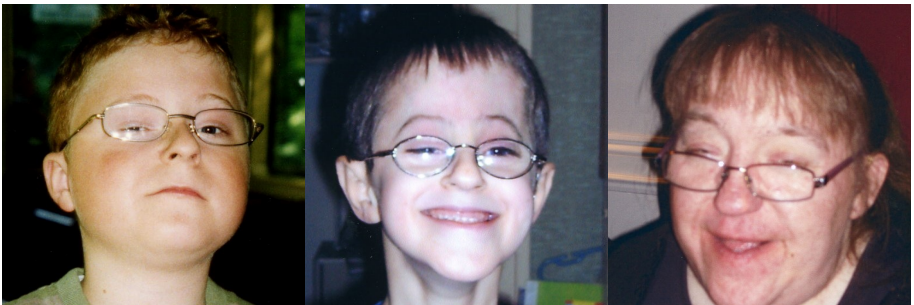




Understanding Chromosome & Gene Disorders

# Duplications of 6p



[rarechromo.org](http://rarechromo.org)

## Duplications of 6p

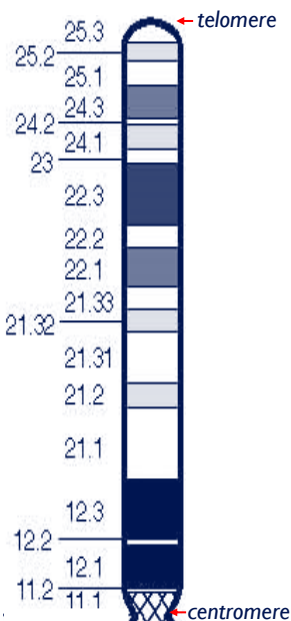
A duplication of 6p means that there is extra material from one of the body's 46 chromosomes – chromosome 6. For healthy development, chromosomes should contain just the right amount of material – not too much and not too little. Extra material is likely to disturb development but how obvious and serious the disturbance is depends on the amount of duplicated material, on which part of the chromosome is duplicated and on what genes are disturbed.

Chromosomes are the structures in the nucleus of the body's cells that carry genetic information (known as genes), telling the body how to develop, grow and function. This genetically important information is made up of DNA. Chromosomes come in 23 pairs, one from each parent, and 22 of the pairs are numbered 1 to 22 approximately from largest to smallest. This makes chromosome 6 one of the larger chromosomes, containing more than 1,000 genes, perhaps as many as 1,600. Each chromosome has a short (p) arm and a long (q) arm. A duplication of 6p means that the extra material is from the short arm of chromosome 6. Duplication of 6p has also been called **trisomy 6p**. Usually only part of the short arm is duplicated; this can then be called **partial trisomy 6p**.

People with a 6p duplication have one intact chromosome 6 but the other has a smaller or larger extra piece of the short arm and this can affect their learning and physical development. Most of the clinical difficulties are probably caused by the presence of an extra copy (instead of the usual two) of a number of genes. However, a child's other genes and personality also help to determine future development, needs and achievements.

## Looking at 6p

You can't see chromosomes with the naked eye, but if you stain them and magnify them under a microscope, you can see that each one has a distinctive pattern of light and dark bands. You can see these bands in the diagram. They are numbered outwards starting from the point where the short and long arms meet (the **centromere**).



## Sources & references

The information in this leaflet is drawn from what is known about 26 people with a duplication of 6p. Sixteen people have been described in the medical literature with a 'pure' duplication of 6p, with no significant material lost or gained from any other chromosome arm (Villa 2007; Domínguez 2003). 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 most articles from *Unique*. The leaflet also draws on *Unique*'s database. When this leaflet was written, *Unique* had 12 members with a pure duplication of 6p. Two members were the subjects of reports in the medical literature.

## The karyotype

Your geneticist or genetic counsellor will be able to tell you about your child's duplication. Your child will almost certainly be given a karyotype, a shorthand notation for their chromosome make-up. It is likely to read something like this

46,XX,dup(6)(p25p22)de novo

46 = The total number of chromosomes in your child's cells

XX = The two sex chromosomes, XX for females; XY for males

dup = A duplication means that material has been repeated

(6) = The duplication consists of material from chromosome 6

(p25p22) = The chromosome has broken in two places. The first break is at p25 and the second break is at p22 so these are the ends of the duplicated section.

de novo = The parents' chromosomes have been checked and no duplication or other abnormality found. The duplication has not been inherited.

## Is there a 6p duplication syndrome?

It's true that certain features - such as unusual facial features, growth delay, a small head and a tall forehead, and hooded eyelids - are found quite frequently in babies and children with a 6p duplication (Schinzel 2001). However, these features are found in other people with quite different chromosome disorders and many children and adults with duplications of 6p don't have most or all of these features. Overall we can't identify a clear enough pattern of similarities to say that there is a 6p duplication syndrome.

