

7q deletions proximal interstitial



A 7q deletion

A 7q deletion is a **chromosome disorder**. A chromosome disorder is a change in chromosome number or structure which results in a set of features or symptoms.

People with a 7q deletion have lost a small but variable amount of genetic material from one of their 46 chromosomes.

Chromosomes and genes

Chromosomes are made up of DNA and are the structure in the nucleus of the body's cells that carry genetic information (known as genes), telling the body how to develop and function. They come in 23 pairs, one from each parent. Twenty-two of the pairs are numbered 1- 22 according to size, from the largest to the smallest. In addition to these 44 chromosomes, each person has another pair of chromosomes, called the sex chromosomes. Girls have two Xs (XX), whereas boys have an X and a Y chromosome (XY).

Each chromosome has a short (p) arm (at the top in the diagram on the next page) and a long (q) arm (the bottom part of the chromosome).

For healthy development, chromosomes should contain just the right amount of material – not too much and not too little. People with a 7q deletion have one intact chromosome 7, but the other chromosome is missing a piece.

This means that there is only one copy instead of the usual two of a number of genes. As chromosome 7 is a medium-sized chromosome, the genes on it represent about 4-6 per cent of the total number of genes in the human genome.

Although the exact numbers and types of genes that are affected by the deletion is often not known, since some genes are missing there can be effects on a person's learning and physical development. It is believed that most of the clinical difficulties are probably caused by having only one copy of a number of genes. We are still learning the about the specific jobs or functions of the genes in these regions. It is important to keep in mind that a child's other genes, environment and unique personality also help to determine future development, needs and achievements.

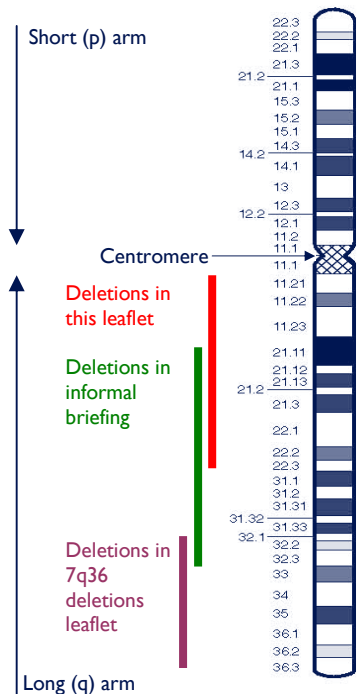
Sources and references

The information in this leaflet is drawn from what is known about people with a deletion from 7q. Many people have been described in the medical literature with a deletion from 7q. The first-named author and publication date are given to allow you to look for the abstracts or original articles on the internet in PubMed (www.ncbi.nlm.nih.gov/pubmed). If you wish, you can obtain most articles from *Unique*. The leaflet also draws on reports from the Chromosome 7 Annotation Project (www.chr7.org) and from *Unique's* database. When this leaflet was written, *Unique* had 56 members with an interstitial deletion of 7q and 21 members with a deletion between the centromere (see next page) and band 7q22.

Looking at 7q

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 on the right. They are numbered outwards starting from the point where the short and long arms meet (the **centromere**). A low number such as q11 is close to the centromere. Material closer to the centromere is called **proximal**. A higher number such as q22, further from the centromere and closer to the tip of the chromosome, is called **distal**. An **interstitial** deletion means that a piece is missing from within the chromosome arm. There are two breakpoints and the sticky broken ends have rejoined.

This leaflet describes the most likely features when chromosome material is lost as far as band 7q22. It does not cover loss of material closer to the tip of the long arm from beyond band 7q22. *Unique* has an informal briefing paper on deletions between 7q21 and 7q32 and publishes a leaflet on deletions that include the tip of the long arm (**7q36 deletions**).



The karyotype

Your geneticist or genetic counsellor will be able to tell you where the chromosome has broken in your child. Your child will almost certainly be given a karyotype, a way of describing their chromosome make-up. It is likely to read something like this

46,XY,del(7)(q11.23q21.2).ish 7q11.23 (WSCRx2)de novo

- 46 The total number of chromosomes in your child's cells
- XY The two sex chromosomes, XY for males; XX for females
- del A deletion, or material has been lost
- (7) The deleted material came from chromosome 7
- (q11.23q21.2) The chromosome has broken in two places. The first break is at q11.23 and the second break is at q21.2 so these are the ends of the missing section
- .ish 7q11.23 (WSCRx2) The diagnosis has been checked using a second technique known as FISH. Using FISH, the so-called 'critical region' for Williams syndrome was found to be present, ie not part of the deletion. The diagnosis is not Williams syndrome (see page 4)
- de novo The parents' chromosomes have been checked and no duplication or other abnormality found. The duplication has not been inherited

You may wish to compare your child with others with the same deletion. It's important to remember that the same deletion can have different effects on different people and there will be differences, sometimes quite marked, between your child and others with an apparently similar karyotype. It is very important to see your child as an individual and not to rely on direct comparisons with others who appear to have the same karyotype.

