**TOPIC**

**DISORDERS IN CELL CYCLE**

**How Chromosome Abnormalities Happen**

Chromosomes are stick-shaped structures in the middle of each cell in the body. Each cell has 46 chromosomes grouped in 23 pairs. When a chromosome is abnormal, it can cause health problems in the body. Abnormal chromosomes most often happen as a result of an error during cell division. Chromosome abnormalities often happen due to one or more of these:

* Errors during dividing of sex cells (meiosis)
* Errors during dividing of other cells (mitosis)
* Exposure to substances that cause birth defects (teratogens)

## Errors during dividing of sex cells (meiosis)

Meiosis (my-OH-sis) is the process in which sex cells divide and create new sex cells with half the number of chromosomes. Sperm and eggs are sex cells. Meiosis is the start of the process of how a baby grows. Normally, meiosis causes each parent to give 23 chromosomes to a pregnancy.  When a sperm fertilizes an egg, the union leads to a baby with 46 chromosomes.

But if meiosis doesn’t happen normally, a baby may have an extra chromosome (trisomy) or have a missing chromosome (monosomy). These problems can cause pregnancy loss. Or they can cause health problems in a child.

A woman age 35 years or older is at higher risk of having a baby with a chromosomal abnormality. This is because errors in meiosis may be more likely to happen as a result of the aging process. Women are born with all their eggs already in their ovaries. The eggs begin to mature during puberty. If a woman is 35 years old, the eggs in the ovaries are also 35 years old. You may be referred for genetic counselling or testing if you’re age 35 or older when you are pregnant. Men make new sperm ongoing. So, age doesn’t increase the risk for chromosome abnormalities for older fathers a lot. But newer studies suggest that rare abnormalities do occur.

## Errors during dividing of other cells (mitosis)

Mitosis (my-TOH-sis) is the dividing of all other cells in the body. It’s how a baby in the womb grows. Mitosis causes the number of chromosomes to double to 92, and then split in half back to 46. This process repeats constantly in the cells as the baby grows. Mitosis continues throughout your lifetime. It replaces skin cells, blood cells, and other types of cells that are damaged or naturally die.

During pregnancy, an error in mitosis can occur. If the chromosomes don’t split into equal halves, the new cells can have an extra chromosome (47 total) or have a missing chromosome (45 total).

## Substances that cause birth defects (teratogens)

A teratogen (ter-AT-uh-jen) is something that can cause or raise the risk for a birth defect in a baby. They are things that a mother may be exposed to during her pregnancy. Teratogens include:

* Some medicines
* Street drugs
* Alcohol
* Tobacco
* Toxic chemicals
* Some viruses and bacteria
* Some kinds of radiation
* Certain health conditions, such as uncontrolled diabetes
* biology
* Consequences of Chromosome Segregatio

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## What is Down syndrome?

Down syndrome (sometimes called Down’s syndrome) is a condition in which a child is born with an extra copy of their 21st chromosome — hence its other name, trisomy 21. This causes physical and mental developmental delays and disabilities.

Many of the disabilities are lifelong, and they can also shorten life expectancy. However, people with Down syndrome can live healthy and fulfilling lives. Recent medical advances, as well as cultural and institutional support for people with Down syndrome and their families, provides many opportunities to help overcome the challenges of this condition.



## What causes Down syndrome?

In all cases of reproduction, both parents pass their genes on to their children. These genes are carried in chromosomes. When the baby’s cells develop, each cell is supposed to receive 23 pairs of chromosomes, for 46 chromosomes total. Half of the chromosomes are from the mother, and half are from the father.

In children with Down syndrome, one of the chromosomes doesn’t separate properly. The baby ends up with three copies, or an extra partial copy, of chromosome 21, instead of two. This extra chromosome causes problems as the brain and physical features develop.

According to the [National Down Syndrome Society (NDSS)](http://www.ndss.org/about-down-syndrome/down-syndrome/), about 1 in 700 babies in the United States is born with Down syndrome. It’s the most common genetic disorder in the United States.

## Types of Down syndrome

There are three types of Down syndrome:

### Trisomy 21

Trisomy 21 means there’s an extra copy of chromosome 21 in every cell. This is the most common form of Down syndrome.

### Mosaicism

[Mosaicism](https://www.healthline.com/health/trisomy-8-mosaicism-syndrome) occurs when a child is born with an extra chromosome in some but not all their cells. People with mosaic Down syndrome tend to have fewer symptoms than those with trisomy 21.

### Translocation

In this type of Down syndrome, children have only an extra part of chromosome 21. There are 46 total chromosomes. However, one of them has an extra piece of chromosome 21 attached.

## Will my child have Down syndrome?

Certain parents have a greater chance of giving birth to a child with Down syndrome. According to the Centers for Disease and Prevention, mothers aged 35 and older are [more likelyTrusted Source](http://www.cdc.gov/ncbddd/birthdefects/downsyndrome/data.html) to have a baby with Down syndrome than younger mothers. The probability increases the older the mother is.

Research shows that paternal age also has an effect. One [2003 study](http://newsroom.cumc.columbia.edu/blog/2003/05/07/columbia-presbyterian-study-links-down-syndrome-fathers-age-3/) found that fathers over 40 had twice the chance of having a child with Down syndrome.

Other parents who are more likely to have a child with Down syndrome include:

* people with a family history of Down syndrome
* people who carry the genetic translocation

It’s important to remember that no one of these factors mean that you’ll have a baby with Down syndrome. However, statistically and over a large population, they may increase the chance that you may.

## What are the symptoms of Down syndrome?

Though the likelihood of carrying a baby with Down syndrome can be estimated by screening during pregnancy, you won’t experience any symptoms of carrying a child with Down syndrome.

At birth, babies with Down syndrome usually have certain characteristic signs, including:

* flat facial features
* small head and ears
* short neck
* bulging tongue
* eyes that slant upward
* atypically shaped ears
* poor muscle tone

An infant with Down syndrome can be born an average size but will develop more slowly than a child without the condition.

People with Down syndrome usually have some degree of developmental disability, but it’s often mild to moderate. Mental and social development delays may mean that the child could have:

* impulsive behavior
* poor judgment
* short attention span
* slow learning capabilities

Medical complications often accompany Down syndrome. These may include:

* [congenital heart defects](https://www.healthline.com/health/congenital-heart-disease)
* [hearing loss](https://www.healthline.com/symptom/hearing-loss)
* poor vision
* [cataracts](https://www.healthline.com/health/cataract) (clouded eyes)
* hip problems, such as [dislocations](https://www.healthline.com/health/dislocation)
* [leukaemia](https://www.healthline.com/health/leukemia)
* [chronic constipation](https://www.healthline.com/health/cic/what-does-it-mean)
* [sleep apnea](https://www.healthline.com/health/sleep/central-sleep-apnea) (interrupted breathing during sleep)
* [dementia](https://www.healthline.com/health/dementia) (thought and memory problems)
* [hypothyroidism](https://www.healthline.com/health/hypothyroidism-primary) (low thyroid function)
* [obesity](https://www.healthline.com/health/obesity)
* late tooth growth, causing problems with chewing
* [Alzheimer’s disease](https://www.healthline.com/health/alzheimers-disease) later in life

People with Down syndrome are also more prone to infection. They may struggle with [respiratory infections](https://www.healthline.com/health/acute-respiratory-disease), [urinary tract infections](https://www.healthline.com/health/urinary-tract-infection-adults), and [skin infections](https://www.healthline.com/health/skin-infection).