It is possible that with new, more sophisticated ways of looking at chromosomes, syndromes will be identified in the future for short segments of 6p. But pure 6p duplications are very rare and not enough people have yet been formally described to be sure of this. Even if such syndromes do emerge, there will still be differences - sometimes quite marked - between individuals.

## Are there people with a 6p duplication who are healthy, have no major medical problems or birth defects and have developed normally?

Yes: in a few people, a very small duplication near the tip of the short arm of the chromosome identified using the microarray technique (a way of analysing thousands of different DNA sequences at the same time) appears to have no effect (Bonaglia 2008; Hengstschaeger 2005; Bonaglia 2003). It is possible that there are other people scarcely affected by a relatively small duplication who have never been identified or reported by the medical profession.

## What is the outlook?

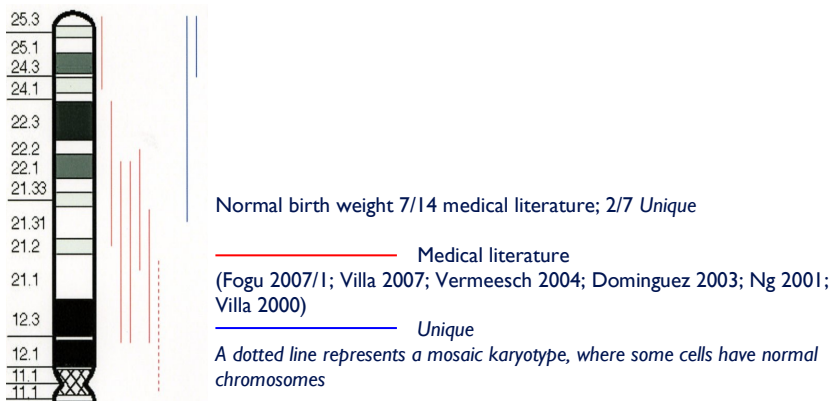
The outlook for any baby or child depends on what segment of chromosome 6 has been duplicated and how this has disrupted early development in the womb. In many children no major internal organs are involved and for them the outlook seems good. There are many healthy older teenagers and adults with particular duplications and you may wish to compare your child with others with the same duplication. All the same, there will be differences between your child and others with an apparently similar karyotype and these can be quite marked. It is important to see your child as an individual and not to rely on direct comparisons with others with the same karyotype. After all, each of us is unique.

## Your baby at birth

Although some babies are born normally at term after an uneventful pregnancy, there is a significant risk that birth will need to be medically managed. In many cases this is because the baby's slow growth in the womb has been noticed and the birth induced. In other cases, babies have moved less than expected during pregnancy or experienced distress during birth and a Caesarean section was performed. After delivery, while some babies breathe normally and have high Apgar scores (a measure of general wellbeing on a scale of 0-10) at one and five minutes, a small but significant number of babies have difficulties and need help with their breathing in the early days of adjustment to life outside the womb.

Although it is repeated in the medical literature babies that babies with a duplication of 6p are **small for gestational age**, this is not true for all. Twelve babies out of 21 were of low weight at birth, but nine were not and there was considerable variation between individual babies. Among the nine babies with a normal birth weight, the range was from 2.9kg (6lb 6oz) to 3.6kg (7lb 15oz) at or near term, while the weights of the small-for-gestational age babies ranged from 1.8kg (4lb) to 2.6kg (5lb 12oz).

## Birth weight

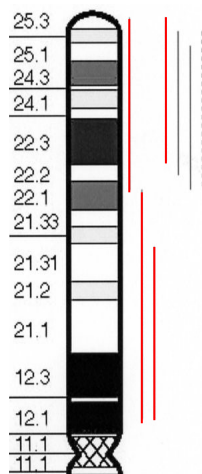


Some babies are sleepy and not as active as you might expect. If this is not your first baby you may notice that their facial features are different from their brothers' and sisters'. It is possible that your baby will need to spend some time in special care. This is an anxious time for parents, especially as medical staff may now seek an underlying cause for any problems and take a blood sample to examine the chromosomes.

Feeding difficulties and a slow weight gain (failure to thrive) are very common among newborn babies with a 6p duplication and can lead to several changes of formula or to abandoning breastfeeding in an attempt to encourage weight gain. Babies tend to feed extremely slowly, so that feeding becomes a major preoccupation and activity.

Sometimes breastfeeding can be maintained, in some cases with supplementary feeds to boost nutritional intake. If necessary, breast milk can be expressed and given by bottle. A few babies are fed by tube (nasogastric (NG-tube), where the tube is fed up the nose and down the throat to the stomach, or gastrostomy (G-tube), feeding direct into the stomach), but most babies manage without tube feeding.

## Choanal atresia



Most babies with a 6p duplication are born with normal, open breathing passages leading from the mouth and nose. There is, however, a small risk that one side or both of the passages leading from the back of the nose will be very narrow or even blocked.