Is there a 7q deletion syndrome?

With a total of around 1150 genes on chromosome 7, it's inevitable that different individuals will have lost different genes. This makes it difficult to describe a specific 7q proximal interstitial deletion syndrome. What is more, many features seen in people with a 7q deletion are quite common in other chromosomal disorders, such as low muscle tone, delays in development, failure to thrive and short stature.

However, people who have lost material from similar bands do share some similarities, as follows:

There is a well-known syndrome caused by loss of genes at **7q11.23** known as **Williams** (or **Williams-Beuren**) syndrome. Williams syndrome causes characteristic heart defects, a distinctive elfin-like face, usually mild learning difficulties with a good short-term verbal memory and poor visuo-spatial abilities, a 'cocktail party' personality and abnormalities of connective tissue, growth and endocrine disorders.

Babies and children who lose only part of the 'critical region' for Williams syndrome, with or without additional loss from closer to the centromere, may have some but not all the typical Williams syndrome features. Depending on which genes have been lost, they may have, for example, heart defects and the Williams-specific cognitive profile, with or without learning difficulties (Blyth 2008).

Babies and children with larger deletions at **7q11.23q21.1** have what has been called 'Williams-plus': they have some features of Williams syndrome but also often have infantile spasms, a type of early-onset epilepsy, and need considerable support with their development and treatment for low muscle tone (hypotonia) (Courtens 2005; Marshall 2008).

Babies and children with a smaller deletion within band **7q21** are likely to be born small with some unusual facial features and then go on to show some delay, typically mild or moderate, in reaching their developmental milestones as well as low muscle tone. Early feeding difficulties are likely to be prominent and babies typically do not grow as well as expected. Some specific birth anomalies occur but they do not affect all babies. These include minor anomalies of the genital area, predominantly in boys; split hand/ foot; a cleft or high palate; hernias, particularly in the groin and at the navel; and epilepsy. A level of hearing loss and unusual teeth are common (Courtens 2005).

Where the **entire 7q21 band** is lost, babies grow slowly before birth and after and have feeding difficulties in infancy. They benefit from support with their development and learning and physical therapy for their low muscle tone (hypotonia). Some have minor anomalies in the genital area, especially boys, some have the split hand/foot anomaly, some have hernias, some have a hearing impairment and some vision impairments. A cleft or high palate is common and some have a heart condition (Courtens 2005).

Where babies and children have a deletion at **7q21q22**, they are typically very short and have a small head (microcephaly); some have a hearing impairment and some have the split hand/foot anomaly. They benefit from support with their learning (Courtens 2005; Tzschach 2007).

Are there people with a 7q deletion who are healthy, have no major medical problems or birth defects and have developed normally?

There are descriptions in the medical literature of people whose development has been unaffected by their unusual chromosomes. In some cases there is a tiny microdeletion, taking out only a very few genes; in others, the chromosome make-up is mosaic, containing cells with normal chromosomes as well as cells with a 7q deletion (Seabright 1978; Caselli 2007). There are also descriptions in the medical literature of individuals with specific features typical of 7q proximal deletions (such as split hand-foot or a jerking movement disorder) but no evidence of developmental delay (Wieland 2004; Asmus 2007).

What are the first signs that a baby or child has the disorder?

The first signs vary somewhat. While a few babies have an obvious birth defect, such as a hand or foot defect, most do not. Among babies with a large deletion from 7q11 to 7q21/2, it is usually obvious at birth that the baby is unwell, has difficulties with feeding, and may be small for dates. Facially, s/he may look a little unusual. Among babies with a smaller deletion encompassing 7q21/2, the disorder may not become apparent until eight or nine months of age when developmental milestones are missed.

Pregnancy

For most of the pregnancies described in the medical literature or to *Unique*, everything went normally. Three/26 mothers had an excess of amniotic fluid (polyhydramnios) and one had too little (oligohydramnios). The slow growth in the womb of four babies was noticed and one mother commented that her bump was very small. One mother felt less fetal movement than in other pregnancies. There was one case of threatened miscarriage at two months, one of premature rupture of the membranes and nine babies were born prematurely, between 32 and 36 weeks.

