

Support and Information



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9p24 deletions



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Sources & references

Researchers have described around 12 people with a 'pure' 9p24 deletion in the medical literature. The oldest person reported was 18 years old.

Unique has nine members with a 'pure' 9p24 deletion/microdeletion.

This leaflet tells you what we know about these people.

The first author's name and publication date of medical articles is given in case you want to look for them on the internet in PubMed. There is a list of articles on page 11.

Articles describing people with a 9p24 deletion and extra material from another chromosome arm (duplication) were not an information source for this leaflet but are listed on page 11.

9p24 deletions

A chromosome 9p deletion means that part of one of the body's chromosomes has been lost or deleted. If the missing chromosome material contains important instructions for the body, learning difficulties, developmental delay and health problems may occur.

How serious these problems are depends on how much of the chromosome has been lost and where the deletion is.

You cannot see chromosomes with the naked eye, but if you stain them and enlarge them under a microscope, you can see that each one has a distinctive pattern of light and dark bands. 9p24 consists of three bands - 24.1, 24.2 and 24.3 - at the top of the diagram on the next page.

Genes and chromosomes

Our bodies are made up of billions of cells, most of which contain a complete set of tens of thousands of genes. Genes act like a set of instructions that control growth, development and how our bodies work.

Genes are carried on microscopically small, thread-like 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'. The chromosomes and genes are made up of a chemical substance called DNA.

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. Each chromosome has a short arm (at the top in the diagram) called p from 'petit', the French for small, and a long arm called q (at the bottom). In a 9p deletion, material has been lost from the short arm of one of the two chromosome 9s.

The point where the short and long arms meet is the **centromere**. The tips of chromosomes are called **telomeres**. The areas close to the tips are the **subtelomeric** regions.

A small piece or a large piece of the chromosome can be missing. The missing piece may be large enough to be identified under a microscope. But it may be so tiny that it can only be identified using new technology with tests such as array-CGH. It is then called a **microdeletion**. These tests are sometimes used to check if certain genes are missing and to be more exact about where the chromosome has broken.

A 9p24 deletion is usually a type of deletion called **terminal**. The chromosome has broken in one place and the part of the chromosome from the breakpoint to the end of the arm is missing. Occasionally a 9p24 deletion is **interstitial**. There are two breakpoints within 9p24 that have rejoined and the bit between them is missing.

References

Techakittiroj 2006: Beijing Da Xue Xue Bao. 2006 Feb 18;38(1): 92-3; Ounap 2004: Am J Med Genet 130A: 415-423; Witters 2004: Ultrasound Obstet Gynecol 23: 414-9; Balliff 2000: Am J Hum Genet 67: 1356-1359; Castorina 2000: Genetic Counseling 11: 3 229-239; Muroya 2000: Jnl Clin Endocrinol Metab 85: 3094-100; Wouters 1999: Ann Genet 1999 42(3): 160-5; Repetto 1998: Am J Med Genet 76: 306-309; McDonald 1997: Am J Med Genet 73(3): 321-6; Shapira 1997: Am J Med Genet 69: 360-4; Veitia 1997: Genomics 41: 271-4; Schimmenti 1995: Am J Med Genet 57(12): 52-6; Kohler 1994: J Med Genet 31(9): 712-4; Teebi 1993: Am J Med Genet 46(3): 288-92; Verbraak 1992: Ophthalmic Paediatric Genet 13: 165-70; Dowman 1989: J Med Genet 26: 525-8; Huret 1988: J Med Genet 1988 25: 741-9; Katsushima 1987: Arch Ophthalmol 105: 323-4.

9p24 deletion with a duplication

In many cases the 9p24 deletion occurs with a duplication (an extra piece) of a different arm of a chromosome. This can change the effects of the 9p24 deletion and so these cases have not been included in the sources for this leaflet. If you wish to know more about any of them, please contact info@rarechromo.org

Break point in 9p24 not specified

1q41 Verbraak 1992
1q42.2 *Unique*
2q33 Katsushima 1987
3p21.3 *Unique*
4p13 Muroya 2000/5
4q27 Wouters 1999
4q27 *Unique* (x2)
4q? *Unique*
5q21 Castorina 2000
5q31 Schimmenti 1995
7p15.3 Teebi 1993
7q21 (Huret 1988)
8p21 McDonald 1997
8p21 *Unique*
8q24.2 *Unique*
9p23p12 Veitia 1997
9q34.1 Shapira 1997
10p12 *Unique*
11p15 Castorina 2000
13q22 *Unique*
16q Dowman 1989
16q22 Muroya 2000/6
22q12 Castorina 2000
X?q26 *Unique*



Break point in 9p24 specified

3p14.2 Witters 2004
16q24 *Unique*
17p13.3 Kohler 1994
7q32 (Ounap 2004)
5q34 *Unique*
8p21.1 *Unique*
10q24.1 *Unique*
14q24.2 *Unique*
16p12.2 *Unique*

Most 9p24 deletions occur when both parents have normal chromosomes. The term that geneticists use for this is **de novo (dn)**. De novo 9p24 deletions are caused by a change that occurred when the parents' sperm or egg cells were formed. We know that chromosomes must break and rejoin when egg and sperm cells are formed but this only occasionally leads to problems.