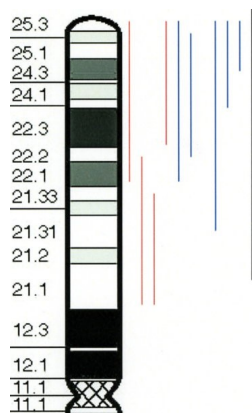
This condition, known as choanal atresia, creates breathing difficulties for the baby and needs correction by surgery. When only one side is blocked, a baby may not show many symptoms and so the condition may not be diagnosed for some time. When both sides are affected, a baby will have some difficulty breathing and so the condition is likely to be diagnosed soon after birth.

Medical literature  
(Fogu 2007/1; Ragoussis 2006 (unpublished); Villa 2000; Nakajima 1995)  
Unique  
A dotted line represents a mosaic karyotype, where some cells have normal chromosomes

## Heart murmur or heart condition

Most babies are born with a healthy heart, but a minority have a heart condition. In some babies, there is a single, simple condition such as a hole between the upper chambers of the heart (atrial septal defect/ ASD) or a narrowing of one or more of the valves through which blood flows within the heart or when it leaves the heart to enter the lungs or to travel around the body. These conditions may improve naturally over time or can sometimes be corrected surgically using minimally invasive surgery. In other babies there are additional heart problems, such as a persistent ductus arteriosus (PDA). This is a channel between the aorta and the pulmonary artery that takes blood to the lungs which usually closes shortly after birth. When it stays open, the lungs receive more blood than they should and the heart has to work too hard. It may close naturally in time but if it does not, it can usually be closed using minimally invasive surgery.

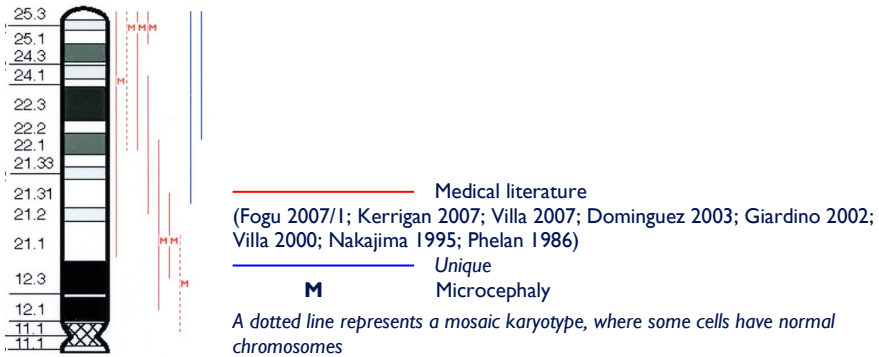
A small number of children are born with a serious or complex heart condition. This can usually be corrected by surgery and outcomes after surgery continue to improve. Occasionally it is not possible to correct the heart condition and this will lead to limitations on a child's activity.



Medical literature  
(Ragoussis 2006 (unpublished); Engelen 2001; Karamanov 2001; Ng 2001)  
Unique  
No heart condition  
A dotted line represents a mosaic karyotype, where some cells have normal chromosomes

“ His heart condition is inoperable – he has cold feet, gets tired easily and sometimes has a blue tinge to his lips after swimming or if he is overexcited - 6p21.3 duplication, 8 years old

## Very small head and brain (microcephaly)



Some babies with a duplication of 6p are born with a very small head relative to their body size. The brain may be small but perfectly formed or there may be further structural anomalies. It has been suggested that an extra dose of a gene or genes in the proximal part of 6p near the centromere may cause the bony plates of the skull to fuse early (craniosynostosis). There are around 60 possible genes between the centromere and band 6p21.1 but one particular gene, known as *BMP5*, is thought to be a possible cause of the early fusion (Villa 2007).

### Facial appearance

A large number of unusual facial features have been noted by geneticists in reports on babies and children with a 6p duplication. Your baby or child may have just one or two of these features or sometimes more and you may find that he or she looks more like others with a 6p duplication than like other members of your own family. The key features include: an unusually small head (microcephaly); a high or prominent forehead; small eyes with narrow openings (blepharophimosis, blepharoptosis), occasionally with tiny skinfolds across the inner corners (epicanthic folds) and also occasionally long eyelashes; ears of an unusual shape or size that are sometimes placed low on the sides of the head; a bulbous nose or a nose with a bulbous tip and with an unusual bridge (wide or high); a small mouth with thin lips (most typically a thin upper lip); and a small lower jaw or a pointed chin.

### Hands

Your child's hands may look somewhat unusual. They may be disproportionately short or long and you may notice features such as incurving fifth fingers, a single crease across the palm or fingers that taper towards the tip. One or more fingers may be clenched and you may find that fingers overlap each other or that two fingers are joined. In one child with a duplication between 6p21.1 and 6p22.2, the flexor tendon was missing from the middle finger of her right hand (Ng 2001).

So long as these unusual features are no more than cosmetic, they do not need treatment. Overlapping or clenched fingers may improve with time or with simple measures like soft splints and joined fingers can be separated surgically, although their function may not be perfect (Unique).