## Screening for Down syndrome during pregnancy

Screening for Down syndrome is offered as a routine part of prenatal care in the United States. If you’re a woman over 35, your baby’s father is over 40, or there’s a family history of Down syndrome, you may want to get an evaluation.

### First trimester

An [ultrasound evaluation](https://www.healthline.com/health/pregnancy/checkups-tests) and blood tests can look for Down syndrome in your fetus. These tests have a higher false-positive rate than tests done at later pregnancy stages. If results aren’t normal, your doctor may follow up with an amniocentesis after your 15th week of pregnancy.

### Second trimester

An ultrasound and quadruple marker screen (QMS) test can help identify Down syndrome and other defects in the brain and spinal cord. This test is done between 15 and 20 weeks of pregnancy.

If any of these tests aren’t normal, you’ll be considered at high risk for birth defects.

### Additional prenatal tests

Your doctor may order additional tests to detect Down syndrome in your baby. These may include:

* **Amniocentesis.** Your doctor takes a [sample of amniotic fluid](https://www.healthline.com/health/amniocentesis) to examine the number of chromosomes your baby has. The test is usually done after 15 weeks.
* **Chorionic villus sampling (CVS).** Your doctor will [take cells from your placenta](https://www.healthline.com/health/chorionic-villus-sampling) to analyze fetal chromosomes. This test is done between the 9th and 14th week of pregnancy. It can increase your risk of a miscarriage, but according to the Mayo Clinic, only by less than [1 percent](https://www.mayoclinic.org/tests-procedures/chorionic-villus-sampling/basics/risks/prc-20013566).
* **Percutaneous umbilical blood sampling (PUBS, or cordocentesis).** Your doctor will take blood from the umbilical cord and examine it for chromosomal defects. It’s done after the 18th week of pregnancy. It has a higher risk of miscarriage, so it’s performed only if all other tests are uncertain.

Some women choose not to undergo these tests because of the risk of [miscarriage](https://www.healthline.com/health/miscarriage). They’d rather have a child with Down syndrome than lose the pregnancy.

### Tests at birth

At birth, your doctor will:

* perform a physical examination of your baby
* order a blood test called a [karyotype](https://www.healthline.com/health/karyotyping) to confirm Down syndrome

## Treating Down syndrome

There’s no cure for Down syndrome, but there’s a wide variety of support and educational programs that can help both people with the condition and their families. The [NDSS](http://www.ndss.org/Resources/Local-Support/) is just one place to look for programs nationwide.

Available programs start with interventions in infancy. [Federal law](http://idea.ed.gov/) requires that states offer therapy programs for qualifying families. In these programs, special education teachers and therapists will help your child learn:

* sensory skills
* social skills
* self-help skills
* motor skills
* language and cognitive abilities
* **Turner syndrome**

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## **Symptoms**

Signs and symptoms of Turner syndrome may vary among girls and women with the disorder. For some girls, the presence of Turner syndrome may not be readily apparent, but in other girls, several physical features and poor growth are apparent early. Signs and symptoms can be subtle, developing slowly over time, or significant, such as heart defects.

### Before birth

Turner syndrome may be suspected prenatally based on prenatal cell-free DNA screening ― a method to screen for certain chromosomal abnormalities in a developing baby using a blood sample from the mother ― or prenatal ultrasound. Prenatal ultrasound of a baby with Turner syndrome may show:

* Large fluid collection on the back of the neck or other abnormal fluid collections (edema)
* Heart abnormalities
* Abnormal kidneys

### At birth or during infancy

Signs of Turner syndrome at birth or during infancy may include:

* Wide or weblike neck
* Low-set ears
* Broad chest with widely spaced nipples
* High, narrow roof of the mouth (palate)
* Arms that turn outward at the elbows
* Fingernails and toenails that are narrow and turned upward
* Swelling of the hands and feet, especially at birth
* Slightly smaller than average height at birth
* Slowed growth
* Cardiac defects
* Low hairline at the back of the head
* Receding or small lower jaw
* Short fingers and toes

### In childhood, teens and adulthood

The most common signs in almost all girls, teenagers and young women with Turner syndrome are short stature and ovarian insufficiency due to ovarian failure that may have occurred by birth or gradually during childhood, the teen years or young adulthood. Signs and symptoms of these include:

* Slowed growth
* No growth spurts at expected times in childhood
* Adult height significantly less than might be expected for a female member of the family
* Failure to begin sexual changes expected during puberty
* Sexual development that "stalls" during teenage years
* Early end to menstrual cycles not due to pregnancy
* For most women with Turner syndrome, inability to conceive a child without fertility treatment

### When to see a doctor

Sometimes it's difficult to distinguish the signs and symptoms of Turner syndrome from other disorders. It's important to get a prompt, accurate diagnosis and appropriate care. See your doctor if you have concerns about physical or sexual development

## **Causes**

Most people are born with two sex chromosomes. Boys inherit the X chromosome from their mothers and the Y chromosome from their fathers. Girls inherit one X chromosome from each parent. In girls who have Turner syndrome, one copy of the X chromosome is missing, partially missing or altered.

The genetic alterations of Turner syndrome may be one of the following:

* **Monosomy.** The complete absence of an X chromosome generally occurs because of an error in the father's sperm or in the mother's egg. This results in every cell in the body having only one X chromosome.



* **Mosaicism.** In some cases, an error occurs in cell division during early stages of fetal development. This results in some cells in the body having two complete copies of the X chromosome. Other cells have only one copy of the X chromosome.
* **X chromosome abnormalities.** Abnormal or missing parts of one of the X chromosomes can occur. Cells have one complete and one altered copy. This error can occur in the sperm or egg with all cells having one complete and one altered copy. Or the error can occur in cell division in early fetal development so that only some cells contain the abnormal or missing parts of one of the X chromosomes (mosaicism).
* **Y chromosome material.** In a small percentage of Turner syndrome cases, some cells have one copy of the X chromosome and other cells have one copy of the X chromosome and some Y chromosome material. These individuals develop biologically as female, but the presence of Y chromosome material increases the risk of developing a type of cancer called gonad blastoma.

