Understanding chromosome disorders

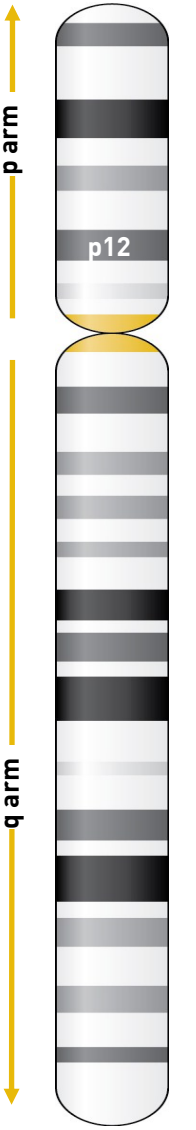
Unique

8p interstitial deletions including 8p12

rarechromo.org

8p interstitial deletions including 8p12

An 8p interstitial deletion including 8p12 is a rare genetic condition caused by a missing part of one of the body's 46 chromosomes – chromosome 8. An interstitial deletion means that the chromosome has broken in two places and the broken ends have fused, leaving out the deleted segment. The size of the missing piece varies between different individuals.



Chromosome 8

For healthy development, chromosomes should contain just the right amount of genetic material – not too much and not too little. An interstitial deletion 8p including 8p12 can result in developmental delay/intellectual disability, anaemia and a disruption of sexual development.

What are chromosomes?

Chromosomes are made up mostly of DNA and are the structures in each of the body's cells that carry the genetic information (in the form of genes) that tells the body how to develop, grow and function. Chromosomes usually come in pairs, with one chromosome from each pair coming from the father and one from the mother.

Of the 46 chromosomes, two area pair of sex chromosomes, XX (two X chromosomes) in females and XY (one X and one Y chromosome) in males. The remaining 44 chromosomes are grouped in 22 pairs, numbered 1 to 22 from largest to smallest. Chromosomes have a short arm, named p (shown at the top in the figure), and a long arm, named q (shown at the bottom in the figure). The two arms of a chromosome meet at a point called the centromere.

Looking at chromosome 8p

You can't see chromosomes with the naked eye, but if you stain them and magnify them many hundreds of times under a microscope, you can see that each one has a distinctive pattern of light and dark bands.

One of those bands is band 8p12. Looking at chromosomes under a microscope, it may be possible to see the genetic material that is missing if the piece is large enough. However, rare chromosome disorders can be caused by subtle changes that are too small to see using a microscope. Molecular DNA technology gives a more precise understanding of the size and position of the deletion. Your geneticist will be able to tell you about the position at which the deleted material can be found on the chromosome 8 of your child. More information on molecular DNA technology can be found in the appendix on page 14.

8p12 interstitial deletion disorder

The disorder was first described in the medical literature in 1977. As of 2015, 17 individuals with an interstitial deletion of 8p including 8p12 have been reported in the medical literature (see Sources & references below). This does not mean that there aren't more children with a deletion of 8p including 8p12. There are children registered in international databases, but often with more limited information known. There are also children with a deletion of 8p including 8p12 who have never been included in medical articles.

Main features in children with an interstitial deletion 8p including 8p12

The features mentioned in this guide have been described in the medical literature in children with an interstitial 8p deletion including 8p12. It is not known if all features are indeed caused by the deletion or if their occurrence in children with the deletion is coincidental. Some of the features can also occur in children without the deletion. Because only a few people with the deletion have been described, not all the effects of the deletion are known.

The features can vary between children, but one or more of the following features can be present:

- Developmental delay and/or intellectual disability (pages 7-9)
- A congenital form of anaemia: hereditary spherocytosis (pages 4-5)
- Delayed, incomplete or absent sexual maturation (pages 11-12)
- Eye problems including nystagmus and strabismus (a squint) (page 10)

How common are interstitial deletions 8p including 8p12?

It is not known exactly how common the deletion is. As previously stated 17 persons have been reported in the medical literature.