## Feet

Some babies with a 6p duplication are born with unusual feet or toes. The feet themselves may be long and or there may occasionally be specific features such as a curved (rocker bottom) sole. The foot may be held at an unusual angle to the leg. The toes may not be evenly placed across the foot and some toes may curve inwards or be joined by skin or tissue. The first ('big') toe may be short or broad and there may be a wide gap ('sandal gap') between the first and second toes.

Some of these features will improve naturally with time and most will not affect walking, although a child with rocker bottom feet may need special insoles to ease walking. Treatment for an abnormal foot or walking position is individually tailored and aims to straighten the foot so that it can grow and develop normally. First-line treatment is non-surgical and may include manipulation, casting, taping, physiotherapy and splinting, followed by bracing to prevent relapse. Ankle or foot supports are often prescribed, as well as special footwear. Surgery and sometimes splinting are considered if non-surgical treatments are not completely successful. The foot position may relapse as the child grows and develops, making further surgery necessary.

## Feeding

Some newborn babies – although not all - will have difficulties feeding and these may extend beyond the newborn period. From the limited information within *Unique* and in the medical literature, it is clear that while babies with a heart complaint are most likely to face feeding challenges, others babies may also be affected. Babies may have difficulty with sucking as newborns and feed very slowly or inadequately to meet their nutritional needs and put on weight, requiring enriched formula and supplements to ensure satisfactory weight gain. Some babies have a low muscle tone (hypotonia), which makes feeding and sucking difficult. Breastfeeding may be achievable, but some babies find the effort too much and thrive better on bottles with teats suitable for premature babies; others are fed expressed breast milk by nasogastric tube. It may be necessary to place a gastrostomy tube to allow feeding direct into the stomach. Progress to sipping, chewing and solid foods also tends to be delayed. Children who have had difficult feeding experiences as babies can be vulnerable to later feeding difficulties, expressed as food refusal or extreme fussiness over texture and taste. Ongoing support is needed to ensure that feeding remains a pleasurable experience (Fogu 2007; Engelen 2001; Ng 2001; Nakajima 1995; *Unique*).

*Unique* data show that some babies and children have gastro oesophageal reflux (where feeds and stomach contents return into the food passage and are often vomited or may be inhaled, causing chest infections, known as aspiration pneumonia) but this has generally been well controlled by giving feeds slowly, positioning a baby semi-upright for feeds and where necessary raising the head end of the bed for sleeping. If these measures are not enough, prescribed medications or anti-reflux milk are usually enough to keep feeds down. Constipation has also been seen but usually responds to increased fluid, fibre or prescribed medication.

## Growth

Many children and adults with a 6p duplication are unusually short and small for their family. Babies born short tend to remain small as children and adults, although their

body weight may be well within normal limits. Growth delay can accelerate in babies who are ill and unable to feed well, although evidence from *Unique* shows that in time they can recover some of their lost growth. At least in some children born within normal size limits, however, a more normal growth trajectory is possible (Fogu 2007; Villa 2007; Vermeesch 2004; Engelen 2001; Ng 2001; *Unique*).

There is very limited information on eventual adult heights, but one *Unique* adult with a mosaic duplication between 6p22 and 6p25 has achieved an adult height of 4' 6" (1.37m).

## Puberty

There is very little information on puberty. In one girl with a mosaic duplication between 6p22 and 6p25, puberty started at a normal age and proceeded normally; a boy with a duplication from 6p21.3 had premature appearance of secondary sexual characteristics (such as body hair) at the age of seven, but tested negative for early puberty (Engelen 2001; *Unique*).

## Development: sitting, moving, walking (gross motor skills)



Delay in reaching the developmental 'milestones' of sitting, becoming mobile and walking is typical. This means that your baby will make progress, generally following the normal developmental sequence, but progress will come slower than normal. How much slower depends chiefly on your baby's innate abilities, but also on opportunities, on stimulation and to some extent on therapeutic interventions. One child with extra material from near the centromere of 6p in the form of a small extra chromosome in some cells of the body showed normal motor development at the age of 2. It is hard to predict eventual mobility, but in general babies who are otherwise well and who lift their heads and learn to roll early tend to be those who go on to become mobile early. Some achieve normal eventual mobility while others need long-term support and physiotherapy to keep them mobile.

From *Unique*'s experience, babies learned to roll over between four and six months, to sit without support between six and 21 months, to become mobile between eight months and two years and to walk between 17 months and three years six months. Not all babies crawled: some shuffled on their bottoms or rolled over and over. Walking may remain unsteady for a long while after it is first achieved and your child may walk with their feet wide apart to improve their balance and need walking aids to help. A buggy may be needed for outdoors or for long expeditions for a long while. Once on their feet, some children acquire skills such as climbing stairs, riding a bike and running but this is not possible for all (Fogu 2007; Kerrigan 2007; Villa 2007; Vermeesch 2004; Ng 2001; Villa 2000; *Unique*).

