

Duplications of 8p



Sources

The information in this leaflet is from the published medical literature and from Unique's experience.

At the time of writing, Unique had 22 member families with a duplication of 8p not involving another chromosome.

Although the pictures on the cover show boys, 8p duplications occur as commonly in girls. Ten families completed a detailed questionnaire in 2004/5. As affected families are more likely to join Unique, this is a biased group.

References

The text contains references to articles in the medical literature. 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. If you wish, you can obtain abstracts and articles from Unique. References to information from Unique are marked U.

8p Duplications

Duplications of the short arm of chromosome 8 (8p) are rare genetic conditions in which people have an extra copy of some of the material of one of the body's 46 chromosomes. Generally speaking, having extra chromosome material increases the risk for problems such as birth defects and growth and developmental delay. However, with 8p duplications the picture is very varied, depending on which part of the chromosome is duplicated and whether the same duplication is present in one of the parents. Some people are healthy and develop normally, but others are mildly or more profoundly affected.

Chromosomes are the microscopic structures in the nucleus of the body's cells that carry genetic information. Each chromosome has a short (p) arm at the top and a long (q) arm at the bottom. Apart from the sex chromosomes X and Y, they are numbered 1 to 22 roughly according to size from largest to smallest. One chromosome from each of the 23 pairs comes from the father and the other from the mother. People with chromosome 8p duplications have an additional copy of some of the material on the short arm of one of their chromosomes 8. The other chromosome 8 is the usual size. Duplication of the whole of the short arm is sometimes called **trisomy 8p**.

Main features

Some people with fairly small amounts of extra 8p material in particular segments are healthy, develop normally and have healthy children. This is especially true in families where different members have the same duplication and are all healthy. There is some uncertainty about the most common features among others, but they appear to include:

- Developmental delay.
- Learning difficulties.
- Floppiness of the skeletal muscles in babies (hypotonia).
- Internal organs are usually unaffected, but one child in five is born with a heart defect.
- Absence or thinning of a band of nerve fibres that join the two hemispheres of the brain. This is called agenesis of the corpus callosum and is discovered when a child has a brain scan.
- Typical facial features (see page 5).

Different types of 8p duplication

The effects of 8p duplications depend mostly on what material has been repeated and the exact points (called breakpoints) where the chromosome has broken. The features described in this leaflet have been found in people who have a duplication of a significant part of 8p. If you wish, your geneticist or genetic counsellor will explain where the breakpoints are in your family and this may help in predicting the outlook for your child.

Some people have most or all of 8p joined to a different chromosome. Other people have a long 8p containing the duplicated material. This doesn't appear to make a big difference to the effects.

Researchers have tried to narrow down the segment of 8p that causes the most important effects but have not yet succeeded in providing a clear, consistent result (Engelen 1995; Fan 2001; U).

There are some special types of 8p duplication.

Inv Dup Del 8p

Some people with extra 8p material have a particular disorder called inverted duplication and deletion of 8p, inv dup del 8p for short.

In this complicated duplication:

1 A large part of 8p is usually duplicated (dup for short). Because this extra segment runs in the opposite direction to normal, it is also described as inverted (inv for short).

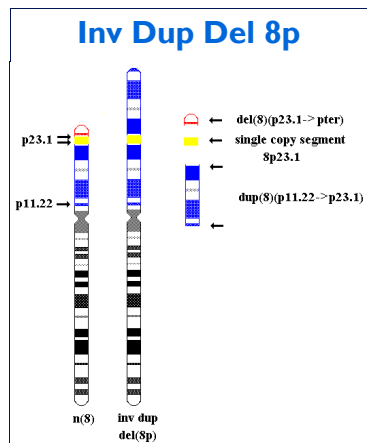
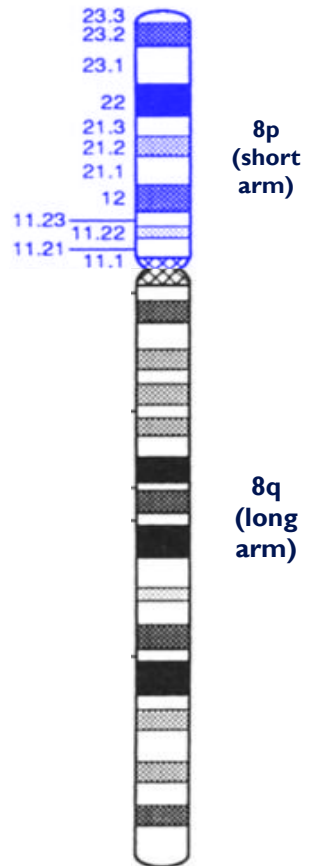
2 The tip of 8p is missing (deleted, or del for short).