Sources & references

The information in this guide is drawn partly from the published medical literature. With the first-named author and publication date you can look for abstracts or original articles on the internet in PubMed (www.ncbi.nlm.nih.gov/pubmed). When this leaflet was written the full text of the articles was used as far as possible, but sometimes only the abstracts were available. As of 2015, 17 people with an interstitial deletion of 8p including 8p12 have been reported in the medical literature (Beighle 1977; Chilcote 1987; Kitatani 1988; Ostergaard 1989; Lux 1990; Cohen 1991; Stratton 1992; Okamoto 1995;Tsukahara 1995; Devriendt 1999; Vermeulen 2002; Dodé 2003; Cau 2005; Klopocki 2006; Stewart 2007).
Also in this guide are included quotes of some Dutch parents who have a child with this deletion and filled out a questionnaire. When Unique formatted this guide, we had 12 members with an interstitial 8p12 deletion with no other chromosome change. Seven families commented on this guide. Unique contributions are in grey boxes marked with the Unique logo.

Outlook

People with the deletion without major physical malformations and/or problems probably have a normal life expectancy. Three adults with the deletion have been described in the medical literature. Unique has two adult members.

Pregnancy

Most mothers of a child with an 8p deletion including 8p12 had a normal, uneventful pregnancy. Delivery was normal and they only discovered their baby was affected after the birth.

One mother had a parvovirus B19 infection during pregnancy, but this did not affect her unborn child (Klopocki 2006). One child was born via Caesarean section after 37 weeks of pregnancy because of intrauterine growth retardation and a low level of amniotic fluid (Stewart 2007).

Unique has information on 6 pregnancies, most of them uncomplicated. One baby was delivered prematurely by planned Caesarean.

Newborn babies. Hereditary spherocytosis

Not all newborn babies with an interstitial 8p deletion including 8p12 necessarily show signs of the deletion at birth. In 8 children reported in the medical literature, the birth weight is reported (Beighle 1977; Chilcote 1987; Cohen 1991; Devriendt 1999; Klopocki 2006; Stewart 2007). Mean birth weight in these children was 2.639 kg (5lb13oz) (range: 1.79-3.48 kg/ 3lb15oz-7lb11oz). Three children reportedly had a low birth weight (Kitatani 1988; Ostergaard 1989; Tsukahara 1995).

Five newborn babies showed signs of jaundice and/or hyperbilirubinaemia. Bilirubin is a waste product of haemoglobin. Haemoglobin is a protein in our red blood cells responsible for oxygen transport (Beighle 1977; Chilcote 1987; Kitatani 1988; Lux 1990; Vermeulen 2002; Dodé 2003). One girl was anaemic at birth.

Jaundice, anaemia and hyperbilirubinemia can be the result of hereditary spherocytosis (HS) in some children with the deletion. HS is a congenital, inherited form of anaemia. In people with HS, the red blood cells have an abnormal shape. Because of this, they are more prone to be broken down in the spleen (an organ that is important within our immune system) which can lead to anaemia, jaundice, a high bilirubin and an increased spleen size (splenomegaly). Nine out of 17 persons with the deletion in the medical literature had HS (Chilcote 1987; Kitatani 1988; Lux 1990; Cohen 1991; Okamoto 1995; Vermeulen 2002; Dodé 2003; Cau 2005). The severity varied. Three children needed regular blood transfusions and eventually had their spleen removed (Chilcote 1987; Lux 1990; Vermeulen 2002; Dodé 2003). After the removal of the spleen, anaemia

resolved. In one girl the spleen was removed when she had her gallbladder removed because of gallstones. This also led to an improvement of her anaemia (Cohen 1991).

Doctors think that HS in people with an interstitial 8p deletion including 8p12 is caused by the deletion of the *ANK1* gene (Lux 1990) in band 8p11.21 at base pairs 41,510,739-41,754,280 (see **Research**, page 15).

Birth weights at Unique range from 1.36kg (3lb) in a preterm baby to 3.35kg (7lb 6oz). One/7 Unique babies has spherocytosis; another has anaemia.

Feeding

Three children had feeding difficulties and/or failure to thrive (Beigle 1977; Chilcote 1987; Devriendt 1999).

