

UNIQUE

UNDERSTANDING GENES & CHROMOSOMES

1q21.1 microdeletions

rarechromo.org

This guide is designed to help families and healthcare professionals looking after people with a 1q21.1 microdeletion. 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.

A 1q21.1 microdeletion is a very rare genetic condition in which a tiny piece is missing from one of the body's 46 chromosomes. The tiny missing bit raises the risk of learning, behaviour and mental health problems and physical abnormalities. But there is wide individual variation. Individuals with a 1q21.1 microdeletion range from people with no symptoms to others with developmental delay and health problems.

Genes and chromosomes

Our bodies are made up of billions of cells, containing tens of thousands of genes. Genes act like a set of instructions, directing our growth and development and how our bodies work. Genes are carried on structures called chromosomes. There are usually 46 chromosomes, 23 inherited from our mother and 23 inherited from our father, so we have two sets of 23 chromosomes in 'pairs'. Apart from two sex chromosomes (two Xs for a girl and an X and a Y for a boy) the chromosomes are numbered 1 to 22, generally from largest to smallest. Chromosome 1 is the largest of the chromosomes. Each chromosome has a short arm (on the left in the diagram at the bottom of page 3) called p from petit, the French word for small, and a long arm called q (on the right).

Looking at chromosome 1q

Chromosomes can't be seen with the naked eye, but if they are stained and magnified under a microscope, each one has a distinctive pattern of light and dark bands. Looking at chromosomes in this way, it is possible to see the points where the chromosome has broken and what material is missing, if the missing piece is large enough. A missing piece visible under the microscope is called a deletion.

In the diagram at the bottom of page 3 you can see the chromosome bands are numbered outwards from the point where the long arm meets the short arm. In a 1q21.1 microdeletion, the chromosome has broken in two places in band q21.1, leaving out the chromosome material between them. This particular deletion is so small that it can only be identified using molecular or DNA technology, in particular a technique using microarrays (array-CGH). This shows gains and losses of tiny amounts of DNA throughout the genome (also called duplications and deletions) and can show whether particular genes are present or not. A deletion so small that it can only be identified in this way is called a microdeletion.

Copy number variant

1q21.1 microdeletions are found in the general population, albeit rarely, as well as in people referred for chromosome testing. However, they are more common in people referred for genetic testing. A 1q21.1 microdeletion is sometimes called a copy number variant. People usually have two copies of each part of any chromosome, including chromosome 1. But it's quite common to have one copy or three copies of tiny parts of any chromosome.

The 1q21.1 band of chromosome 1 is an area where people in the general population do sometimes have one copy or three copies. Having just one copy or three copies appears to make no difference to development in some people. But since a lot of people with a copy number variant in 1q21.1 do have developmental problems, it seems that the deletion can make some people more vulnerable to difficulties.