3 The duplicated segments are separated by band 8p23.1 which remains neither duplicated nor deleted.

People with inv dup del 8p share some features with other 8p duplications but they tend to be rather more severely affected. Some researchers have suggested that direct duplications of 8p tend to have more mild effects than inverted duplications, but this is not at all certain.

Unique publishes a separate leaflet on Inv Dup Del 8p.

Chromosome 8



Natural (euchromatic) variants

In some families, extra material is seen within band **8p23.1** which resembles a duplication but has turned out on closer molecular genetic analysis to be harmless copy number variation of a short stretch of DNA within band 8p23.1. Most people have two copies of this segment on both chromosomes 8 giving a total of four copies. However, some people have as few as three or as many as seven copies. Rare families have been found with between nine and 12 copies which can appear almost identical to genuine 8p23.1 duplications (Barber, 2005). The similarity in their appearance accounts for the controversy in the literature about their significance (Tsai, 2002; Kennedy, 2002).

People with high copy numbers are healthy and develop normally and the unusual chromosome findings usually come to light by chance. The expanded material contains three genes that are important players in the immune system and it is possible that people with high copy numbers have an enhanced resistance to infection (Barber 1998; Gibbons 1999; Barber 2000; Hollox 2003).

Small, harmless duplications that run in families

In some families, other harmless duplications have been found. These have been found within the region **8p22 to 8p23.1** and **8p23.1 to 8p23.3** (Engelen 1995; Engelen 2000).

Another normal variant within band **8p22** has recently come to light in three generations of the same family, where all members were unaffected by the extra chromosome material (Chan 2005).

Other small duplications in families

In some families a healthy parent can pass a duplication between bands **8p21.3 and 8p23.1** to a child who then will have some developmental delay or birth defects, particularly involving the formation of the heart. This can occur in parents who have the duplication in all of their white blood cells (the material that is usually tested) or only in some of them (a condition called mosaicism).

Most of these family duplications have been found in chromosome material at the upper end of the short arm. However, there has also been a report of a relatively harmless duplication between **8p12 and 8p21.1** that occurred in an adult with mild developmental delay and no health problems.

The medical literature suggests that the effects of the duplication on the child are usually mild, with minor birth defects, but that is not certain and in one instance at least, a father passed an 8p23.1 duplication to a child, apparently with severe effect (Dhooge 1994; Engelen 1995; Brooks 1998; Moog 2000; Fan 2001; U).

How rare are 8p duplications?

They are almost certainly very rare, but probably no one will ever know for certain because people who are healthy and unaffected will never be investigated. Inv dup del 8p is one of the most common types and is estimated to occur in 1:22,000 to 1:30,000 newborn babies.

Might the pregnancy be different?

Babies with 8p duplications appear to be just as likely to be born at or near term as other babies. Premature birth at 34 weeks has been reported but the rate appears to be no higher than in other pregnancies. Among 11 *Unique* families, two babies were born prematurely, at 34 or 35 weeks and two at 37 weeks. Two mothers developed high blood pressure and one carried a large amount of amniotic fluid (polyhydramnios). Most babies were a good size and their weight at term fell within the normal range. The range in the *Unique* series was between 4lb 13oz (2183g) and 9lb 10oz (4138g) (Allen 1982; U).

How might it affect my newborn baby?