“ After sitting for a long time, she becomes stiff and finds walking difficult. She is OK after a few minutes but needs a rest every so often. No reason can be found for this - mosaic duplication between 6p22 and 6p25, adult (In a mosaic duplication, some cells have the duplication while others do not.)

One of the causes of the delay in mobility is altered muscle tone. Your baby may have a low muscle tone (hypotonia) and feel floppy to handle. This generally improves over time and may resolve with physiotherapy and exercises. In some children, muscle tone is raised (hypertonia), so that muscles remain taut and unable to stretch. This can give rise to tripping and toe-walking, in which case a surgical intervention known as heel-cord lengthening may improve your child's gait.

### **Development: hand use and coordination (fine motor skills) and self care**

Most children, though not all, experience delay in controlling their hand use. They may show a weak hand grip, drop things or knock them over easily and find achieving a pincer grip between thumb and forefinger and manipulating small objects a particular challenge. In *Unique's* experience, slower-developing children may continue to need help to feed, dress and care for themselves throughout childhood and even as adults. Some children do achieve relative independence in these activities although they still tend to be slower than other normally-developing children.

In terms of self care, some youngsters achieve a level of collaborative independence in dressing, washing and personal care tasks, although most need regular reminders to complete the task in hand. It may not be appropriate for parents to expect toileting to occur at the same age as other unaffected children. Data from *Unique* suggest that daytime bladder and bowel control may be achieved with a slight to moderate delay, while in others control may remain precarious or not prove consistently possible (Engelen 2001; Ng 2001; *Unique*).

“ He has little grip and can't hold properly but has a soft sponge ball to squeeze for practice. He still needs help to dress and undress, brush his teeth and wash. He is toilet trained but needs prompting, wiping and his pants pulled up - *duplication from 6p21.3, at 8 years*

“ He can perform personal care with very little help - *duplication from 6p24.2 to 6p25.3, at 10 years*

“ She used chubby pencils and crayons as a child but as an adult uses normal implements. She is toilet trained, brushes her own teeth and dresses herself but needs help to hurry her up in the mornings - *mosaic duplication between 6p22 and 6p25, adult*

### **Learning**

Most children will need extra support with learning. How much support will be needed usually only becomes apparent over time, and not enough experience has yet built up in youngsters with a 6p duplication to make reliable predictions. However, it seems likely that some children may learn at a fairly normal pace or experience only borderline or mild delay in their early school years. One child with a small extra chromosome containing material between 6p21.1 and the centromere in some cell lines had an IQ of 81 at two years (Villa 2007; Ng 2001). This is not possible for all and within *Unique's* membership are children with a moderate to severe learning delay.

In terms of longer term outcome, two adults were assessed to have moderate cognitive delays (Giardino 2002; *Unique*). It is important to remember that youngsters with a moderate learning disability are capable of considerable depth and complexity in their learning and may learn some reading and writing skills.

Some youngsters will need extensive support and skilled one: one teaching to develop and maintain the skills they need for daily living and for them the focus of education should be on living skills rather than academic attainments.

Any family with a child with a 6p duplication should ensure that she or he is regularly and thoroughly assessed and placed in a calm, stimulating and supportive learning environment where his or her strengths and abilities are recognised and built upon and weaknesses minimised. This may be a mainstream school, one where the child's special needs can be more specifically catered for or a home-schooling environment may be thought most suitable (Villa 2007; Ng 2001; Giardino 2002; Phelan 1986; Chiyo 1975; Unique).

“ He has moderate to severe learning difficulties and has difficulty sitting still to do things. He reads reading tree books, signs and words he recognizes and tries to write his name as well as other words; has statement - *duplication from 6p21.3, at 8 years*

“ He has moderate learning difficulties but no difficulties with concentration. He can read around 40 words of 3-4 letters, writes his name, address and family names and draws people, trees and houses. He has a moderate amount of learning support and is home schooled - *duplication from 6p24.2 to 6p25.3, at 10 years*

“ She is moderately learning disabled but has no attention or concentration difficulties. She cannot read but recognises signs, writes her name and copies letters and can draw a house with windows, a cake with candles and a face. She is not good with numbers but has a very good memory and is excellent at jigsaws and household skills. She can peg washing on the line after taking it from the machine; she can break eggs into a jug, assemble and use a mixer; she can boil a kettle and make a pot of tea; make toast and sandwiches and serve them to guests - *mosaic duplication between 6p22 and 6p25, adult*

## Speech and communication

Information on speech and communication is available on only 11 youngsters and in most cases the information is sketchy. This shows that generally the development of speech and language appears to reflect the child's cognitive abilities and that many youngsters face challenges in making words and speech clearly understandable.

Communication skills such as reciprocal smiling, facial expressions and vocal noises emerge before first words, which have been heard between 18 months and four years. Most children are taught some sign language and learn to use it, either alongside speech or as an interim way of expressing themselves until understandable speech takes over. In some children the typical progression follows from single words to short phrases and then longer sentences with more complex grammar, but others continue to communicate in the one word utterances or short phrases.