1q21.1 microdeletion: two sizes

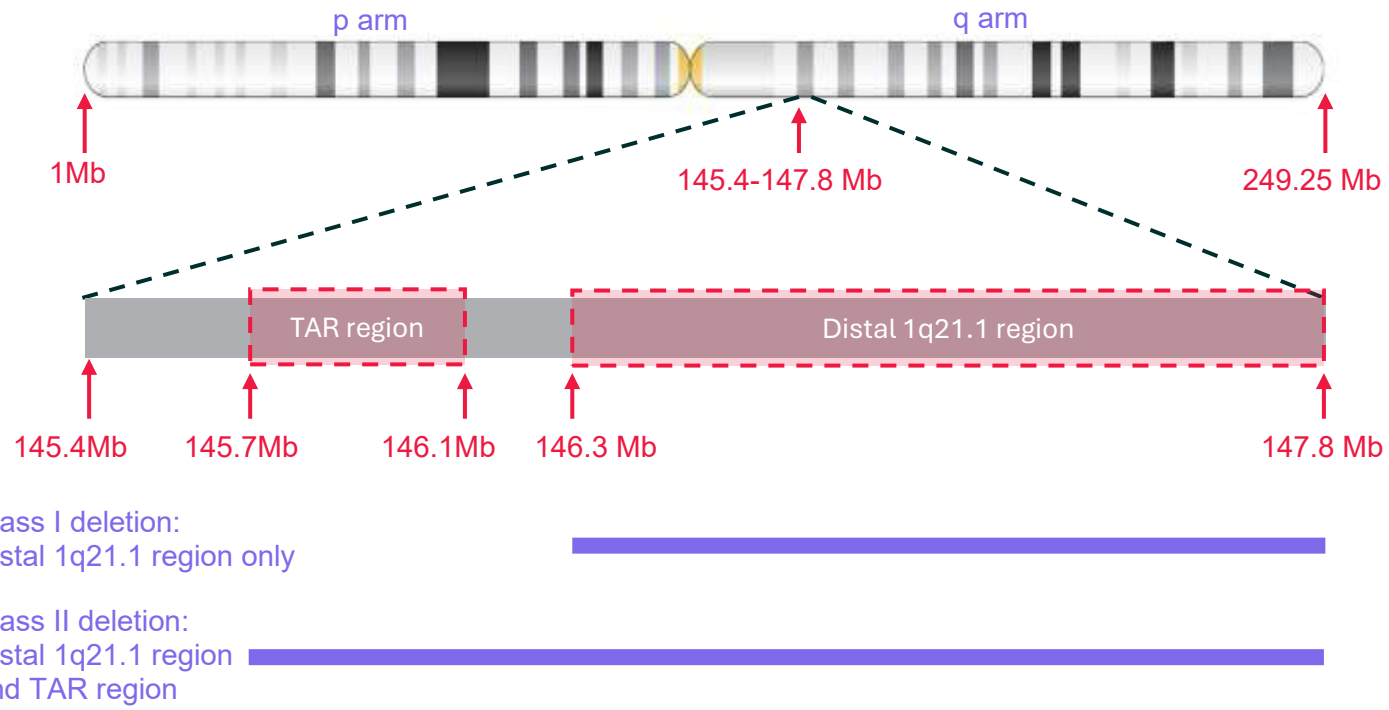


Diagram adapted from Nature Genetics Vol 40 (12) p1469 by kind permission of Dr Ankita Patel and subsequently updated. The numbers in this diagram refer to the human genome build 19 (hg19; see page 4 for more details). Your child's report may refer to a different human genome build. Please contact Unique or your genetic specialist for any help with understanding the report.

There are broadly two sizes of 1q21.1 microdeletion. The first type is smaller. It's called distal because it's closer to the tip of the long arm of the chromosome than the larger second type of microdeletion. A class 1 deletion spans around one million base pairs, or one so-called megabase (Mb) of DNA. Base pairs are the chemicals in DNA that form the ends of the 'rungs' of its ladder-like structure. Chromosome 1 has around 247 Mb in total and band 1q21.1 alone contains around 5.4 Mb.

bp = one base pair
kb = 1,000 base pairs
Mb = a million base pairs

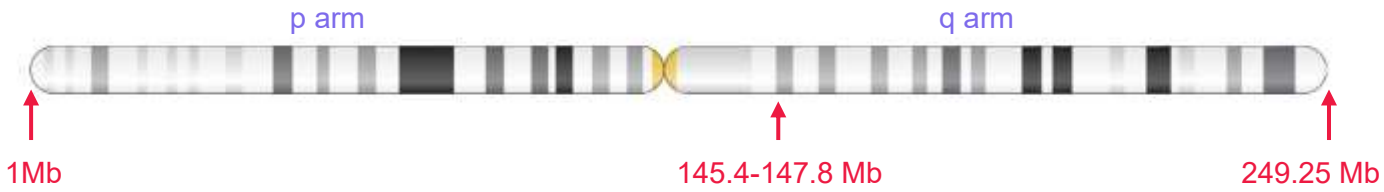
In a class 1 deletion, DNA is typically missing between around 146 Mb and 147.8 Mb, as you can see in the diagram above. The Mb numbers show a position on chromosome 1 between position 1Mb (the tip of the short arm) and position 247.975 Mb (the tip of the long arm). We know that the missing section includes at least nine known genes and there may be more (Brunetti-Pierri 2008; Mefford 2008).

