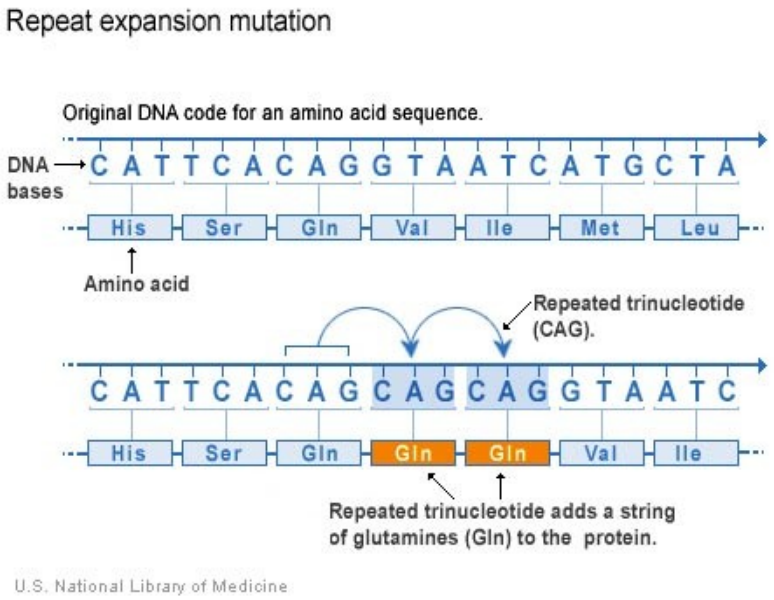
In this example, one nucleotide (adenine) is deleted from the DNA code, changing the amino acid sequence that follows.



A section of DNA is accidentally duplicated when a chromosome is copied.



A frameshift mutation changes the amino acid sequence from the site of the mutation.



In this example, a repeated trinucleotide sequence (CAG) adds a series of the amino acid glutamine to the resulting protein.

Can a change in the number of genes affect health and development?

People have two copies of most genes, one copy inherited from each parent. In some cases, however, the number of copies varies—meaning that a person can be born with one, three, or more copies of particular genes. Less commonly, one or more genes may be entirely missing. This type of genetic difference is known as copy number variation (CNV).

Copy number variation results from insertions, deletions, and duplications of large segments of DNA. These segments are big enough to include whole genes. Variation in gene copy number can influence the activity of genes and ultimately affect many body functions.

Researchers were surprised to learn that copy number variation accounts for a significant amount of genetic difference between people. More than 10 percent of human DNA appears to contain these differences in gene copy number. While much of this variation does not affect health or development, some differences likely influence a person's risk of disease and response to certain drugs. Future research will focus on the consequences of copy number variation in different parts of the genome and study the contribution of these variations to many types of disease.

For more information about copy number variation:

The Howard Hughes Medical Institute discusses the results of recent research on copy number variation in the news release, Genetic Variation: We're More Different Than We Thought (http://www.hhmi.org/news/genetic-variation-were-more-different-we-thought).

More information about copy number variation (https://www.dnalc.org/view/552-Copy-Number-Variants.html) is available in a video from Cold Spring Harbor Laboratory.

For people interested in more technical data, several institutions provide databases of structural differences in human DNA, including copy number variation:

- Database of Genomic Variants (http://dgv.tcag.ca/dgv/app/home)
- The Sanger Institute: Database of Chromosomal Imbalance and Phenotype in Humans using Ensembl Resources (DECIPHER (https://decipher.sanger.ac.uk/))

Can changes in the number of chromosomes affect health and development?

Human cells normally contain 23 pairs of chromosomes, for a total of 46 chromosomes in each cell (image on page 16). A change in the number of chromosomes can cause problems with growth, development, and function of the body's systems. These changes can occur during the formation of reproductive cells (eggs and sperm), in early fetal development, or in any cell after birth. A gain or loss of chromosomes from the normal 46 is called aneuploidy.

A common form of aneuploidy is trisomy, or the presence of an extra chromosome in cells. "Tri-" is Greek for "three"; people with trisomy have three copies of a particular chromosome in cells instead of the normal two copies. Down syndrome is an example of a condition caused by trisomy (image on page 17). People with Down syndrome typically have three copies of chromosome 21 in each cell, for a total of 47 chromosomes per cell.

Monosomy, or the loss of one chromosome in cells, is another kind of aneuploidy. "Mono-" is Greek for "one"; people with monosomy have one copy of a particular chromosome in cells instead of the normal two copies. Turner syndrome is a condition caused by monosomy (image on page 18). Women with Turner syndrome usually have only one copy of the X chromosome in every cell, for a total of 45 chromosomes per cell.

Rarely, some cells end up with complete extra sets of chromosomes. Cells with one additional set of chromosomes, for a total of 69 chromosomes, are called triploid (image on page 19). Cells with two additional sets of chromosomes, for a total of 92 chromosomes, are called tetraploid. A condition in which every cell in the body has an extra set of chromosomes is not compatible with life.

In some cases, a change in the number of chromosomes occurs only in certain cells. When an individual has two or more cell populations with a different chromosomal makeup, this situation is called chromosomal mosaicism (image on page 20). Chromosomal mosaicism occurs from an error in cell division in cells other than eggs and sperm. Most commonly, some cells end up with one extra or missing chromosome (for a total of 45 or 47 chromosomes per cell), while other cells have the usual 46 chromosomes. Mosaic Turner syndrome is one example of chromosomal mosaicism. In females with this condition, some cells have 45 chromosomes because they are missing one copy of the X chromosome, while other cells have the usual number of chromosomes.

Many cancer cells also have changes in their number of chromosomes. These changes are not inherited; they occur in somatic cells (cells other than eggs or sperm) during the formation or progression of a cancerous tumor.

For more information about chromosomal disorders:

A discussion of how chromosomal abnormalities happen (https://www.genome.gov/11508982#6) is provided by the National Human Genome Research Institute.

The Centre for Genetics Education offers a fact sheet about changes in chromosome number or size (http://www.genetics.edu.au/Publications-and-Resources/Genetics-Fact-Sheets/FactSheetChromosomeChanges).

Information about chromosomal changes (http://www.eurogentest.org/index.php?id=611), including changes in the number of chromosomes, is available from EuroGentest.

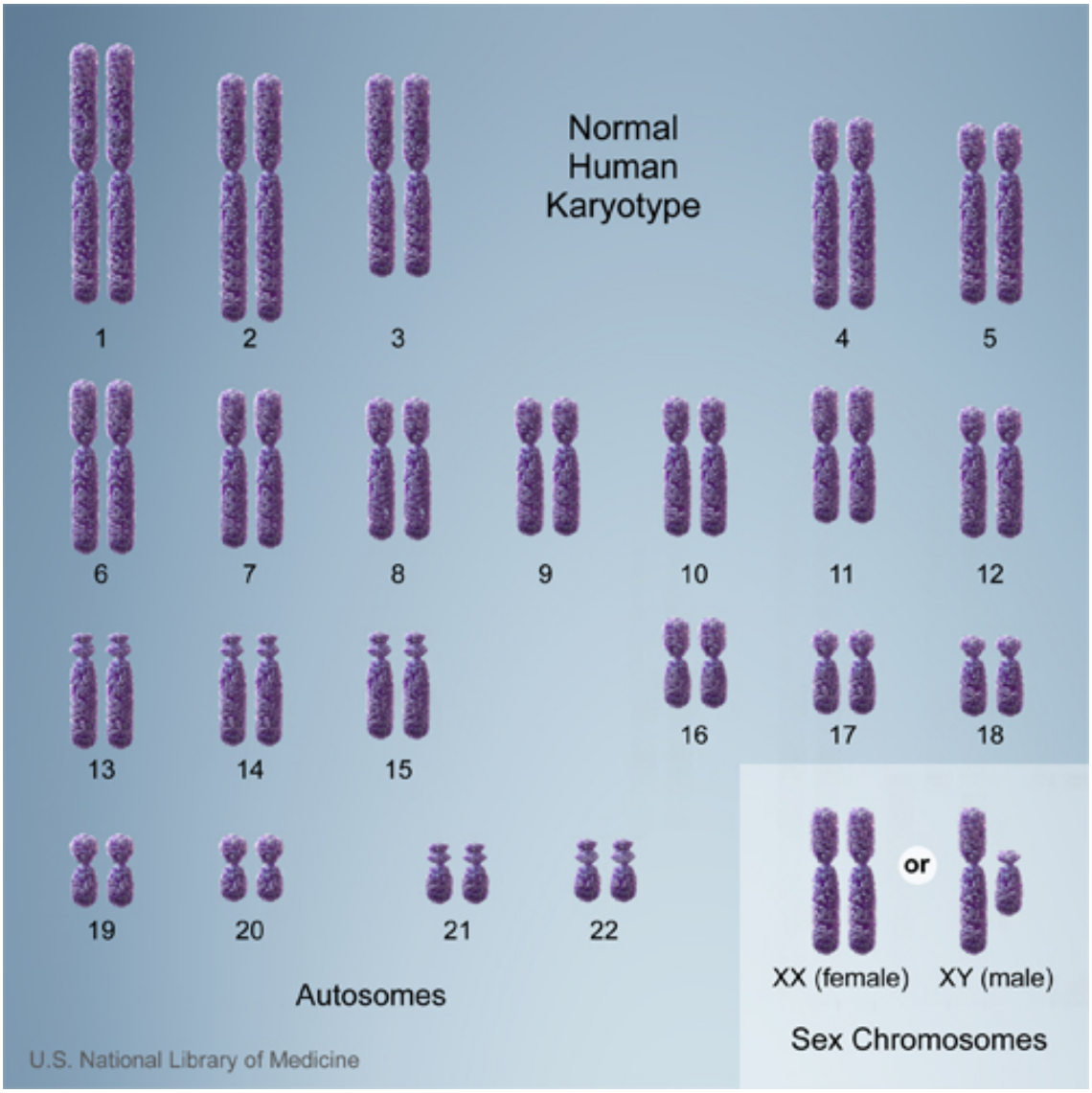
The University of Leicester's Virtual Genetics Education Center provides an explanation of numerical chromosome aberrations (http://www2.le.ac.uk/departments/genetics/vgec/healthprof/topics/patterns-of-inheritance/chromosomal-abnormalities#numerical-aberrations).