Although visible birth defects can occur in babies with 8p duplications, they are not very common and most babies appear healthy at birth. All the same, your baby is likely to feel very soft and floppy to hold. This is caused by a condition called hypotonia, where the skeletal muscles are unusually unresponsive to signals from the brain.

Many babies also cry and suck very weakly and they may have difficulties at first co-ordinating sucking with swallowing.

Some babies have unusual signs that are typical of 8p duplications but are not usually important to development. Some babies have deep creases in the soles of their feet, especially between the big and second toes, or the palms of their hands. The fingers may also be clenched and the little (fifth) finger may curve inwards.

Among the visible birth defects that have been described are a cleft palate/ lip, hernias in the groin (inguinal), unusually angled feet or feet with a curved sole and no arch (known as rocker bottom feet) (Gibbons 1999; U).

“A did not cry after delivery, but was alert and looking around immediately. She did not exhibit any typical ‘baby’ expressions; she always had a very serious expression on her face. She didn’t giggle, cry or babble or put anything in her mouth. Although she was very intent and focused, she hardly made a sound. She was very interested in people’s faces and hands. She would stare so intently for so long that people would get uncomfortable.”

Appearance

As they grow, most children with 8p duplications will look little different from other children. All the same, certain cosmetic features are typical of children with 8p duplications. Most of them have no effect on your child and doctors only point them out because they help them to make the right diagnosis. They include a high, rounded forehead, a prominent nose with a wide bridge and an upturned and slightly bulbous tip, a wide mouth with a thick, even ‘pouting’ lower lip and a short neck. A more important feature is a small lower jaw that can cause difficulties later on if the upper and lower teeth don’t meet when the mouth is closed.

Growth



Many chromosome disorders affect growth so that children and adults are unusually short, but the picture with 8p duplications appears quite variable, suggesting that this disorder has no consistent effect on growth. Among *Unique's* adult members, one woman is 4'11" (147cm) tall – eight inches (20cm) below average adult height for a woman, while one young man measures 6'2" (185cm), five inches (12.3cm) above average adult height for men. There is no gender difference: *Unique* members include tall women and short men with 8p duplications.

Despite being born a normal weight, many babies with an 8p duplication find feeding and putting on weight very difficult in the early months. Health professionals call this failure to thrive. The failure to thrive is an important factor in many children's poor growth in their early years.

Food and eating

Babies will need support with feeding in the early weeks. In addition to their typically weak sucking action and low tone in the muscles of the face, most have poor lip closure, allowing milk to flow out of the mouth. This is made especially difficult in babies with a cleft of the soft palate (a split in the soft part at the back of the roof of the mouth) or in babies whose soft palate does not close properly, allowing milk to enter the nasal spaces and come out of the nose. Some babies also have noticeable reflux, the regurgitation of the stomach contents up the food pipe (oesophagus), causing an extreme form of possetting that is distressing to the baby. Reflux is usually manageable if babies are fed semi upright and sleep with the head end of their cot slightly raised. Thickened feeds generally stay down better and some babies may respond to anti reflux medication. If simple measures do not work, it is possible to improve the action of the valve between the stomach and the food pipe in a surgical operation called a fundoplication.

In *Unique's* experience, most babies were tube fed for the first few weeks. Ideally, they will receive expressed breast milk and one baby graduated to breastfeeding. Babies who were bottle fed needed an adapted teat for premature babies or a teat for babies with a cleft palate. In a minority (three out of 13), failure to thrive was severe enough for a gastrostomy tube to be fitted, allowing feeds to be given direct into the stomach as a temporary measure.

Beyond babyhood, feeding patterns improved, with most babies moving on to solid food at the appropriate age. However, some children had dental problems and chewing difficulties and problems feeding themselves persisted for most children, but

by secondary school age, all the families who gave information noted their child's good appetite.

Constipation is common in children with chromosome disorders, especially children with small appetites who drink little and those who are not very active. In one child constipation was made worse by redundant loops in the bowel. Most children took regular prescribed or natural stool softeners or bowel movement stimulants, but despite this one child developed faecal impaction.

