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UNDERSTANDING GENES
& CHROMOSOMES



Ring chromosome 4

rarechromo.org

This guide is designed to help families and healthcare professionals looking after people with ring chromosome 4. It contains information about the cause, the ways in which it can affect people and suggestions about the help and management that can benefit people with this condition.

What is ring chromosome 4?

Ring chromosome 4 is a rare genetic condition where a chromosome 4 has formed a ring structure instead of its typical rod-like structure. People can have different size ring chromosomes, and the effects can vary from person to person. Most but not all people with a ring chromosome 4 have developmental delay, learning difficulties and varying degrees of intellectual disability. Having a ring chromosome 4 is also often associated with poor growth involving height, weight and head size throughout life, unique facial features and structural changes to the body (such as the heart, digestive tract, urinary structures and limbs). As is common with genetic conditions, each person can be affected differently - even among affected members within the same family. Not everyone with ring chromosome 4 will have all the possible features and each person with a certain feature won't necessarily be affected by it to the same level as other people with that feature.

How common is ring chromosome 4?

Ring chromosome 4 is extremely rare. Currently (2026) about 50 individuals with a ring chromosome 4 have been reported in the medical literature, but more are known to have been diagnosed. It is expected that more people will be diagnosed with this condition as awareness increases and genetic testing improves. Current routine genetic tests, while able to detect missing and additional chromosomal material, are less able to detect ring chromosomes but research is being carried out in an attempt to improve this.

What features and symptoms do people with ring chromosome 4 have?

As is common with many genetic conditions, children and adults with a ring chromosome 4 can have a range of features and symptoms. When a ring chromosome forms, some genetic material can be lost or duplicated, and some features are related to the loss (deletion) or gain (duplication) of genetic material on their ring chromosome. Some features are shared with people who have just a deletion (and no ring chromosome), such as people with Wolf Hirshhorn syndrome. As more people are diagnosed, and information is shared, the range of features, and the likelihood of a child or adult having these features, will become clearer.

Common features

Most people with a ring chromosome 4 have:

- Growth delay
- Small head size (microcephaly)
- Short stature
- Characteristic facial features including unusually-shaped ears, a gap in the iris of the eye (iris coloboma), wide-set eyes (hypertelorism), small mouth, small chin (micrognathia) and a short neck
- Anomalies of the limbs
- Anomalies of the heart (cardiac anomalies)
- Anomalies of the kidneys and genitals (urogenital anomalies)
- Anomalies of the digestive system (gastrointestinal anomalies)
- Some degree of developmental delay ranging from very mild to moderate/severe/profound
- Some degree of intellectual disability (ID) or learning difficulties (LD) ranging from very mild to moderate/severe/profound
- Cleft lip or palate or other palate anomalies

Other possible features include:

- Seizures
- Hearing loss
- Spinal curvature – scoliosis (sideways curve) and kyphosis (forward curve of upper back)

Wolf-Hirschhorn Syndrome

Ring chromosome 4 can be associated with a condition called Wolf-Hirschhorn syndrome. Wolf-Hirschhorn syndrome occurs when an important region of chromosome 4, called the Wolf-Hirschhorn critical region, is lost during ring formation. Individuals with Wolf-Hirschhorn syndrome often have the following features or conditions (Battaglia 2008):

- Delayed growth
- Learning (developmental) disability
- Unique facial features such as a high-bridged, prominent bone between the eyebrows (prominent glabella), high forehead, wide-set eyes (hypertelorism), protruding eyes, high-arched eyebrows, skin folds covering the inner eye (epicanthal folds), short nose-to-lip region (short philtrum) and a small jaw (micrognathia)
- Seizures

Unique publishes a separate guide to **Wolf-Hirschhorn syndrome**

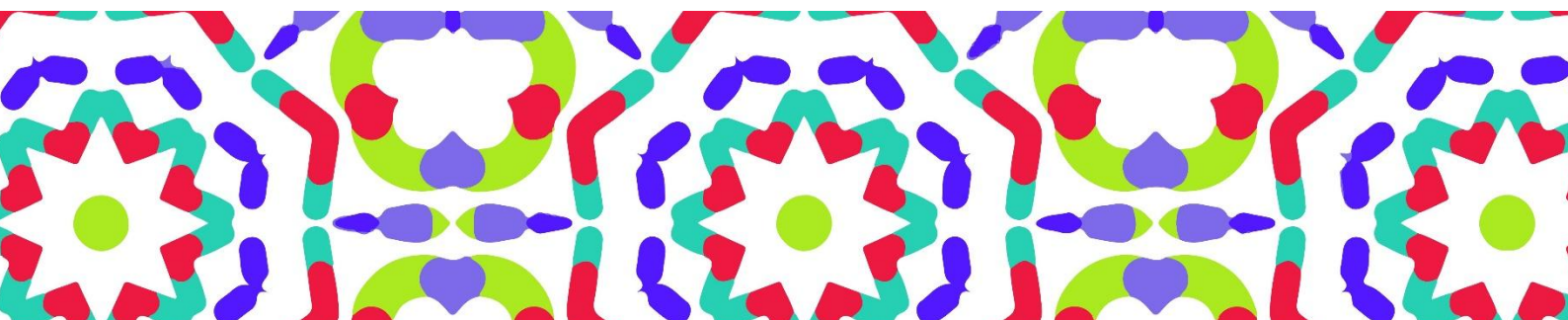
Pregnancy and birth

While many pregnancies are unremarkable and proceed without complication, some concerns during pregnancy have been reported, often following mid-pregnancy anomaly scans (20-week ultrasounds). From reports in the medical literature, the most common prenatal finding is slow growth in the womb (intrauterine growth retardation IUGR) (Bone 2024). Some scans also noted unusually small amounts of amniotic fluid (oligohydramnios).

The majority of pregnancies go to term but a few babies are born prematurely. Many babies show some signs of difficulty at birth, related to poor growth. Birth weights, heights and head circumferences are usually well below the expected range and may lead medical providers to keep babies in hospital after delivery for additional care. A couple of babies have been found to have missing kidneys (both) and severely low levels on amniotic fluid (oligohydramnios) seen on prenatal imaging. They were born with poor lung development and life-threatening breathing problems, but this is very rare.



Our son was born at 39 weeks and 1 day after a normal, healthy pregnancy. Following an emergency C-section, he was airlifted to another hospital four hours away, where he spent six weeks. Genetic testing was performed because of his heart condition, but we had to wait until he was four months old for an official diagnosis. That uncertainty was difficult for our family, as it seemed that every day brought a new diagnosis.” Age 10 years, partial mosaic trisomy ring chromosome 4



Appearance

Certain facial features are found more often in children with a ring chromosome 4 than in other children. These features may mean that you see unexpected similarities between your child and others with a ring chromosome 4. The most common characteristic features include unusually-shaped or low-set ears, a gap in the iris of the eye (iris coloboma), wide-set eyes (hypertelorism), small mouth, small chin (micrognathia) and a short neck. Other possible features vary greatly between individuals but may include cleft lip or palate, a prominent forehead (frontal bossing), a tiny dimple in front of the ear (pre-auricular pit), skin folds at the inner corner of the eye (epicanthal folds) or drooping of the upper eyelids (ptosis).