### Effect of the chromosomal errors

The missing or altered X chromosome of Turner syndrome causes errors during fetal development and other developmental problems after birth — for example, short stature, ovarian insufficiency and heart defects. Physical characteristics and health complications that arise from the chromosomal error vary greatly.

## **Risk factors**

The loss or alteration of the X chromosome occurs randomly. Sometimes, it's because of a problem with the sperm or the egg, and other times, the loss or alteration of the X chromosome happens early in fetal development.

Family history doesn't seem to be a risk factor, so it's unlikely that parents of one child with Turner syndrome will have another child with the disorder.

## **Complications**

Turner syndrome can affect the proper development of several body systems but varies greatly among individuals with the syndrome. Complications that can occur include:

* **Heart problems.** Many infants with Turner syndrome are born with heart defects or even slight abnormalities in heart structure that increase their risk of serious complications. Heart defects often include problems with the aorta, the large blood vessel that branches off the heart and delivers oxygen-rich blood to the body.
* **High blood pressure.** Women with Turner syndrome have an increased risk of high blood pressure — a condition that increases the risk of developing diseases of the heart and blood vessels.
* **Hearing loss.** Hearing loss is common with Turner syndrome. In some cases, this is due to the gradual loss of nerve function. An increased risk of frequent middle ear infections can also result in hearing loss.
* **Vision problems.** Girls with Turner syndrome have an increased risk of weak muscle control of eye movements (strabismus), near sightedness and other vision problems.
* **Kidney** **problems.** Girls with Turner syndrome may have some malformation of the kidneys. Although these abnormalities generally don't cause medical problems, they may increase the risk of high blood pressure and urinary tract infections.
* **Autoimmune disorders.** Girls and women with Turner syndrome have an increased risk of an underactive thyroid (hypothyroidism) due to the autoimmune disorder Hashimoto's thyroiditis. They also have an increased risk of diabetes. Some women with Turner syndrome have gluten intolerance (celiac disease) or inflammatory bowel disease.
* **Skeletal problems.** Problems with the growth and development of bones increase the risk of abnormal curvature of the spine (scoliosis) and forward rounding of the upper back (kyphosis). Women with Turner syndrome are also at increased risk of developing weak, brittle bones (osteoporosis).
* **Learning disabilities.** Girls and women with Turner syndrome usually have normal intelligence. However, there is increased risk of learning disabilities, particularly with learning that involves spatial concepts, math, memory and attention.
* **Mental health issues.** Girls and women with Turner syndrome may have difficulties functioning well in social situations and have an increased risk of attention-deficit/hyperactivity disorder (ADHD).
* **Infertility.** Most women with Turner syndrome are infertile. However, a very small number of women may become pregnant spontaneously, and some can become pregnant with fertility treatment.

# **Pregnancy complications.** Because women with Turner syndrome are at increased risk of complications during pregnancy, such as high blood pressure and aortic dissection, they should be evaluated by a cardiologist before pregnancy.[**Klinefelter syndrome**](https://www.mayoclinic.org/diseases-conditions/klinefelter-syndrome/symptoms-causes/syc-20353949)

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[Symptoms & causes](https://www.mayoclinic.org/diseases-conditions/klinefelter-syndrome/symptoms-causes/syc-20353949). Most men with Klinefelter syndrome produce little or no sperm but assisted reproductive procedures may make it possible for some men with Klinefelter syndrome to father children.

## **Symptoms**

Signs and symptoms of Klinefelter syndrome vary widely among males with the disorder. Many boys with Klinefelter syndrome show few or only mild signs. The condition may go undiagnosed until adulthood or it may never be diagnosed. For others, the condition has a noticeable effect on growth or appearance.

Signs and symptoms of Klinefelter syndrome also vary by age.

### Babies

Signs and symptoms may include:

* Weak muscles
* Slow motor development — taking longer than average to sit up, crawl and walk
* Delay in speaking
* Problems at birth, such as testicles that haven't descended into the scrotum

### Boys and teenagers

Signs and symptoms may include:

* Taller than average stature
* Longer legs, shorter torso and broader hips compared with other boys
* Absent, delayed or incomplete puberty
* After puberty, less muscle and less facial and body hair compared with other teens
* Small, firm testicles
* Small penis
* Enlarged breast tissue (gynecomastia)
* Weak bones
* Low energy levels
* Tendency to be shy and sensitive
* Difficulty expressing thoughts and feelings or socializing
* Problems with reading, writing, spelling or math

### Men

Signs and symptoms may include:

* Low sperm count or no sperm
* Small testicles and penis
* Low sex drive
* Taller than average height
* Weak bones
* Decreased facial and body hair
* Less muscular compared with other men
* Enlarged breast tissue
* Increased belly fat

## **Causes**

Klinefelter syndrome occurs as a result of a random error that causes a male to be born with an extra sex chromosome. It isn't an inherited condition.

Humans have 46 chromosomes, including two sex chromosomes that determine a person's sex. Females have two X sex chromosomes (XX). Males have an X and a Y sex chromosome (XY).

Klinefelter syndrome can be caused by:

* One extra copy of the X chromosome in each cell (XXY), the most common cause
* An extra X chromosome in some of the cells (mosaic Klinefelter syndrome), with fewer symptoms
* More than one extra copy of the X chromosome, which is rare and results in a severe form

Extra copies of genes on the X chromosome can interfere with male sexual development and fertility.

## **Risk factors**

Klinefelter syndrome stems from a random genetic event. The risk of Klinefelter syndrome isn't increased by anything a parent does or doesn't do. For older mothers, the risk is higher but only slightly.

## **Complications**

Klinefelter syndrome may increase the risk of:

* Anxiety and depression
* Social, emotional and behavioral problems, such as low self-esteem, emotional immaturity and impulsiveness
* Infertility and problems with sexual function
* Weak bones (osteoporosis)
* Heart and blood vessel disease
* Breast cancer and certain other cancers
* Lung disease
* Metabolic syndrome, which includes type 2 diabetes, high blood pressure (hypertension), and high cholesterol and triglyceride

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# XYY Syndrome

## What is XYY syndrome?

Most people have 46 chromosomes in each cell. In males, this typically includes one X chromosome and one Y chromosome (XY). XYY syndrome is a genetic condition that occurs when a male has an extra copy of the Y chromosome in each of their cells (XYY). Sometimes, this mutation is only present in some cells. Males with XYY syndrome have 47 chromosomes because of the extra Y chromosome.

This condition is also sometimes called Jacob’s syndrome, XYY karyotype, or YY syndrome. According to the National Institutes of Health, XYY syndrome occurs in [1 out of every 1,000](http://ghr.nlm.nih.gov/condition/47xyy-syndrome#diagnosis) boys.