How can an 8p duplication affect a child's ability to learn?

The extra chromosome material will affect the speed at which many children learn and set some limits on their eventual achievement. Just how slight or far reaching the effects are will become clear as your child develops, but the possible range is really very broad, from no effect at all in children who have or inherit a small, stable duplication to a more profound effect in others. It is not always possible to predict from the chromosomes what the effects on learning will be, but by your child's first birthday it will be easier to suggest the outlook from the chromosomes, the results of clinical investigations and observations of your child's development.

Many children are characterised as having a moderate or severe learning disability but each has individual strengths and abilities. A facility for music and rhythm is a common theme in parental reports and children's generally sociable nature enhances their learning relationships. Educational reports suggest that learning is most effective when a multi-sensory approach is used. One child had a remarkable imagination, at the age of 6 converting scraps of paper into cars, people and animals. On the downside, attention span and memory can be short and formal academic skills are slow to emerge. Some older children with small duplications do read and write, but this is not possible for all.

From *Unique's* database, one young man with an 8p23.1p23.3 duplication (not inherited) had achieved the preliminary stages of the UK school leaver's examinations in English, mathematics, science and information technology by the age of 16.

Families say ...

“ At age 8, he is operating at an 18 month level. He is very friendly, loves to try his best to dance and sing and smiles almost constantly. He learns by observing and tries to mimic words and actions. He loves music and dancing - 8p11.2p23.3 duplication.

“ He shows a good comprehension because he was stimulated very early. Attending a regular school helps his self esteem and he enjoys playing music, singing songs and running with his classmates - 8p21p23 duplication, age 8.

“ At a chronological age of 10, he is considered to be at a 2 year level in most areas. His strengths are that he is very social and loving. He has a hard time focusing so he does not do well learning. He learns best when visual,, auditory and kinaesthetic modalities are used together - 8p21.3p23.1 duplication.

Families say ...

- “ Up to the age of 4 years C used to use vocal noises and hand gestures to communicate, from the age of 4 to 8 years he used Makaton signing and vocal noises. Since the age of 9, he has communicated verbally, albeit with difficulty, but he can now make himself understood with ease, and is able to hold full conversations with his peers as well as others.*
- “ C can use speech normally, although due to improper breath control, he seems to have a lot of pauses within his sentences.*
- “ C does frequently set out to hold a conversation, but by the time he has said half of his first sentence he has forgotten what he was actually saying.*
- “ C progressed very slowly, then a little further, then seemed to go backwards, then forwards again, and has progressed steadily up to two years ago, when he seems to have hit a plateau - 8p23.1p23.3 duplication, age 16.*

What type of school do children attend?

The great majority of children in the *Unique* series attended a special school. Almost all had a statement of special educational need or its local equivalent.

Speech and communication

Speech and language delay appears to be in line with children's ability to learn. First words typically emerged between two and five years although one child who did not speak until the age of 9 as a teenager had reasonable verbal understanding and among the most fluent speech in *Unique's* membership. Some children have marked hypotonia of the face muscles, dribble readily and face difficulties in making the sounds of speech.

Most children understand and acquire some speech and, while limited, their language allows them to express their needs and wishes. A few children do not communicate using speech.

Sitting, moving, walking ...

As babies, children with 8p duplications had marked hypotonia and were late to achieve skills such as holding their head steady, sitting, crawling and walking. There was a wide range in the ages at which individual children acquired these skills. On average they learned to roll over between seven months and three years, to sit without support between eight months and three years and to crawl or shuffle between 11 months and seven years, although some children by-passed this stage and moved direct to walking. Those children who walk generally achieved this between 2 and 3 but in a few children this skill emerged earlier and a sizeable number of children aged 6 to 8 have not yet learned this skill or have acquired it and then lost it.