The breaking and rejoining is part of a natural process and as a parent you cannot change or control it. Children from all parts of the world and from all types of background have 9p24 deletions. No environmental, dietary or lifestyle factors are known to cause them. There is nothing that either parent did before or during pregnancy that can be shown to have caused the deletion to occur and equally nothing could have been done to prevent it.

Can it happen again?

The possibility of having another pregnancy with a 9p24 deletion depends on the parents' chromosomes. If both parents have normal chromosomes, the deletion is very unlikely to happen again.

If a blood test shows that either parent has a chromosome change involving 9p24, the possibility is increased of having other pregnancies with chromosome changes. Usually one parent has a balanced translocation. Occasionally one parent has the same chromosome change as the child.

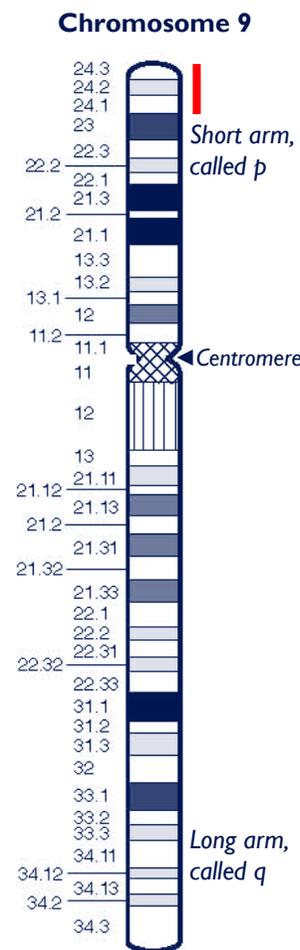
Once the family chromosome change or translocation is known, a test can be done in any future pregnancy to find out whether the baby's chromosomes are affected. Discussing the chromosome change with other family members gives them the opportunity to have a blood test to see if they too carry it. A genetic specialist can give you more guidance for your family.



Two pairs of brothers, one with a 9p24 deletion (on left in each picture), one with normal chromosomes (right).

Will my child with a 9p24 deletion also have children with a 9p24 deletion?

Adults with 9p24 deletions may form close relationships and want to have children. Boys with a serious genital anomaly are not likely to be fertile but it is likely that in boys with minor anomalies or none at all and in girls fertility can 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 degree of learning difficulty.



How important is the amount of deleted material?

Your genetic specialist can tell you more about the chromosome material that has been lost. You will almost certainly be given a **karyotype**, a shorthand code for your child's chromosomes that shows the points where the chromosome has broken and rejoined. Where part or all of the chromosome between points known as markers D9S285 at 9p22.3 and D9S286 at 9p24.1 has been lost, a syndrome known as 9p- or 9p deletion syndrome occurs (see *Unique's* leaflet **9p deletions**).

When the chromosome has broken in the 9p24 bands, the effects are less certain. Some people have been described in the medical literature with a tiny deletion from very close to the end of the chromosome who have no developmental difficulties (Techakittiroj 2006; Balliff 2000; Repetto 1998). Yet the 9p24 bands are known to contain some genes that are important for development. So people with a 9p24 deletion do not all have the same problems or features. There will be differences between your child and others and these differences can be quite marked. It is important to see your child as an individual and not to make direct comparisons with others. After all, each of us is unique. But some features are similar in people with a 9p24 deletion. This leaflet describes the things that are similar.

How many people have a 9p24 deletion?

The technology for finding some very small 9p24 microdeletions has not been widely available for long, so we do not know yet how often they occur. As well as the people described in this leaflet, there are likely to be thousands more people who have not been diagnosed.

Your baby at birth

What was unusual?

How many affected?