The National Organization for Rare Disorders offers an overview of triploidy (http://rarediseases.org/rare-diseases/triploidy/).

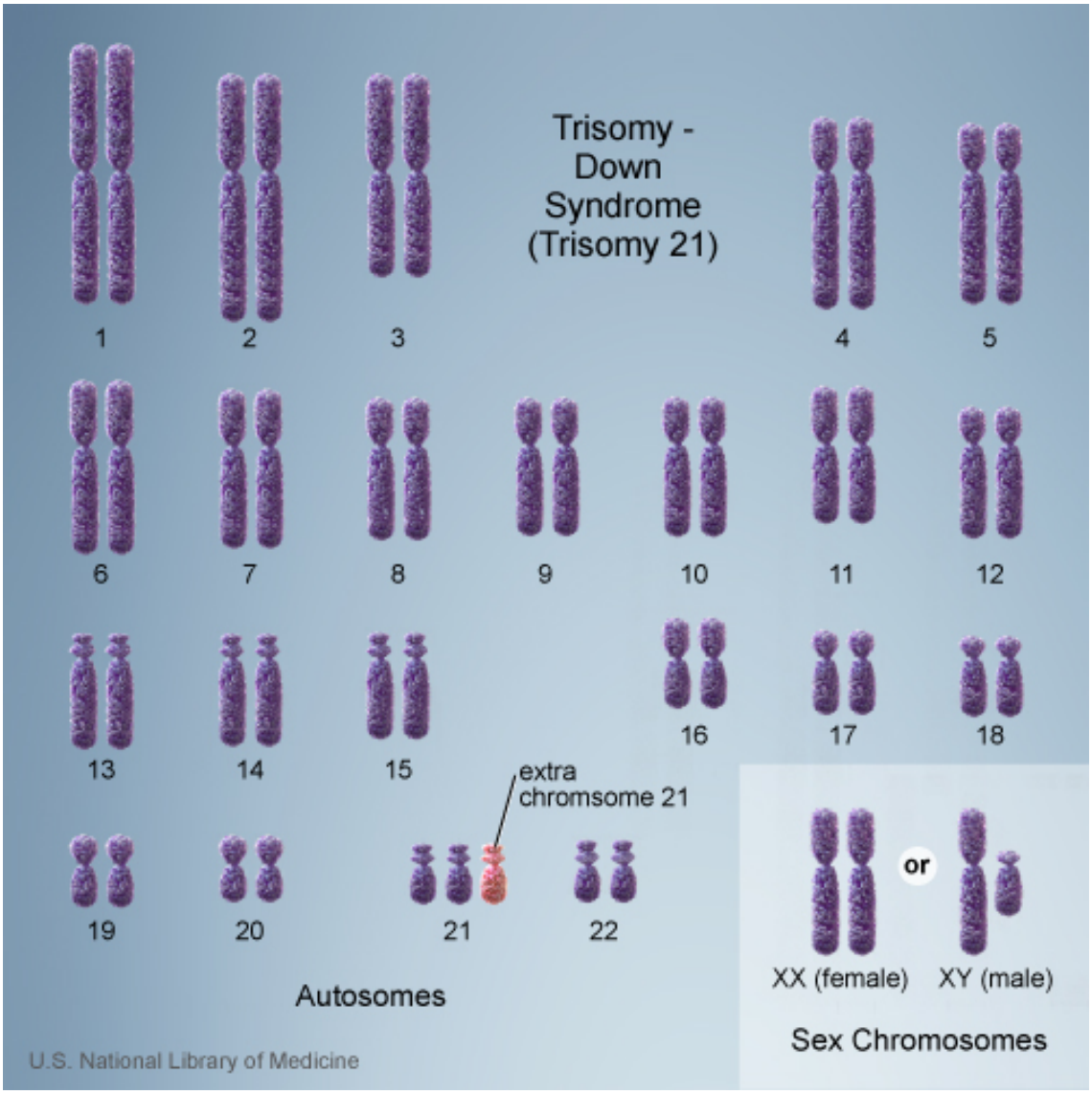
Chromosomal Mosaicism (http://mosaicism.cfri.ca/index.htm), a web site provided by the University of British Columbia, offers detailed information about mosaic chromosomal abnormalities.

MedlinePlus offers an encyclopedia article about chromosomal mosaicism (https://medlineplus.gov/ency/article/001317.htm).