Some children with a chromosome disorder have difficulties swallowing and sucking. Feeding difficulties are partly caused by low muscle tone (hypotonia) in these children. Hypotonia has only been reported in two children with an interstitial 8p deletion including 8p12 (Devriendt 1999; Klopocki 2006).

Three children had a high palate (Beighle 1977; Kitatani 1988; Tsukahara 1995) and two children had a cleft (split) palate (Stratton 1992; Cau 2005). One girl had a bifid uvula (Klopocki 2006). These features can cause problems with sucking and swallowing although they do not necessarily do so.

Ten/12 Unique families had difficulty with feeding and/or growth, but the amount of difficulty varied a lot. Among the babies with the greatest problems were those with other health problems with breathing, the heart or a cleft throat. Three babies had a high or cleft palate (split in the roof of the mouth), but only one of their families reported feeding difficulties. One baby breastfed, but weakly, and only took a bottle at 15 months after a year of practice. At least two babies needed feeding through a naso-gastric tube, and both - as well as 2 others - later needed a gastrostomy for feeds direct to the stomach, one until 9 years. Common difficulties were swallowing, reflux (bringing feeds back, and risking inhaling them), being late to wean, and failure to put on enough weight. Many children are prescribed high energy drinks; families of older children report a persistently poor appetite.

“ He got a gastronomy button at 8 months together with a tracheostomy. At 1½ he started to learn to drink via online coaching (www.notube.com). Due to his many allergies he gets special milk with vegetables or fruit. He drinks around one third of his 200 ml portion and gets the rest via button. He can drink very well and does not choke a lot. **”** 4¾ years

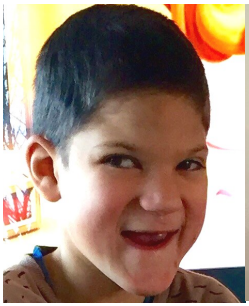
Growth

Ten out of 17 children reported in the medical literature are said to have growth delay or short stature (Beighle 1977; Kitatani 1988; Lux 1990; Cohen 1991; Tsukahara 1995; Devriendt 1999; Vermeulen 2002; Dodé 2003; Cau 2005;Klopocki 2006). Based on height, children often belong to the smallest 3% (3 in 100) of the population. One girl, aged 2½ years, had a feeding tube inserted because of her feeding difficulties. One child had growth hormone deficiency (Vermeulen 2002; Dodé 2003).

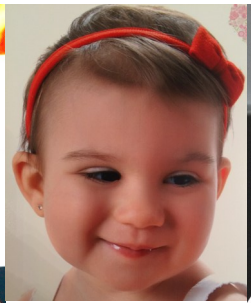
“ Our daughter has growth problems. We added a food thickener to her bottle. This increased the amount of food she was eating. She is still small for her age. This is a symptom of this deletion.**”**

Six/7 children at Unique are short for their age; none has taken growth hormone. An 8-month baby wore 0-3 month baby clothes; at 12 years he was the size of a 7-year-old (122cm/4’ in height, 3 stone/19kg in weight) and wore size 11 shoes. Other children: are under the first percentile on the growth chart at 19 months; measure 92cm/3’ at almost 5 years; 117cm/3’10” and very thin at 8 years; and 145cm/4’9” at 17 years.

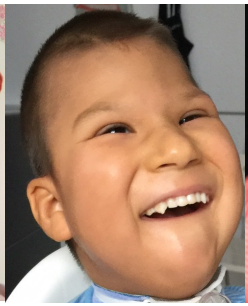
Appearance



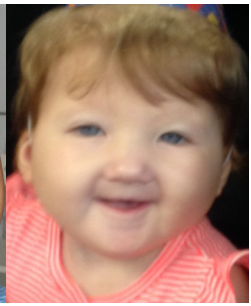
7½ years



20 months



4½ years



16 months

Based on the medical literature, it is difficult to draw a clear picture of the appearance of children with the deletion. Most children look like other members of their family. There are a few facial features that have been reported in multiple children with the deletion. Five children had a small head (Beighle 1977; Kitatani 1988; Ostergaard 1989; Cohen 1991; Devriendt 1999). Another girl had a relatively long head compared to its width (dolichocephaly) (Tsukahara 1995). Two people had a prominent forehead (Beighle 1977; Cau 2005).
Both wide spaced eyes as well as narrow eyes have been reported (Beighle 1977; Devriendt 1999). Two people had small eyes (Dodé 2003; Klopocki 2006). Two sisters had upslanting palpebral fissures (eyes) (Chilcote 1989). One boy had an extra fold of skin covering the inner corner of the eye (epicanthus) (Kitatani 1988).