Your baby at birth

Most babies are small and light at birth, regardless of the size or position of their deletion. Some are extremely small, as small or smaller than the smallest three per cent of all newborn babies. Among babies with a 7q11q21/2 deletion, birth weights ranged from 2.1 kg (4lb 10oz) at term to 3.2 kg (7lb 1oz), with an average of 2.53 kg (5lb 9oz). Among babies with a 7q21q22 deletion, average birth weight around term was slightly higher at 2.7kg (5lb 15oz) but ranged widely from 1.2kg (2lb 10oz) to 3.4 kg (7lb 8oz).

Despite their small size, most babies are in reasonable condition at birth, scoring between 4 and 8 on the Apgar scale (a measure of general wellbeing on a scale of 0-10) at one minute and between 8 and 9 at five minutes after birth. Most typically, difficulties arise with feeding, with a high proportion of babies feeding slowly and not sucking strongly enough to satisfy their nutritional needs. These difficulties are not universal and some babies, particularly those with smaller deletions at 7q21q22, breast or bottle feed efficiently. Where babies do have feeding problems, however, they can be severe and persistent and can be coupled with reflux, where feeds and stomach contents return up the food passage and are regurgitated. To help meet nutritional needs, babies may be given a high-calorie formula and fed from a bottle or through a naso-gastric tube passed through the nose and down the throat. Some babies still fail to feed and put on weight or have persistent reflux and are fed through a gastrostomy tube direct into the stomach.

Will my baby look different?

You and the doctors may notice that your baby has a slightly unusual facial appearance. A large number of unusual facial features have been noted by geneticists in reports on babies and children with a 7q deletion. 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 7q deletion than like other members of your own family – or you may find that your baby looks just like the rest of the family. The unusual features are not specific to 7q deletions and are found in people with many other chromosome disorders.

They include: a broad, prominent forehead; a low nasal bridge; low set ears that may be an unusual shape or size; a large mouth with downturned corners; prominent lips; delicate features; pale, translucent skin and blond or red hair.

Your baby's head may be an unusual size or shape. Most typically, it is small

(microcephaly) but a large head

(macrocephaly) has also been seen. Their head may be short from front to back (brachycephaly), narrow and elongated (dolicocephaly) or longer from front to back on one side than the other or asymmetrical (plagiocephaly). The unusual shape may be due in part to early fusion of some of the bony plates that make up the skull (craniosynostosis) and if this is warranted, treatment may be by surgery (Allanson 1988; Wu 1999; Morimoto 2003; *Unique*).



Nine months old, with unaffected brother,
seven years

What about visible birth defects?

Most babies do not look out of the ordinary at birth and while there is a known association between certain birth defects and 7q proximal interstitial deletions, the numbers of affected babies are small. One baby was born with a cleft lip and a small group with a specific developmental anomaly of the hands or feet known as ectrodactyly where one or more fingers or toes is missing and the hand or foot appears to be split. Neither of these anomalies has been seen in *Unique* families (Del Porto 1983; Pfeiffer 1984; Fryns 1985; Tajara 1989; Nunes 1994; McElveen 1995; Fukushima 2003; *Unique*).

Hands

Where material is missing from band 7q21.3-q22 at a site known as *SHFM1* (split hand foot malformation 1), the possibility exists that one or both hands or feet may be split, with missing fingers or toes and webbing between the remaining digits. When one hand or foot is affected, it is usually the right one. But even when *SHFM1* is missing, not everyone has the hand-foot anomaly (McElveen 1995; Haberlandt 2001; Fukushima 2003; Tzschach 2007).

Your baby's hands may have other, much less obvious but still slightly unusual features. Many of these features are not specific to babies or children with a 7q deletion but are also found in other chromosome disorders. The fifth and possibly the fourth finger may curve inwards on one hand or both (clinodactyly); fingers may be tapered or short and stumpy and one or more finger creases may not be visible. Finger joints have been reported that do not straighten. Thumbs may be broad and flat. The hands may be small. Nails may be unusually curved. One child developed painful finger swellings at the age of 14 (Klep de Pater 1979; Young 1984; Frydman 1986; Fryns 1987; Allanson 1988; Chitayat 1988; Zackowski 1990; Wu 1999; Manguoglu 2005; *Unique*).

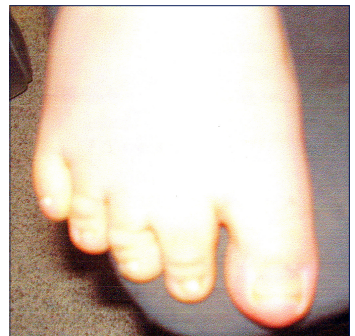


This child has a 7q11.23q21.2 deletion

Feet

Apart from the split foot anomaly, which typically affects both feet, unusual features of the feet are relatively minor. Feet may be very small. There may be specific features such as a low instep, prominent heels or a curved sole (rockerbottom feet). Toes may occasionally curl under or over neighbouring toes and there may be a wide space between the 1st and 2nd toes. Toenails have been described as small, concave or missing.