Children may not acquire speech, but often understand more than they can say and can still communicate well using gestures and signing. Among those without speech, communication devices are popular and helpful. Some children have difficulty making particular sounds of speech, including one child with a tongue tie (Fogu 2007; Villa 2007; Vermeesch 2004; Ng 2001; Unique).

“ His Makaton and speech have greatly improved and he speaks in sentences, although these are not always clear to strangers as he has difficulty with s & l sounds due to tongue tie - *duplication from 6p21.3, at 8 years*

“ He had speech delay and was taught signing but now uses mostly speech in sentences with normal grammar, although he still finds some sounds hard to make - *duplication from 6p24.2 to 6p25.3, at 10 years*

## Behaviour

*Unique* has fairly detailed information on the behaviour of five youngsters with a 6p duplication. There are also brief descriptions of two youngsters in the medical literature (Villa 2007; Ng 2001). This is too small a number for a definitive picture to emerge but the remarks that follow may give families helpful insights into their own child's behaviour.

Both children described in the medical literature, one with a duplication between 6p22.2 and 6p21.1 and the other with a small extra chromosome containing material between 6p21.1 and the centromere in some cell lines, had high activity levels and poor concentration, adding up to a diagnosis of attention deficit hyperactivity disorder (ADHD), treated in one case with medication.

A *Unique* child with a duplication from 6p21.3 was also diagnosed with ADHD and autism and treated with a fish oil supplement as well as standard behaviour modification techniques. A further child with a duplication between 6p23 and 6p25.3 was diagnosed with a sensory disorder after displaying highly unusual behaviours but improved significantly with occupational therapy (*Unique*).

Two children within *Unique* have no behaviour problems at all, displaying on the contrary exemplary manners. A 12-year-old girl was nominated by her school and won a national Child of Achievement award for 'her zest and love for life'. As an adult she has excellent manners, is good at sharing and loveable, interacting very well socially. A 10-year-old boy with a duplication between 6p24.2 and 6p25.3 interacts very well socially and is very sensitive to correction, becoming sad when corrected.

“ We use an egg timer to calm him and say how long something is going to take to happen. He also has a good boy token system – he gets a party popper after his bath if he gets five tokens. He also loves kisses and cuddles and says 'I love you, mama'. He's a little miracle - *duplication from 6p21.3, at 8 years*

“ Although she has special needs, she is very much aware of others worse off than herself. She has a wicked sense of humour and cheers everyone up - *mosaic duplication between 6p22 and 6p25, adult*



## Other clinical concerns

### ■ Seizures

Most children and adults with a 6p duplication are not known to have had seizures. There are four reports in the medical literature (Kerrigan 2007; Villa 2007; Vermeesch 2004; Phelan 1986) and two from *Unique*, in each case well-controlled with medication. There was no obvious relationship between brain size (microcephaly, see above) or abnormal structure and the occurrence of seizures.

### ■ Spine

Three youngsters have been described with a spinal curvature, but it was not severe enough to require anything other than monitoring. Sideways curvature of spine so on x-ray it appears like a C or an S rather than a straight line. In many children a slight curve will correct itself in time but progressive scoliosis can lead to problems sitting and if it is severe can cause heart and lung problems. Treatment depends on the severity and progression of the curve but may involve wearing a body brace and surgery to fuse the vertebrae (Giardino 2002; *Unique*).

A sacral dimple (dimple or hole in the skin just above the crease between the buttocks) was seen in four babies. This may be shallow so you can see the base, but stools can collect there before your child is toilet trained, so keeping it clean and protected is important. A sacral pit may be deep and even connect to the spinal canal or the colon. If there is any concern about this, your baby's spine will be imaged, usually with ultrasound or an MRI scan (Morton 1980; Chiyo 1975; *Unique*).

### ■ Minor genital anomalies

A minor genital developmental anomaly occurs occasionally. Undescended testicles - one or both - were seen in three boys and two others were born with a hydrocele, an accumulation of fluid round the testis in the scrotum. Treatment for undescended testicles depends on the suspected cause and is usually needed if the testicles do not descend naturally in time. Generally speaking, the testicles can be brought down in a short operation under general anaesthetic called an orchidopexy. A hydrocele can develop when the passage through which the testicles descend into the scrotum fails to close. Fluid from the abdomen comes through the passage into the scrotum. A hydrocele at birth is usually fixed by a surgical operation in which the fluid is removed from the hydrocele and the passage between the abdomen and scrotum is sealed off.

One boy had a narrow foreskin opening (phimosis) and another had an inguinal hernia, which shows as a bulge in the area where the lower abdomen meets the upper thigh (the groin). The cause is that an opening in the lower part of the wall of the abdomen that is open during fetal life but closes before birth does not in fact close. The remaining opening may be small, only allowing fluid through, or it may be large enough for something such as a loop of the intestine or another organ to get stuck in it. An inguinal hernia should always be assessed by your child's doctors and your child may need surgery to repair it (Fogu 2007; Ragoussis 2006 (unpublished); Villa 2000; Karamanov 2001; *Unique*).