Nine people had abnormalities concerning their ears (Beighle 1977; Chilcote 1987; Ostergaard 1989; Cohen 1991; Tsukahara 1995, Devriendt 1999; Vermeulen 2002; Dodé 2003). Ears may be low set or abnormally shaped. Two sisters had small pits in front of their ears.

Six people had a small lower jaw (Chilcote 1989; Tsukahara 1995; Vermeulen 2002; Dodé 2003), while a girl of 19 had a prominent lower jaw (Beighle 1977). Two people are said to have a thin upper lip (Tsukahara 1995; Klopocki 2006). Five individuals had abnormalities of their hand and/or feet (Beighle 1977; Kitatani 1988; Devriendt 1999; Dodé 2003; Stewart 2007). These include an abnormal position of the hand and/or feet, abnormalities of the nails, short or long fingers or fusion of fingers.

Five/10 Unique children had something unusual about their hands: a single palm crease on one or both hands (3); very small hands (1); long fingers (2); and puffy finger tips (1). Three babies were born with unusual feet: in 3, the second toe overlaps the third. One baby was born with a club foot.

Learning and psychomotor development

Most children with the deletion reported in the medical literature have developmental delay and/or intellectual disability (Beighle 1977; Chilcote 1987; Kitatani 1988, Ostergaard 1989, Lux 1990; Cohen 1991; Tsukahara 1995, Okamoto 1995, Devriendt 1999; Cau 2005; Klopocki 2006; Stewart 2007). These reports might be somewhat biased, since these features often are the reason for genetic testing. The severity of any developmental delay or intellectual disability varies. Some children are said to have mild developmental delay (Cau 2005), while the delay may be severe in others (Lux 1990). One man has normal intelligence. He was referred for genetic testing because of delay in growth and hypogonadotrophic hypogonadism (see pages 11-12) and fertility problems.

6 years

One young woman had low scores for speech and communication (IQ 70) and performing tasks (IQ 76) (Beighle 1977). One girl, age 2½ years, sat at 14 months, crawled at 15 months and spoke her first words at 22 months (Klopocki 2006).

“ Her level of development is 50-55% of that of her peers. But she continues to make progress at her own pace. She has a learning level of a 6-year-old child. She is very active and can do almost everything - walking, jumping, dancing and riding a bike with support etc. Everything she learns is a milestone for her and for us! She can do so much more than we could have imagined 9 years ago and this has made us very happy. She is open-minded, honest and friendly, and we are very proud of her! ” - 10 years

Learning and psychomotor development (continued)

Developmental delay affects all Unique members and typically is global. Babies are late to hold their heads steady and to sit: among 6 children, sitting without support evolved between 8 months and almost 4 years. Mobility also comes late, and some babies never crawl, using other means such as rolling, creeping, pulling themselves forward on their arms or bottom-shuffling. Four children learned to walk between 2 years, 2 months and 12 years, but walking may not be possible for all. Low muscle tone is one factor in the late mobility.

" Our son had low muscle tone as a baby but today it is more a coordination problem that makes movements difficult and it takes many repetitions for him to learn new things. Once put in a sitting position, he can sit without help and when laid down, rolls from side to side. We do standing training and since a year ago he has been able to hold his own weight. He progresses at a very slow pace but there is always some improvement. He is very cooperative and patient when we do training. However, he shows when he has had enough and squinches up his face. " - 4¾ years

" He still has balance problems as he is very hypermobile. This affects him when climbing, and with balance on uneven ground." - Almost 11 years

Learning difficulties reported to Unique are in the moderate to severe range, with babies and children needing much repetition and practice to learn new skills. Low muscle tone and hypermobile joints can make holding toys and writing implements hard. A child of 3½ could count to 12 and knew some colours; by the age of 12, his development was as of a 4-year-old. At nearly 11, another boy struggled with writing in the 5th class at school as his hands tired with gripping pens and pencils. A child of almost 5 enjoys reaching out to grab things and mouth them, especially a vibrating stick.