The second type is a larger deletion of around 1.35 to 2 Mb, including 25 known genes. DNA is missing between around 145.4 Mb and 147.8 Mb, as you can see in the diagram above. This includes a region of the chromosome known to cause a syndrome known as TAR syndrome (Brunetti-Pierri 2008; Mefford 2008; Stefansson 2008).

TAR syndrome

T – Thrombocytopaenia. Reduced platelets in the blood, leading to spontaneous bruising and lengthy bleeding.

AR - absent radius. The outer, shorter bone in the forearm is missing.



Karyotype

You may receive a laboratory report including a karyotype. A karyotype is a way of describing what the chromosomes look like. It is likely to read something like this:

46, XY, del(1)(q21.1q21.1)

46	The number of chromosomes in your child's cells
XY	The two sex chromosomes: XY for males; XX for females
del	A deletion, that is, material is missing
(1)	The deletion is from chromosome 1
(q21.1q21.1)	The chromosome has two breakpoints, both in band 1q21.1. The material between these two breakpoints is missing

Array CGH report

Most often, a deletion of 1q21 is detected using a molecular technique. The laboratory will send a report that will usually look like one of these:

46,XY,del(1)(q21.1).arr cgh (RP11-337C18,RP11-533N14,RP11-102F23)x1

46	The number of chromosomes in your child's cells
XY	The two sex chromosomes: XY for males; XX for females
del	A deletion, or material is missing
(1)	The deletion is from chromosome 1
(q21.1q21.1)	The chromosome has broken in band 1q21.1
arr cgh	The analysis used microarray technology
(RP11-337C18, RP11-533N14, RP11-102F23)x1	Three different markers, whose position in the 1q21.1 band is known, have been shown to be missing

arr[hg19] 1q21.1(145167814-146090213)x1

arr	The analysis was by array (arr) comparative genomic hybridisation (cgh)
1q21.1	The chromosome involved is 1 and the position of the deletion is in band q21.1
145167814-146090213)x1	The base pairs between 145167814 and 146090213 have been shown to be missing. Take the first long number from the second and you get 922,399 (0.922 Mb or 922kb). This is the number of base pairs that are deleted
[hg 19]	Human Genome build 19. The human genome is updated as more information is found; each new version is called a 'build'. In each build, the base pair may well change slightly. In January 2013, hg19 is the newest build. Confusingly, hg19 is also sometimes called Genome Reference Consortium genome 37, GRCh37
x1	Means there is one copy of these base pairs, not two – one on each 1 – as you would normally expect

Are there people with a 1q21.1 microdeletion who have developed normally and have no health, learning or behaviour difficulties?

Yes, there are. The 1q21.1 microdeletion can be 'silent'. Some of the parents of children with a 1q21.1 microdeletion have the same microdeletion but do not have any unusual features, delayed development or behaviour problems. Other parents who also have the deletion are extremely mildly affected. Some children with a 1q21.1 microdeletion also develop normally.

The effect of some genetic variants ranges from being barely perceptible to being obvious and severe. In this sense they are like infections such as flu that can be mild or serious (Brunetti-Pierri 2008; Mefford 2008).

Most likely features

- Small head
- Increased possibility of mild or moderate developmental delay
- Slightly unusual facial features
- Increased possibility of behavioural or mental health problems
- Heart problem
- Loose joints or double-jointedness

Other features

- Seizures
- Disturbances in the lens of the eye
- Increased risk of other inborn anomalies

Most likely features

Small head

Studies have shown that around two thirds of people with this microdeletion have a small head or a head that is small compared with their overall size. This suggests that the microdeletion influences brain growth. Some people with an extra copy of this section of chromosome 1 (a microduplication) have an unusually large head and this also supports the idea that the microdeletion influences head growth. Researchers have identified a gene called HYD1N (see diagram, page 3 and Some genes in 1q21.1, page 11) that is likely to be important in determining head growth.

There is also a possible link between head size and mental health problems, particularly schizophrenia. This does not mean that everyone with a 1q21.1 microdeletion and a small head will develop schizophrenia. On the other hand, it does mean that healthcare professionals should be alert to early warning signs (Brunetti-Pierri 2008; Mefford 2008).