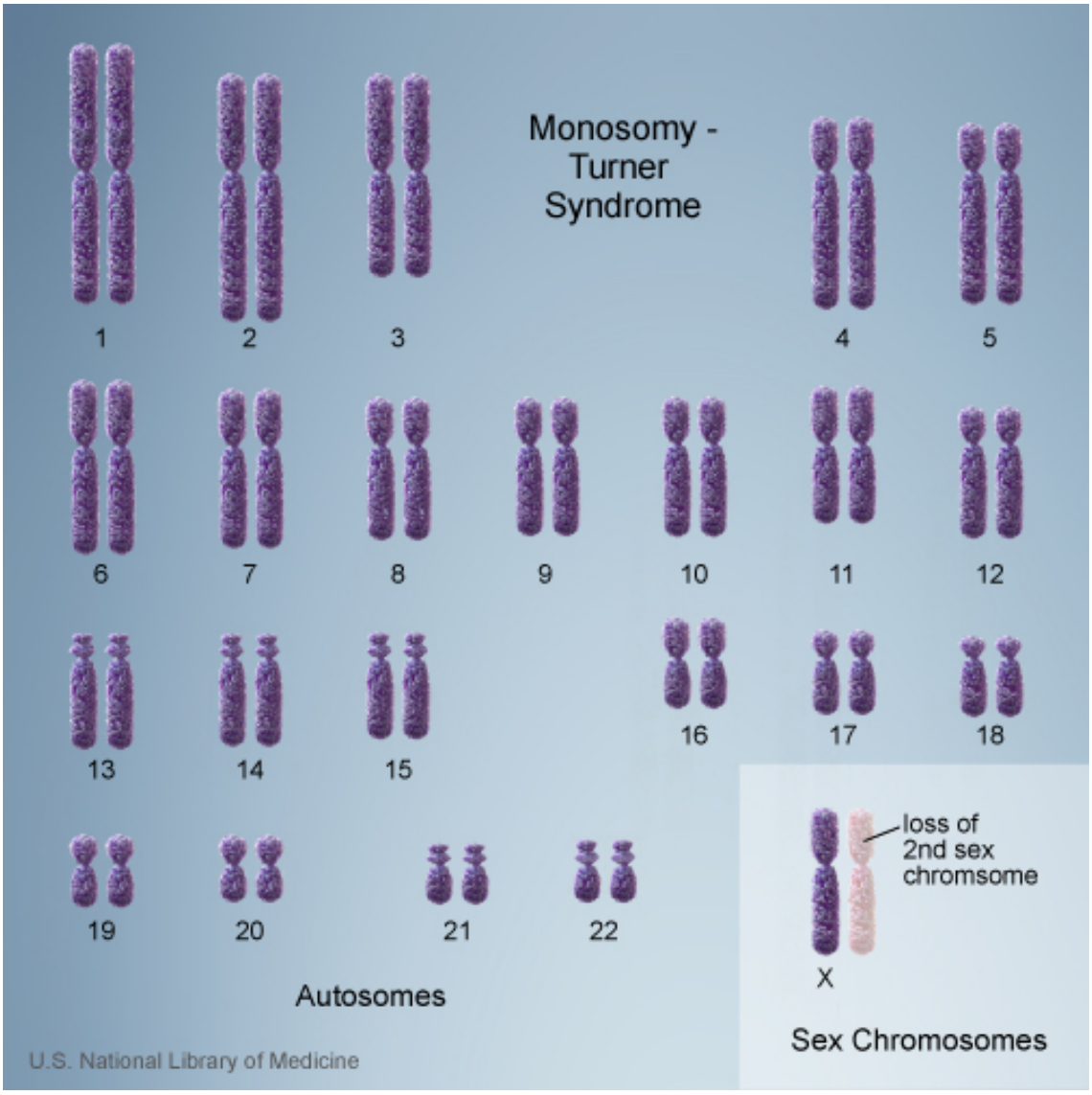
Images



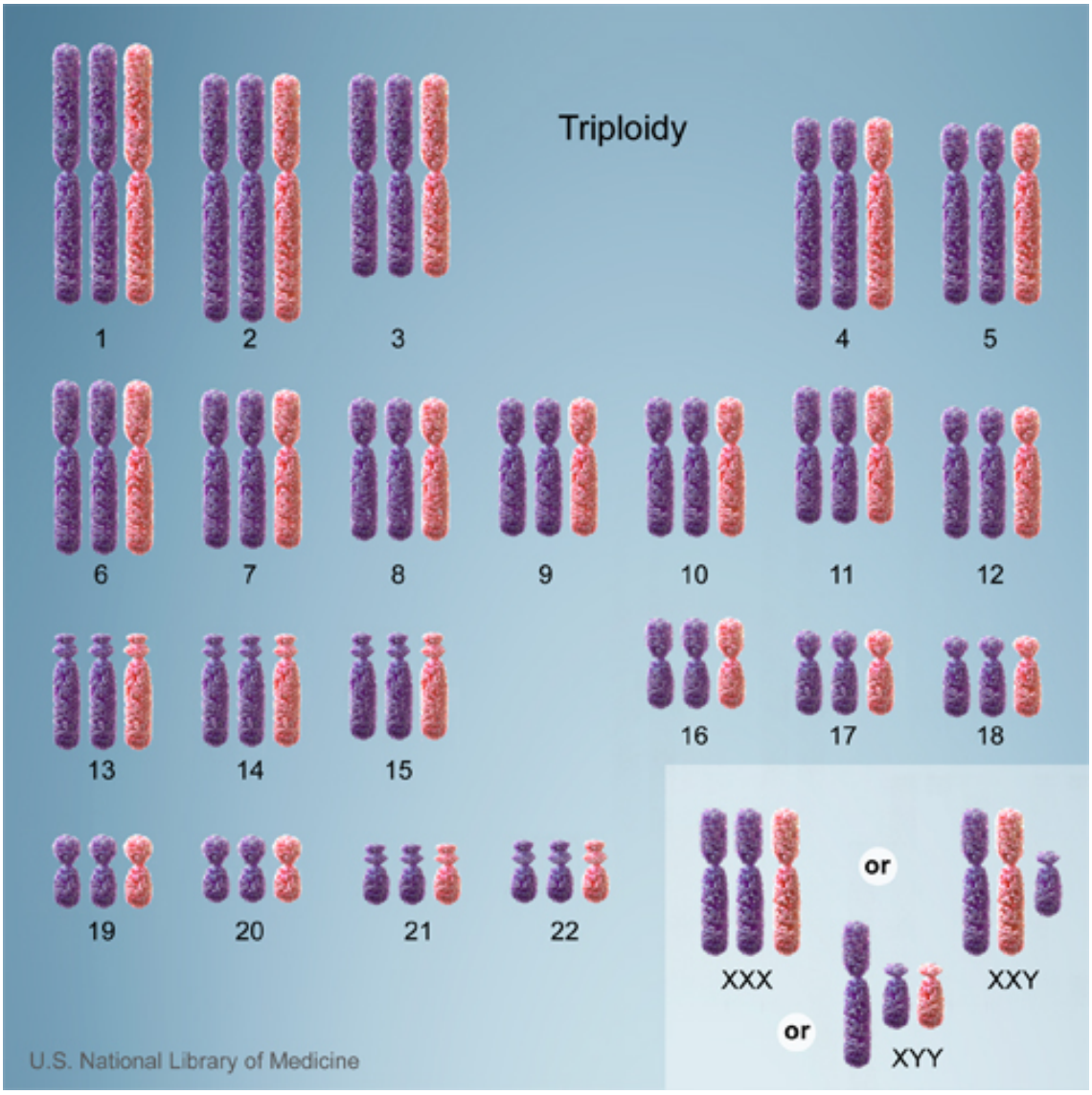
Human cells normally contain 23 pairs of chromosomes,
for a total of 46 chromosomes in each cell.



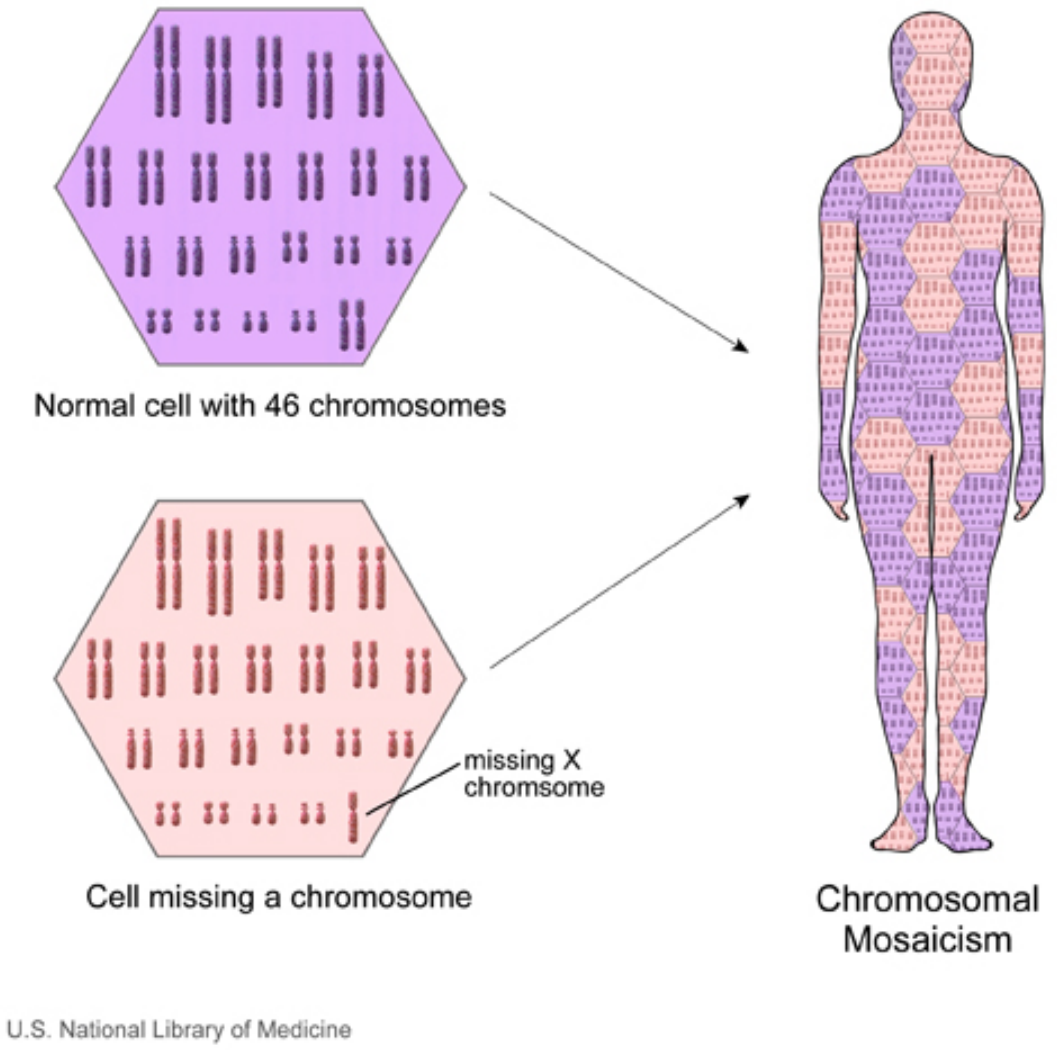
Trisomy is the presence of an extra chromosome in cells. Down syndrome is an example of a condition caused by trisomy.