### ■ Kidneys

Three children have been reported with kidney anomalies. Among *Unique*'s children, these include kidney reflux, also known as vesico-ureteric reflux, where the urine flows

from the bladder up towards the kidneys. If infected urine flows into the kidneys, this can damage them. As the bladder wall thickens and matures with age, many children grow out of reflux. Meanwhile, children with kidney reflux are treated with a low dose of long term antibiotics to prevent urinary tract infections and, in turn, kidney infections. Other problems include hydronephrosis, where the kidneys get dilated because of one of many causes (treatment depends on the cause) and abnormally formed kidneys, leading to failure at 10 years of age and a kidney transplant (Ragoussis 2006 (unpublished); Engelen 2001; *Unique*).

## ■ Infections

Babies and young children with a chromosome disorder appear to generally have a higher rate of childhood respiratory tract infections including ear and chest infections than children with no disorder and this is true of those with a 6p duplication. However, there is no information that children with a 6p duplication have immune deficiency. Episodes of pneumonia may be triggered in young babies by milk or reflux inhalation and chest infections including pneumonia can be a frequent winter feature in early childhood. Infections can be severe and may even be life threatening, although there is no evidence among *Unique*'s members that this is the case (Fogu 2007; Ragoussis 2006 (unpublished)).

## ■ Other problems

A high level of protein in the urine is sometimes found (Ragoussis 2006 (unpublished); Giardino 2003; Wauters 1993). A high level of protein may cause no symptoms but will usually require further investigation. A baby was born with a blocked anus and partially blocked rectum (Fogu 2007). Another was born with a small umbilical hernia, which develops when a small opening in the abdominal muscles that allows the umbilical cord to pass through does not close after birth. Many umbilical hernias close naturally by the age of three or four but a very large hernia or one that stays open after this age can be closed surgically (Crolla 1998). A baby with a 6p22.2p25.2 duplication was born with a non-functioning or absent thyroid gland and takes replacement therapy (*Unique*).

## Eyesight

Most reports to *Unique* and in the medical literature contain no mention of vision problems, suggesting that many and perhaps most children have good functional vision. The most frequent problem is ptosis or blepharoptosis, where the upper eyelid droops so the eye is not fully open. When the eyelid obscures vision, it can be repaired surgically using synthetic material or tendon from the upper thigh (Kerrigan 2007; Ragoussis 2006 (unpublished); Dominguez 2003; Giardino 2002; *Unique*). Four children are described with strabismus (a squint), in two cases associated with short sight. This can be treated by patching the stronger eye, exercises, glasses to correct any refractive error and surgery to realign the muscles that hold the eye in place (Engelen 2001; Giardino 2002; Chiyo 1975; *Unique*). One baby had clouding over the cornea (the front of the eyeball); and a child with a duplication from 6p24.2 to 6p25.3 had a corneal transplant to restore his vision (Villa 2000; *Unique*) while another child had small corneas (Ragoussis 2006 (unpublished)). A child with a duplication between 6p12.1 and 6p22.1 had pigmentary dystrophy of the retina (Fogu 2007) and three children were short sighted (Ragoussis 2006 (unpublished); Giardino 2002; *Unique*).

Retinopathy of prematurity is a condition that occurs in premature, low birthweight babies. Overexpression of the VEGF (vasculo endothelial growth factor) gene at 6p12 in a baby with 6p duplication may increase the severity of the condition (Mandal 2007).

## Hearing

Most children with a 6p duplication have normal hearing. However, children with delayed development may sometimes appear to be deaf because they do not react quickly enough to aural stimuli. A significant minority are prone to frequent ear infections as babies and young children, which can lead to a build-up of fluid behind the ear drums and the need for aeration by temporarily fitting tiny tubes into the ear drums to improve hearing (Ng 2001; *Unique*).

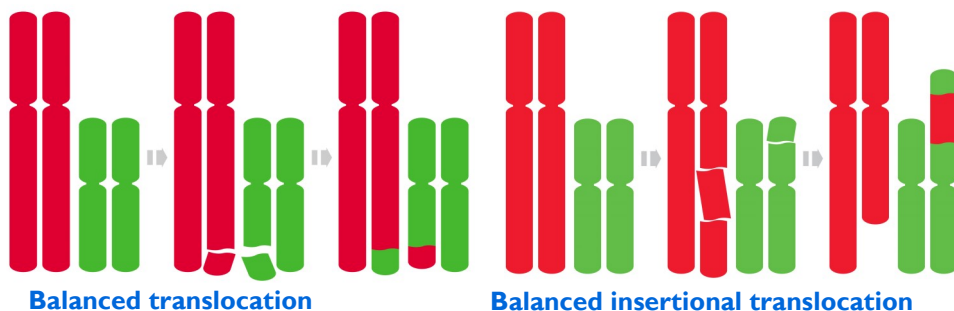
Two children have been described with a permanent sensorineural hearing loss leading to hearing impairment and necessitating wearing hearing aids. Both have a duplication of 6p22p25, one in mosaic form, the other in all cells (*Unique*).

