**GENETIC DISEASES**

A genetic disease is any disease caused by an abnormality in the genetic [makeup](https://www.medicinenet.com/beauty_quiz/quiz.htm) of an individual. The genetic abnormality can range from minuscule to major -- from a discrete mutation in a single base in the DNA of a single gene to a gross chromosomal abnormality involving the addition or subtraction of an entire chromosome or set of chromosomes. Some people inherit genetic disorders from the parents, while acquired changes or mutations in a preexisting gene or group of genes cause other genetic diseases. Genetic mutations can occur either randomly or due to some environmental exposure.

There are a number of different types of genetic disorders and include:

1. **Single gene inheritance**
2. **Multifactorial inheritance**
3. **Chromosome abnormalities**
4. **Mitochondrial inheritance**

**Single gene inheritance**

Single gene inheritance is also called Mendelian or monogenetic inheritance. Changes or mutations that occur in the DNA sequence of a single gene cause this type of inheritance. There are thousands of known single-gene disorders. These disorders are known as monogenetic disorders (disorders of a single gene).

Single-gene disorders have different patterns of genetic inheritance, including

* autosomal dominant inheritance, in which only one copy of a defective gene (from either parent) is necessary to cause the condition;
* autosomal recessive inheritance, in which two copies of a defective gene (one from each parent) are necessary to cause the condition; and
* X-linked inheritance, in which the defective gene is present on the female, or X-chromosome. X-linked inheritance may be dominant or recessive.

Some examples of single-gene disorders include [cystic fibrosis](https://www.medicinenet.com/cystic_fibrosis/article.htm), alpha- and beta-thalassemias, [sickle cell anemia](https://www.medicinenet.com/sickle_cell/article.htm) ([sickle cell disease](https://www.medicinenet.com/sickle_cell/article.htm)), [Marfan syndrome](https://www.medicinenet.com/marfan_syndrome/article.htm), [fragile X syndrome](https://www.medicinenet.com/fragile_x_syndrome/article.htm), Huntington's disease, and [hemochromatosis](https://www.medicinenet.com/iron_overload/article.htm).

**Fragile X syndrome** is a genetic condition that causes a range of developmental problems including learning disabilities and cognitive impairment. Usually, males are more severely affected by this disorder than females. Affected individuals usually have delayed development of speech and language by age 2. Most males with fragile X syndrome have mild to moderate intellectual disability, while about one-third of affected females are intellectually disabled. Children with fragile X syndrome may also have anxiety and hyperactive behavior such as fidgeting or impulsive actions. They may have attention deficit disorder (ADD), which includes an impaired ability to maintain attention and difficulty focusing on specific tasks. About one-third of individuals with fragile X syndrome have features of [autism spectrum disorder](https://ghr.nlm.nih.gov/condition/autism-spectrum-disorder) that affect communication and social interaction. Seizures occur in about 15 percent of males and about 5 percent of females with fragile X syndrome.

Most males and about half of females with fragile X syndrome have characteristic physical features that become more apparent with age. These features include a [long and narrow face](https://ghr.nlm.nih.gov/art/large/narrow-face.jpeg), large ears, a prominent jaw and forehead, unusually flexible fingers, [flat feet](https://ghr.nlm.nih.gov/art/large/flat-feet.jpeg), and in males, enlarged testicles (macroorchidism) after puberty.

**Huntington disease** is a progressive [brain](https://ghr.nlm.nih.gov/art/large/side-view-of-brain.jpeg) disorder that causes uncontrolled movements, emotional problems, and loss of thinking ability (cognition).

Adult-onset Huntington disease, the most common form of this disorder, usually appears in a person's thirties or forties. Early signs and symptoms can include irritability, [depression](https://ghr.nlm.nih.gov/condition/depression), small involuntary movements, poor coordination, and trouble learning new information or making decisions. Many people with Huntington disease develop involuntary jerking or twitching movements known as chorea. As the disease progresses, these movements become more pronounced. Affected individuals may have trouble walking, speaking, and swallowing. People with this disorder also experience changes in personality and a decline in thinking and reasoning abilities. Individuals with the adult-onset form of Huntington disease usually live about 15 to 20 years after signs and symptoms begin.