Monosomy is the loss of one chromosome in cells. Turner syndrome is an example of a condition caused by monosomy.



Cells with one additional set of chromosomes,
for a total of 69 chromosomes, are called triploid.



When an individual has two or more cell populations with a different chromosomal makeup, this situation is called chromosomal mosaicism.

Can changes in the structure of chromosomes affect health and development?

Changes that affect the structure of chromosomes can cause problems with growth, development, and function of the body's systems. These changes can affect many genes along the chromosome and disrupt the proteins made from those genes.

Structural changes can occur during the formation of egg or sperm cells, in early fetal development, or in any cell after birth. Pieces of DNA can be rearranged within one chromosome or transferred between two or more chromosomes. The effects of structural changes depend on their size and location, and whether any genetic material is gained or lost. Some changes cause medical problems, while others may have no effect on a person's health.

Changes in chromosome structure include:

Translocations (image on page 24)**,** (image on page 25)

A translocation occurs when a piece of one chromosome breaks off and attaches to another chromosome. This type of rearrangement is described as balanced if no genetic material is gained or lost in the cell. If there is a gain or loss of genetic material, the translocation is described as unbalanced.

Deletions (image on page 26)

Deletions occur when a chromosome breaks and some genetic material is lost. Deletions can be large or small, and can occur anywhere along a chromosome.

Duplications (image on page 27)

Duplications occur when part of a chromosome is copied (duplicated) too many times. This type of chromosomal change results in extra copies of genetic material from the duplicated segment.

Inversions (image on page 28)

An inversion involves the breakage of a chromosome in two places; the resulting piece of DNA is reversed and re-inserted into the chromosome. Genetic material may or may not be lost as a result of the chromosome breaks. An inversion that involves the chromosome's constriction point (centromere) is called a pericentric inversion. An inversion that occurs in the long (q) arm or short (p) arm and does not involve the centromere is called a paracentric inversion.

Isochromosomes (image on page 29)

An isochromosome is a chromosome with two identical arms. Instead of one long (q) arm and one short (p) arm, an isochromosome has two long arms or two short arms. As a result, these abnormal chromosomes have an extra copy of some genes and are missing copies of other genes.

Dicentric chromosomes (image on page 30)

Unlike normal chromosomes, which have a single constriction point (centromere), a dicentric chromosome contains two centromeres. Dicentric chromosomes result from the abnormal fusion of two chromosome pieces, each of which includes a centromere. These structures are unstable and often involve a loss of some genetic material.

Ring chromosomes (image on page 31)

Ring chromosomes usually occur when a chromosome breaks in two places and the ends of the chromosome arms fuse together to form a circular structure. The ring may or may not include the chromosome's constriction point (centromere). In many cases, genetic material near the ends of the chromosome is lost.

Many cancer cells also have changes in their chromosome structure. These changes are not inherited; they occur in somatic cells (cells other than eggs or sperm) during the formation or progression of a cancerous tumor.

For more information about structural changes to chromosomes:

The National Human Genome Research Institute provides a list of questions and answers about chromosome abnormalities (https://www.genome.gov/11508982), including a glossary of related terms.

Chromosome Deletion Outreach offers a fact sheet on this topic titled Introduction to Chromosomes (http://chromodisorder.org/Display.aspx?ID=35). This resource includes illustrated explanations of several chromosome abnormalities.

The Centre for Genetics Education provides a fact sheet about chromosome changes (http://www.genetics.edu.au/Publications-and-Resources/Genetics-Fact-Sheets/FS4).

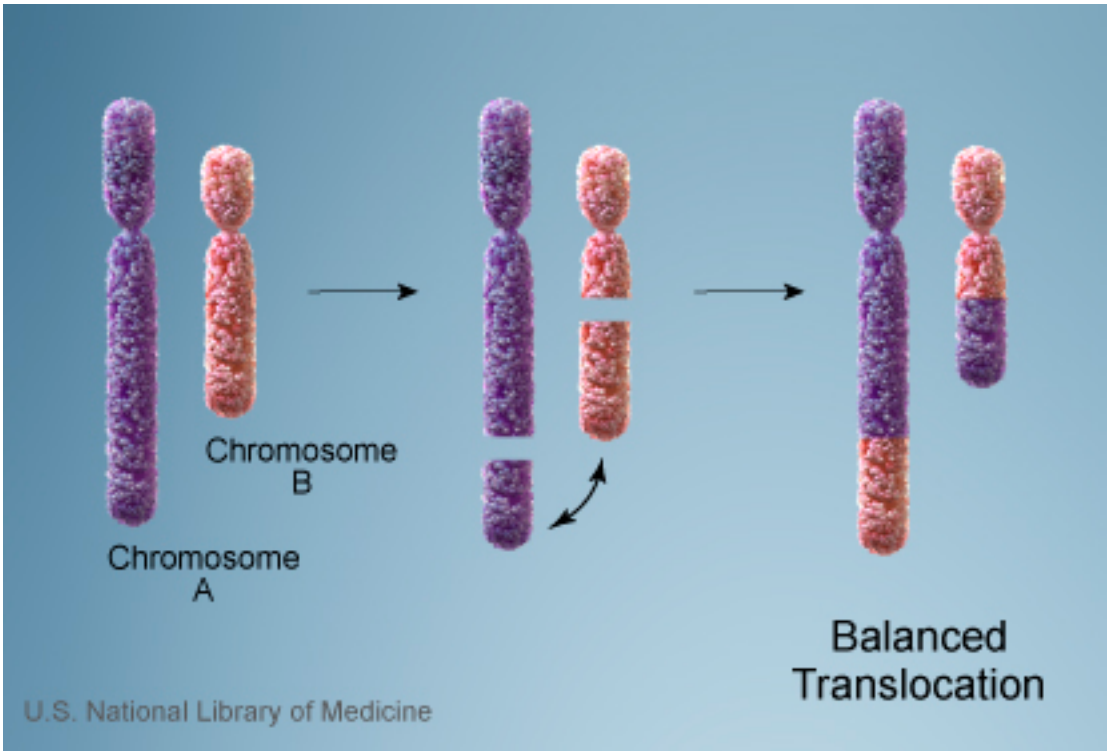
EuroGentest offers fact sheets about chromosome changes (http://www.eurogentest.org/index.php?id=611) and chromosome translocations (http://www.eurogentest.org/index.php?id=612).