Higher risk pregnancy (bleeding in first 3 months; low levels of amniotic fluid (2/10); small for dates (3/10); little fetal movement; pre-eclampsia)	7/10
Preterm labour, actual or threatened	4/10
Birth weight in normal range at term	5/5
Normal feeding/ breastfeeding	6/8
Genital anomalies in boys	1/3
Cataract in one eye	2/8

Range of birth weights at term: 2.6kg (5lb 12oz) to 3.9kg (8lb 10oz)

■ Higher risk pregnancy

Something abnormal was reported in six pregnancies out of eight. There were concerns over the baby's growth rate in three pregnancies although only one of these babies was small for dates at birth. In the second half of two pregnancies, a low level of amniotic fluid was noticed (oligohydramnios) but in neither case was there an underlying abnormality of the kidneys - a common cause of oligohydramnios.

Despite these pregnancy concerns, all babies for whom we have information except one were born healthy and in good condition. The exception was a baby delivered early at 36 weeks because of oligohydramnios who developed respiratory distress syndrome and required special care and supportive oxygen as a newborn. By the age of three he was entirely healthy (Repetto 1998; *Unique*).

■ Preterm labour, actual or threatened

Three pregnancies were threatened with premature labour, but only one baby was delivered very early at 32 weeks and his subsequent development was normal and healthy. In the other two cases, delivery was delayed until 36-7 weeks and both babies thrived after delivery.

■ Birth weight in normal range at term

Despite concerns over the baby's growth rate during pregnancy, all babies for whom *Unique* has information were an appropriate weight for their gestation, although there was a very broad range of birth weights.

■ Normal feeding/ breastfeeding

Unusually for a group of babies with a chromosome disorder, feeding problems were not common after birth and most families reported that their baby breastfed well and without difficulty. Only two families reported any real feeding difficulty, in one case where their baby fed very slowly and needed to use premature baby teats with a bottle (she was not premature) and in another case where the baby developed an allergy both to dairy and soy products.

Despite efficient, problem-free breastfeeding, one baby showed signs of gastro oesophageal reflux, bringing back part of his feeds. This settled by the age of two. Mild to moderate reflux can usually be controlled by careful positioning of your baby in a semi upright position to feed, by keeping the head end of the cot raised and if necessary by the use of prescribed medication or anti-reflux milks.

■ Genital anomalies in boys

Some baby boys with a 9p24 deletion are born with a genital anomaly. It is not yet known how commonly the genital anomalies occur, but reports from support groups including *Unique* suggest that they are much less common than the medical literature suggests, where 22 cases were reported by 2004 (Ounap 2004).

The genital abnormalities are believed to be caused by the loss of two sex-determining genes close to the tip of 9p24.3, called *DMRT1* and *DMRT2*. We do not know why some boys are affected while others are not, but these genes may have a sensitive threshold above which normal male development occurs, while if the threshold is not met some anomaly occurs.

Caring for your child with a 9p24 deletion

Children and adolescents will generally need a high level of personal care. Their low muscle tone makes it more difficult for them to grasp and manipulate objects such as cutlery and most children will continue to need help or supervision with dressing and washing even as adults. Toilet training is also usually delayed. Children's partial understanding of their surroundings means that they need continued supervision both at home and at school and families of older children report that they need a regular routine and frequent reminders to keep them on track.

Therapies available to your child depend partly on your local services, but most children benefit from early physiotherapy and speech therapy. Early intervention with play therapy and occupational therapy is helpful but it is not certain how long the benefit lasts.

Behaviour

Most families report that young babies and children have a sociable and pleasant temperament and enjoy the company of their family and peers at school. Young children may experience difficulties in interacting with typically developing children and understanding boundaries and may benefit from being taught social skills. However, any difficulties appear to be generally mild. Many families report that their child particularly enjoys interacting with animals.

Among teenagers and especially those with a more marked learning disability, challenging behaviour may develop but this is not consistent and generally lessens with maturity and behaviour modification although considerable ongoing input may be needed.

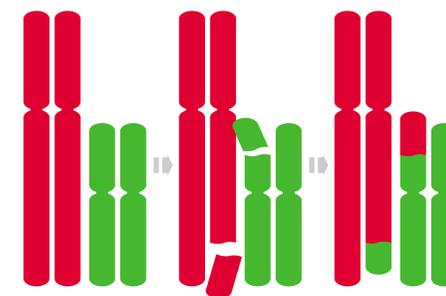
“ He is known to make everybody he meets welcome and loved. He is very sweet to everybody: outgoing, personable, independent but able to play with others too, and with an animated personality. He is loveable at the right times, funny at the right times and charming ” – 3 years

“ She is very loving but shows little emotion. Socially, she stays in contact with the family where she went for respite and occasionally sees old school friends ” – 18 years

Why did the 9p24 deletion occur?

Some 9p24 deletions are the result of a rearrangement in one parent's chromosomes. This is usually a **balanced translocation** in which material has changed places between chromosomes but no material has been lost or gained and the parent usually has no difficulties with health or development.