**Cystic fibrosis** is an inherited condition that causes sticky mucus to build up in the lungs Symptoms of cystic fibrosis include: recurring [chest infections](https://www.nhs.uk/conditions/chest-infection/), wheezing, [coughing](https://www.nhs.uk/conditions/cough/), [shortness of breath](https://www.nhs.uk/conditions/shortness-of-breath/) and damage to the airways [(bronchiectasis)](https://www.nhs.uk/conditions/bronchiectasis/), difficulty putting on weight and growing, [jaundice](https://www.nhs.uk/conditions/jaundice/), [diarrhoea](https://www.nhs.uk/conditions/diarrhoea/), [constipation](https://www.nhs.uk/conditions/constipation/), a bowel obstruction in newborn babies (meconium ileus) – surgery may be needed. People with the condition can also develop a number of related conditions, including [diabetes](https://www.nhs.uk/conditions/diabetes/), thin, weakened bones [(osteoporosis)](https://www.nhs.uk/conditions/osteoporosis/), [infertility](https://www.nhs.uk/conditions/infertility/) in males, and liver problems.

In the UK, all newborn babies are screened for cystic fibrosis as part of the [newborn blood spot test](https://www.nhs.uk/conditions/pregnancy-and-baby/newborn-blood-spot-test/) (heel prick test) carried out shortly after they're born. If the screening test suggests a child may have cystic fibrosis, they'll need these additional tests to confirm they have the condition:

* a sweat test – to measure the amount of salt in sweat, which will be abnormally high in someone with cystic fibrosis
* a genetic test – where a sample of blood or saliva is checked for the faulty gene that causes cystic fibrosis

These tests can also be used to diagnose cystic fibrosis in older children and adults who didn't have the newborn test. The genetic test can also be used to see whether someone is a "carrier" of cystic fibrosis in cases where the condition runs in the family. This test can be important for someone who thinks they may have the faulty gene and wishes to have children.

**Multifactorial inheritance**

Multifactorial inheritance is also called complex or polygenic inheritance. Multifactorial inheritance disorders are caused by a combination of environmental factors and mutations in multiple genes. For example, different genes that influence [breast cancer](https://www.medicinenet.com/breast_cancer_facts_stages/article.htm) susceptibility have been found on chromosomes 6, 11, 13, 14, 15, 17, and 22. Some common chronic diseases are multifactorial disorders.

Examples of multifactorial inheritance include [heart disease](https://www.medicinenet.com/heart_disease_coronary_artery_disease/article.htm), [high blood pressure](https://www.medicinenet.com/high_blood_pressure_hypertension/article.htm), [Alzheimer's](https://www.medicinenet.com/alzheimers_disease_causes_stages_and_symptoms/article.htm) disease, [arthritis](https://www.medicinenet.com/arthritis/article.htm), [diabetes](https://www.medicinenet.com/diabetes_mellitus/article.htm), [cancer](https://www.medicinenet.com/cancer/article.htm), and [obesity](https://www.medicinenet.com/obesity_weight_loss/article.htm).

Multifactorial inheritance also is associated with heritable traits such as fingerprint patterns, height, eye color, and skin color.

**Alzheimer's disease** is a progressive disorder that causes brain cells to waste away (degenerate) and die. Alzheimer's disease is the most common cause of dementia — a continuous decline in thinking, behavioral and social skills that disrupts a person's ability to function independently and it is characterized by symptoms like impairment of memory and eventually by disturbances in reasoning, planning, language, and perception. The likelihood of having Alzheimer's disease increases substantially after the age of 70, and it may affect around 38% of persons over the age of 85.

The early signs of the disease may be forgetting recent events or conversations. As the disease progresses, a person with Alzheimer's disease will develop severe memory impairment and lose the ability to carry out everyday tasks. People with Alzheimer's may:

* Repeat statements and questions over and over
* Forget conversations, appointments or events, and not remember them later
* Routinely misplace possessions, often putting them in illogical locations
* Get lost in familiar places
* Eventually forget the names of family members and everyday objects
* Have trouble finding the right words to identify objects, express thoughts or take part in conversations

**Chromosome abnormalities**

Many types of chromosomal abnormalities exist, but they can be categorized as either numerical or structural. Numerical abnormalities are whole chromosomes either missing from or extra to the normal pair. Structural abnormalities are when part of an individual chromosome is missing, extra, switched to another chromosome, or turned upside down.

Chromosomal abnormalities can occur as an accident when the egg or the sperm is formed or during the early developmental stages of the fetus. The age of the mother and certain environmental factors may play a role in the occurrence of genetic errors.