The University of Leicester's Virtual Genetics Education Center provides an explanation of structural chromosome aberrations (http://www2.le.ac.uk/

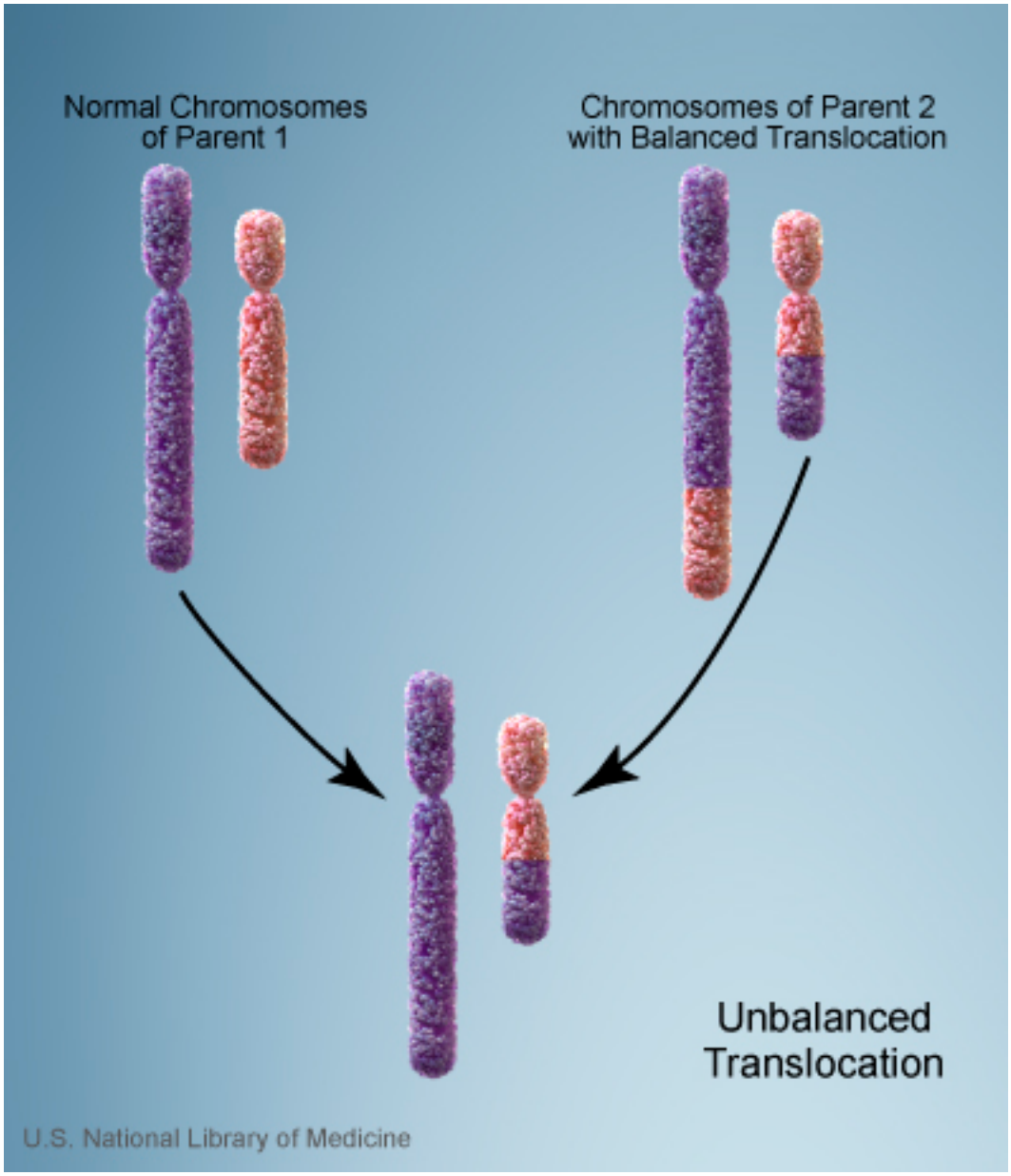
departments/genetics/vgec/healthprof/topics/patterns-of-inheritance/chromosomal-abnormalities#structural-aberrations).

The Atlas of Genetics and Cytogenetics in Oncology and Haematology provides a technical introduction to chromosomal aberrations (http://atlasgeneticsoncology.org/Deep/Chromaber.html) and a detailed discussion of ring chromosomes (http://atlasgeneticsoncology.org/Deep/RingChromosID20030.html), particularly their role in cancer.

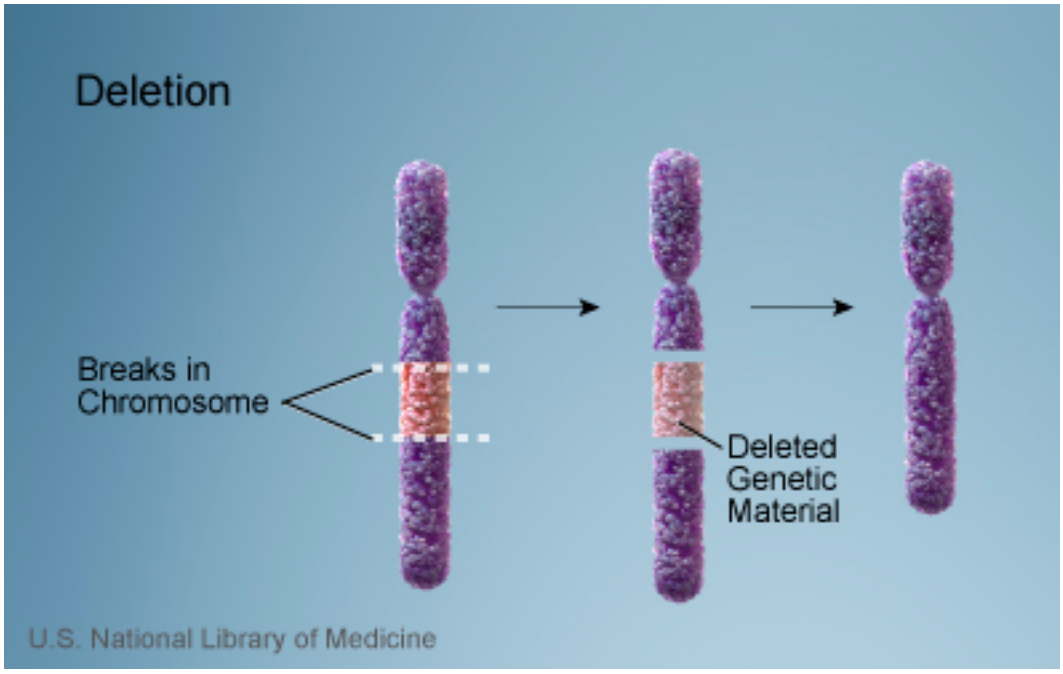
Images



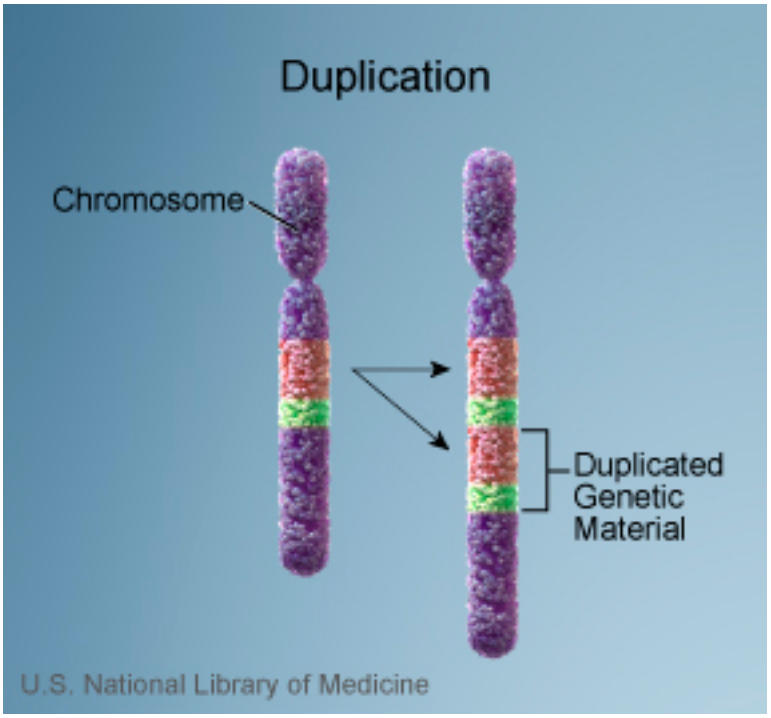
In a balanced translocation, pieces of chromosomes are rearranged but no genetic material is gained or lost in the cell.