The typical pattern of muscle tone in children with an 8p duplication appears to be marked floppiness of the upper body with increased tone and tautness in the muscles of the lower body. Balance may also be affected and in the lower body the joints often become increasingly contracted. To counteract this tendency, most children needed a programme of daily stretching exercises to keep the joints in the body below the waist flexible. Many needed to wear braces overnight

to straighten the knees and orthotic ankle supports or support boots for walking. Despite regular physiotherapy, some children needed the hamstring tendons behind the knee and the Achilles tendon in the lower leg releasing and lengthening to allow the knee and ankle joints to straighten and flex. Mobility has been achieved and maintained in some children by more extensive surgery releasing tendons in the foot and fusing bones to maintain position. To maintain their mobility, children typically needed intensive and regular physiotherapy following surgery.

The *Unique* series showed that this pattern of increasing joint contractures in the lower body was not universal. Some children progressed from walking around their third year to running around ages three to six and climbing stairs shortly afterwards. This group of children tended to have a smaller duplication in the 8p21.3 to 8p23.1 region, while children with larger duplications appeared to be at greater risk of joint contractures needing surgical correction.

Using their hands

Hand use and hand-eye co-ordination were significantly delayed in all children in the *Unique* series, but there was no consistent pattern of delay. Pincer grip (between thumb and forefinger) and pointing appeared to develop late in most children but other skills such as transferring objects from one hand to the other and developing a tripod grip for writing tools showed a less consistent pattern.

Medical concerns

■ Heart

Babies with an 8p duplication will have a thorough cardiac investigation because of the known association between the disorder and heart defects. Many different defects have been described in the medical literature including three cases of hypoplastic left heart, where there is underdevelopment of the left side of the heart, as well as a case of narrowing of the tricuspid valve between the upper and lower chambers on the right side of the heart, large holes (septal defects) between the right and left chambers, narrowing of the aorta that takes the blood flow from the heart to the body, failure of an opening between the two upper chambers to close after birth (patent foramen ovale) and a right displacement of the heart.



Families say ...

“Physical therapy and occupational therapy have helped the most with mobility skills, especially since they have been consistent from the age of five months old through to the present.

“A could pick up a pin off the floor with a thumb and forefinger grip but struggles with screw tops on bottles as she turns them the wrong way..

The *Unique* series suggested a more encouraging story. Of 22 babies with an 8p duplication, a heart defect was found in four but treatment was necessary in none. The defects found were an aberrant right subclavian artery (supplying blood to the neck and arms), two septal defects and an aortic valve defect, all of which rectified themselves naturally (Giglio 2000; Fan 2001; Tsai 2002; U).

■ Anomalies of brain structure

Children diagnosed with an 8p duplication will usually have a brain scan. In some cases, an anomaly will be revealed, most typically absence of the broad band of nerve fibres that connects the two hemispheres of the brain known as the corpus callosum. In some children the corpus callosum is only partly developed or is very

thin. The effects of agenesis (absence) of the corpus callosum (ACC) depend on any other abnormalities. There is no standard treatment for ACC but any symptoms that may develop will be treated. It has been suggested that a duplication covering the bands 8p21 to 8p22 is always found in people with corpus callosum anomalies and this agrees with *Unique's* experience (Walker 1987; U).

In some babies the fluid-filled cavities within the brain are enlarged, giving less space for the brain tissue and increasing pressure inside the brain. In young children where the skull plates are not yet fused, this can make the head increase in size. The increase in cerebrospinal fluid (CSF), the liquid in the brain's cavities, can be caused by interference with normal flow due to abnormalities of brain structure at the back of the head.

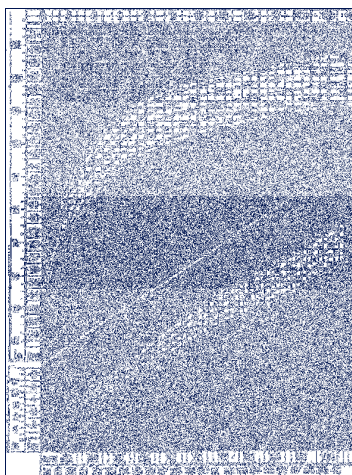


Chart showing rapid head growth in a baby with an 8p21.3p23.1 duplication.