Among Unique members with the microdeletion, head size is variable. Three out of seven members have a large or relatively large head, one is average and three small.

Increased risk of developmental delay and learning difficulties

Some children with a 1q21.1 microdeletion develop at a normal rate and cope well academically without support. Others are slow to reach their developmental milestones, need extra help at school and may need special schooling. This means that a baby or child with the microdeletion should be monitored vigilantly for delay and extra help and therapies should be sought and offered promptly.

The microdeletion does not make it possible to predict how mild or severe the delay and the learning difficulties will be. The spectrum includes people who have no noticeable problems – and a few people who are profoundly affected. In most cases the delay is mild or moderate (Mefford 2008; Unique).

Among Unique members, the range of developmental delay is very broad indeed, from none to profound. Babies and toddlers may be late to reach their developmental milestones
(sitting, crawling, walking) and fine motor control and toilet training may also be delayed. Low muscle tone was found in around a quarter of children in one study as well as among Unique members.

Unique's experience is that when seizures have been hard to control a more severe degree of learning disability has become apparent (Mefford 2008; Unique).



6 weeks 10 months Toddler

Slightly unusual facial features

Most children and adults with a 1q21.1 microdeletion look like other members of their family. They may, however, have one or two slightly unusual facial features such as an unusually prominent forehead, deep-set eyes and a somewhat bulbous nose. These features do not usually make them stand out. But they may mean that your child has a passing resemblance to others with the microdeletion. Unique families have commented that the broad forehead can make their child's face look triangular. Where more than one child in a family has the microdeletion, the unusual facial features are not necessarily the same.

A gallery of adults and children with the microdeletion has been published (BrunettiPierri 2008) and is available to families from Unique on request.

Heart problem

It is uncertain whether having a 1q21.1 microdeletion puts a baby at risk of being born with a heart problem. Some researchers have found a high incidence of heart problems, but others have not. In a study of the complex heart anomaly known as Tetralogy of Fallot, one per cent of affected children had a 1q21 deletion. Heart problems have not been identified among Unique members (Greenway 2009; Brunetti-Pierri 2008; Mefford 2008; Christiansen 2004; Unique). A gene known as GJA5 has been identified that may contribute to heart problems (see diagram, page 3 and Some genes in 1q21.1, page 11).

The heart problems diagnosed in individual children may be single or multiple. As well as Tetralogy of Fallot, they include:

- **Patent ductus arteriosus** – a channel known as the ductus arteriosus is a normal short cut in the circulation of the unborn baby. The channel usually closes naturally soon after birth. When it stays open, the lungs receive more blood than they should and the heart has to work too hard. It can be closed using minimally invasive surgery by inserting a coil via an artery in the thigh or it can be clipped or tied shut.
- **Atrial septal defects** (ASDs) - holes in the muscular wall between the two filling parts of the heart. Some blood flows through from the left to the right side, increasing the amount of blood flowing to the lungs. Treatment depends on the type of defect, whether it closes spontaneously and its size. Treatment can include medical management, taking medications to help the heart to work better, control of potential infection to the inner surfaces of the heart and surgical repair with stitches or a special patch.
- **Ventricular septal defects** (VSDs) - holes in the wall between the two pumping chambers of the heart (ventricles). This allows blood to flow from the left to the right chamber, increasing the blood flow to the lungs. Treatment is determined individually. Small VSDs may close spontaneously; a larger VSD usually needs surgical repair to prevent lung problems that would develop from extra blood flow.
- **Transposition of the great vessels** - the main blood vessels (aorta and pulmonary artery) leading from the heart are reversed. A baby usually needs surgery very soon after birth.
- **Truncus arteriosus** - instead of having separate blood vessels leading out of each side of the heart, a baby with a truncus arteriosus has a single blood vessel leaving the heart that then branches into vessels that go to the lungs and the body. This great vessel usually sits over both the ventricles and the upper part of the wall between the two chambers is missing,, resulting in a VSD. Early surgical repair is usually needed.
- **Aortic valve abnormalities** - the aortic valve regulates blood flow from the left ventricle into the aorta, the blood vessel leading to the body. The valve may be weakened or inefficient, causing blood to flow back into the left ventricle of the heart. The valve normally has three flaps or valves, but a bicuspid valve has only two. In many cases no treatment is needed but a valve replacement may be needed.