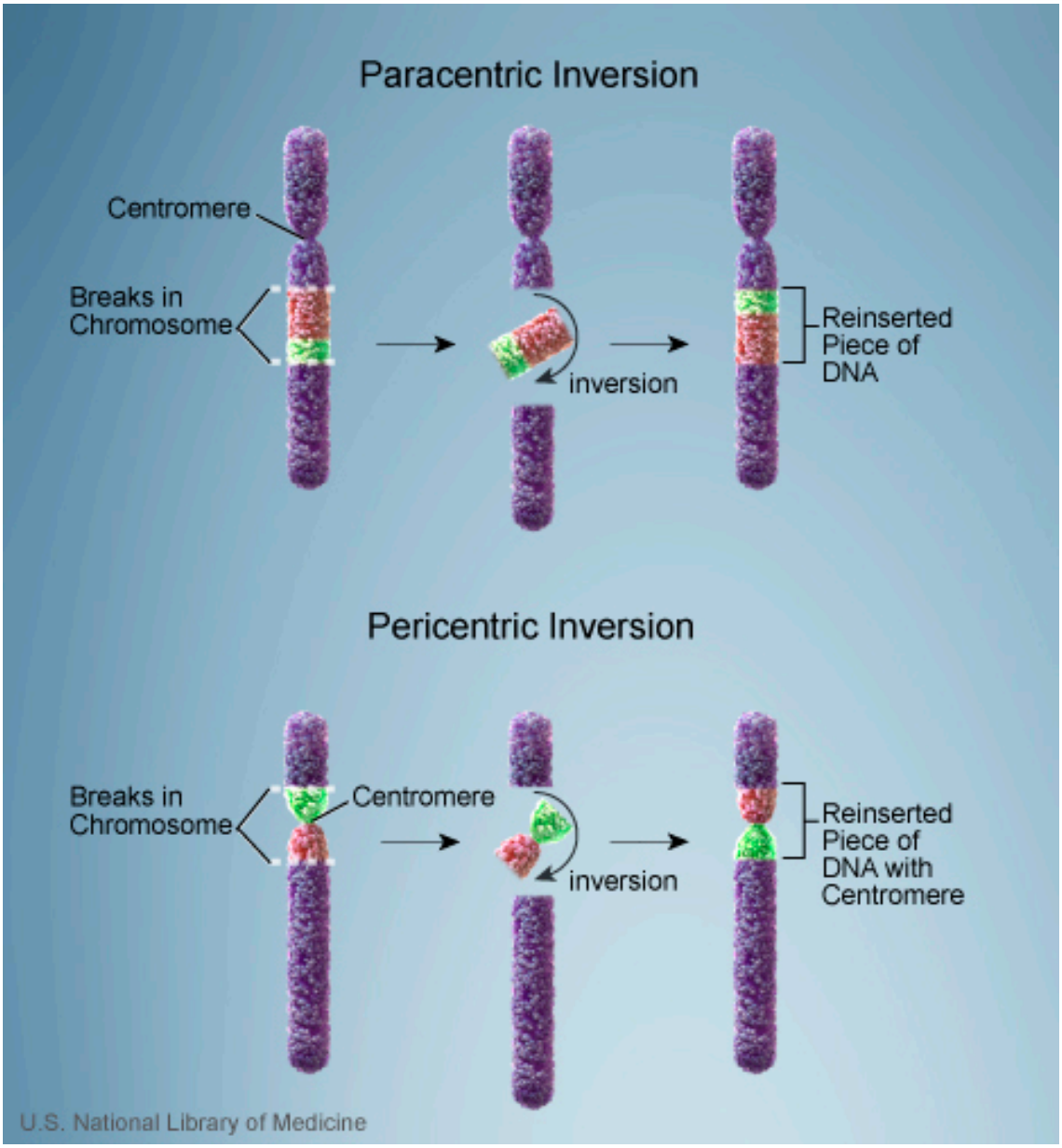
An unbalanced translocation occurs when a child inherits a chromosome with extra or missing genetic material from a parent with a balanced translocation.



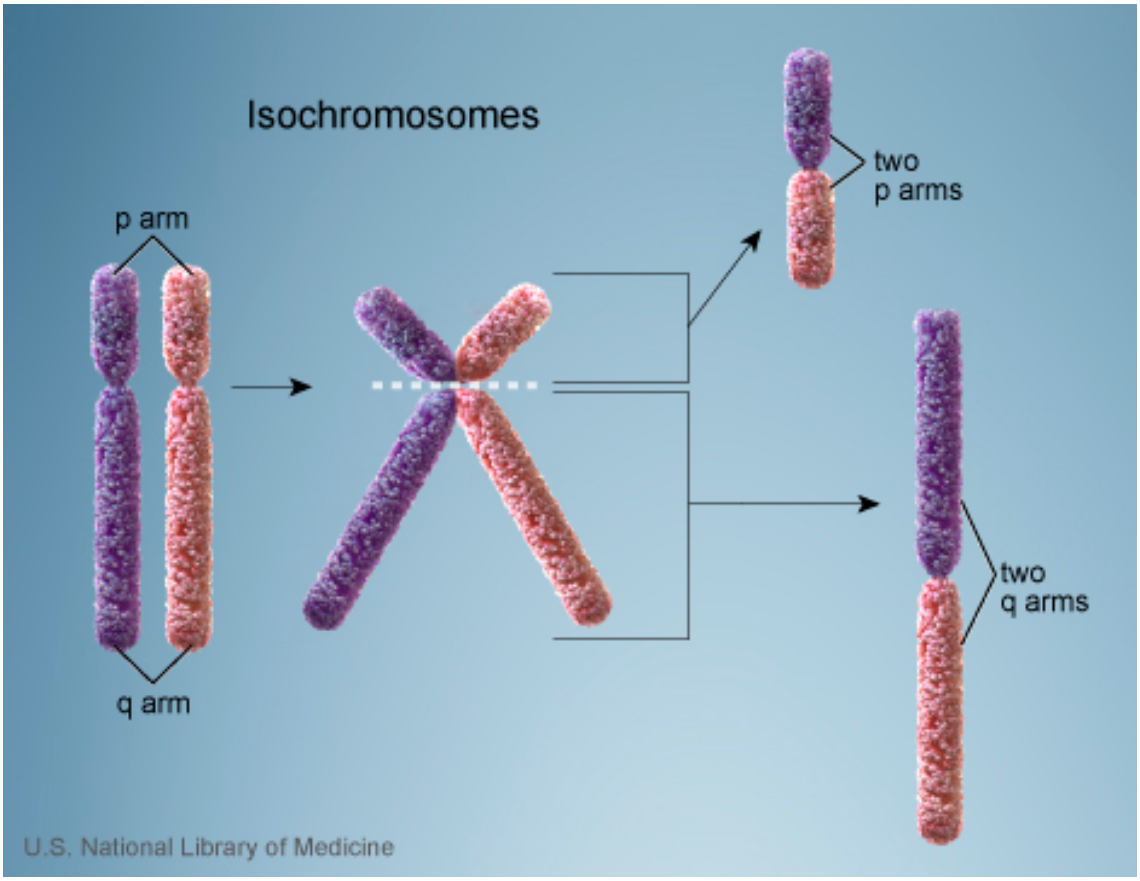
A deletion occurs when a chromosome breaks and some genetic material is lost.