Many of these features will not affect walking, although a child with flat feet may need special footwear or arch supports and babies with curling toes may benefit from soft splints to straighten them. A baby was born with one club foot (talipes equinovarus). 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 (Young 1984; Fryns 1987; Fagan 1989; Tajara 1989; Zackowski 1990; Gillar 1992; Manguoglu 2005; *Unique*).



Right foot of the same child

Minor genital anomalies

Minor anomalies of the genital system are not unusual in the general population and appear to be somewhat more common among babies and children, especially boys, with a chromosome disorder. In this group, 9/16 boys were affected.

One or both testicles may not have descended into the scrotum by birth. Treatment for undescended testicles (cryptorchidism) depends on the suspected cause but whatever it is, treatment is usually needed if the testicles do not descend naturally in time.

The testicles can generally be brought down in a short operation under general anaesthetic called an orchidopexy. Some boys were born with hypospadias, where the hole that is normally at the end of the penis is located on the underside instead. Other reported anomalies were a very small penis and a divided scrotum. In two boys, the genitalia did not immediately indicate the baby's sex.

The genitalia are less often affected in girls but in this group there were two/14 reports of small, unformed labia (Gibson 1982; Fryns 1985; Frydman 1986; Fryns 1987; Fagan 1989; Tajara 1989; Zackowski 1990; Mizugishi 1998; Fukushima 2003; Manguoglu 2005; *Unique*).

Heart

Most babies with a proximal interstitial 7q deletion were born with a healthy heart: 8/44 were born with a heart defect. A child whose deletion includes the Williams syndrome critical region has a raised risk of heart problems, specifically a narrowing of the blood vessel that takes blood from the heart to the rest of the body (aorta – supraaortic stenosis, SVAS).

Among other heart problems, the most frequent was pulmonary stenosis, where the entrance to the artery that takes blood to the lungs is unusually narrow. In 2/3 babies, the narrowing was mild and resolved naturally. In three babies, the lower, pumping chambers of the heart were enlarged, suggesting that they were working hard. One baby had a thickened valve between the left pumping chamber of the heart and the aorta that takes blood to the body. Two babies had holes between the upper or lower heart chambers (Pfeiffer 1984; Fryns 1985; Frydman 1986; Gillar 1992; Mizugishi 1998; Wu 1999; Morimoto 2003; *Unique*).

Hernias

Hernias occur fairly frequently in newborn babies and appear to be even more frequent in this group, especially those with a 7q11q21/2 deletion. This is probably due to the effects of losing the elastin *ELN* gene on the development of connective tissue. Umbilical (at the navel) and inguinal (in the groin) hernias occur with equal frequency and one baby was diagnosed with a diaphragmatic hernia (Klep de Pater 1979; multiple other references; *Unique*).

In an [inguinal hernia](#), part of the bowel loops through an opening in the inguinal canal. In fetal development, the testes descend into the scrotum through this opening which usually then closes. If it fails to close, or re-opens, part of the intestine can bulge through it. The hernia usually appears as a swelling in the groin or enlargement of the scrotum. An inguinal hernia usually needs surgical repair. An [umbilical hernia](#) shows as an abnormal bulge that can be seen or felt at the umbilicus (belly button). The hernia develops when a small opening in the abdominal muscles that allows the umbilical cord to pass through

does not close after birth. Part of the lining of the abdomen, part of the intestine and sometimes fluid from the abdomen passes through the opening causing the hernia. 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. A [diaphragmatic hernia](#) is a hole in the muscular wall separating the heart and lungs from the contents of the abdomen. Part of the bowel, stomach or liver take space in the chest, potentially depriving the lungs and heart of room to develop properly. Once a baby's condition has been stabilised, usually with a ventilator, the hernia will be repaired and support given for breathing for as long as the baby needs it, which may be weeks, months or even years.

Feeding

Many newborn babies have difficulties establishing feeding and some of these are documented in the medical literature (Klep de Pater 1979; Gibson 1982; Pfeiffer 1984; Young 1984; Chitayat 1988; Nunes 1994; Mizugishi 1998; Wu 1999; Fukushima 2003; Morimoto 2003). Some level of feeding difficulty appears almost universal – while one or two *Unique* babies breastfed, none was able to maintain their weight and grow on breastmilk alone. Some babies breastfed extremely slowly and in insufficient quantities; others were unable to suck properly, others to swallow or protect themselves from aspiration by coughing. Some babies thrived better on breastmilk given from bottles with teats suitable for premature babies or those with a cleft palate but the great majority needed high calorie supplements to maintain their growth rate.