" Our daughter is a very, very happy little girl! She smiles through all that she has been through in her short life. She brings us a lot of joy and has touched a lot of people. Her big brother and sister love doting on her and she loves all the attention! She has taught us all to appreciate the small things in life and not to take things for granted. She has also helped to raise awareness about chromosome disorders in our small, close-knit community." - 19 months

Speech

Eight/8 Unique children show some speech delay, but the amount varies a lot. One boy of 3 years is trying to form sentences, while others of the same age are not yet talking at all. One child is hampered by his tracheostomy (breathing tube in the neck). The age at which parents heard first words is 8 months - 5½ years.

“ With the tracheostomy he cannot really learn to make noises or sounds. However he tries to and is somehow successful. He loves music and when someone is singing, and when he has his special speaking valve he ‘sings’ with enthusiasm sometimes at a very high volume, and enjoys it a lot. However, this is exhausting for him. ” - 4¾ years

“ He only used very few words and a few signs until 7½ years when he suddenly started to say a lot of words. At 8 years he speaks in sentences, but still not with correct pronunciation and he misses out some words. One still needs to know him well to understand. He is very social and has always been very good at communicating. Even when he spoke almost no words and only used a few signs he still managed to get people he knew to understand what he meant and to have conversations. ” - 8 years

Medical concerns

Head and brain

Three children described in the medical literature underwent brain imaging by MRI (Devriendt 1999; Klopocki 2006; Stewart 2007). Results were normal in one. The results in the other two children showed enlargement of the ventricles and absent or small corpus callosum (the structure in the brain that connects the left and right hemispheres). In one child there was a reduction of white matter (white matter hypoplasia: white matter consists of nerve fibres and an insulating sheath, myelin).

Five/5 children at Unique have microcephaly or a small head. One baby’s head grew at the normal rate for the first 6 months, than tailing off so by 18 months he was in the smallest 3 per cent of the population.

“ Small, but still growing, so not diagnosed with microcephaly. ” 8 years

Only one child has had brain imaging, which showed a slightly small brain and underdeveloped corpus callosum (see above).

Heart

Most children with an interstitial 8p deletion including 8p12 have no abnormalities of their heart. Heart problems are more common in children in whom the deletion involves the band or bands near the tip of the short arm of chromosome 8. Doctors think that a deletion of band 8p23 plays an important part in the heart problems seen in these children.

Four children described in the medical literature with an 8p interstitial deletion including 8p12 have heart problems (Ostergaard 1989; Tsukahara 1995; Dodé 2003; Stewart 2007). In two, there is no detailed description of the problems . One 24-year-old woman had a patent ductus arteriosus (PDA). The ductus arteriosus is a short channel between the pulmonary artery and the aorta, the two main blood vessels leading from the heart, which normally closes soon after birth (Dodé 2003). One boy had a hole between the left and right upper and lower chambers of the heart (atrial septal defect/ASD and ventricular septal defect/ VSD) (Stewart 2007).

Three/6 Unique babies were born with a heart problem; two needed surgery; in both it was successful. One baby had DORV (double outlet right ventricle, where both the major blood vessels lead from the same side of the heart instead of different sides). Another had holes between both the upper and lower chambers of the heart. A third baby had a common condition called PDA (see above); this resolved naturally. A boy of 11 has a fast heartbeat, but needs no treatment at present.

Vision

Fewer than half of the people described in the medical literature (8/17) have eye problems. Six had nystagmus (uncontrolled eye movements) (Chilcote 1987; Devriendt 1999; Dodé 2003; Klopocki 2006; Stewart 2007). Three have strabismus (a squint) (Beighle 1977; Cau 2005;Klopocki 2006). One young woman also had myopia (short sight) (Beighle 1977). A boy's eyes also bulged so that he could not fully close them (Cau 2005). Three children, in addition to nystagmus or strabismus, had abnormalities of the optical nerve (Dodé 2003; Klopocki 2006; Stewart 2007). One of these children was found to have additional eye problems after an eye examination. This child had severe visual problems (Stewart 2007).