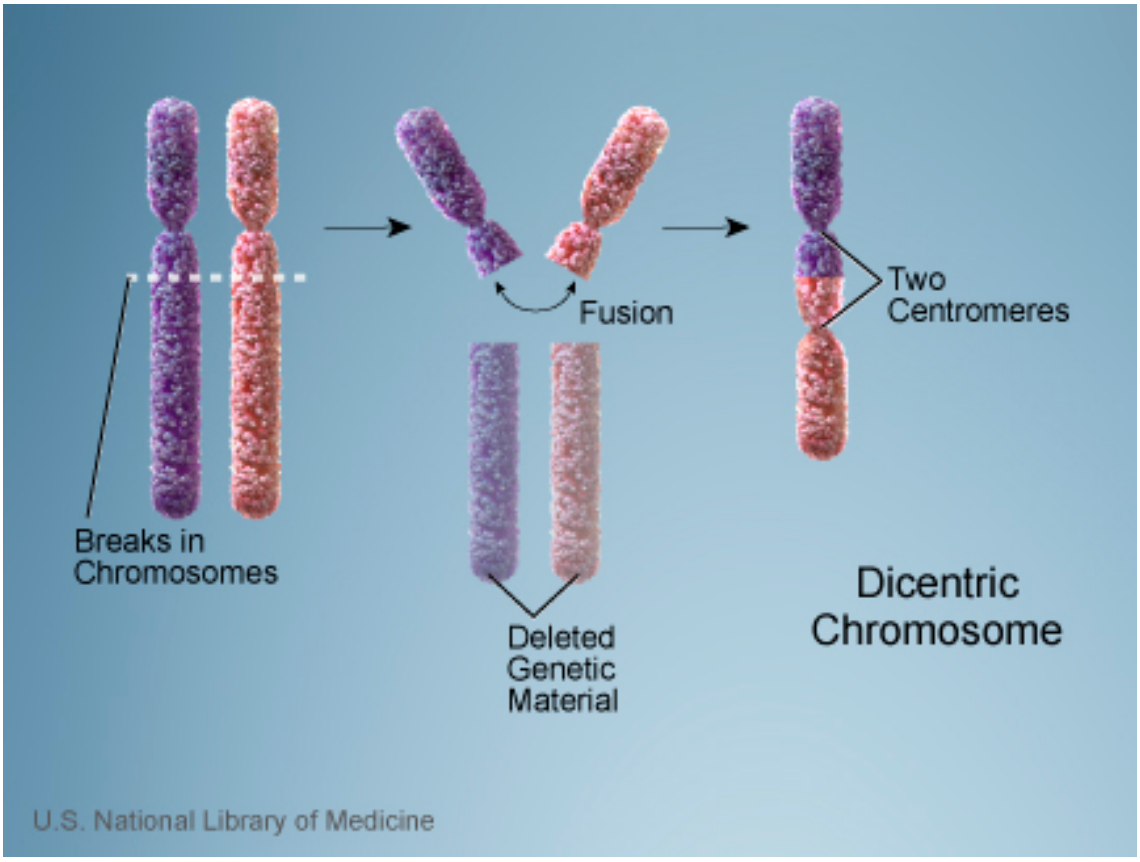
A duplication occurs when part of a chromosome is copied (duplicated) abnormally, resulting in extra genetic material from the duplicated segment.



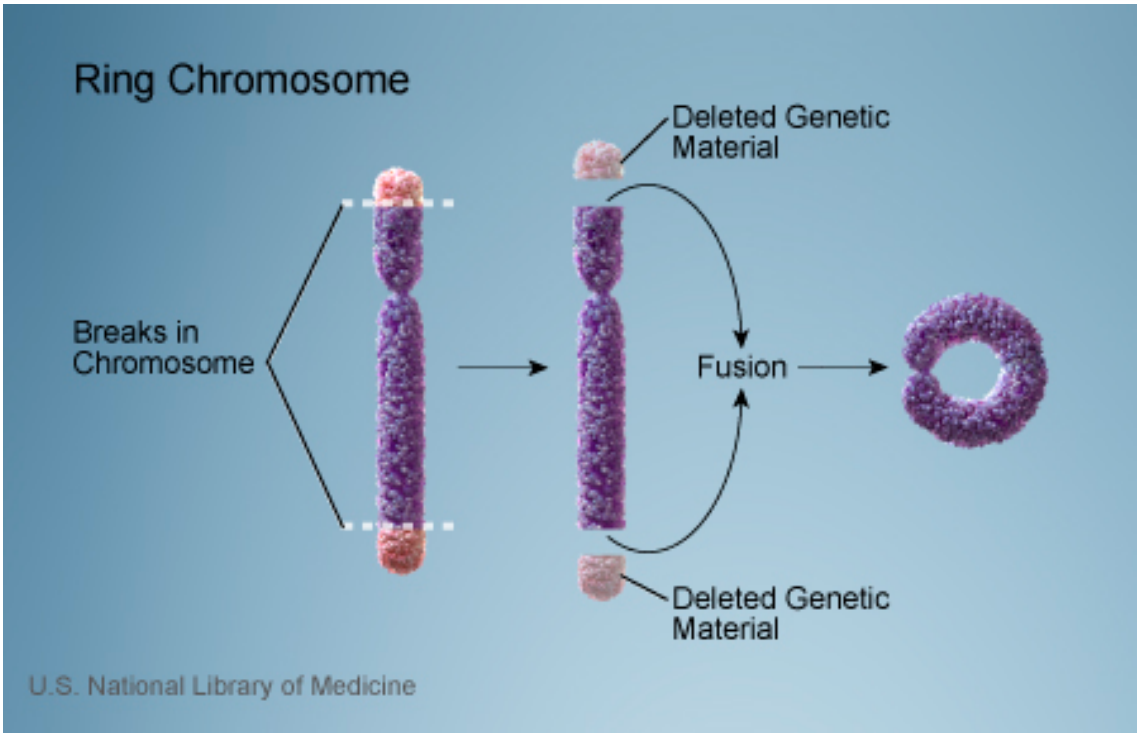
Inversions occur when a chromosome breaks in two places and the resulting piece of DNA is reversed and re-inserted into the chromosome. Inversions that involve the centromere are called pericentric inversions; those that do not involve the centromere are called paracentric inversions.



An isochromosome is an abnormal chromosome with two identical arms, either two short (p) arms or two long (q) arms.



Dicentric chromosomes result from the abnormal fusion of two chromosome pieces, each of which includes a centromere.



Ring chromosomes usually occur when a chromosome breaks in two places and the ends of the chromosome arms fuse together to form a circular structure.

Can changes in mitochondrial DNA affect health and development?

Mitochondria (image on page 34) are structures within cells that convert the energy from food into a form that cells can use. Although most DNA is packaged in chromosomes within the nucleus, mitochondria also have a small amount of their own DNA (known as mitochondrial DNA or mtDNA). In some cases, inherited changes in mitochondrial DNA can cause problems with growth, development, and function of the body's systems. These mutations disrupt the mitochondria's ability to generate energy efficiently for the cell.

Conditions caused by mutations in mitochondrial DNA often involve multiple organ systems. The effects of these conditions are most pronounced in organs and tissues that require a lot of energy (such as the heart, brain, and muscles). Although the health consequences of inherited mitochondrial DNA mutations vary widely, frequently observed features include muscle weakness and wasting, problems with movement, diabetes, kidney failure, heart disease, loss of intellectual functions (dementia), hearing loss, and abnormalities involving the eyes and vision.

Mitochondrial DNA is also prone to somatic mutations, which are not inherited. Somatic mutations occur in the DNA of certain cells during a person's lifetime and typically are not passed to future generations. Because mitochondrial DNA has a limited ability to repair itself when it is damaged, these mutations tend to build up over time. A buildup of somatic mutations in mitochondrial DNA has been associated with some forms of cancer and an increased risk of certain age-related disorders such as heart disease, Alzheimer disease, and Parkinson disease. Additionally, research suggests that the progressive accumulation of these mutations over a person's lifetime may play a role in the normal process of aging.

For more information about conditions caused by mitochondrial DNA mutations:

Genetics Home Reference provides background information about mitochondria and mitochondrial DNA (https://ghr.nlm.nih.gov/primer/basics/mtdna) written in consumer-friendly language.

The Cleveland Clinic offers a basic introduction to mitochondrial disease (http://my.clevelandclinic.org/health/diseases_conditions/hic-what-are-mitochondrial-diseases/hic_Myths_and_Facts_About_Mitochondrial_Diseases). Additional information about mitochondrial disorders (https://www.cincinnatichildrens.org/service/m/mitochondrial-disorders/patients/) is available from Cincinnati Children's Hospital Medical Center.

An overview of mitochondrial disorders (http://www.ncbi.nlm.nih.gov/books/NBK1224/) is available from GeneReviews.

The Muscular Dystrophy Association offers an introduction to mitochondrial disorders as part of their fact sheet called Mitochondrial Myopathies (https://www.mda.org/disease/mitochondrial-myopathies).

The Neuromuscular Disease Center at Washington University provides an in-depth description of many mitochondrial conditions (http://neuromuscular.wustl.edu/mitosyn.html).

Images

Mitochondria provide the cell's energy.

What are complex or multifactorial disorders?

Researchers are learning that nearly all conditions and diseases have a genetic component. Some disorders, such as sickle cell disease and cystic fibrosis, are caused by mutations in a single gene. The causes of many other disorders, however, are much more complex. Common medical problems such as heart disease, diabetes, and obesity do not have a single genetic cause—they are likely associated with the effects of multiple genes in combination with lifestyle and environmental factors. Conditions caused by many contributing factors are called complex or multifactorial disorders.

Although complex disorders often cluster in families, they do not have a clear-cut pattern of inheritance. This makes it difficult to determine a person's risk of inheriting or passing on these disorders. Complex disorders are also difficult to study and treat because the specific factors that cause most of these disorders have not yet been identified. Researchers continue to look for major contributing genes for many common complex disorders.