- **Aortic abnormalities**—these include dilation of the aorta as it leaves the heart and coarctation (narrowing) of the aorta. The narrowing forces the left side of the heart to pump harder to push blood through. Treatment is tailored to the individual but, if necessary, the narrowed section can be surgically removed or made larger. Another abnormality seen is interrupted aortic arch, where the aorta is blocked leaving no direct way for red blood from the heart to reach body parts 'downstream' from the blockage. It needs surgical repair as soon as possible.

Loose joints or double-jointedness

One study has pinpointed very loose joints or double-jointedness in around a quarter of people with a 1q21.1 microdeletion. The same study found that a similar number of people had a low muscle tone (hypotonia). In some people the two conditions coincided. In others they didn't. Among the Unique group, low muscle tone was fairly common but very lax joints were not seen (Mefford 2008; Unique).

Early physiotherapy and regular exercises can improve hypotonia very much in some children. Children with very lax joints may need supports, splints or special footwear while learning to walk.

Increased risk of behavioural or mental health problems

Children and adults with a 1q21.1 microdeletion can be affectionate and sociable with no behaviour problems. But as a group, they appear to be at risk for a range of behaviour difficulties and mental health problems. We do not know yet whether these unusual behaviours and mental health problems are a result of the 1q21.1 microdeletion or a chance association. This is particularly true when a parent and child have a similar behaviour pattern and both have the 1q21.1 microdeletion.

The increased frequency of behaviour difficulties suggests vulnerability in this area and means that children and adults should be monitored and families offered early support. The key concerns that have emerged so far are listed below.

- Attention deficit with hyperactivity. This has only been observed in children with learning difficulties or developmental delay
- Antisocial behaviour. Seen in parent: child pairs and those whose deletion has not been inherited
- Aggressiveness. This has only been seen in children with learning disabilities
- Autistic-like behaviour. This has only been seen in children with learning disabilities
- Anxiety. Seen in parent: child pairs and those whose deletion has not been inherited
- Depression. This has been seen in parent: child pairs
- Hallucinations

Schizophrenia is more common among people with a 1q21.1 microdeletion than in the general population. It is possible that small head size may be somehow involved, but the link is not yet clear. People with the 1q21.1 microdeletion and schizophrenia respond to neuroleptic drugs in the normal way (Brunetti-Pierri 2008; International Schizophrenia Consortium; Stefansson 2008).

Unique families report marked mood swings in their children, with fierce temper outbursts (screaming, aggressive) and stubborn refusal to conform. However, patterns vary and children and adults can also behave delightfully.

> ***"On a good day, he is such a light in our lives. He can certainly make anyone laugh!"***
> **– 5 years**

"She can be engaging, charming, fun loving and affectionate, with a good sense of humour and of rhythm. She is totally innocent, with no guile, totally honest and living in the moment. But she is very Jekyll and Hyde and has prolonged screaming outbursts lasting up to three hours at a time." – 25 years

Other features

Seizures

Seizures have been reported in 6/55 people in the medical literature and in 3/10 Unique members. In the Unique members, seizures started in the first year of life. In one case they resolved by two years, but another child has a type of seizure disorder known as LennoxGastaut syndrome with different types of seizure that are very difficult to control. An adult has absence, complex partial and other unidentified seizure types that lead to long periods of being pale, sleepy, vacant and 'out of it' (Brunetti-Pierri 2008; Mefford 2008; Christiansen 2004; Unique).

Disturbances in the lens of the eye

Cataracts (clouding of the lens of the eye) have been seen in 5/44 people with a 1q21.1 microdeletion, including two sisters, although their father who also carries the deletion had no cataracts. Cataracts have not been seen in Unique members with the deletion. The type of cataracts varies from being dense and diagnosed at birth to subtle cataracts only found after a specific search. Cataracts that cause no visual problems do not need treatment but if the cataract affects vision, surgery to remove it is usually considered.