Development

Gross and fine motor skills

Developmental delay has been reported in most children with a ring chromosome 4 so far (2026). The degree of delay ranges from mild to profound. Developmental “milestones”, including rolling, sitting, walking, playing with toys, using cutlery, using zips and buttons and toilet training, are often delayed, although there is a wide range of eventual ability, with some children acquiring mobility and other skills around the same age as “typical” children and others showing more obvious delay. For example, one child discussed in medical literature sat at 12 months and stood alone at 17 months, as expected (Anderson 1997). However, another child was unable to roll, crawl or walk at age 4.5 years (Laleye 2006). Low muscle tone (hypotonia) has been noted in several children and may affect mobility. Some children have atypical limb or foot positioning that can affect movement and the way they walk (gait). For some, independent walking may not be achieved. Others will walk without concern. Early intervention with physiotherapy or occupational therapy may be beneficial for those with motor difficulties.

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Intellectual development and learning

Many children with a ring chromosome 4 have learning (intellectual) disability (LD/ID) or learning difficulties. LD/ID ranges from very mild (unaffected or almost unaffected neurodevelopment) to severe but is usually in the mild to moderate range. Children with very mild intellectual changes will thrive without any interventions. However, some children will require significant additional support with their learning throughout their education. Early intervention can prove particularly beneficial and formal testing to assess specific, individual needs is recommended to help each child reach their full potential. Some adults have intelligence within the standard range.

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Speech and language

Children with a ring chromosome 4 typically experience some degree of speech and language delay. The eventual range of achievement is broad. Some children develop limited expressive language, while others achieve language skills within the expected range and attend mainstream school. A common observation from the medical literature is that a child's understanding of language (receptive language) is significantly better than their ability to speak (expressive language). Structural features sometimes seen in ring chromosome 4, such as a cleft lip and/or cleft palate, high arched palate or a small lower jaw (micrognathia), may also affect speech development. Additionally, hearing loss has been reported in some children, which can further impact

speech and language development. Speech therapy may be beneficial for those with speech or language difficulties.

Unique publishes a separate guide to **Communication**

Feeding

Feeding issues in the new-born period are possible. Due to small mouth size and potential structural anomalies including cleft lip and palate, some babies will suck weakly or have difficulty swallowing. This can contribute to poor weight gain. If the poor feeding is significant, newborns may be admitted to the neonatal intensive care unit (NICU) or nursery after delivery for additional support.

Unique publishes a separate guide to **Feeding**

Growth and stature

Almost all individuals with a ring chromosome 4 described in the medical literature so far (2026) are noted as having growth delay and short stature. Most also have a smaller than expected head size (microcephaly). Beyond infancy, height and weight remain below the typical range in childhood, adolescence and adulthood. This is also seen in people with no or very little missing or extra genetic information on their ring chromosome; these features are assumed to be caused by the chromosome having a ring structure rather than the loss or gain of genetic material, this is known as **Ring syndrome**.

Having a ring chromosome, for any chromosome, not just chromosome 4, can cause a condition called **ring syndrome**. Which is when children have growth issues, often starting before birth and continuing throughout life. Some people may also have developmental delay. Starting after conception, embryos grow and develop by division of cells. As cells divide, more and more cells are made. Ring syndrome happens because of what occurs to the ring chromosome when cells divide during growth. Ring chromosomes usually do not divide the same way that unaffected chromosomes do, and sometimes the ring can become larger or be lost. The cells with larger or missing rings often do not survive. This cell death results in less cells overall and poor growth.

Supporting our son's development has required ongoing care and advocacy. Over the years, he has seen specialists in cardiology, urology, nephrology, endocrinology, and neurology. He has received speech, physical, and occupational therapy, and we have advocated for assessments and studies, including neurodevelopmental and psychological testing and sleep studies.

Despite these challenges, our son has a good quality of life. He attends school, enjoys video games and animals, and likes playing with his friends. He impresses us every day with his intelligence, interests, and personality.” Age 10 years, partial mosaic trisomy ring chromosome 4



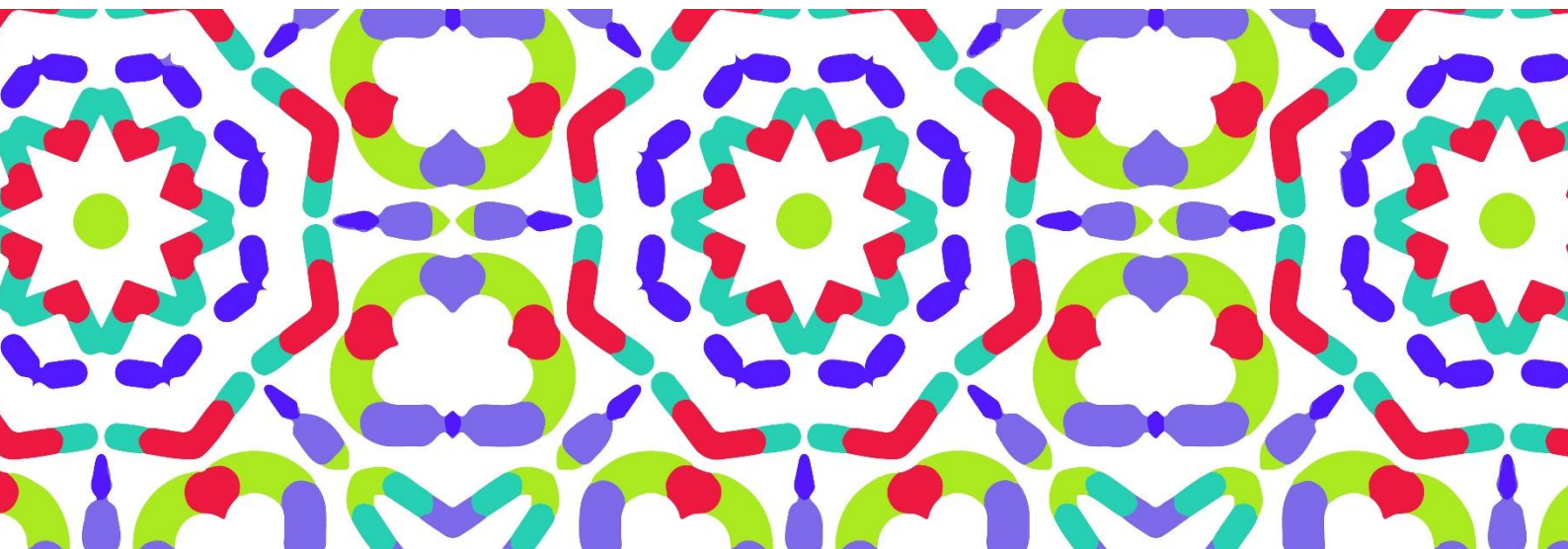
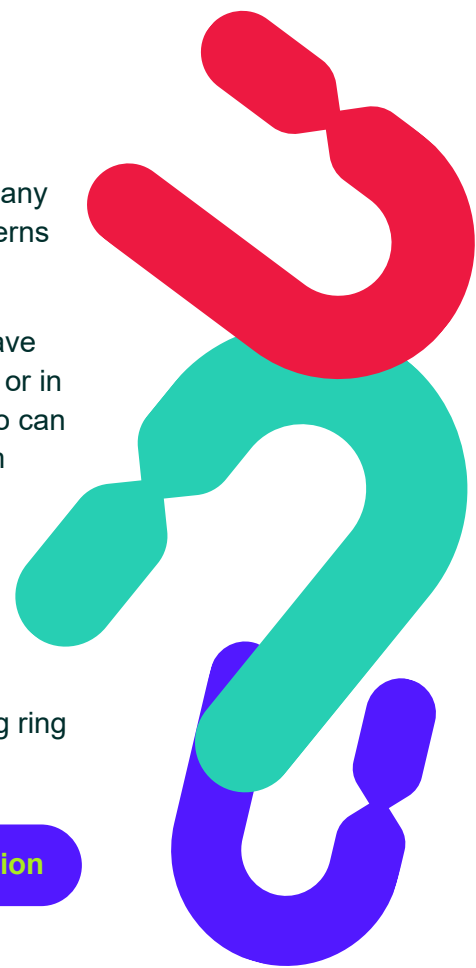
Adulthood

Experiences of adulthood are likely to vary considerably and will depend on many factors. These include the level of any LD/ID, possible on-going medical concerns and improvements in early intervention and therapies/treatments.