## Teeth

Generally speaking, children with chromosome disorders appear to have more dental problems than others. Information on nine children in the group shows that in two children the gums were thickened and in one the teeth erupted early; one child has marked under- or overbite, caused by a mismatch between the teeth of the upper or lower jaw (Villa 2007; Giardino 2002; Ng 2001; Villa 2000; *Unique*).

## How did this happen?

A duplication can arise in a number of different ways. A blood test to check both parents' chromosomes is needed first. Most 6p duplications are accompanied by a loss of material from another chromosome and are the result of a rearrangement in one parent's chromosomes (Villa 2007; Dominguez 2003). This is usually a rearrangement known as a **balanced translocation** in which material has swapped places between chromosomes. As no genetically relevant material has been lost or gained, the parent usually has no clinical or developmental problems, although they may have difficulties with fertility or childbearing. Balanced translocations involving one or more chromosomes are not rare: one person in 500 has one, making a total world population of over 13 million balanced translocation carriers. Another change sometimes found in parental chromosomes is an **insertional translocation** in which a piece of 6p has inserted itself into another chromosome. The eggs or sperm of someone with these changes risk containing too much or too little chromosome material.



Some 6p duplications occur when both parents have normal chromosomes. The term that geneticists use for this is **de novo** (dn). De novo 6p duplications are thought to be caused by a change that occurred when the parents' sperm or egg cells were formed or possibly just after fertilisation. We know that chromosomes must break and rejoin in quite a complex process when egg and sperm cells are formed but this only occasionally leads to problems.

Very occasionally exactly the same 6p duplication is found in a child and one parent, who appears unaffected by it. This can mean that the 6p duplication is not the cause of any problems found in the child. It can also mean that the chromosome duplication has been 'switched on' in the child by some new factor, such as which parent the duplication came from (Bonaglia 2008; Delatycki 1999). What is certain is that as a parent there is nothing you did to cause the 6p duplication and nothing you could have done to prevent it. No environmental, dietary or lifestyle factors are known to cause these types of chromosome changes. They are no-one's fault.

### **Can it happen again?**

The possibility of having another pregnancy with a 6p duplication depends on the parents' chromosomes. If both parents have normal chromosomes, the duplication is very unlikely to happen again.

If either parent has a chromosome rearrangement involving 6p, the possibility is greatly increased of having other affected pregnancies. If they wish, parents should have the opportunity to meet a genetic counsellor to discuss their specific recurrence risks and options. 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. Testing is very accurate, although not all of these tests are available in all parts of the world.

### **Could my child with a 6p duplication have similarly affected children?**

Adults with small 6p duplications may form close relationships and want to have children. It is not certain whether the duplication affects fertility but it is likely that at least in some people fertility will be normal. There is a small number of known families in which a tiny duplication, especially one that is only detected by FISH or microarray techniques, has been passed directly from one parent to one or more of their children. One is a duplication of 6p25 passed from an unaffected mother to a daughter with developmental problems (Bonaglia 2008; Hengstschlager 2005).

In each pregnancy, someone with the duplication has a 50 per cent risk of passing it on and a 50 per cent chance of having a child without the duplication. Their ability to look after a child is very likely to be closely related to their own degree of learning difficulty.

### **Note**

This leaflet focuses only on pure duplications of 6p. However in many cases reported in the medical literature, the 6p duplication occurs together usually with a deletion in another chromosome arm. As these people do not show the effects of a 'pure' duplication, they are not considered in this leaflet. *Unique* holds a list of the cases described in the medical literature and the karyotypes of those in *Unique*, and this is available to members on request.

# Support and Information



Understanding Chromosome & Gene Disorders

## Rare Chromosome Disorder Support Group

The Stables, Station Road West, Oxted, Surrey RH8 9EE, United Kingdom

Tel: +44(0)1883 723356

[info@rarechromo.org](mailto:info@rarechromo.org) | [www.rarechromo.org](http://www.rarechromo.org)

## Join Unique for family links, information and support.

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

[www.rarechromo.org/donate](http://www.rarechromo.org/donate) Please help us to help you!

## Chromosome 6 research project

The C6 project works with families to collect detailed information with the aim of linking specific disease characteristics with specific regions of chromosome 6.

<https://www.chromosome6.org/>

## Facebook page for chromosome 6

[www.facebook.com/groups/chromosome6](https://www.facebook.com/groups/chromosome6)

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 updated 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 reviewed by Dr Jiannis Ragoussis, Head of Genomics, Wellcome Trust Centre for Human Genetics, Oxford and by Professor Maj Hulten BSc, PhD, MD, FRCPath, Professor of Medical Genetics, University of Warwick, UK 2008.

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