For the most part, people with XYY syndrome live typical lives. Some may be taller than average and face learning difficulties or speech problems. They may also grow up with minor physical differences, such as weaker muscle tone. Besides these complications, though, males with XYY syndrome don’t usually have any distinguishing physical features, and they have normal sexual development.

## What causes XYY syndrome?

XYY syndrome is the result of a random mix-up, or mutation, during the creation of a male’s genetic code. Most cases of XYY syndrome are not inherited. Researchers don’t believe that there’s any genetic predisposition to it. That is, men with XYY syndrome are not more or less likely than other men to have children with XYY syndrome. The random error can occur during the formation of sperm or at different times during the formation of an embryo. In the latter case, a male may have some cells that are not affected. This means that some cells may have XY genotype while others have XYY genotype.

## What are the symptoms of XYY syndrome?

The signs and symptoms of XYY syndrome differ from person to person and age to age.

Symptoms in a baby who has XYY syndrome can include:

* hypotonia (weak muscle tone)
* delayed motor skill development, such as with walking or crawling
* delayed or difficult speech

Symptoms in a young child or teenager with XYY syndrome can include:

* an autism diagnosis
* attention difficulties
* delayed motor skill development, such as with writing
* delayed or difficult speech
* emotional or behavioral issues
* hand trembling or involuntary muscle movements
* hypotonia (weak muscle tone)
* learning disabilities
* taller-than-average height

# **Patau syndrome**

* **Patau syndrome** is a [syndrome](https://en.wikipedia.org/wiki/Syndrome) caused by a [chromosomal](https://en.wikipedia.org/wiki/Chromosome) abnormality, in which some or all of the [cells](https://en.wikipedia.org/wiki/Cell_(biology)) of the body contain extra genetic material from [chromosome 13](https://en.wikipedia.org/wiki/Chromosome_13_(human)). The extra genetic material disrupts normal development, causing multiple and complex organ defects.
* This can occur either because each cell contains a full extra copy of chromosome 13 (a disorder known as **trisomy 13** or **trisomy D**), or because each cell contains an extra partial copy of the chromosome or because of [mosaic](https://en.wikipedia.org/wiki/Mosaicism) Patau syndrome. Full trisomy 13 is caused by [nondisjunction](https://en.wikipedia.org/wiki/Nondisjunction) of chromosomes during [meiosis](https://en.wikipedia.org/wiki/Meiosis) (the mosaic form is caused by nondisjunction during [mitosis](https://en.wikipedia.org/wiki/Mitosis)).

## **Signs and symptoms**

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* Nervous system
  + [Intellectual disability](https://en.wikipedia.org/wiki/Intellectual_disability) and [motor disorder](https://en.wikipedia.org/wiki/Developmental_coordination_disorder)
  + [Microcephaly](https://en.wikipedia.org/wiki/Microcephaly)
  + [Holoprosencephaly](https://en.wikipedia.org/wiki/Holoprosencephaly) (failure of the forebrain to divide properly).
  + Structural eye defects, including [microphthalmia](https://en.wikipedia.org/wiki/Microphthalmia), [Peters' anomaly](https://en.wikipedia.org/wiki/Anterior_segment_mesenchymal_dysgenesis), [cataract](https://en.wikipedia.org/wiki/Cataract), iris or fundus ([coloboma](https://en.wikipedia.org/wiki/Coloboma)), retinal dysplasia or [retinal detachment](https://en.wikipedia.org/wiki/Retinal_detachment), sensory [nystagmus](https://en.wikipedia.org/wiki/Pathologic_nystagmus), [cortical visual loss](https://en.wikipedia.org/wiki/Cortical_visual_loss), and [optic nerve hypoplasia](https://en.wikipedia.org/wiki/Optic_nerve_hypoplasia)
  + [Meningomyelocele](https://en.wikipedia.org/wiki/Meningomyelocele) (a [spinal](https://en.wikipedia.org/wiki/Spinal_cord) defect)
* Musculoskeletal and cutaneous
  + [Polydactyly](https://en.wikipedia.org/wiki/Polydactyly) (extra digits)
  + [Cyclopia](https://en.wikipedia.org/wiki/Cyclopia)
  + [Proboscis](https://en.wikipedia.org/wiki/Proboscis_(anomaly))
  + [Congenital trigger digits](https://en.wikipedia.org/wiki/Congenital_trigger_thumb)
  + [Low-set ears](https://en.wikipedia.org/wiki/Low-set_ears)[[3]](https://en.wikipedia.org/wiki/Patau_syndrome#cite_note-Ostler2004-3)
  + Prominent heel
  + Deformed feet known as [rocker-bottom feet](https://en.wikipedia.org/wiki/Rocker-bottom_feet)
  + [Omphalocele](https://en.wikipedia.org/wiki/Omphalocele) ([abdominal](https://en.wikipedia.org/wiki/Abdomen) defect)
  + Abnormal [palm](https://en.wikipedia.org/wiki/Hand) pattern
  + Overlapping of fingers over [thumb](https://en.wikipedia.org/wiki/Thumb)
  + [Cutis aplasia](https://en.wikipedia.org/wiki/Cutis_aplasia) (missing portion of the skin/hair)
  + [Cleft palate](https://en.wikipedia.org/wiki/Cleft_palate)
* Urogenital
  + Abnormal [genitalia](https://en.wikipedia.org/wiki/Genitalia)
  + [Kidney defects](https://en.wikipedia.org/wiki/Kidney_defects)
* Other
  + [Heart defects](https://en.wikipedia.org/wiki/Heart_defects) ([ventricular septal defect](https://en.wikipedia.org/wiki/Ventricular_septal_defect)) ([Patent Ductus Arteriosus](https://en.wikipedia.org/wiki/Patent_Ductus_Arteriosus))
  + [Dextrocardia](https://en.wikipedia.org/wiki/Dextrocardia)
  + [Single umbilical artery](https://en.wikipedia.org/wiki/Single_umbilical_artery)[[4]](https://en.wikipedia.org/wiki/Patau_syndrome#cite_note-urlTrisomy_13:_MedlinePlus_Medical_Encyclopedia-4)

## **Causes**

Patau syndrome is the result of [trisomy](https://en.wikipedia.org/wiki/Trisomy) 13, meaning each cell in the body has three copies of chromosome 13 instead of the usual two. A small percentage of cases occur when only some of the body's cells have an extra copy; such cases are called mosaic Patau.

Patau syndrome can also occur when part of chromosome 13 becomes attached to another chromosome (translocated) before or at conception in a [Robertsonian translocation](https://en.wikipedia.org/wiki/Robertsonian_translocation). Affected people have two copies of chromosome 13, plus extra material from chromosome 13 attached to another chromosome. With a translocation, the person has a partial trisomy for chromosome 13 and often the physical signs of the syndrome differ from the typical Patau syndrome.