Adults with ring chromosome 4 have varying levels of independence. A few have gone on to have families of their own. Some continue to live with their parents or in supported settings such as a group/residential care home, with caregivers who can provide support. Others may live independently but require some support from family or friends with certain tasks. Levels of employment and the nature of employment varies but some people with a ring chromosome 4 do undertake some form of paid or unpaid employment.

Two adults in the medical literature with a ring chromosome 4 only discovered that they had this genetic syndrome when faced with reproduction-related difficulties (Bone 2024). There is limited information about the impact of having ring chromosome 4 and infertility, making it difficult to say if there is a link.

Unique publishes a separate guide to **Transition**



Medical concerns

The following medical concerns have been found in children with a ring chromosome 4. They are not found in all children so not all children with ring chromosome 4 will be affected.



Heart

Heart conditions have been found in 30% of people reported so far with ring chromosome 4 (Bone 2024), which can be present at birth (congenital) or present later in life. In children for whom heart problems are suspected, these can be diagnosed using tests like an echocardiogram (ultrasound scan of the heart). The type of heart condition is variable but includes anomalies affecting the size and structure of the heart muscle and valves. The most commonly reported are holes between the chambers of the heart. This can affect the upper heart chambers (atrial septal defect (ASD)) or the lower heart chambers (ventricular septal defect (VSD)). Other possible heart conditions include the failure of closure of the small vessel that carries blood between the aorta and the pulmonary artery during the foetal period (persistent ductus arteriosus (PDA)) and the incorrect connection of major heart vessels (transposition of the greater arteries (TGA)). Additionally, one individual described in the medical literature has a heart on the right side of the chest (dextrocardia) (Hou & Wang 1996), rather than the left. Some of these conditions are relatively minor and resolve naturally with time. Medical treatment may be necessary for others, and some may require surgery.

 *Our son's medical history is complex. He underwent heart procedures at five days and eight weeks old, followed by a Ross-Konno procedure at five months and another eight-week hospitalization. Since then, he has had several heart catheterizations and a valve replacement last summer." Age 10 years, partial mosaic trisomy ring chromosome 4*

Kidney and urinary tract

Some babies with a ring chromosome 4 are born with structural anomalies of the kidneys and urinary tract. Reported anomalies include:

- Having only **one kidney** (one-sided (unilateral) renal agenesis). Individuals born with one kidney can be otherwise healthy with limited renal concerns. However, this kidney needs to work harder, which can lead to conditions such as high blood pressure or kidney disease later in life
- At least one baby with a ring chromosome 4 has been born **without kidneys** (bilateral renal agenesis) (Bone 2024). Sadly, newborns with no kidneys cannot survive outside the womb. This is because without functioning kidneys, not enough fluid is excreted into the amniotic sac. Very little amniotic fluid (oligohydramnios) prevents the lungs from developing as they should
- Some individuals with a ring chromosome 4 have one kidney located in a **lower position** in the pelvis than expected (unilateral ectopic kidney). These kidneys may or may not have normal function, and they can be more susceptible to swelling, kidney stones, or lead to backwards urine flow (**vesicoureteral reflux (VUR)**)
- **VUR** has been noted in one individual with ring chromosome 4, even though their kidneys were in the expected place (Bone 2024)
- A condition called oligomeganephronia, where the kidneys contain **too few filtering units** (nephrons), has also been reported in an adolescent with ring chromosome 4 (Anderson 1997). This condition can progress to kidney failure over time
- **Under-sized kidneys** (hypoplastic kidneys)
- **Kidney tissue** that does not develop as expected during foetal life (kidney dysplasia)
- Small kidneys with **fluid-filled sacs** (hypoplastic kidneys with cysts)

 *He has bilateral hydronephrosis and hydroureter. After one heart procedure, he developed a blood clot that injured his right kidney and caused it to become atrophic. He has lived with one functioning kidney for 10 years. He also has a history of congenital hypothyroidism, which has since resolved.” Age 10 years, partial mosaic trisomy ring chromosome 4*

Genitals

Minor anomalies of the genitals in boys have been reported in about half of males with a ring chromosome 4. Most common among these are hypospadias, where the hole normally at the end of the penis lies on the underside; undescended testes (cryptorchidism); a small or abnormally formed testis; and retractile testicle/testis, where one or both testicles move between the groin and the scrotum due to an overactive muscle. The following structural changes are less common but have been seen in at least one individual in the medical literature: incomplete closure of the scrotal midline, an absent testis and a tightening of the foreskin (phimosis). Many of these anomalies can also be seen in children without ring chromosome 4 and are not of major concern. If necessary, most can be corrected with surgery. In females, genital anomalies are less common but have been reported. At least one individual was reported to have underdevelopment of the outer folds of the vulva (hypoplasia of the labia majora).

Gastrointestinal system

Some babies are born with structural anomalies of the gastrointestinal system, though these are not present in all children with a ring chromosome 4. Some of these anomalies may cause vomiting or nausea, loose stools or abdominal pain. However, these symptoms are common and may be seen in individuals with typical gastrointestinal systems. Structural changes can be visualized using medical imaging technologies such as X-ray or magnetic resonance imaging (MRI). Often surgical intervention is required. Gastrointestinal conditions that have been described include babies born with:

- **Midgut malrotation**, where the intestines rotate and localize in an abnormal location, impacting function. This is the most frequently seen gastrointestinal anomaly in individuals with a ring chromosome 4
- **Duodenal atresia**, a blockage of the first portion of the small intestine
- **Bowel obstruction**, a blockage of the small or large intestine preventing proper flow
- **Short bowel**, which is when a portion of the small intestine is missing
- **No gallbladder** (gallbladder aplasia), which may lead to abdominal pain, nausea or vomiting
- **Congenital diaphragmatic hernia (CDH)**, a condition in which abdominal organs move up into the chest due to an incompletely formed diaphragm

Hands, feet and limbs

Children with a ring chromosome 4 often have anomalies of the hands and feet. Most common among these are:

- **Finger(s) that curve inwards (clinodactyly)**, which most often involves the fifth finger. This is the most common limb change reported by families
- **Underdeveloped (hypoplastic), small, misplaced or misshapen thumbs**. One individual was reported to have an extra thumb (polydactyly) which was surgically corrected (Kishi 2018)
- **Abnormal radial ray development**, where structures on the thumb-side of the arm do not form as expected. This atypical development can range from mild to severe
- **Club foot (talipes equinovarus)**, with the foot turned inwards and the soles pointing towards each other

- Other foot anomalies: outward turned foot (valgus feet), rocker-bottom feet or overlapping toes
- Stiff joints (contractures) due to muscle, tendon or skin tightening, seen to impact the knees and elbows
- Absence of one upper extremity

Some children are only mildly affected and will not require treatment. Others may benefit from massage, orthotics and physiotherapy. Treatment is tailored to the individual child, and in some cases surgical correction will best enhance eventual mobility.