A gene called GJA8 has been identified that may contribute to problems with the lens of the eye (see diagram, page 3 and Some genes in 1q21.1, page 11).

In people with a 1q21.1 microdeletion other eyesight problems include long or short sight, a squint (strabismus), Duane anomaly (restricted turning of eye, associated with narrowing of the eye), abnormally small eyes, dislocated lenses, coloboma (a developmental defect) and double vision. Some problems can be corrected with glasses although some children will not tolerate wearing them. Other problems, such as a squint, can generally be corrected with surgery. Unique has one member with this deletion who is registered as blind.

Increased risk of other inborn anomalies

A wide range of other minor or more serious conditions identified at birth have been seen, but they don't seem to follow a particular pattern. They include: missing ribs; extra fingers or toes; webbed or incurving toes; clubfeet; unusual brain structure; hydrocephalus (increased fluid in the brain); minor genital anomalies; birthmarks; tongue tie; hernia in the groin; cleft palate; lung malformation; small kidneys (renal hypoplasia), which can also have abnormal tissue (renal hypodysplasia) or absent kidney/s (renal agenesis) (BrunettiPierri 2008; Mefford 2008; Sanna-Cherchi 2012; Westland 2015; Verbitsky 2015 & 2019; Unique).



9 years

At birth

Among Unique members, babies - even brothers and sisters - are very different at birth. Some babies are born small and light, while others have grown well in the womb and are a good size at birth. Some babies have physical anomalies, while others are perfectly formed. Apgar scores, a measure of wellbeing with a score out of 10, range from low to full marks. Some babies have feeding difficulties, problems latching on to the breast and bring their feeds back frequently. Other problems noted by Unique members among newborn babies are mild jaundice, a blocked tear duct, coughing up blood and gasping for breath and suspected deafness.

Feeding

Among five Unique members, all have had feeding difficulties. These have included sucking weakly at breast or bottle, bringing feeds back, lack of appetite, choking on lumps, failing to chew, gastro-oesophageal reflux, delayed gastric emptying, uncoordinated swallowing and tongue thrusting. While three babies were breastfed, in one instance using techniques for babies with low muscle tone, others needed tube feeding and treatment for reflux, including a low-allergen milk formula. Two babies' feeding difficulties were so severe that they were fed for a time by gastrostomy tube direct to the stomach. One of these babies was born with a cleft palate (a hole in the roof of the mouth). Two babies grew into very picky eaters who accepted only a limited range of food textures.

Growth

Four out of five Unique members were very short as children including one who was a normal weight and length at birth. A delay in bone age appears to be common. Four out of five were very thin, including one who was tall for his age. One child grew into a short adult with a stocky physique. Limb length is variable even within the same family, and some children are short-limbed while others are long-limbed. One very thin child had a large stomach, perhaps due to slack abdominal muscles.

Health and wellbeing

Infections are common in childhood and some children with chromosome disorders seem particularly prone to them and to suffer worse when they catch them. Ear and chest infections seem to be particularly common. However, there is no evidence that children with 1q21.1 microdeletions are more prone to infection than other children although one Unique member has low levels of natural infection-fighting antibodies.

It isn't certain whether any of the illnesses reported are linked with the 1q21.1 microdeletion or just occurred by chance in the same person. They include: a dry mouth and eyes, with possible diagnosis of the autoimmune disorder Sjögren's syndrome; rheumatoid arthritis; urinary reflux and enlarged kidneys (hydronephrosis); precocious puberty; multiple sclerosis; asthma; multiple allergies; anaemia (Brunetti-Pierri 2008; Unique).

Hearing

Among Unique members, 5/10 have some hearing loss. In three cases, this was temporary and caused by a build-up of fluid in the middle ear (glue ear), readily treated by insertion of aeration tubes into the eardrum. A fourth child and possibly a fifth have permanent nerve deafness in one ear (Unique).

Why are people with a 1q21.1 microdeletion so different from each other?