Most cases of Patau syndrome are not inherited but occur as random events during the formation of reproductive cells (eggs and sperm). An error in cell division called [non-disjunction](https://en.wikipedia.org/wiki/Non-disjunction) can result in reproductive cells with an abnormal number of chromosomes. For example, an [egg](https://en.wikipedia.org/wiki/Ovum) or [sperm](https://en.wikipedia.org/wiki/Spermatozoon) cell may gain an extra copy of the chromosome. If one of these atypical reproductive cells contributes to the genetic makeup of a child, the child will have an extra chromosome 13 in each of the body's cells. [Mosaic](https://en.wikipedia.org/wiki/Mosaicism) Patau syndrome is also not inherited. It occurs as a random error during cell division early in [fetal](https://en.wikipedia.org/wiki/Fetal) development.

Patau syndrome due to a translocation can be inherited. An unaffected person can carry a rearrangement of genetic material between chromosome 13 and another chromosome. This rearrangement is called a balanced translocation because there is no extra material from chromosome 13. Although they do not have signs of Patau syndrome, people who carry this type of balanced translocation are at an increased risk of having children with the condition.

## **Treatment**

Medical management of children with Trisomy 13 is planned on a case-by-case basis and depends on the individual circumstances of the patient. Treatment of Patau syndrome focuses on the physical problems with which each child is born. Many infants have difficulty surviving the first few days or weeks due to severe neurological problems or complex [heart defects](https://en.wikipedia.org/wiki/Heart_defects). Surgery may be necessary to repair heart defects or [cleft lip](https://en.wikipedia.org/wiki/Cleft_lip) and [cleft palate](https://en.wikipedia.org/wiki/Cleft_palate). Physical, occupational, and speech therapy will help individuals with Patau syndrome reach their full developmental potential. Surviving children are described as happy and parents report that they enrich their lives.[[6]](https://en.wikipedia.org/wiki/Patau_syndrome#cite_note-6) The cited study grouped [Edwards syndrome](https://en.wikipedia.org/wiki/Edwards_syndrome), which is sometimes survivable beyond toddlerhood, along with Patau, hence the median age of 4 at the time of data collection

# **Edwards syndrome**

**Edwards syndrome**, also known as **trisomy 18**, is a [genetic disorder](https://en.wikipedia.org/wiki/Genetic_disorder) caused by the presence of a third copy of all or part of [chromosome 18](https://en.wikipedia.org/wiki/Chromosome_18_(human)).[[2]](https://en.wikipedia.org/wiki/Edwards_syndrome#cite_note-NIH2012-2) Many parts of the body are affected.[[2]](https://en.wikipedia.org/wiki/Edwards_syndrome#cite_note-NIH2012-2) Babies are often [born small](https://en.wikipedia.org/wiki/Intrauterine_growth_retardation) and have [heart defects](https://en.wikipedia.org/wiki/Congenital_heart_defects).[[2]](https://en.wikipedia.org/wiki/Edwards_syndrome#cite_note-NIH2012-2) Other features include a [small head](https://en.wikipedia.org/wiki/Small_head), [small jaw](https://en.wikipedia.org/wiki/Small_jaw), clenched fists with overlapping fingers, and severe [intellectual disability](https://en.wikipedia.org/wiki/Intellectual_disability).[[2]](https://en.wikipedia.org/wiki/Edwards_syndrome#cite_note-NIH2012-2)

Most cases of Edwards syndrome occur due to problems during the formation of the [reproductive cells](https://en.wikipedia.org/wiki/Reproductive_cells) or during [early development](https://en.wikipedia.org/wiki/Embryonic_development).[[2]](https://en.wikipedia.org/wiki/Edwards_syndrome#cite_note-NIH2012-2) The rate of disease increases with the [mother's age](https://en.wikipedia.org/wiki/Advanced_maternal_age).[[2]](https://en.wikipedia.org/wiki/Edwards_syndrome#cite_note-NIH2012-2) Rarely, cases may be [inherited from a person's parents](https://en.wikipedia.org/wiki/Heredity).[[2]](https://en.wikipedia.org/wiki/Edwards_syndrome#cite_note-NIH2012-2) Occasionally, not all cells have the extra chromosome, known as [mosaic trisomy](https://en.wikipedia.org/wiki/Mosaic_trisomy), and symptoms in these cases may be less severe.[[2]](https://en.wikipedia.org/wiki/Edwards_syndrome#cite_note-NIH2012-2) An [ultrasound during pregnancy](https://en.wikipedia.org/wiki/Prenatal_ultrasound) can increase suspicion for the condition, which can be confirmed by [amniocentesis](https://en.wikipedia.org/wiki/Amniocentesis)

## **Signs and symptoms[**[**edit**](https://en.wikipedia.org/w/index.php?title=Edwards_syndrome&action=edit&section=1)**]**



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Children born with Edwards syndrome may have some or all of these characteristics: kidney malformations, structural heart defects at birth (i.e., [ventricular septal defect](https://en.wikipedia.org/wiki/Ventricular_septal_defect), [atrial septal defect](https://en.wikipedia.org/wiki/Atrial_septal_defect), [patent ductus arteriosus](https://en.wikipedia.org/wiki/Patent_ductus_arteriosus)), intestines protruding outside the body ([omphalocele](https://en.wikipedia.org/wiki/Omphalocele)), [oesophageal atresia](https://en.wikipedia.org/wiki/Esophageal_atresia), [intellectual disability](https://en.wikipedia.org/wiki/Intellectual_disability), developmental delays, growth deficiency, [feeding difficulties](https://en.wikipedia.org/wiki/Feeding_difficulties), [breathing difficulties](https://en.wikipedia.org/wiki/Breathing_difficulties), and [arthrogryposis](https://en.wikipedia.org/wiki/Arthrogryposis) (a muscle disorder that causes multiple joint [contractures](https://en.wikipedia.org/wiki/Contractures) at birth).[[6]](https://en.wikipedia.org/wiki/Edwards_syndrome#cite_note-What_is-6)[[7]](https://en.wikipedia.org/wiki/Edwards_syndrome#cite_note-medline-7)