Palate

Anomalies of the roof of the mouth (palate), ranging from those that may be invisible to the casual onlooker such as a high/arched palate to more obvious conditions such as a cleft palate, have been reported. Anomalies of the palate, particularly cleft palate, can cause difficulties in feeding, hearing, teething and speech production. As well as helping aesthetically, surgical repair eases these problems and may even eliminate them altogether. Approximately 20% of individual with a ring chromosome 4 recorded in the medical literature have a cleft lip or palate (Bone 2024).

CLAPA (Cleft Lip and Palate Association) offers support for people affected by cleft lip and palate

Ears and Hearing

Many individuals with ring chromosome 4 have changes to the appearance of their ears. Some possible changes seen include low-set, misshapen, rotated or unusually large ears. Small pits in front of the ear (preauricular pits) can also occur. Most often, the appearance does not impair the functioning of the ear, however, it is possible.

Hearing loss, ranging from mild to severe, has been noted in several individuals with ring chromosome 4. It is recommended that all individuals born with ring chromosome 4 have hearing tests.

Many types of hearing loss can be managed by using hearing aids. As children are at risk of speech delay, parental concerns should be acted on early and home- or school-based therapy provided.

Unique publishes a separate guide to **Hearing**

Eyes and sight

Eye and vision anomalies are common in children with ring chromosome 4. A thorough evaluation by a paediatric ophthalmologist is recommended at diagnosis. Known concerns include a condition where one or both eyes turn inward (strabismus) which can result in a 'lazy eye' and vision issues if untreated. Additionally, some individuals have iris coloboma, where a piece of the coloured portion of the eye (iris) is missing. This results in the pupil appearing elongated and on its own, would not impact vision, but may indicate other possible eye anomalies requiring assessment. Drooping of the upper eyelid (ptosis) has also been seen. Most eye findings can be corrected with glasses or patching, and few require surgery.



Brain

A few children with a ring chromosome 4 have a structural brain anomaly, which can be detected by MRI (magnetic resonance imaging) or a CT (computerised tomography) scan of their brain. The changes seen vary but include:

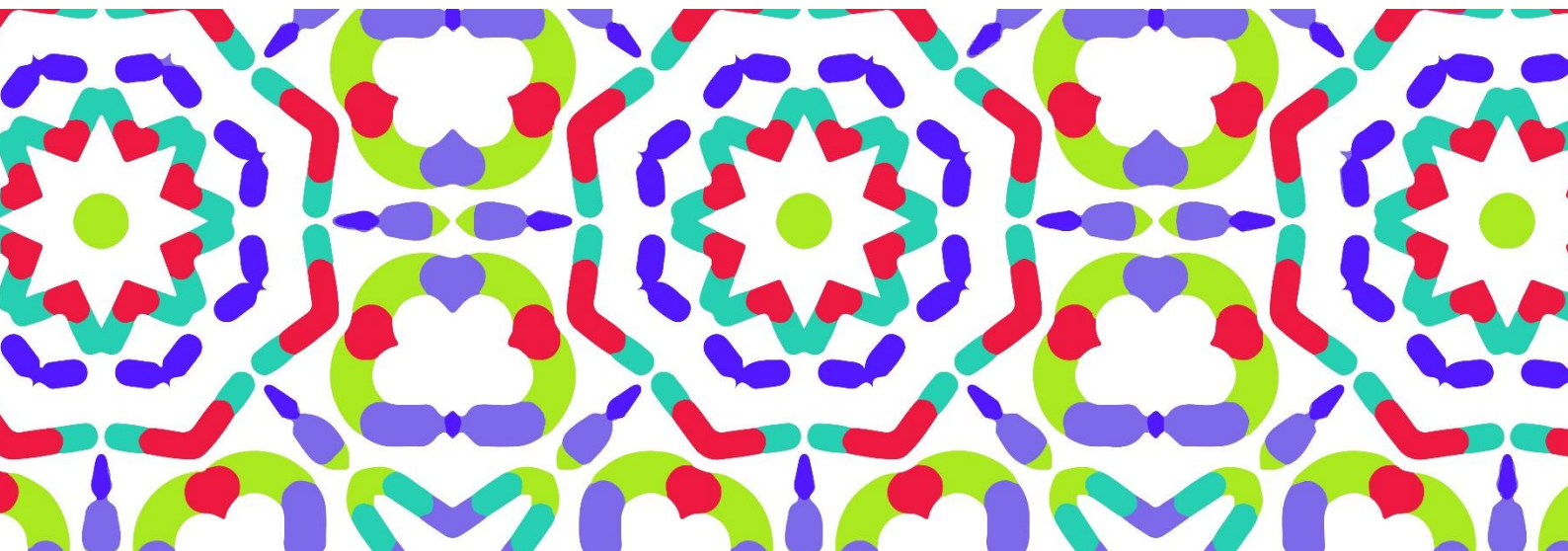
- Underdevelopment (hypoplasia) or partial/complete absence (agenesis) of the white matter connecting the two halves of the brain (corpus callosum)

Seizures

Occasionally, children with ring chromosome 4 experience some form of seizure (a sudden and unexpected change in the electrical activity in the brain). Depending on the part(s) of the brain affected, symptoms vary, but include temporary confusion, uncontrollable jerking movements and loss of consciousness or awareness. Age of onset can vary considerably, while seizures may be isolated to a single incident or occur more regularly. More than one type of seizure may be present in the same individual.

Electroencephalograph (EEG) and video telemetry (video EEG) are medical tests that can be used to measure and record the electrical activity of the brain and are tools that, when used alongside other tests, can help diagnose the type of seizure experienced. Seizures can cause a lot of worry for families and can be frightening to observe, but in the majority of cases they self-resolve or resolve with medical treatment. If a child has a seizure for the first time, it is important to remove nearby hazards so they can't hurt themselves and contact a medical professional.

 *I have learned to focus on enjoying today rather than allowing fear about the future to overshadow our time together. Our son's medical history still brings uncertainty, but it also reminds me to be present, appreciate the good moments, and make happy memories." Age 10 years, partial mosaic trisomy ring chromosome 4*

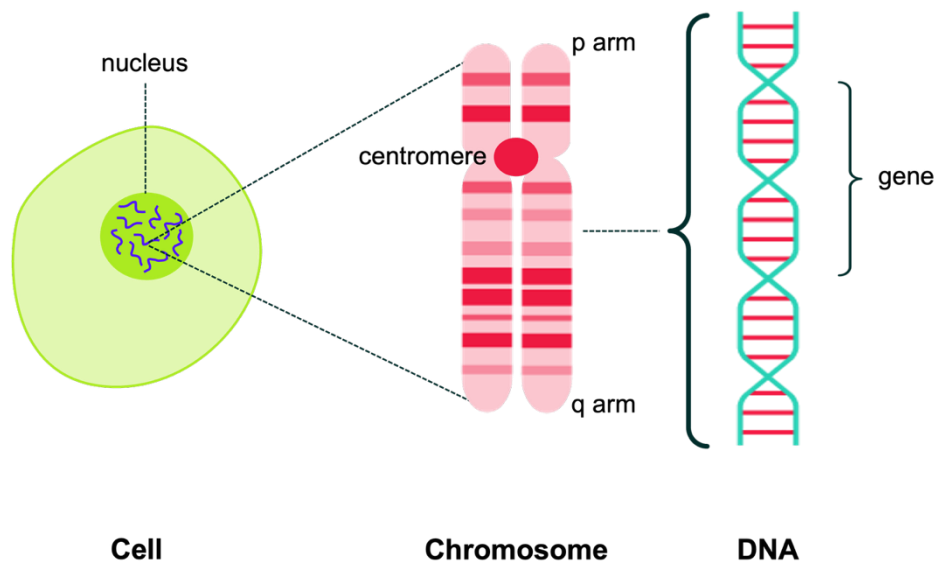


This section includes some more complicated scientific terms and concepts - don't worry if it's a lot to take in, you can always come back to this section later if you want to.