Eight/9 Unique families report eyesight problems. Most common are nystagmus (6); apparent errors of refraction - long or short sight (5) and strabismus (squint - 5), in one child causing him to use only one eye at a time. Only one family reported an anomaly of the optic nerve that takes messages to the brain.

" No optic nerve abnormalities but a severe cerebral sight disturbance. He does not really look at faces, and does not follow moving things, but he can recognize some things that he sees often. " - 4¾ years

" His symptoms are similar to being nearsighted, but the optician cannot right the problem with glasses. They think maybe his eye sight is maturing slowly. " - 8 years

Hearing

Hearing problems do not appear to be common in children with an interstitial 8p deletion including 8p12. One 12-year -old boy probably has a combination of sensorineural and conductive hearing loss (Cau 2005). In conductive hearing loss, sound is not conducted properly from the middle ear to the inner ear. In sensorineural hearing loss the hearing nerves in the inner ear do not function properly. Sensorineural hearing loss is permanent. Another boy had conductive hearing loss because the bones in his inner ear were fused (Cohen 1991).

The only type of hearing loss reported by Unique families is glue ear, a fluctuating deafness very common in young children.
" Very narrow ear canals, but hears very well."

Puberty and genitals

Minor anomalies of the genitals are common in babies with chromosome disorders, most often affecting boys.

Among 9 boys reported in the medical literature (Kitatani 1988; Ostergaard 1989; Lux 1990; Stratton 1992; Okamoto 1995; Devriendt 1999; Vermeulen 2002; Dodé 2003; Cau 2005; Stewart 2007), six had undescended testes (cryptorchidism). Four boys also had a small penis (micropenis). Three boys had an inguinal hernia.

A micropenis can result from hypogonadotrophic hypogonadism.
The reproductive organs (testicles in men and ovaries in women) produce hormones. This process is controlled by hormones produced in the brain. The hormones produced in the reproductive organs (testosterone in men and oestrogen in women) set off puberty: body hair develops, the penis and testes grow and the production of semen increases in men and in women breasts grow and the menstrual cycle commences. In hypogonadotrophic hypogonadism the production of hormones to set off the production of hormones in the reproductive organs is insufficient. This results in delayed, incomplete or absent sexual maturation.

Five children or adults described in the literature have hypogonadotrophic hypogonadism (Beighle 1977; Stratton 1992; Vermeulen 2002; Dodé 2003; Klopocki 2006). A brother and sister had failure of sexual maturation, but the article did not state that this was because of hypogonadotrophic hypogonadism. In a 12-year-old boy this diagnosis is also not mentioned. This boy had a micropenis and was unable to smell (anosmia) (Cau 2005). Anosmia can occur in hypogonadotrophic hypogonadism. This is also called Kallmann syndrome. One man had fertility problems as a result of the hypogonadotrophic hypogonadism (Vermeulen 2002; Dodé 2003). Several other youngsters were to young for their

fertility to be assessed. Puberty and sexual maturation in youngsters with hypogonadotrophic hypogonadism can often be induced by the administration of hormones.

Doctors have shown that hypogonadotrophic hypogonadism in people with the deletion is caused by the loss of the *FGFR1* gene at bands 8p11.22-3 between base pairs 41,510,739-41,754,280 (see **Research**, page 15) (Dodé 2003).

Only one/8 boys at Unique was born with undescended testicles, corrected in a small operation together with a groin (inguinal) hernia. One girl has no sense of smell. Two teenagers, a girl and a boy, were late starting puberty.

Other

Two children with the deletion had frequent respiratory tract infections (Beighle 1977; Cau 2005). One boy died at age 2½ years because of a severe respiratory tract infection. In addition, he had a heart defect (Ostergaard 1989). A nine-year-old girl had epilepsy (Chilcote 1987). One boy, aged 13 months, had a sacral dimple (Kitatani 1988). Another boy had an abnormal left kidney (Stewart 2007). One girl had reduced tear production, reduced sensitivity to pain, sleep problems and peripheral neuropathy, damage to the nerves in the hands and feet (Klopocki 2006). One boy underwent surgery because of shortened Achilles tendons. His sister who also carried the deletion had diabetes mellitus. In addition, some vertebrae in her neck were fused which resulted in wry neck (Cohen 1991).One boy had dental abnormalities (Cau 2005).