Some physical malformations associated with Edwards syndrome include small head ([microcephaly](https://en.wikipedia.org/wiki/Microcephaly)) accompanied by a prominent back portion of the head ([occiput](https://en.wikipedia.org/wiki/Occiput)), low-set, malformed ears, abnormally small jaw ([micrognathia](https://en.wikipedia.org/wiki/Micrognathia)), [cleft lip](https://en.wikipedia.org/wiki/Cleft_lip)/[cleft palate](https://en.wikipedia.org/wiki/Cleft_palate), upturned nose, narrow eyelid openings, widely spaced eyes ([ocular hypertelorism](https://en.wikipedia.org/wiki/Ocular_hypertelorism)), drooping of the upper eyelids ([ptosis](https://en.wikipedia.org/wiki/Ptosis_(eyelid))), a short breast bone, clenched hands, [choroid plexus cysts](https://en.wikipedia.org/wiki/Choroid_plexus_cysts), underdeveloped thumbs and/or nails, [absent radius](https://en.wikipedia.org/wiki/Absent_radius), [webbing](https://en.wikipedia.org/wiki/Webbed_toes) of the second and third toes, [clubfoot](https://en.wikipedia.org/wiki/Clubfoot) or [rocker bottom feet](https://en.wikipedia.org/wiki/Rocker_bottom_feet), and in males, [undescended testicles](https://en.wikipedia.org/wiki/Undescended_testicles).[[6]](https://en.wikipedia.org/wiki/Edwards_syndrome#cite_note-What_is-6)[[7]](https://en.wikipedia.org/wiki/Edwards_syndrome#cite_note-medline-7)

*In utero*, the most common characteristic is cardiac anomalies, followed by [central nervous system](https://en.wikipedia.org/wiki/Central_nervous_system) anomalies such as head shape abnormalities. The most common intracranial anomaly is the presence of choroid plexus cysts, which are pockets of fluid on the brain. These are not problematic in themselves, but their presence may be a marker for trisomy 18.[[8]](https://en.wikipedia.org/wiki/Edwards_syndrome#cite_note-pmid17357350-8)[[9]](https://en.wikipedia.org/wiki/Edwards_syndrome#cite_note-pmid17206726-9) Sometimes, excess [amniotic fluid](https://en.wikipedia.org/wiki/Amniotic_fluid) or [polyhydramnios](https://en.wikipedia.org/wiki/Polyhydramnios) is exhibited.[[6]](https://en.wikipedia.org/wiki/Edwards_syndrome#cite_note-What_is-6) Although uncommon in the syndrome, Edwards syndrome causes a large portion of prenatal cases of [Dandy–Walker malformation](https://en.wikipedia.org/wiki/Dandy%E2%80%93Walker_malformation).[[10]](https://en.wikipedia.org/wiki/Edwards_syndrome#cite_note-:13-10)[[11]](https://en.wikipedia.org/wiki/Edwards_syndrome#cite_note-:1-11)

## **Genetics**

Edwards syndrome is a chromosomal abnormality characterized by the presence of an extra copy of genetic material on the 18th chromosome, either in whole ([trisomy](https://en.wikipedia.org/wiki/Trisomy) 18) or in part (such as due to [translocations](https://en.wikipedia.org/wiki/Chromosomal_translocation)). The additional chromosome usually occurs before [conception](https://en.wikipedia.org/wiki/Fertilisation). The effects of the extra copy vary greatly, depending on the extent of the extra copy, genetic history, and chance. Edwards syndrome occurs in all human populations, but is more prevalent in female offspring.[[12]](https://en.wikipedia.org/wiki/Edwards_syndrome#cite_note-emed-12)

A healthy egg and/or sperm cell contains individual chromosomes, each of which contributes to the 23 pairs of chromosomes needed to form a normal cell with a typical human [karyotype](https://en.wikipedia.org/wiki/Karyotype) of 46 chromosomes. Numerical errors can arise at either of the two [meiotic](https://en.wikipedia.org/wiki/Meiotic) divisions and cause the failure of a chromosome to segregate into the daughter cells ([nondisjunction](https://en.wikipedia.org/wiki/Nondisjunction)). This results in an extra chromosome, making the [haploid](https://en.wikipedia.org/wiki/Haploid) number 24 rather than 23. Fertilization of eggs or insemination by sperm that contain an extra chromosome results in trisomy, or three copies of a chromosome rather than two.[[13]](https://en.wikipedia.org/wiki/Edwards_syndrome#cite_note-13)

Trisomy 18 (47, XX, +18) is caused by a meiotic nondisjunction event. With nondisjunction, a [gamete](https://en.wikipedia.org/wiki/Gamete) (*i.e.*, a sperm or egg cell) is produced with an extra copy of chromosome 18; the gamete thus has 24 chromosomes. When combined with a normal gamete from the other parent, the [embryo](https://en.wikipedia.org/wiki/Embryo) has 47 chromosomes, with three copies of chromosome 18.

A small percentage of cases occur when only some of the body's cells have an extra copy of chromosome 18, resulting in a mixed population of cells with a differing number of chromosomes. Such cases are sometimes called [mosaic](https://en.wikipedia.org/wiki/Mosaic_(genetics)) Edwards syndrome. Very rarely, a piece of chromosome 18 becomes attached to another chromosome (translocated) before or after conception. Affected individuals have two copies of chromosome 18 plus extra material from chromosome 18 attached to another chromosome. With a translocation, a person has a partial trisomy for chromosome 18, and the abnormalities are often less severe than for the typical Edwards syndrome.

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**Triple X syndrome,**

Triple X syndrome, also called trisomy X or 47, XXX, is a genetic disorder that affects about 1 in 1,000 females. Females normally have two X chromosomes in all cells — one X chromosome from each parent. In triple X syndrome, a female has three X chromosomes. 

Many girls and women with triple X syndrome don't experience symptoms or have only mild symptoms. In others, symptoms may be more apparent — possibly including developmental delays and learning disabilities. Seizures and kidney abnormalities occur in a small number of girls and women with triple X syndrome.

Treatment for triple X syndrome depends on which symptoms, if any, are present and their severity.

## **Symptoms**

Signs and symptoms can vary greatly among girls and women with triple X syndrome. Many experiences no noticeable effects or have only mild symptoms.

Being taller than average height is the most typical physical feature. Most females with triple X syndrome experience normal sexual development and can become pregnant. Some girls and women with triple X syndrome have intelligence in the normal range, but possibly slightly lower when compared with siblings. Others may have intellectual disabilities and sometimes may have behavioral problems.

Occasionally significant symptoms may occur. If signs and symptoms are present, they are often variable. Signs and symptoms in girls and women with triple X syndrome may include an increased risk of:

* Delayed development of speech and language skills, as well as motor skills, such as sitting up and walking
* Learning disabilities, such as difficulty with reading (dyslexia), understanding or math
* Behavioral problems, such as attention-deficit/hyperactivity disorder (ADHD) or symptoms of autism spectrum disorder
* Psychological problems, such as anxiety and depression
* Problems with fine and gross motor skills, memory, judgment and information processing

Sometimes triple X syndrome may be associated with these signs and symptoms:

* Vertical folds of skin that cover the inner corners of the eyes (epicanthal folds)
* Widely spaced eyes
* Abnormally curved pinky fingers
* Flat feet
* Abnormally shaped breastbone
* Weak muscle tone (hypotonia)
* Seizures
* Kidney abnormalities
* Premature ovarian failure or ovary abnormalities
* Developmental delays

### When to see a doctor

If you're concerned about your child's development, make an appointment to talk with your family doctor or pediatrician. Your doctor can help determine the cause and suggest appropriate action.