Genes and chromosomes

Genes are instructions which have important roles in our growth and development. They are made of DNA and are incorporated into organised structures called **chromosomes**. Chromosomes therefore contain our genetic information. Chromosomes are located inside our **cells**, the building blocks of our bodies. In people with genetic conditions, one or more of their genes don't instruct the body as expected, which can lead to changes in how their body works.

Most of our cells normally contain 46 chromosomes, organised as 23 pairs. We usually inherit one chromosome of each pair from our biological mother and the other from our biological father. Chromosome pairs are numbered 1 to 22 and the 23rd pair are the sex chromosomes, which determine biological sex (whether we are male or female). Females usually have two X chromosomes (XX) and males usually have an X and a Y chromosome (XY). Ring chromosomes can occur in any chromosome.

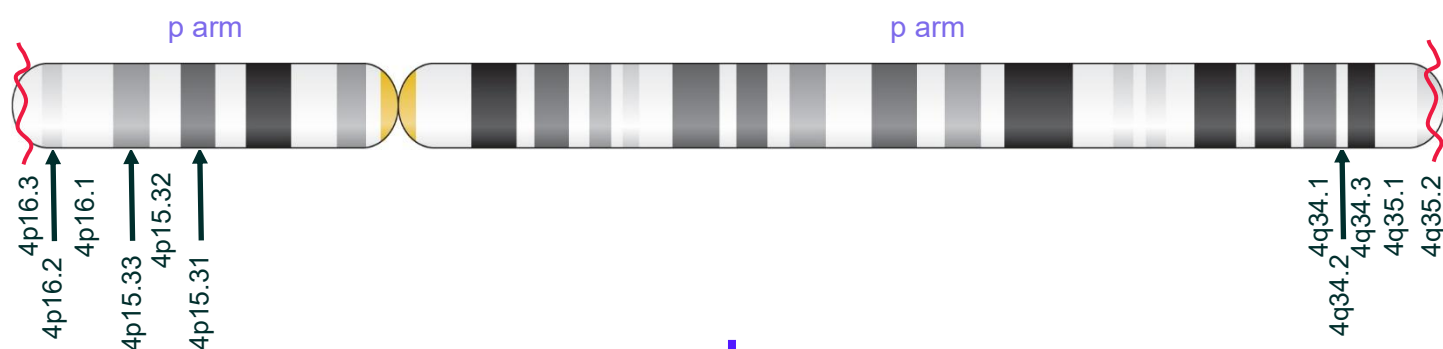


What is a ring chromosome?

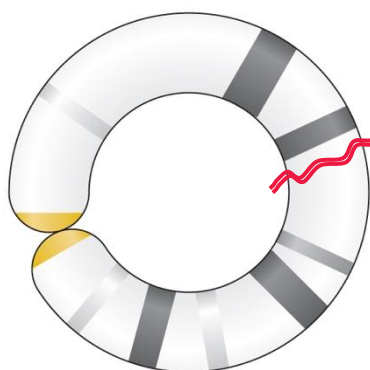
Our chromosomes typically have a rod-like structure. A ring chromosome occurs when the two ends of a single chromosome fuse together to form a circular ring structure. When this happens, part of the chromosome can be lost and/or duplicated, but there isn't always a loss or duplication of genetic material.

As seen in the image on the following page, chromosomes have a short 'p' arm and a long 'q' arm. Additionally, you may notice that the chromosome has stripes. These stripes are called bands. When chromosomes are prepared in a specific way, these bands can be seen under a microscope along the full length of the chromosome. The bands are numbered outwards starting from the point where the short p arm and long q arm meet, at a place called the centromere. Bands can act like landmarks, allowing us to localize where on a chromosome extra or missing pieces of chromosome occur (if they are large enough to be seen – smaller deletions and duplications are now able to be identified using different laboratory techniques, as explained later in this guide).

Chromosome 4



Ring chromosome 4



Since we usually have two copies of chromosome 4 in our cells, we also have two copies of each important gene on this chromosome. If we lose a copy of an important gene, we usually have a second functional copy on our other chromosome 4. However, sometimes just having one copy is not enough or having an extra copy is too much, and a genetic condition occurs. There are a number of important genes at the ends of chromosome 4 and if these genes are deleted or duplicated when a ring chromosome 4 forms then there are missing or extra copies of genes, respectively, which can affect how the body develops and functions.

Since the number of genes lost or gained when a ring chromosome forms is very variable, individuals with ring chromosome 4 may have very different features. If two individuals have lost different genes, their bodies may develop very differently. If the same genes are lost, individuals may develop similarly.

Unique publishes general guides to **deletions and microdeletions** and **duplications and microduplications** as well as **various guides** to chromosome 4 deletions and duplications

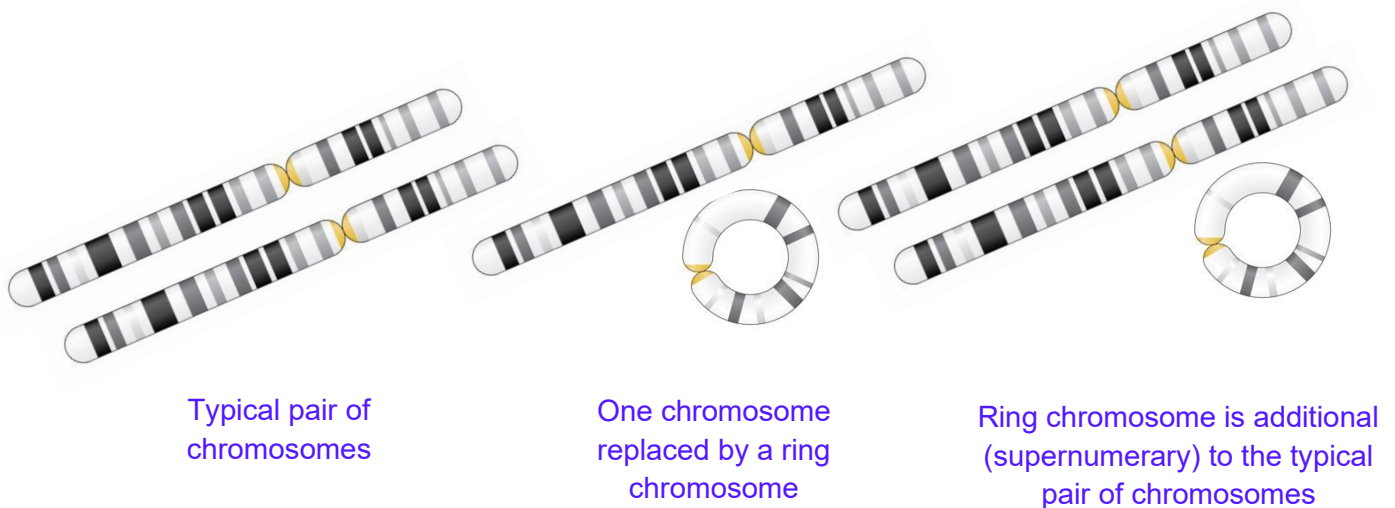
Wolf-Hirshhorn syndrome – when a ring chromosome 4 has a specific segment of chromosome 4 deleted near the end of the p arm, the person will have features that overlap with those of Wolf-Hirshhorn syndrome, which is a condition caused by a chromosome 4p16 deletion without a ring chromosome formation.