■ Limbs and feet

The rate of positional defects of the feet in babies is raised, but it is uncertain whether this is specifically due to the 8p duplication. Among the foot problems mentioned in the medical literature are various types of club foot (talipes equinovarus, calcaneovalgus) and rocker bottom foot.

The *Unique* membership described a broader and less easily classifiable range of positional anomalies, including markedly flat feet, a tendency to stand on the outer edge of the feet and an inturning left foot. Children with large duplications covering most of 8p were much more likely to have a positional foot defect. In most children, the unusual position was corrected with physiotherapy and splinting, but three children needed surgical correction (Clark 1980; Moreno Fuenmayor 1980; Pezzolo 1990; U).

■ Joints

In some children with 8p duplications, there is a characteristic stiffening of the joints in the lower body during childhood, making regular stretching, physiotherapy and bracing necessary to maintain mobility. However, this does not affect all children. In affected children tendons behind the knee and in the lower leg may need to be surgically released to allow the knees and ankles to straighten. Although this was more common in children with large 8p duplications, it also affected some of those with a smaller extra segment of 8p21.3 to 8p23.1 (Clark 1980; Moreno Fuenmayor 1980; U).

■ Spine

Children with 8p duplications have an increased tendency for the spine to curve sideways, causing the classic C or S-shaped bend of scoliosis. Scoliosis that progresses can lead to problems sitting and if it is severe can cause heart and lung problems. In *Unique's* experience, this was more common in children with large duplications. As this tendency is well known, children with 8p duplications can expect to have a spinal x-ray and monitoring if any scoliosis is progressive. Lesser degrees of scoliosis can be treated with physiotherapy or a body brace, but if it is more severe, surgery is most likely to help.

■ Cleft

The risk that a baby will be born with a cleft palate, sometimes with a cleft lip as well, is raised in 8p duplications. Many degrees of cleft have been described in the medical literature, from a division in the finger-like projection of soft, fleshy tissue that hangs down at the back of the roof of the mouth (bifid uvula) to a submucous cleft, where the split in the roof of the mouth is covered by the mucous membrane that lines all the mouth's surfaces, to an obvious cleft in either the muscular tissue at the back of the roof of the mouth (soft palate) or the bony roof (hard palate). In some children the palate is intact but is abnormally high. A cleft palate may be accompanied by a cleft in the upper lip, on one side or both.



Unique's membership showed that around half of all babies with an 8p duplication had an abnormal palate. Of 10 babies with a defect, three had a high palate, three had a cleft palate and four had a cleft lip as well. The cleft was independent of the size or position of the duplication. One child with a small duplication in band 8p23.1 inherited from a healthy parent had a bilateral cleft lip and palate (Funderburk 1978; Fineman 1979; Moreno Fuenmayor 1980; Memo 1988; U).

Other medical concerns

Having any chromosome disorder raises the risk of certain birth defects. These also occur in children with normal chromosomes but are found more frequently when a

child has a chromosome disorder. Some of the features listed below may be specifically due to an 8p duplication but as so few people have the disorder, this cannot yet be certain.

Gallbladder

There have been three reports of babies with an 8p duplication born with no gallbladder. This was not seen in the *Unique* series (Funderburk 1978; Moore 1992).

Genitals

Genital development may be disturbed or delayed, most often in boys. The testicles may not be felt in the scrotum at birth and a surgical operation may be needed to bring them down and fix them in early childhood. In the *Unique* series, this was the only genital anomaly described. The penis may also be unusually small (Fineman 1979; MorenoFuenmayor 1980; U).

Hernias

Visible hernias can occur in the groin (inguinal), around the umbilicus (umbilical) and along the midline of the abdomen (diastasis recti abdominis). The *Unique* series showed that only one or two children were affected and the hernias occurred in the groin and at the abdominal midline.