Chromosomal abnormalities can have many different effects, depending on the specific abnormality. For example, an extra copy of chromosome 21 causes Down syndrome (trisomy 21). Chromosomal abnormalities can also cause miscarriage, disease, or problems in growth or development.

The most common type of chromosomal abnormality is known as aneuploidy, an abnormal chromosome number due to an extra or missing chromosome. Most people with aneuploidy have trisomy (three copies of a chromosome) instead of monosomy (single copy of a chromosome). Down syndrome is probably the most well-known example of a chromosomal aneuploidy. Besides trisomy 21, the major chromosomal aneuploidies seen in live-born babies are: trisomy 18; trisomy 13; 45, X (Turner syndrome); 47, XXY (Klinefelter syndrome); 47, XYY; and 47, XXX and 46, XX or XY, 5p- (Cri du chat syndrome, or the "cry of the cat" syndrome).

Structural chromosomal abnormalities result from breakage and incorrect rejoining of chromosomal segments. A range of structural chromosomal abnormalities result in disease. Structural rearrangements are defined as balanced if the complete chromosomal set is still present, though rearranged, and unbalanced if information is additional or missing. Unbalanced rearrangements include deletions, duplications, or insertions of a chromosomal segment. Ring chromosomes can result when a chromosome undergoes two breaks and the broken ends fuse into a circular chromosome. An isochromosome can form when an arm of the chromosome is missing and the remaining arm duplicates.

Balanced rearrangements include inverted or translocated chromosomal regions. Since the full complement of DNA material is still present, balanced chromosomal rearrangements may go undetected because they may not result in disease. A disease can arise as a result of a balanced rearrangement if the breaks in the chromosomes occur in a gene, resulting in an absent or nonfunctional protein, or if the fusion of chromosomal segments results in a hybrid of two genes, producing a new protein product whose function is damaging to the cell.

**Cri-du-chat (cat's cry) syndrome**, also known as 5p- (5p minus) syndrome, is a chromosomal condition that results when [a piece of chromosome 5 is missing](https://ghr.nlm.nih.gov/art/large/chromosome-5p-deletion-in-cri-du-chat-syndrome.jpeg). [Infants with this condition](https://ghr.nlm.nih.gov/art/large/cri-du-chat-infant.jpeg) often have a high-pitched cry that sounds like that of a cat. The disorder is characterized by intellectual disability and delayed development, small head size ([microcephaly](https://ghr.nlm.nih.gov/art/large/microcephaly.jpeg)), low birth weight, and weak muscle tone (hypotonia) in infancy. [Affected individuals](https://ghr.nlm.nih.gov/art/large/cri-du-chat-ya-flowers.jpeg) also have distinctive facial features, including widely set eyes (hypertelorism), low-set ears, a small jaw, and a rounded face. Some children with cri-du-chat syndrome are born with a heart defect.

**Mitochondrial inheritance**

Since the first identification of mitochondrial DNA mutations associated with disease in 1988, there has been an explosion in the recognition of distinct nuclear and mitochondrial genetic causes of mitochondrial disease. Due to an improved understanding of mitochondrial pathology, the recognized incidence has escalated and the minimal prevalence of mitochondrial disease is now estimated at 1 in 5000 across all ages. Affected children present across nearly all pediatric disciplines, with a predominance of neurologic, muscular, cardiac, gastrointestinal, and ophthalmologic manifestations. While the diagnostic evaluation of suspected primary mitochondrial disease has embraced the rapidly changing landscape of genetic information, the overall diagnostic yield remains low for the highly heterogeneous group of mitochondrial disorders that are caused by mutations across two genomes. Strictly speaking, no cures for mitochondrial disease are known.

Examples of mitochondrial diseases include: [Myoneurogenic gastrointestinal encephalopathy](https://en.wikipedia.org/wiki/Myoneurogenic_gastrointestinal_encephalopathy) (MNGIE), MELAS syndrome and Myoclonic epilepsy with ragged-red fibers (MERRF).

**Myoclonic epilepsy with ragged-red fibers (MERRF)** is a disorder that affects many parts of the body, particularly the muscles and nervous system. In most cases, the signs and symptoms of this disorder appear during childhood or adolescence. The features of MERRF vary widely among affected individuals, even among members of the same family.