Other features observed at Unique include:

- Dental problems (6) including late teething (2); missing milk teeth (1); milk teeth late to fall out (1); severely worn , eroded or decayed adult teeth (3); missing adult teeth (1).
- Sleep problems (4) including difficulty falling asleep after waking at night (2); and poor sleep (2).
- Overly mobile joints (3).
- Severe breathing difficulties requiring surgery (2) - tracheostomy (breathing tube) and ongoing problems with serious respiratory infections; supraglottoplasty (removal of floppy tissue round voice box for laryngomalacia) and oxygen at night for central and obstructive sleep apnoea.
- Spinal curve (2) including scoliosis (1) and curve that may be caused by attempts to balance body (1). Dimple at base of spine (1).
- Epilepsy (1); suspected absence seizures (1).

Other features observed at Unique include:

- Unexplained episodes of lightheadedness possibly occurring at times of fever.
- Hirschsprung's disease, causing poo to get stuck in the bowels (1), surgically treated with a type of colostomy, where the bowel is diverted to end at a bag attached to the wall of the abdomen. Another child had constipation as a baby.
- Breath holding (1) when upset, until losing consciousness.
- High cholesterol despite a healthy diet (1).
- Multiple allergies and baby eczema (1).

> " Our son has a very sunny personality. He is almost always happy (even though he can switch moods within seconds) and wants to deliver hugs to everyone. He absolutely loves it when someone sings to him, and he has a very distinct taste in what he likes and does not in regards to music. He is very good at jigsaw puzzles, even though he has poor fine motor skills. He brings us love, joy and pride every day, just like his big brother without disabilities does. " - 8 years

If one person in a family with the interstitial deletion 8p including 8p12 is mildly affected, will others in the same family also be mildly affected?

It is difficult to answer this question as there are only a few families in which multiple family members carry the deletion (Chilcote 1987; Cohen 1991).

Why did this happen?

When children are conceived the genetic material is copied in the egg and sperm that makes a new child. The biological copying method is not perfect and occasionally random rare changes occur in the genetic code of children that are not seen in the DNA of their parents. The term doctors use for this is de novo. This happens naturally and is not due to your lifestyle or anything you did to cause a change. Most parents of children with an interstitial 8pdeletion including 8p12 are not found carry the deletion.

One mother is described in the medical literature who passed the deletion on to her children (Cohen 1991). Their mother carried the deletion in some of her cells. She showed no signs or symptoms because the part of chromosome 8 that was deleted in her children was present as a separate fragment in other cells of her body. It is therefore important that both parents of a child with the deletion have their own chromosomes tested.

In either situation there is nothing you could have done to have stopped this. No one is to blame and nobody is at fault.

Can it happen again?

The risk of having another child affected by a rare chromosome disorder depends on the genetic code of the parent. If the chromosomes in both parents are normal, the chance of having another child affected is very low.

Nonetheless, there is a small changce that part of the egg cells of the mother or part of the sperm cells of the father carries the change ("germline mosaicism"). This means that parents who are not found to carry the change have a very small chance of having another affected child. This has been described once in the medical literature in two sisters with a deletion 8p including 8p12 (Chilcote 1987).

The chance of recurrence is much higher if one of the parents is found to carry the deletion of a chromosomal rearrangement that involved the short arm of chromosome 8. Each family situation is different and a clinical geneticist can give you specific advice on the chance of recurrence in your family and options for prenatal diagnosis and preimplantation genetic diagnosis. PGD requires the use of in vitro fertilisation and embryo biopsy, and only healthy embryos are transferred to the mother's uterus. If the parents choose to conceive naturally, prenatal diagnosis options include chorionic villus sampling (CVS) and amniocentesis to test the baby's chromosomes.