Occasionally, when the deletion is very small, one parent appears to have the same deletion as the child. A blood test to check the parents' chromosomes will show what the situation is.



Balanced translocation

difficulties in forming certain consonants and possibly in tongue control. This means that in the early years speech is much more understandable to people who know the child well.

Communication is supported by object and picture substitution and in some children by learning to sign as well as by children's generally sociable temperament. Families have found early intervention with speech therapy very helpful.

“ She is still way behind her peers but her speech and understanding are getting better every day. She receives speech therapy at school every two weeks with work sent home for parents to use ”

“ She has difficulties saying sounds such as *l, r, f, pl, bl, cl, st* and *sn* ” – 6 years

“ He has been talking in broken English since the age of seven and we have seen a major improvement. The outcome from speech therapy has been good and he is now able to hold a conversation ” – 8 years

Sitting, moving: gross motor skills



Children's mobility is generally somewhat delayed but in *Unique's* experience even the most severely affected youngsters are able to walk and the most mildly affected experience only a slight delay in reaching their mobility milestones and particularly if they receive appropriate physiotherapy may reach them at an appropriate age.

Babies are typically floppy (hypotonic) and acquire head control late, although some children may have increased muscle tone (hypertonia) and stiff joints.

Unique members have learned to roll between nine and 12 months and to sit alone between seven and 15 months. Children have become mobile by

Two years old

commando crawling (creeping), bottom shuffling (scooting) or crawling between 11 months and four years. First supported or unsupported steps may be possible in some children as early as 18 months but usually emerge later after practice.

Many children have a degree of low muscle tone (hypotonia) but this generally lessens with physiotherapy and with increasing mobility. There may also be difficulties with balance but some children do learn to run, to climb stairs and to jump.

“ His biggest challenge is his lack of balance. He tends to trip and fall very easily. When close to a wall or object he can stand still without moving around but when he has nothing close to him, he tends to shift his feet around attempting to keep balance. He does tire more easily than others his age and his left side (arm, leg and eye) is much weaker ” – 3 years

“ She joins in all activities indoors and outdoors, and her dad is teaching her and sister to play tee-ball. She can run and jump ” – 6 years

“ She manages stairs well but has a wide gait and her walking is slow due to uneven leg length and is becoming slower as she becomes heavier. She moves well in familiar areas but is unsteady outside and uses a wheelchair on longer outings ” – 15 years

Effects on the external sex organs can be fairly mild, including hypospadias, where the hole usually at the end of the penis is on the underside instead and testes that are undescended at birth. Sometimes the effects can be more severe and include sex reversal, ambiguous or apparently female sex organs. The internal sex organs may also be involved.

These anomalies only affect baby boys. In baby girls, the external sex organs develop normally and experience so far shows that girls go through puberty in the normal way and at the normal age (Ounap 2004; *Unique*).

If your baby has ambiguous genitals or sex reversal, as parents you can expect to be fully informed and supported. A decision about gender assignment will be reached in consultation with you and will depend in part on your baby's existing structures. A series of surgical operations and possibly hormone treatment may be needed. *Unique* does have experience of babies with sex reversal and can put families who would like contact in touch with each other.

■ Cataract in one eye

Two babies have been born with a cataract (an opaque area within the lens of the eye) but both cataracts were small and neither needed surgical removal (Repetto 1998; *Unique*).

Other birth issues

One baby was born with glaucoma, raised pressure within the eye, which runs the risk of damaging the optic nerve. Initially, babies are usually examined under anaesthetic and if the eye pressure is found to be raised, surgery is carried out to drain off excess fluid.

One baby was born with developmental hip dysplasia, treated by wearing a harness for 12 weeks (*Unique*).

Will my baby or child look different?

You and your child's doctors may notice that your child has a slightly unusual facial appearance for your family and you may notice similarities between your child and the pictures in this leaflet. Among *Unique* members, two families remarked that their child had subtly cupped ears. Two families remarked that their child had a long groove between the nose and upper lip and one family observed that the upper lip was thin and tight. Facial features typical of a larger deletion (a keel-shaped head when viewed from on top, upslanting eyes) have occasionally been reported in the medical literature (de Vries 2003; *Unique*).

A geneticist may remark that your child's fingers have relatively long middle joints. This is typical of children with a larger deletion. One family observed that their daughter had mild incurving of the fifth fingers, but this is not specific to a 9p deletion (*Unique*).

“ No-one realises that she has a disability until they ask her a question ” – age 5

“ A beautiful boy who looks so normal ” – age 8



Two years



Seven years

Will my baby be healthy?