MERRF is characterized by muscle twitches (myoclonus), weakness (myopathy), and progressive stiffness (spasticity). When the muscle cells of affected individuals are stained and viewed under a microscope, these cells usually appear abnormal. These abnormal muscle cells are called ragged-red fibers. Other features of MERRF include recurrent seizures (epilepsy), difficulty coordinating movements (ataxia), a loss of sensation in the extremities (peripheral neuropathy), and slow deterioration of intellectual function (dementia). People with this condition may also develop hearing loss or optic atrophy, which is the degeneration (atrophy) of nerve cells that carry visual information from the eyes to the brain. Affected individuals sometimes have short stature and a form of heart disease known as cardiomyopathy. Less commonly, people with MERRF develop fatty tumors, called lipomas, just under the surface of the skin.

**GENETIC TESTING**

As the cost of genetic analysis decreases and as research advances, it is becoming increasingly possible to include a person’s genetic makeup in the repertoire of tools that inform their health and well-being. Similarly, genetic analysis can be used in reproductive healthcare to learn about the DNA of an embryo in a Petri dish or a fetus in the womb, often as a way to gain medical insights at early stages of development. Two such genetic technologies are: **preimplantation genetic diagnosis (PGD)** and **non-invasive prenatal testing (NIPT)**, which allow people to screen embryos and fetuses, respectively, for a variety of characteristics.

**Prenatal testing**

Technology is transforming the ways that a person could learn about the genetic makeup of the fetus they are carrying. Previously, the only way doctors could analyze the DNA of a fetus was through an invasive procedure, either amniocentesis (typically at 15-20 weeks of pregnancy) or chorionic villus sampling (CVS; typically at 11-13 weeks of pregnancy). Since these invasive procedures involve collecting tissue or fluid from inside the womb, they both carry a small risk (how small remains a matter of debate, but could be anywhere from a .005% to 1% chance) of miscarriage. In 2011, a new generation of non-invasive prenatal tests (NIPT) became available for analyzing fetal DNA through a blood sample taken from a pregnant person’s arm. NIPT can be performed as early as 9 weeks of pregnancy and, as with any blood test performed during pregnancy, NIPT does not increase the risk for miscarriage.

NIPT is most commonly used to screen for extra or missing copies of certain chromosomes, that can result in conditions such as Down Syndrome. NIPT can also assess the chromosomal sex of the fetus. This test is more accurate than previous generations of prenatal blood tests, which did not look directly at fetal DNA. Importantly, NIPT is not diagnostic. Because NIPT can be performed at an early stage of pregnancy and only requires a blood sample, it has been rapidly adopted by medical professionals and raises challenges around informed consent. As a result, people are grappling with how to handle genetic information about the developing fetus that is increasingly available to prospective parents. Ethical and practical questions abound about how this information might be used. These questions include (i) whether information learned via NIPT could improve medical care; (ii) how NIPT could impact pregnancy termination rates; and (iii) whether the availability of NIPT might add to the stigmatization of people with perceived disabilities.

**Embryo testing**

Preimplantation genetic diagnosis (PGD) allows for the genetic diagnosis of embryos created by in vitro fertilization (IVF) - the fusion of egg and sperm in a lab. Based on the results of this analysis, one or more embryos can be selected for transfer into the womb. PGD can be used to assess whether an embryo has genetic variants that are associated with fatal diseases, such as Tay-Sachs disease and Huntington’s Disease, with the goal of avoiding them. Thousands of healthy children have been born as a result of this technology, free of the genetic diseases that have, in many cases, devastated the older generations of their families. At the same time, PGD has raised ethical issues, as it gives individuals the capacity to select one embryo over another, and therefore brings to the forefront issues about autonomy, medical interventions, and disability.

**GENE THERAPY**

Gene therapy is an experimental technique that uses genes to treat or prevent disease. In the future, this technique may allow doctors to treat a disorder by inserting a gene into a patient’s cells instead of using drugs or surgery. Researchers are testing several approaches to gene therapy, including:

* Replacing a mutated gene that causes disease with a healthy copy of the gene.
* Inactivating, or “knocking out,” a mutated gene that is functioning improperly.
* Introducing a new gene into the body to help fight a disease.

Although gene therapy is a promising treatment option for a number of diseases (including inherited disorders, some types of cancer, and certain viral infections), the technique remains risky and is still under study to make sure that it will be safe and effective. Gene therapy is currently being tested only for diseases that have no other cures.