Hands

Very loose finger joints, making the fingers unusually flexible, small fingernails and a single crease on the fingers are all typical of 8p duplications as is an additional finger and clenched fingers. More generally typical of chromosome disorders is a sharply incurved fifth finger. These differences are chiefly cosmetic apart from the extra finger which can be removed in a straightforward daycare surgical operation. The very flexible finger joints can also delay hand control, and your child's physiotherapist or occupational therapist will advise on approaches to strengthen the fingers (Chiyo 1975; Fineman 1979; MorenoFuenmayor 1980; Pezzolo 1990; U).

Kidneys, urinary tract and bladder

Kidney and urinary tract disorders are common in children with chromosome conditions. In one baby described in the medical literature, the kidneys had extensive calcium deposits. In the *Unique* series, one child was born with dilated kidneys and an unspecified structural anomaly but this caused no further problems. A teenager with a duplication of band 8p23.1 to 8p23.3 developed Henoch-Schonlein purpura, a puzzling condition that inflames the blood vessels, causing crops of tiny blood blisters that eventually fade. He was one of few children in whom the illness affected the kidneys and he went into kidney failure. However, there is no reason to assume that this event was linked with the 8p duplication (Fan 2001; U).

Intestines

In two *Unique* members, extra bowel loops or incorrect position of the bowel have played a role in long term severe constipation. In one child, emergency surgery was needed to reposition the bowel (U).

Seizures

Seizures have not often been reported in the medical literature and affected only 4/22 children in the *Unique* series. The seizure type varied and there appeared to be no obvious link with either duplication size or structural brain anomalies. Two children with agenesis of the corpus callosum (ACC, see page 10) also had seizures, but so did two children in whom magnetic resonance imaging showed a normal brain. In one baby with ACC, seizures started at 13 weeks as absences and resolved at eight months. They resumed at 16 months but were controlled with anti-epileptic medication and by age 6 were very infrequent. In one child seizures were well controlled from the age of 5. In other children, seizures were either reasonably controlled or, in one teenager, they resolved by the age of 17.

Infections

Children with chromosome disorders have a generally increased rate of respiratory infections. Ear infections are also especially common. There is one research report of a child with an unusual lobe pattern of the right lung (Pezzolo 1990; U).

Ears and hearing

Nine of 22 children in the *Unique* series were reported to have a hearing loss, in each case caused not by permanent nerve deafness but by an obstruction to sound reaching the inner ear (conductive deafness). This type of deafness, called glue ear, is extremely common in children with or without chromosome disorders and is usually outgrown by the age of 7 or 8. All affected children had grommets (tubes) inserted to stabilise the air pressure inside the middle ear and improve sound conduction and one child also wore hearing aids to the age of 2½. One child who did not have a hearing loss was noted to have narrow ear canals. One child with a structural defect of the middle ear needed reconstructive surgery (U).

Eyes and vision

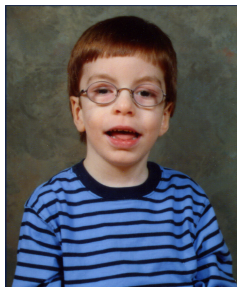
Two problems that are relatively common in children with a chromosome disorder are strabismus (squint) and blocked tear ducts. Two children in the *Unique* series (nine per cent) needed surgery to clear the tear ducts. Although squint was noted in four children, it resolved without surgical intervention in all of them.

In other children, vision was reported to be normal but one child with a duplication between 8p21.3 and p23.1 had noticeably reduced functional vision and received teaching from a vision therapist.

At age 5, it was noted that 'When asked to color pictures on the screen, D will only

Families say ...

"D tends to metabolise anti epileptic medications very quickly. In good spells, he would have 2-7 seizures a week and went through regular periods of 5-100 or more seizures a daily. After an illness such as a sinus infection he would sometimes have a huge increase in seizure activity for weeks or months. We were looking into alternative treatments such as ketogenic diet and vagus nerve stimulation when his seizures came under control for no apparent reason at the age of 5. When he was having the seizures on a regular basis his development was very slow - age 6.



use his left hand and often leaves the right side of the picture blank. When moved over to the right he continued to colour the left side with his left hand and would not cross the midline to finish the picture. In other activities he has no hesitation to cross midline to reach for objects' (U).