Appendix

Results of the chromosome test

In an interstitial deletion 8p including 8p12, the result is likely to read something like one of the following examples:

arr[hg19] 8p22p12(18656021-36218432)x1

arr The analysis was performed using the (arr) technique: array CGH or SNP array.

hg19 This shows which 'build' of the human genome (hg) was used. Builds are updated regularly, and when they are, base numbers shift. hg19 Is the build current when this guide was compiled.

8p22p12 The chromosome involved is chromosome 8 and DNA has been lost between bands numbered 22 and 12 on the short (p) arm.

(18,656,021-36,218,432)x1 DNA consists of base pairs. All base pairs are numbered from the top of the chromosome to the end. In this example, the base pairs between 18,656,021and 36,218,432 are present once (x1) instead of the usual twice. This is the deletion. If you subtract the smaller number from the larger number the result is 17,562,411 Base pairs (or 17,562Kb, or 17.56 Mb). In summary, doctors call this an 8p22p12 deletion from base pair 18.6 million to 36.2 million (Mb) on chromosome 8 which is 17.56Mb in size.

1 base pair = bp
1,000 base pairs = 1kb
1,000,000 base pairs = 1Mb

46,XY,del(8)(p11.1p21.1)

46	The total number of chromosomes in your child's cells
XY	The two sex chromosomes, XY in men, XX in women
del(8)	A **del**etion, or material is missing from chromosome 8
(p11.1p21.1)	The part of chromosome **8** that is missing is from the short arm of chromosome 8 (**p**) and involves bands **11.1** to **21.1**

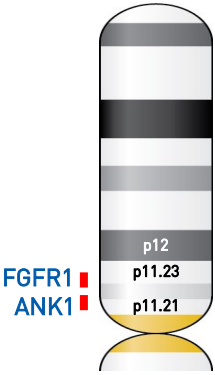
Research involving 8p

The features of an interstitial 8p deletion including 8p12 are likely to be the result of the missing genetic material and missing genes located on this part of the chromosome. It is important, therefore, to have the exact location and length of the missing material determined. When researchers compare the features in different individuals with the deletion, genes can be identified that contribute to the different features of 8p deletions.

As a result of earlier research, researchers have established that the *FGFR1* gene at bands 8p11.22-3 between base pairs 41,510,739-41,754,280 is probably responsible for the hypogonadotrophic hypogonadism (see pages 11-12).

The *ANK1* gene in band 8p11.21 between base pairs 41,510,739-41,754,280 is responsible for hereditary spherocytosis (see **Newborn babies**, pages 4-5) (Lux 1990).

Establishing the role of individual genes is important and can help future research. Often this does not directly result in better treatments. Furthermore, deletion of a gene does not mean that the associated feature is always present. Other genetic and environmental factors also influence this risk.



Chromosome 8p

" Our son is such a happy and cooperative boy. When he is not well, he is patient and trusts that we are there to help him. He is practically never in a bad mood, only when something is not right with him. It is amazing to watch his small steps, it is like looking at development in slow motion. He seems to be satisfied with life and when our lives as parents are hectic and overloaded, he shows us the important things in life – breathing well and enjoying the moment, not thinking about the future. " - 4¾ years

Support and Information

Rare Chromosome Disorder Support Group

G1, The Stables, Station Road West, Oxted, Surrey
RH8 9EE, United Kingdom
Tel/Fax: +44(0)1883 723356

info@rarechromo.org | www.rarechromo.org

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www.rarechromo.org/html/MakingADonation.asp
Please help us to help you!

Websites, Facebook groups and other links

Project 8p: Join

Project 8p: Patient Navigator

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Unique lists external message boards and websites in order to be helpful to families looking for information and support. This does not imply that we endorse their content or have any responsibility for it.
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. Unique does its best to keep abreast of changing information and to review its published guides as needed. The text was written by Dr Laura van Dussen, MD, Erfocentrum, Netherlands, and Unique and reviewed by Prof Dr C. van Ravenswaaij-Arts (UMC Groningen) and Mieke van Leeuwen (VGnetwerken). With special thanks to Annet van Betuw (VanBetuwAdvies), Marja de Kinderen (PROK Project management and training), Joyce Schaper (Chromosome Foundation) and Sarah Wynn, BSc(Hons) PhD DIC (Unique).
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