One reason for the differences is that the amount of missing chromosome material and number of missing genes is larger in some people. But people in the same family with the same size microdeletion can be very differently affected. We don't yet understand all the reasons for this, but one possible explanation is undiscovered genes. The 1q21.1 band of chromosome 1 has such a complex structure that its precise sequence has not been completely mapped. There are still 15 gaps in the map and it's possible that genes exist in these gaps that contribute to the effects of the microdeletion.

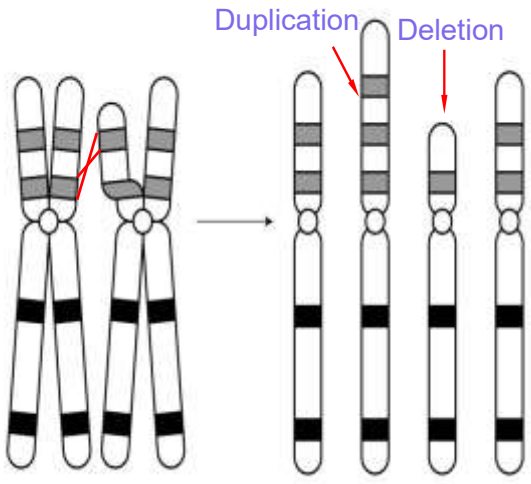
How did this happen?

1q21.1 microdeletions can occur out of the blue for no obvious reason, or they can be inherited from either the mother or the father. The only way to be certain is to check the chromosomes of both parents. The parents' chromosomes should be checked even if they are themselves completely healthy with no developmental problems at all.

If one parent has the same microdeletion, it has been inherited. If both parents have usual chromosomes, the 1q21.1 microdeletion is a new occurrence. The genetic term for this is de novo (dn). A new 1q21.1 microdeletion has been caused by a mistake that occurred when the parents' sperm or egg cells were formed or in the very earliest days after fertilisation. This is part of a natural process and as a parent there is nothing you can do to change or control it.

At one point, all the chromosomes including the two chromosome 1s pair up and swap segments. To pair up precisely, each chromosome 'recognises' matching or nearmatching DNA sequences on its partner chromosome. However, throughout the chromosomes there are many DNA sequences that are so similar that it is thought that mispairing can occur.

The 1q21.1 region has an extremely complex structure. Three-quarters of it consists of at least four blocks of DNA that are more than 90 per cent similar to each other. It is quite likely that these very similar blocks have caused a mismatch. When researchers examined the breakpoints in the chromosome in individual people, they found that they fell within these near-matching DNA sequences. In most people, the breakpoints occurred within parts of them that are virtually identical.



Although no-one has ever seen this happen, it is believed that when the exchange of genetic material, known as 'crossing over' - occurs after mismatching, it is unequal, looping and cutting out a short length of the chromosome.

What is certain is that as a parent there is nothing you could have done to prevent this from happening. No environmental, dietary, workplace or lifestyle factors are known to cause 1q21.1 microdeletions. There is nothing that either parent did before or during pregnancy that caused the microdeletion.

The diagram shows mismatching in the short arm of a chromosome.

If one person in a family with the 1q21.1 microdeletion is mildly affected, will others in the same family also be mildly affected?

Not necessarily. There is a lot of variation between different members of the same family. We know that if one person is mildly affected, others may be more severely and obviously affected.

Can it happen again?

Where both parents have normal chromosomes, it is unlikely that another child will be born with a 1q21.1 microdeletion or any other chromosome disorder. Very rarely (less than 1%), both parents have normal chromosomes by a blood test, but a few of their egg or sperm cells carry the microdeletion. This is called germline mosaicism, and it means that parents whose chromosomes appear normal when their blood is tested can have more than one child with the deletion.

In families where the 1q21.1 microdeletion has been inherited from a parent, the possibility of having another child - either a girl or a boy - with the 1q21.1 microdeletion rises to 50% in each pregnancy. However, the effect of the microdeletion on the child's development, health and behaviour cannot be reliably predicted.

Your genetics centre should be able to offer counselling before you have another pregnancy.

Will my child with a 1q21.1 microdeletion have similarly affected children?