General health

Children in the *Unique* series were generally healthy and apart from a susceptibility to infections of the upper and lower respiratory tracts were no more likely than anyone else to need unplanned hospital treatment.

Therapies

The *Unique* series showed that children with 8p duplications needed a very high level of therapy input from babyhood onwards. Physiotherapy was especially important in helping children to achieve their mobility milestones and all children needed input from the speech and language services, although their progress was often slow. Some children had access to swimming therapy, horse riding or music but it was not clear that they progressed better than children with more limited opportunities. It was also not clear whether children who started therapy early eventually achieved at a higher level than those for whom therapies did not start until their second or third years.

Support and independence

Self care skills were not well developed in the *Unique* series, and only two out of five teenagers and adults were toilet trained. Some teenagers with small duplications were able to help with daily tasks such as dressing, undressing and eating. As a group, therefore, people with 8p duplications appear likely to need 1:1 support into adulthood and will achieve only a limited measure of independence.

Puberty

There is very little published experience of puberty in youngsters with 8p duplications. Taken together with *Unique's* experience, it suggests that while puberty may proceed at the usual time and pace, in at least some youngsters full sexual development will never be complete (Clark 1980; U).

Behaviour

It is uncertain whether any particular behaviour pattern is typical for children with 8p duplications but from parental reports, children were typically happy and sociable. From

Families say ...

“ Music therapy helped in several ways, mainly with his self esteem - age 8.

“ Very much along the lines of the average teenager, but mood swings and compulsions have been greatly exaggerated - age 16.

“ Some behavioural issues but overall a sweet and loving boy - age 10.

Families say ...

around age 5, bouts of oppositional behaviour might develop and children could be aggressive towards themselves and others. Children with chromosome disorders are subject to the same influences as other children, but the effects tend to be less modulated and more extreme. Challenging behaviour typically developed in response to stress or fatigue and was especially evident at puberty. The behaviours that children then showed could be very difficult for parents to handle and all families needed ready access to a good behaviour support, psychology or mental health service. Attention deficit is not a noticeable feature of 8p duplication, but was noted in two children with a small (8p21/2 – 8p23.1) duplication, who responded well to methylphenidate (Ritalin) (U).

“A happy boy, always smiling, likes music, very sociable with other children, sometimes shows a very strong personality, sometimes afraid of high places and new situations, observes others at play before joining in - age 8.

Can someone pass on an 8p duplication?

It is best to discuss the inheritance pattern of your child's 8p duplication with a geneticist or genetic counsellor. In general, parents with simple duplications are most likely to have chromosomally normal children or offspring with the same duplication 8 as themselves. The risk of transmitting a duplication may be as high as 50 per cent.

However, the laboratory analysing the chromosomes will take care to distinguish simple duplications from insertions or more complex rearrangements which may carry a risk of forming other types of gain or loss of chromosomal material.

In some families, one parent has a balanced translocation between two (or occasionally more) chromosomes. Chromosome material has changed places but as nothing has been added or taken away, the parent is usually healthy. These parents will also usually have chromosomally normal children or offspring with the same balanced translocation as themselves. However, when eggs or sperm are created, there is a chance that there will be too much or too little chromosome material.

There are many other cases in the medical literature of families in which a small 8p duplication has been passed direct from parent to child. There are three main groups:

- 1 families in which different healthy members have the same duplication, so in this family at least it is harmless.
- 2 families in which a healthy parent passes the same duplication to a child who is not very severely affected. It may not be certain whether the child's problems derive from the chromosome disorder or something else.
- 3 families in which the duplication is a natural variant and has no effect.

Support and Information



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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. Unique does its best to keep abreast of changing information and to review its published guides as needed. The guide was compiled by Unique and reviewed by Dr John Barber, Wessex Clinical Genetics Service and by Professor Maj Hultén, BSc, PhD, MD, FRCPath, Professor of Medical Genetics, University of Warwick, 2005.

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