## **Causes**

## Although triple X syndrome is genetic, it's usually not inherited — it's due to a random genetic error.

Normally, people have 46 chromosomes in each cell, organized into 23 pairs, including two sex chromosomes. One set of chromosomes is from the mother and the other set is from the father. These chromosomes contain genes, which carry instructions that determine everything from height to eye color.

The pair of sex chromosomes — either XX or XY — determines a child's sex. A mother can give the child only an X chromosome, but a father can pass on an X or a Y chromosome:

* If the child receives an X chromosome from the father, the XX pair makes the child genetically a female.
* If the child receives a Y chromosome from the father, the XY pair means the child is genetically a male.

Females with triple X syndrome have a third X chromosome from a random error in cell division. This error can happen before conception or early in the embryo's development, resulting in one of these forms of triple X syndrome:

* **Nondisjunction.** In most cases, either the mother's egg cell or the father's sperm cell divides incorrectly, resulting in an extra X chromosome in the child. This random error is called nondisjunction, and all the cells in the child's body will have the extra X chromosome.
* **Mosaic.** Occasionally, the extra chromosome results from an incorrect cell division caused by a random event early in the embryo's development. If this is the case, the child has a mosaic form of triple X syndrome, and only some cells have the extra X chromosome. Females with the mosaic form may have less obvious symptoms.

Triple X syndrome is also called 47, XXX syndrome because the extra X chromosome results in 47 chromosomes in each cell instead of the usual 46.

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## Chromosomal Basis of Inherited Disorders

## Disorders in Chromosome Number

#### Key Points

* Aneuploidy is caused by nondisjunction, which occurs when pairs of homologous chromosomes or sister chromatids fail to separate during meiosis.
* The loss of a single chromosome from a diploid genome is called monosomy (2n-1), while the gain of one chromosome is called trisomy (2n+1).
* If homologous chromosomes fail to separate during meiosis I, the result is no gametes with the normal number (one) of chromosomes.
* If sister chromatids fail to separate during meiosis II, the result is two normal gametes each with one copy of the chromosome, and two abnormal gametes in which one carries two copies and the other carries none.
* Aneuploidy can be lethal or result in serious developmental disorders such as Turner Syndrome (X monosomy) or Downs Syndrome (trisomy 21).

#### Key Terms

* **aneuploidy**: the state of possessing a chromosome number that is not an exact multiple of the haploid number
* **nondisjunction**: the failure of chromosome pairs to separate properly during meiosis

### Disorders in Chromosome Number

Of all the chromosomal disorders, abnormalities in chromosome number are the most obviously identifiable from a karyotype and are referred to as aneuploidy. Aneuploidy is a condition in which one or more chromosomes are present in extra copies or are deficient in number, but not a complete set. To be more specific, the loss of a single chromosome from a diploid genome is called monosomy (2n-1). The gain of one chromosome is called trisomy (2n+1). They are caused by nondisjunction, which occurs when pairs of homologous chromosomes or sister chromatids fail to separate during meiosis. Misaligned or incomplete synapsis, or a dysfunction of the spindle apparatus that facilitates chromosome migration, can cause nondisjunction. The risk of nondisjunction occurring increases with the age of the parents.

Nondisjunction can occur during either meiosis I or II, with differing results. If homologous chromosomes fail to separate during meiosis I, the result is two gametes that lack that chromosome and two gametes with two copies of the chromosome. If sister chromatids fail to separate during meiosis II, the result is one gamete that lacks that chromosome, two normal gametes with one copy of the chromosome, and one gamete with two copies of the chromosome. If a gamete with two copies of the chromosome combines with a normal gamete during fertilization, the result is trisomy; if a gamete with no copies of the chromosomes combines with a normal gamete during fertilization, the result is monosomy.

**Nondisjunction in Meiosis**: Nondisjunction occurs when homologous chromosomes or sister chromatids fail to separate during meiosis, resulting in an abnormal chromosome number. Nondisjunction may occur during meiosis I or meiosis II.

Aneuploidy often results in serious problems such as Turner syndrome, a monosomy in which females may contain all or part of an X chromosome. Monosomy for autosomes is usually lethal in humans and other animals. Klinefelter syndrome is a trisomy genetic disorder in males caused by the presence of one or more X chromosomes. The effects of trisomy are like those of monosomy. Down syndrome is the only autosomal trisomy in humans that has a substantial number of survivors one year after birth. Trisomy in chromosome 21 is the cause of Down syndrome; it affects 1 infant in every 800 live births.

## Chromosomal Structural Rearrangements

* A chromosome inversion is the detachment, 180° rotation, and reinsertion of part of a chromosome; this may have no effect on the organism, but if the inversion occurs within a gene or moves a gene away from its regulatory elements it can have an adverse effect.
* Pericentric inversions include the centromere, while paracentric inversions occur outside of the centromere; a pericentric inversion can change the length of the chromosome arms above and below the centromere.
* A pericentric inversion on chromsome 18 appears to have been involved in the evolution of humans.
* A translocation occurs when a segment of a chromosome dissociates and reattaches to a different, nonhomologous chromosome and can be benign or detrimental; in reciprocal translocations, there is no gain or loss of genetic information, so these are usually benign.
* **inversion**: a segment of DNA in the context of a chromosome that is reversed in orientation relative to a reference karyotype or genome
* **translocation**: a transfer of a chromosomal segment to a new position, especially on a nonhomologous chromosome

### Chromosomal Structural Rearrangements

Cytologists have characterized numerous structural rearrangements in chromosomes, but chromosome inversions and translocations are the most common. Both are identified during meiosis by the adaptive pairing of rearranged chromosomes with their former homologs to maintain appropriate gene alignment. If the genes carried on two homologs are not oriented correctly, a recombination event could result in the loss of genes from one chromosome and the gain of genes on the other. This would produce aneuploid gametes.

### Chromosome Inversions

A chromosome inversion is the detachment, 180° rotation, and reinsertion of part of a chromosome. Inversions may occur in nature as a result of mechanical shear, or from the action of transposable elements (special DNA sequences capable of facilitating the rearrangement of chromosome segments with the help of enzymes that cut and paste DNA sequences). Unless they disrupt a gene sequence, inversions only change the orientation of genes and are likely to have milder effects than aneuploid errors. However, altered gene orientation can result in functional changes because regulators of gene expression could be moved out of position with respect to their targets, causing aberrant levels of gene products.

An inversion can be pericentric and include the centromere, or paracentric and occur outside of the centromere. A pericentric inversion that is asymmetric about the centromere can change the relative lengths of the chromosome arms, making these inversions easily identifiable.