Some rings, however, do not have any missing or extra copies of genes. The tips of the chromosomes fuse without removing or adding genes. This often causes small growth and may cause mild developmental delays because ring chromosomes do not behave the same way as rod shaped chromosomes, and a person is said to have **ring syndrome** (as described earlier).

Ring chromosomes can replace rod-like chromosomes, or they can occur as an additional chromosome. If a ring chromosome is present in addition to the usual set of chromosomes, it is known as a **supernumerary ring chromosome**. Sometimes a ring chromosome is not found in all cells, this is known as **mosaicism**. Mosaicism may be associated with milder features, but this is hard to predict when a baby is diagnosed. Since the symptoms can be mild, a parent may be found to have mosaicism on their genetic test after their child is diagnosed with ring chromosome 4. It is also possible, but extremely rare, for **double rings** to form that can have quite unusual structures.

Sometimes a ring chromosome is lost and another chromosome 4 is 'rescued' by duplicating the unaffected chromosome 4. This results in both copies of chromosome 4 coming from the same parent, this is called **uniparental disomy (UPD)**.

Unique publishes separate guides to **Mosaicism** and **uniparental disomy (UPD)**



What causes ring chromosome 4?

Ring chromosome 4 is thought to happen by chance and can occur by different mechanisms. Some, but not all, rings form when a piece of chromosome, at one or both ends, are lost and the two ends fuse together. The size of the lost pieces of chromosome can vary considerably from virtually undetectable amounts to large sections. Other rings can form by a different mechanism, and pieces of chromosome might be duplicated. It is not always known why ring chromosomes form, but they are not due to anything either parent did or did not do, they are not associated with any lifestyle, dietary or other factors, it's just something that happened by chance.

Genetic Test Results

Many years ago, in order to investigate genetic conditions, a standard genetic test called a karyotype would be carried out, usually on a blood sample. This type of test involved the preparation of chromosomes, by a specific method, so that they could be viewed under a microscope. This method can show the presence of a ring chromosome and whether it is in addition to the expected set of chromosomes (**supernumerary**) or if it replaces a rod-shaped chromosome. It can also determine if all cells have the ring chromosome or if it is **mosaic** (not found in all cells). Other unusual and incredibly rare ring structures can also be visualized, such as double rings or interlocking rings.

Following this type of test, people with a ring chromosome, and sometimes the parents of a child with a ring chromosome, receive a genetic test result that contains the abbreviation r (for ring). If the ring was not found in all cells analysed, mos (for mosaic) would be noted. Sometimes images of chromosomes, called a [karyotype](#), are provided.

The results of genetic (genomic) testing are likely to be provided by a geneticist, a genetic counsellor or the clinician who ordered the test.

Depending on the test that was carried out, the results of a [karyotype test](#) that can identify a ring chromosome 4 might look like one of these examples:

46,XY,r(4)

- 46 signifies that 46 chromosomes were counted, which is the expected number of chromosomes
- XY signifies that X and Y chromosomes were identified, so the person is male (a female would be XX)
- r signifies the presence of a ring chromosome
- 4 signifies that the ring chromosome is made from chromosome number 4

Mos 47,XX,+r4[3]/46,XX[27]

- mos signifies that the ring chromosome is not found in all cells, it is mosaic
- 47 signifies that 47 chromosomes were counted, we usually have 46 chromosomes in each cell, so the ring chromosome is an extra, or supernumerary, chromosome
- XX signifies that two X chromosomes were identified, so the person is female (a male would be XY)
- r signifies the presence of a ring chromosome
- 4 signifies that the ring chromosome is made from chromosome number 4
- [3] signifies that three cells were found to contain the ring chromosome
- 46 signifies that there are also cells that have the expected number of chromosomes, 46
- XX signifies that the cells with the expected number of chromosomes also have two X chromosomes as expected
- [27] signifies that 27 cells were found to have the expected number of 46 chromosomes

A karyotyping test as described above is no longer the first choice of genetic test in most developed countries, when a genetic condition is suspected. Genetic testing has improved dramatically in the last few years and other more detailed and precise tests are now more commonly used. Examples of such tests (in 2026) are called [chromosome microarray \(CMA\)](#) tests (such as [array CGH](#) or a [SNP array](#)) or [DNA sequencing](#) tests (either [genome \(GS\)](#) or [exome \(ES\)](#) sequencing).

Unique publishes separate guides to [DNA sequencing](#), [array CGH](#) and [SNP arrays](#)

Unfortunately, these tests, in their standard form, are not able to identify a ring chromosome structure. However, if both ends of a chromosome are found to be altered, a ring chromosome might be suspected and a karyotype offered.

If you or your child were found to have a ring chromosome by a karyotype test many years ago, you or your child may be offered a more recent form of genetic testing if this is of interest to you. These types of tests can identify deletions and duplications of DNA and genes within the ring chromosome that would have been too small to notice in a karyotype test. The position of each gene on each chromosome is now known, so the results of a chromosome microarray or sequencing test will be able to identify which, if any, genes have been affected.

An example result of a **chromosome microarray (CMA) test** is shown here for a ring chromosome 4 that was identified by karyotyping, but the array test also identified a small deletion (called a microdeletion) containing important genes, too small to be identified by a karyotype test:

arr[hg38] 4p16.3 (72555-1962072)x1 dn

arr	signifies the analysis was by chromosome microarray (arr)
hg38	signifies Human Genome build 38. This is the reference DNA sequence that the base pair numbers refer to. As more information about the human genome is found, new 'builds' of the genome are made, and the base pair numbers may be adjusted. This means gene positions change depending on the version used
4p16.3	The chromosome involved is chromosome 4 and the position of the deletion is on the p arm in band 16.3
72555-1962072	the base pairs between 72,555 and 1,962,072 have been shown to be deleted. Take the first long number from the second and you get 1,889,517 (1.962Mb). This is the number of base pairs that are deleted
x1	means there is one copy of these base pairs, instead of two. There should be one on each chromosome 4, so this a deletion
dn	means <i>de novo</i> . The biological parents' chromosomes have been checked and no deletion or other chromosome change has been found at position 4p16.3. The deletion is very unlikely to be inherited and has almost certainly occurred for the first time in this family with this child mat here would mean that the deletion has been inherited from the biological mother pat here would mean that it has been inherited from the biological father

Unique publishes a separate guide to
Interpreting Genetic Test Results

When we met with the geneticist, they were not hopeful about our son's prognosis. We were told to take him home, keep him comfortable, and seek services as needed. We were also told that a follow-up with genetics was unnecessary. Despite those expectations, our son continued to make progress. He weaned from his feeding tube and learned to sit, stand, crawl, walk, talk, and attend school, even though some people thought he might never reach those milestones.