It appears that most babies with a 9p24 deletion are healthy and are only diagnosed when they miss their early developmental milestones. Even babies with health problems in the newborn period seem to outgrow them and become healthy children and adolescents. *Unique's* experience is that there are only single reports of particular health problems, which suggests that there may be no connection between the health concern and the chromosome deletion.

In *Unique's* experience, individual children have had the following conditions: hypothyroidism, treated with replacement thyroxine; seizures, well controlled on medication; increased vulnerability to respiratory infections at age 2 to 3 years; asthma. Additionally, one child had a ventricular septal defect (a hole between the lower chambers of the heart), but this did not need surgical closure.

Is there a typical growth pattern?

Most babies are born a normal weight and size, although in some cases their head circumference may be relatively small. The evidence from *Unique* is that there is no typical growth pattern and children generally are the same height and body build as the rest of their family. One child with an interstitial deletion between 9p24.1 and 9p24.3 was relatively short but unusual stature has not been found in other children up to and beyond puberty (*Unique*).

Are there any effects on eyesight?

Eyesight concerns seem to be fairly common, affecting 5/8 *Unique* members, and children can expect to have a careful ophthalmological examination. Apart from the babies born with congenital cataracts and glaucoma (see page 5), two children have an astigmatism, two have a 'lazy eye' (amblyopia), one is long sighted, and two have a degree of strabismus (squint).

If necessary, an astigmatism (usually caused by an abnormal curvature of the front part of the eye) can be corrected with glasses. A 'lazy eye' is usually treated by correcting any underlying eye disorder that is causing the problem and then by making the eye with poorer vision work harder, usually by restricting the use of the good eye. All forms of squint usually benefit from surgery to realign the muscles that control eye movement.

Is hearing affected?

No families have reported any underlying hearing impairment, although young children with a 9p24 deletion may develop the temporary form of hearing loss known as glue ear that is common among all young children and is relieved by inserting tubes (grommets) into the ear drum.

Are there people with this deletion who have been healthy, have developed normally and completed their education without any major difficulties?

There are certainly adults with a tiny submicroscopic deletion at 9p24 who apparently developed normally and were only discovered when their chromosomes were checked after one of their children had genetic testing. We do not know how often this occurs (Techakittiroj 2006; Balliff 2000; Repetto 1998).

The situation is different when a child has had genetic testing because of their own developmental delay or health problems. Parents of some children with a 9p24 deletion

have reported catch-up and age-appropriate development but we do not know yet how long they maintain this. We do know that the effects on development can be quite different between individuals.

This makes it difficult to be certain how much support children are likely to need with their learning. Among *Unique's* membership, we have enough detail on six members to be able to suggest that with appropriate early intervention, some children appear to have little or no learning disability in the early years of education. This will not be true for all and there will be a range of learning difficulty that appears to be generally mild or moderate but can occasionally be severe.

Most young children attend mainstream (regular) schools for their primary education, with learning support to enable them to access the full curriculum. Common learning strengths include a good memory and a sociable temperament. Weaknesses may include manipulating writing tools, as many children have an underlying hypotonia (low muscle tone) but most young children have shown that they are able to manage a computer switch, mouse and keyboard.

Reading, drawing and writing skills have generally emerged in the primary school years, although not in the most severely affected, and *Unique's* experience is that children have generally transferred to a special needs setting for their secondary education, as their needs will be met more appropriately there.

Among older children, one girl with moderate learning difficulties left school at 16 and has since attended college to study animal and horse care.

“ We have not had any signs of learning disabilities yet. His teachers are very impressed with his knowledge of colours, shapes, letters and numbers. He knows his ABCs and so far seems to be very quick on picking up educational type learning. He seems to remember well during different games and where things are after only seeing once. He enjoys being read to ” – age 3

“ She has a good memory and learns if interested. She does not read or write but makes pencil marks on paper ” – age 15

How may communication be affected?

As with other areas of development, there is a wide range of achievement in speech and language, with some older teenagers able to talk appropriately for their age while others communicate without speech.

Eye contact and smiles are typically delayed and in *Unique's* experience first smiles arrive between three and six months. Babies communicate their needs by crying, facial expression and, as they mature, by gestures, intonation, vocal noises and approximations. Recognisable words emerge late, in *Unique's* experience after the second birthday, but they may come later and in some children may not emerge at all. By 2 or 3, children may be communicating with a variety of vocal noises and intonations as well as using gestures and usually single words. Longer phrases may develop in the later pre-school and early primary school years and some children are able to hold conversations. Understanding of situations and language is also likely to be impaired but in general children appear to understand better than they can speak, although responses are often delayed. Sound production is affected in some children, with