**Inversions can be pericentric or paracentric**: Pericentric inversions include the centromere, and paracentric inversions do not. A pericentric inversion can change the relative lengths of the chromosome arms; a paracentric inversion cannot.

When one homologous chromosome undergoes an inversion, but the other does not, the individual is described as an inversion heterozygote. To maintain point-for-point synapsis during meiosis, one homolog must form a loop, and the other homolog must mold around it. Although this topology can ensure that the genes are correctly aligned, it also forces the homologs to stretch and can be associated with regions of imprecise synapsis.

**Inversion heterozygotes**: When one chromosome undergoes an inversion, but the other does not, one chromosome must form an inverted loop to retain point-for-point interaction during synapsis. This inversion pairing is essential to maintaining gene alignment during meiosis and to allow for recombination.

Not all structural rearrangements of chromosomes produce nonviable, impaired, or infertile individuals. In rare instances, such a change can result in the evolution of a new species. In fact, a pericentric inversion in chromosome 18 appears to have contributed to the evolution of humans. This inversion is not present in our closest genetic relatives, the chimpanzees. Humans and chimpanzees differ cytogenetically by pericentric inversions on several chromosomes and by the fusion of two separate chromosomes in chimpanzees that correspond to chromosome two in humans.

The pericentric chromosome 18 inversion is believed to have occurred in early humans following their divergence from a common ancestor with chimpanzees approximately five million years ago. Researchers characterizing this inversion have suggested that approximately 19,000 nucleotide bases were duplicated on 18p, and the duplicated region inverted and reinserted on chromosome 18 of an ancestral human.

A comparison of human and chimpanzee genes in the region of this inversion indicates that two genes—ROCK1 and USP14—that are adjacent on chimpanzee chromosome 17 (which corresponds to human chromosome 18) are more distantly positioned on human chromosome 18. This suggests that one of the inversion breakpoints occurred between these two genes. Interestingly, humans and chimpanzees express USP14 at distinct levels in specific cell types, including cortical cells and fibroblasts. Perhaps the chromosome 18 inversion in an ancestral human repositioned specific gene and reset their expression levels in a useful way. Because both ROCK1 and USP14 encode cellular enzymes, a change in their expression could alter cellular function. It is not known how this inversion contributed to hominid evolution, but it appears to be a significant factor in the divergence of humans from other primates.

### Translocations

A translocation occurs when a segment of a chromosome dissociates and reattaches to a different, nonhomologous chromosome. Translocations can be benign or have devastating effects depending on how the positions of genes are altered with respect to regulatory sequences. Notably, specific translocations have been associated with several cancers and with schizophrenia. Reciprocal translocations result from the exchange of chromosome segments between two nonhomologous chromosomes such that there is no gain or loss of genetic information.

**Reciprocal translocations do not involve loss of genetic information**: A reciprocal translocation occurs when a segment of DNA is transferred from one chromosome to another, nonhomologous chromosome.

## X-Inactivation

The presence of extra X chromosomes in a cell is compensated for by X-inactivation in which all but one X chromosome are silenced.

#### Key Points

* Extra copies of the X chromosome are silenced by becoming Barr bodies.
* X chromosomal abnormalities are typically associated with mild mental and physical defects, as well as sterility.
* Conditions associated with aneuploidy of the sex chromosomes include individuals with three X chromosomes, called triplo-X; the XXY genotype, known as Klinefelter syndrome; and Turner syndrome, characterized as X monosomy.
* X-inactivation is a form of dosage compensation, in which an organism attempts to equalize the amount of X chromosome gene products in males and females.
* Since males only have one X chromosome, females inactivate one of theirs so that only one X chromosome is active in each gender.

#### Key Terms

* **dosage compensation**: a genetic regulatory mechanism that equalizes the phenotypic expression of characteristics determined by genes on the X chromosome so that they are equally expressed in males and females.
* **Barr body**: a sex chromosome inactivated by packing in heterochromatin
* **X inactivation**: a process by which one of the two copies of the X chromosome present in female mammals is inactivated

### Sex Chromosome Nondisjunction in Humans

Humans display dramatic deleterious effects with autosomal trisomies and monosomies. Therefore, it may seem counterintuitive that human females and males can function normally, despite carrying different numbers of the X chromosome. Rather than a gain or loss of autosomes, variations in the number of X chromosomes are associated with relatively mild effects. In part, this occurs because of a molecular process called X inactivation. Early in development, when female mammalian embryos consist of just a few thousand cells (relative to trillions in the newborn), one X chromosome in each cell inactivates by tightly condensing into a quiescent (dormant) structure called a Barr body. The chance that an X chromosome (maternally or paternally derived) is inactivated in each cell is random, but once the inactivation occurs, all cells derived from that single cell will have the same inactive X chromosome or Barr body.

By this process, a phenomenon called dosage compensation is achieved. Females possess two X chromosomes, while males have only one; therefore, if both X chromosomes remained active in the female, they would produce twice as much product from the genes on the X chromosomes as males.

**Sex Chromosome Nondisjunction**: The symptoms of Klinefelter’s syndrome (XXY) in a human male.

So how does X-inactivation help alleviate the effects of extra X chromosomes? An individual carrying an abnormal number of X chromosomes will inactivate all but one X chromosome in each of her cells. If three X chromosomes are present, the cell will inactivate two of them. If four X chromosomes are present, three will be inactivated, and so on. This results in an individual that is relatively phenotypically normal. However, even inactivated X chromosomes continue to express a few genes, and X chromosomes must reactivate for the proper maturation of female ovaries. As a result, X-chromosomal abnormalities are typically associated with mild mental and physical defects, as well as sterility. If the X chromosome is absent altogether, the individual will not develop in utero.

Several errors in sex chromosome number have been characterized. Individuals with three X chromosomes, called triplo-X, are phenotypically female, but express developmental delays and reduced fertility. The XXY genotype, corresponding to one type of Klinefelter syndrome, corresponds to phenotypically male individuals with small testes, enlarged breasts, and reduced body hair. More complex types of Klinefelter syndrome exist in which the individual has as many as five X chromosomes. In all types, every X chromosome except one undergoes inactivation to compensate for the excess genetic dosage. This be several Barr bodies in each cell nucleus. Turner syndrome, characterized as an X0 genotype (i.e., only a single sex chromosome), corresponds to a phenotypically female individual with short stature, webbed skin in the neck region, hearing and cardiac impairments, and sterility.

### Duplications and Deletions

In addition to the loss or gain of an entire chromosome, a chromosomal segment may be duplicated or lost. Duplications and deletions often produce offspring that survive but exhibit physical and mental abnormalities. Duplicated chromosomal segments may fuse to existing chromosomes or may be free in the nucleus. Cri-du-chat (from the French for “cry of the cat”) is a syndrome associated with nervous system abnormalities and identifiable physical features that result from a deletion of most of 5p (the small arm of chromosome 5).