Your child with a 1q21.1 microdeletion may well want to have children. We have not known about the condition for long enough to be certain if it affects fertility, but it is likely that fertility will be normal. In each pregnancy, someone with the deletion has a 50 per cent risk of passing it on and a 50 per cent chance of having a child without the deletion. Their ability to look after a child is very likely to be closely related to their own learning ability.

Some genes in 1q21.1

The part of 1q21.1 that most people have lost is rich in genes. You can see the approximate position of three of these genes in the diagram on page 3.

The HYD1N gene found on chromosome 16q22.2 has a part copy (paralogue) that was inserted into 1q21.1 during evolution. The HYD1N gene on 1q21.1 is only active in the brain. In individuals in whom it is missing, head size is small, while individuals who have an extra copy of this gene have a large head. This strongly suggests that the HYD1N gene plays a role in determining head size (Brunetti-Pierri 2008; Mefford 2008).

GJA5 is a gene that produces a protein known as Connexin40. It's expressed in the upper chambers (atria) of the heart and not having enough is associated with congenital heart problems. Some people who do not have this gene have normal hearts, though, and the reason for this is not fully understood (Mefford 2008; Christiansen 2004).

GJA8 is a gene that produces a protein known as Connexin50 whose job is to keep the lens in the eye transparent. The gene is expressed in the cornea of the eye, in the retina and the brain. Some people who have lost GJA8 have cataracts which can be very subtle or obvious (Mefford 2008).

The GJA8 gene has also been associated with schizophrenia (Stefansson 2008; Christiansen 2004).

Sources and references

The information in this guide is drawn from what is known about around 60 people with a 1q21.1 microdeletion, aged between birth and 31 years. The first named author and publication date are given to allow you to look for the abstracts or original articles on the internet in PubMed (www.ncbi.nlm.nih.gov/pubmed). If you wish, you can obtain articles from Unique. The guide also draws on Unique's database (Christiansen 2004; Redon 2006; Mefford 2008; Brunetti-Pierri 2008; Stefansson 2008; Greenway 2009; SannaCherchi 2012; Westland 2015; Verbitsky 2015 & 20 19; Unique).

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 I rarechromo.org

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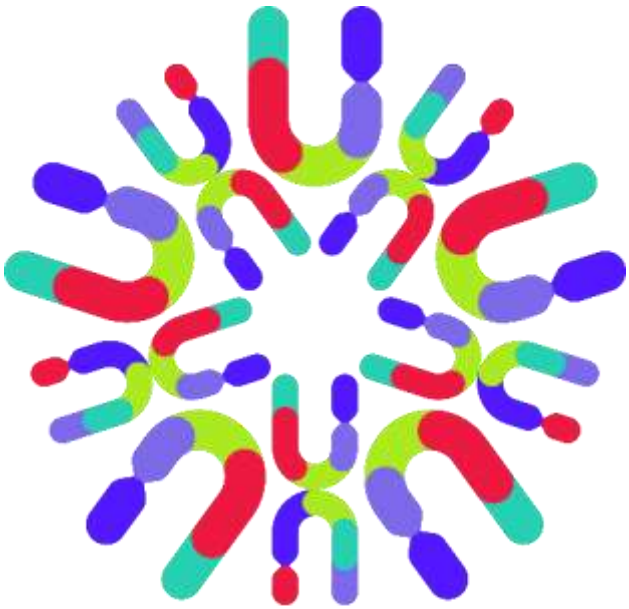
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This information guide is not a substitute for personal medical advice. Families should consult a medically qualified clinician in all matters relating to genetic diagnosis, management and health. Information on genetic changes is a very fast-moving 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 compiled by Unique and reviewed by Dr Heather Mefford, Acting Assistant Professor, Genetics, University of Washington School of Medicine, USA and by Professor Maj Hultén, Professor of Medical Genetics, University of Warwick, UK. The CAKUT (congenital anomalies of kidney and urinary tract) information in this guide was updated in 2021 by Dr. Emily Groopman, MD/PhD (Broad Institute of MIT and Harvard, Cambridge, MA, USA; Boston Children's Hospital, Boston, MA, USA)

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