Because his chromosome abnormality is so rare, there has been little information about what to expect, which concerns might be related to it, or how to find other families with a similar diagnosis. We have often had to ask questions, seek appropriate services, and navigate each new issue as it arose."
Age 10 years, partial mosaic trisomy ring chromosome 4



Why did this happen?

When children are conceived, their parents' genetic material (DNA) is copied in the egg and sperm that makes a new child. The biological copying method is not perfect, and random changes occur in the genetic code of all children that are not seen in the DNA of their parents. This happens naturally and is not due to the parents' diet, environment or lifestyle. Most of these DNA changes have no obvious effect. But in rare instances these random DNA changes can lead to health issues or affect development. When such a random change disrupts the function of the chromosome, and/or an important gene, or set of genes within a chromosome then a child will be affected.

In almost all people identified so far [2026] with ring chromosome 4, the genetic change was a random (or '*de novo*') change, meaning the change occurred for the first time in that family in the affected individual. Rarely ring chromosome 4 is inherited from an affected parent (typically the parent has mild features/ID). Very rarely one parent may have the same ring chromosome 4 in some of their egg or sperm cells and pass it on to their child (this is known as *germline mosaicism*). However, it is important to recognize that no one should be blamed for variants in their DNA and no parent is at fault when a new DNA change occurs in their child.

Can it happen again?

The possibility of having another child affected by a rare gene disorder depends on the genetic code of the parents. In most people reported with a ring chromosome 4 so far (2026) the altered chromosome has been found to be *de novo* (dn), which means neither parent was found to have the same ring chromosome as their child. Therefore, the chance of having another child with a ring chromosome 4 is usually less than 1%.

One reason why there is some residual chance of recurrence is due to the rare phenomenon called *germline mosaicism* that was mentioned above. This is when a parent carries a genetic change, but it is limited to some of their egg or sperm cells. The genetic change would not, therefore, be detected in the parents' blood tests. It is also possible that a parent has a ring chromosome present in some of the cells of their body but not all (the parent is then known to have *somatic mosaicism*), and the chances of having a child with the ring chromosome is likely to be more than 1%.

Unique publishes a short general guide to *Mosaicism*

From the medical literature published so far (2026), there is no evidence of parents passing down a ring chromosome 4. However, there is one report of recurrence of ring chromosome 4 in a sibling (Phillips 2021), which was likely due to germline mosaicism. However, the effect on each child's development, health and behaviour cannot be reliably predicted. Your genetics centre should be able to offer counselling before you have another pregnancy.

If your child with a ring chromosome 4 goes on to have children of their own, the chances of passing on the variant to their child would be 50% in each pregnancy (unless they have mosaicism or a supernumerary ring chromosome). Your child's ability to look after their own child is very likely to be closely related to their own learning ability and behaviour.

A clinical geneticist or genetic counsellor can provide specific advice for each family about the chance of having further children with a ring chromosome 4. Additionally, prenatal testing or preimplantation genetic testing options with IVF are available.

Unique publishes separate guides to *Planning your next child*, *Prenatal genetic testing and diagnosis*, *A clinical genetics appointment* and *Supporting siblings of children with a rare genetic condition*

Can a ring chromosome 4 be cured?

There is no cure for a ring chromosome 4 since most of the effects of the genetic change took place during a baby's formation and development. However, knowing the diagnosis means that appropriate monitoring and interventions can be put in place.

Management

No clinical practice guidelines for ring chromosome 4 have been published (2026). The following suggestions have been provided by clinicians, who have personal experience of managing/treating individuals with ring chromosome 4, to improve quality of life and reduce complications.

Children and adults with ring chromosome 4 should be under the care of a multidisciplinary team. The team should include a geneticist and paediatrician (for children) who can oversee care so that development and behaviour can be monitored, and the best help given in the form of different therapies. Individuals may also have evaluations with various specialist doctors

Immediately following diagnosis

When not carried out as part of the diagnostic process, an evaluation of the features of a ring chromosome 4 that are present in the child or adult who has been diagnosed with this genetic condition is recommended. This can determine which of the features of ring chromosome 4 are present and how severe they are.

The following assessments are recommended:

- A [cardiac assessment with imaging \(echocardiogram\)](#) to look for [heart anomalies](#)
- A [renal assessment](#) with ultrasound to look for renal anomalies
- An [audiological \(hearing\) assessment](#) to check for hearing loss and determine severity if present
- A [vision assessment](#) to see if any interventions are needed
- A [neurodevelopmental assessment](#) to determine whether conditions such as learning (intellectual) disability are present

[Genetic counselling](#) for affected individuals and their families should also be offered together with the provision of signposting to [family support and resources](#).

Supportive care

How a person with a ring chromosome 4 is cared for is likely to require co-ordinated care by a multidisciplinary team of specialists. Depending on their health issues, this may include a/an:

Paediatrician – a doctor who specialises in the physical, mental and social health of children from birth to young adulthood.

Neurologist – a doctor who specialises in conditions of the brain, spinal cord and nervous system.

Cardiologist – a doctor who specialises in heart conditions.

Endocrinologist – a doctor who specialises in hormones and their effect on the body.

Urologist – a doctor who specialises in diagnosing and treating conditions affecting the urinary system.

Nephrologist – a doctor who specialises in conditions affecting the kidneys.

Surgeon – a doctor who is specially trained to perform medical operations.



Ophthalmologist – a doctor who specialises in conditions affecting the eyes.

Audiologist – a health care professional who diagnoses, treats and helps manage a condition that involves hearing or balance.

Occupational therapist (OT) – a health care professional who uses activities to aid self-management of a condition and can provide equipment.

Physiotherapist/physical therapist (PT) – a health care professional who uses exercise, movement, manual therapy, education and advice to help with the body's strength and mobility.

Speech and language therapist (SALT) – a health care professional who helps with speech, language communication and sometimes feeding/swallowing difficulties.

Psychiatrist – a doctor who specialises in mental health.

Specialist nurses and/or other healthcare professionals may need to systematically and comprehensively plan a child or adult's treatment.

Treatments and therapies

Early intervention can be beneficial and formal testing to assess specific, individual needs is recommended. An **education, health and care plan (EHCP)** in the UK, **individualized education plan (IEP)** in the US, or equivalent document in other countries, may be issued after a child has undergone an assessment, to help ensure that the educational, health and social provisions deemed necessary to support the child's needs are delivered.

Treatment will depend on the specific features and symptoms experienced by the person with ring a chromosome 4 but may include:

Physiotherapy for low muscle tone (hypotonia) and gross motor delays, which usually includes exercises to build core strength, improve balance, and enhance coordination for/to help children achieve motor milestones like sitting, crawling, and walking and to improve overall mobility.

Occupational therapy for fine motor skill delays and sensory sensitivities, which can include activities to improve hand strength and coordination for daily tasks (e.g. feeding and dressing) and sensory integration therapy to help individuals better process and respond to sensory information from their environment.

Speech therapy for a range of speech and language delays or difficulties and feeding/swallowing difficulties. For children with moderate to severe difficulties, this can include regular sessions focusing on Augmentative and Alternative Communication (AAC) methods (e.g. sign language, picture exchange systems and high-tech communication devices) and provides a functional means of communication for individuals who are non-verbal or have very limited speech.

Behavioural therapy for features of autism, ADHD and anxiety, which can include structured therapies like Applied Behaviour Analysis (ABA) to help manage challenging behaviours, improve social skills and develop coping strategies.

Medications may be prescribed depending on an individual's clinical features. For example, an anti-seizure medication (ASM) may be needed to help control seizures if present.