For more information about complex disorders:

A fact sheet about the inheritance of multifactorial disorders (http://www.genetics.edu.au/Publications-and-Resources/Genetics-Fact-Sheets/FactSheetEnvironmenralGeneticInteractions) is available from the Centre for Genetics Education.

The Children's Hospital of Wisconsin provides basic information about multifactorial inheritance (http://www.chw.org/medical-care/genetics-and-genomics-program/medical-genetics/multifactorial-inheritance/) and examples of multifactorial disorders.

GeneEd from the National Library of Medicine and the National Human Genome Research Institute provides a list of educational resources about multifactorial inheritance and complex disease (https://geneed.nlm.nih.gov/topic_subtopic.php?tid=5&sid=8).

The National Human Genome Research Institute describes how researchers study complex disorders (https://www.genome.gov/10000865).

If you would like information about a specific complex disorder such as diabetes or obesity, MedlinePlus (https://medlineplus.gov/) will lead you to fact sheets and other reliable medical information. In addition, the Centers for Disease Control and Prevention provides a detailed list of diseases and conditions (http://www.cdc.gov/DiseasesConditions/) that links to additional information.

What does it mean to have a genetic predisposition to a disease?

A genetic predisposition (sometimes also called genetic susceptibility) is an increased likelihood of developing a particular disease based on a person's genetic makeup. A genetic predisposition results from specific genetic variations that are often inherited from a parent. These genetic changes contribute to the development of a disease but do not directly cause it. Some people with a predisposing genetic variation will never get the disease while others will, even within the same family.

Genetic variations can have large or small effects on the likelihood of developing a particular disease. For example, certain mutations in the *BRCA1* or *BRCA2* genes greatly increase a person's risk of developing breast cancer and ovarian cancer. Variations in other genes, such as *BARD1* and *BRIP1*, also increase breast cancer risk, but the contribution of these genetic changes to a person's overall risk appears to be much smaller.

Current research is focused on identifying genetic changes that have a small effect on disease risk but are common in the general population. Although each of these variations only slightly increases a person's risk, having changes in several different genes may combine to increase disease risk significantly. Changes in many genes, each with a small effect, may underlie susceptibility to many common diseases, including cancer, obesity, diabetes, heart disease, and mental illness.

In people with a genetic predisposition, the risk of disease can depend on multiple factors in addition to an identified genetic change. These include other genetic factors (sometimes called modifiers) as well as lifestyle and environmental factors. Diseases that are caused by a combination of factors are described as multifactorial on page 35. Although a person's genetic makeup cannot be altered, some lifestyle and environmental modifications (such as having more frequent disease screenings and maintaining a healthy weight) may be able to reduce disease risk in people with a genetic predisposition.

For more information about genetic predisposition to disease:

The World Health Organization offers information about genetic predisposition to several common diseases (http://www.who.int/genomics/public/geneticdiseases/en/index3.html), including cancer, diabetes, cardiovascular disease, and asthma.

The Genetic Science Learning Center at the University of Utah provides more information about calculating the risk of genetic diseases and predicting

disease based on family history (http://learn.genetics.utah.edu/content/history/geneticrisk/).

The Coriell Personalized Medicine Collaborative explains genetic and nongenetic risk factors (https://cpmc.coriell.org/genetic-education/genetic-and-non-genetic-risk) for complex diseases.

More detailed information about the genetics of breast and ovarian cancer (http://www.cancer.gov/types/breast/hp/breast-ovarian-genetics-pdq) is available from the National Cancer Institute.

What information about a genetic condition can statistics provide?

Statistical data can provide general information about how common a condition is, how many people have the condition, or how likely it is that a person will develop the condition. Statistics are not personalized, however—they offer estimates based on groups of people. By taking into account a person's family history, medical history, and other factors, a genetics professional can help interpret what statistics mean for a particular patient.

Some statistical terms are commonly used when describing genetic conditions and other disorders. These terms include:

Common statistical terms

Statistical term	Description	Examples
Incidence	The incidence of a gene mutation or a genetic disorder is the number of people who are born with the mutation or disorder in a specified group per year. Incidence is often written in the form “1 in [a number]” or as a total number of live births.	About 1 in 200,000 people in the United States are born with syndrome A each year. An estimated 15,000 infants with syndrome B were born last year worldwide.
Prevalence	The prevalence of a gene mutation or a genetic disorder is the total number of people in a specified group at a given time who have the mutation or disorder. This term includes both newly diagnosed and pre-existing cases in people of any age. Prevalence is often written in the form “1 in [a number]” or as a total number of people who have a condition.	Approximately 1 in 100,000 people in the United States have syndrome A at the present time. About 100,000 children worldwide currently have syndrome B.
Mortality	Mortality is the number of deaths from a particular disorder occurring in a specified group per year. Mortality is usually expressed as a total number of deaths.	An estimated 12,000 people worldwide died from syndrome C in 2002.

Statistical term	Description	Examples
Lifetime risk	Lifetime risk is the average risk of developing a particular disorder at some point during a lifetime. Lifetime risk is often written as a percentage or as “1 in [a number].” It is important to remember that the risk per year or per decade is much lower than the lifetime risk. In addition, other factors may increase or decrease a person's risk as compared with the average.	Approximately 1 percent of people in the United States develop disorder D during their lifetimes. The lifetime risk of developing disorder D is 1 in 100.

For more information about understanding and interpreting statistics:

The New York Department of Health provides a basic explanation of statistical terms (http://www.health.ny.gov/diseases/chronic/basicstat.htm), including incidence, prevalence, morbidity, and mortality.

More detailed information about health statistics is available from Woloshin, Schwartz, and Welch's Know Your Chances: Understanding Health Statistics (http://www.ncbi.nlm.nih.gov/books/NBK115435/), which is available through the NCBI Bookshelf.

The National Cancer Institute offers additional tools for understanding cancer statistics (http://www.cancer.gov/about-cancer/what-is-cancer/statistics).

How are genetic conditions and genes named?

Naming genetic conditions

Genetic conditions are not named in one standard way (unlike genes, which are given an official name and symbol by a formal committee). Doctors who treat families with a particular disorder are often the first to propose a name for the condition. Expert working groups may later revise the name to improve its usefulness. Naming is important because it allows accurate and effective communication about particular conditions, which will ultimately help researchers find new approaches to treatment.

Disorder names are often derived from one or a combination of sources:

- The basic genetic or biochemical defect that causes the condition (for example, alpha-1 antitrypsin deficiency);
- One or more major signs or symptoms of the disorder (for example, hypermanganesemia with dystonia, polycythemia, and cirrhosis);
- The parts of the body affected by the condition (for example, craniofacial-deafness-hand syndrome);
- The name of a physician or researcher, often the first person to describe the disorder (for example, Marfan syndrome, which was named after Dr. Antoine Bernard-Jean Marfan);
- A geographic area (for example, familial Mediterranean fever, which occurs mainly in populations bordering the Mediterranean Sea); or
- The name of a patient or family with the condition (for example, amyotrophic lateral sclerosis, which is also called Lou Gehrig disease after the famous baseball player who had the condition).

Disorders named after a specific person or place are called eponyms. There is debate as to whether the possessive form (e.g., Alzheimer’s disease) or the nonpossessive form (Alzheimer disease) of eponyms is preferred. As a rule, medical geneticists use the nonpossessive form, and this form may become the standard for doctors in all fields of medicine.

Naming genes

The HUGO Gene Nomenclature Committee (http://www.genenames.org/) (HGNC) designates an official name and symbol (an abbreviation of the name) for each known human gene. Some official gene names include additional information in parentheses, such as related genetic conditions, subtypes of a condition, or inheritance pattern. The HGNC is a non-profit organization funded by the U.K. Medical Research Council and the U.S. National Institutes of Health. The Committee has named more than 13,000 of the estimated 20,000 to 25,000 genes in the human genome.

During the research process, genes often acquire several alternate names and symbols. Different researchers investigating the same gene may each give the gene a different name, which can cause confusion. The HGNC assigns a unique name and symbol to each human gene, which allows effective organization of genes in large databanks, aiding the advancement of research. For specific information about how genes are named, refer to the HGNC's Guidelines for Human Gene Nomenclature (http://www.genenames.org/about/guidelines).

Genetics
Home
Reference

https://ghr.nlm.nih.gov/

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services

Published on December 21, 2016