Surgery may also be needed to correct heart, abdominal, kidney or vision-related anomalies.



Surveillance

It is recommended that the following evaluations are considered to monitor an individual's existing symptoms, how they respond to care and treatment and whether any new symptoms emerge over time:

- Monitor for growth and adequate nutritional intake
- Neurodevelopmental and learning assessments at key stages or when there are concerns to optimise an EHCP/IEP
- Consider an ENT consultation for a palate review (particularly if there are feeding difficulties or speech concerns)
- Consider a baseline echocardiogram
- Consider a baseline renal ultrasound to assess for kidney and urinary tract anomalies
- Consider baseline audiologic assessments and reassessments if concern
- Consider a low threshold to investigate for seizures with a neurologic review (including MRI and EEG)
- Baseline and periodic vision assessments by an ophthalmologist
- Assessment of the need for social support, such as respite care and home nursing care, or genetic counselling and family planning advice

Research into new treatments for ring chromosome 4

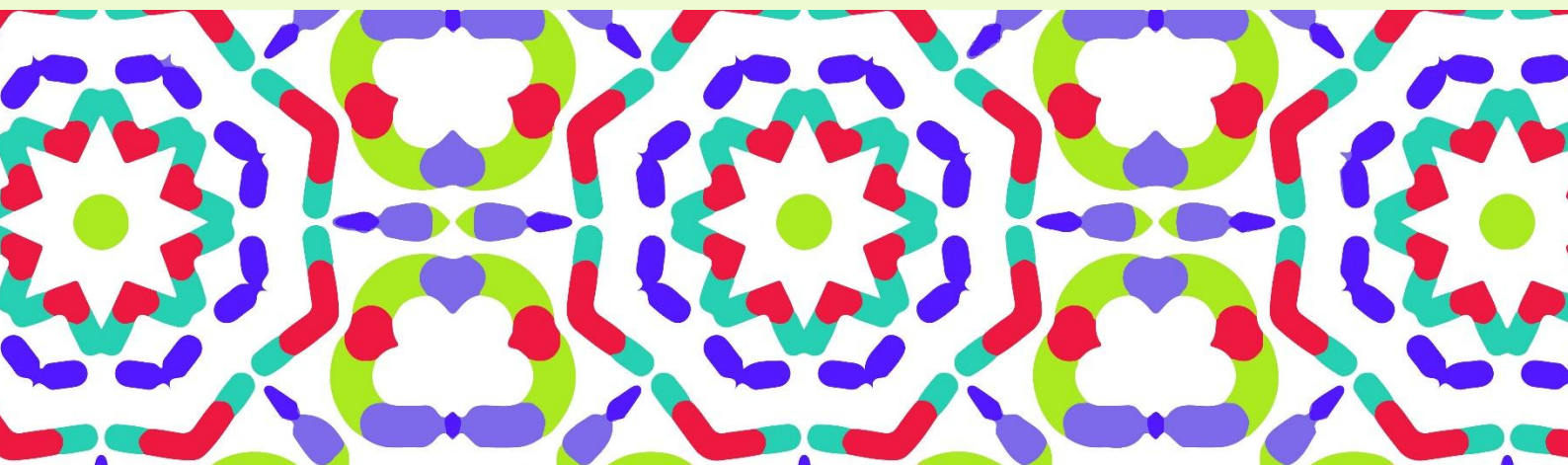
The genetic change causing ring chromosome 4 affects development of the body before birth. Therefore, a complete cure is unlikely, even in the future, since the body has already formed by the time a diagnosis is made. However, research into improved treatments and management for various features of ring chromosome 4, like delayed growth, is ongoing.

Details of clinical trials related to a particular condition or gene can be found at [ClinicalTrials.gov](https://clinicaltrials.gov) and [EU Clinical Trials Register](https://european-clinical-trials-register.eu).

Families say:

It can be hard not to compare your child with others, but every child is unique and may be affected differently. Some children may thrive socially, others may succeed academically, and some may learn to walk, talk, or sit up when no one believed they could. Each child's progress is their own.

To other families, I would say: take things one step at a time, keep asking questions, and never be afraid to advocate for your child and family. Celebrate every achievement, including the small steps others may not notice, and allow yourself to enjoy the day you have with your child."



Sources

The information in this booklet is drawn from the published medical literature and information from Unique members. In 2026, Unique had 11 members with a ring chromosome 4. The first-named author and publication date for articles in the medical literature are given to allow you to look for the abstracts or original articles on the internet in PubMed (pubmed.ncbi.nlm.nih.gov/).

References

Anderson CE, Wallerstein R, Zamerowski ST, Witzleben C, Hoyer JR, Gibas L, Jackson LG (1997) Ring chromosome 4 mosaicism coincidence of oligomeganephronia and signs of Seckel syndrome. *Am J Med Genet* 72(3):281–285. [Link to article](#)

Bone, K.M., Chernos, J., Thomas, M.A. (2024). Ring Chromosome 4. In: Li, P., Liehr, T. (eds) *Human Ring Chromosomes*. Springer, Cham. [Link to article](#)

Giersch, A.B.S. (2014). *Introduction to Cytogenetics*. In *Pathobiology of Human Disease*. Elsevier. [Link to article](#)

Kishi Y, Ikeda H (2018) A case of thumb polydactyly which ulnar thumb has no active motion in ring chromosome 4. *J Hand Surg Asian-Pac* 23(4):566–570. [Link to article](#)

Laleye A, Alao MJ, Adjagba M, Hans C, Delneste D, Gnamey DK, Ayivi B, Darboux RB (2006) Wolf Hirshhorn syndrome in a case of ring chromosome 4: Phenotype and molecular cytogenetic findings. *Genet Couns* 17(1):35–40. [Link to article](#)

Phillips EA, Caluseriu O, Schlade-Bartusiak K, Chernos J, McLeod DR, Thomas MA (2021) Clinical and molecular characterization of an almost complete ring chromosome 4 in two sisters, with recurrence due to gonadal mosaicism. *30(4):173–176*. [Link to article](#)

Hou JW, Wang TR (1996) Amelia, dextrocardia, asplenia, and congenital short bowel in deleted ring chromosome 4. *J Med Genet* 33(10):879–881. [Link to article](#)



Inform Network Support



Rare Chromosome Disorder Support Group
The Stables, Station Road West, Oxted, Surrey, RH8, 9EE, UK
Tel: +44(0)1883 723356
help@rarechromo.org | rarechromo.org

Join Unique for family links, information and support:

[Become a member](#)

Please help us to help you!

Unique is a charity without government funding, existing entirely on donations and grants.
If you can, please make a donation:

[Donate via our website](#)

Websites, Facebook groups and other links:

- [4p minus support group](#) (for people with a 4p deletion)

This information guide is not a substitute for personal medical advice. Families should consult a medically qualified clinician in all matters relating to genetic diagnosis, management and health. Information on genetic changes is a very fast-moving field and while the information in this guide is believed to be the best available at the time of publication, some facts may later change.

This guide was written by Sarah Gartly (BSc), Cumming School of Medicine, University of Calgary, Dr. Mary Ann Thomas (MD, CM), Department of Medical Genetics and Pediatrics, Cumming School of Medicine, University of Calgary and Unique (AP) and reviewed by Dr. Mary Ann Thomas (MD, CM), Department of Medical Genetics and Pediatrics, Cumming School of Medicine, University of Calgary.

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