In addition to their early feeding difficulties, a significant proportion of *Unique* babies had 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). This can sometimes be 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 help to keep feeds down.

However, in this group of babies, it was fairly common to need feeding by gastrostomy tube direct into the stomach.

Beyond the newborn period, *Unique* has information on feeding histories from 14 children. These show a range of further challenges, including food intolerances; difficulties with chewing and a preference for semi-solid foods such as yoghurts and custards; and a tendency to stuff the mouth.

Weaning can present problems, with many families reporting reluctance to take lumpy food, to chew or to accept anything but a narrow range of tastes and textures.

Reluctance to chew can be especially persistent.



Ten years old
Uncertain breakpoints between 7q21.12 & 7q22.1

Palate (roof of the mouth)

A cleft (split) in the palate has been reported occasionally in babies with a 7q proximal interstitial deletion. This can occur where the deletion is between 7q11 and 7q21 or within the 7q22 bands (Klep de Pater 1979; Pfeiffer 1984; Allanson 1988; Nunes 1994; *Unique*). The cleft is caused by an error in fusion when the fetus is forming in the first three months of pregnancy. A cleft palate causes difficulties both in feeding and in speech production. Surgical repair of the palate eases these difficulties and may eliminate them altogether.

Meanwhile, babies with a cleft palate will need feeding support and this may also be true for babies with an unusually high but intact palate. A high palate can make latching on and sucking more difficult and some babies make better progress with a nipple shield or, if bottle fed, with a variable-flow teat or one specially adapted for premature babies. After weaning, solids may become lodged in the palate; regular sips of drink can help to prevent this.

Growth

The majority of children and adults with a 7q proximal deletion between 7q11 and 7q21 are unusually short and small for their family. In many children, the slow growth rate starts before birth; in some, it sets in or accelerates after birth. Most children and adults are below the average height for their age and many are exceptionally small, as small or smaller than the shortest three per cent of the population. While some children maintain their growth rate on a percentile chart, in others the growth rate falls off over time. The characteristic build for a child with a 7q proximal deletion is both short and slender. Adults are also on the short side, and may be exceptionally so. Body build is variable, with a tendency in children to slender limbs and a protruding tummy, due in part to low muscle tone (Young 1984; Allanson 1988; Fagan 1989; Wu 1999; Fukushima 2003; *Unique*).

Children with a deletion from 7q21 to 7q22 generally achieve a more average height, although some are short, with a petite build (Fagan 1989; Nunes 1994; Tzschach 2007; *Unique*).

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

Delay is typical in reaching the developmental 'milestones' of sitting, becoming mobile and walking. This delay is common but may not affect a very small number of children with a tiny microdeletion (Wieland 2004). This means that your baby will make progress, generally following the expected developmental sequence, but progress will come slower than in other children. How much slower depends chiefly on your baby's innate abilities, but also on opportunities, on stimulation and to some extent on therapeutic interventions. Abnormal muscle tone is a major contributory factor: some children have generalised low tone (hypotonia), while others have low tone in the upper body and raised tone (hypertonia) in the lower limbs. Low tone makes a child or baby feel floppy to handle and generally improves and may resolve with maturity, physiotherapy and exercises. In some children, muscle tone increases, so that muscles remain unable to stretch. It is hard to predict eventual mobility, but while in some it is fairly normal, others may need supported seating and walking and a wheelchair long term.

From *Unique*'s experience, babies learned to roll over between four and 28 months, to sit without support between six months and six years, to become mobile between 11

months and five years and to walk without support between 20 months and five years. Not all babies crawled: some shuffled on their bottoms, scooted, rolled or slid along. Not all walked, and among those who did, walking often remained unsteady for a long while after it was first achieved. Your child may walk with their feet wide apart to improve their balance and they may find uneven surfaces a particular challenge. Once on their feet, a few children rapidly acquire skills such as climbing stairs, running and even swimming, but - like walking itself - this is not possible for all.

Data from *Unique* show that mobility was more significantly delayed among those with a more proximal deletion between 7q11 and 7q21 than among those with a 7q21q22 deletion (Klep de Pater 1979; Pfeiffer 1984; Fryns 1987; Gillar 1992; Wu 1999; Morimoto 2003; *Unique*).

Where the *SGCE* gene at 7q21.3 is deleted, in some children there may be a raised risk of myoclonus dystonia, a syndrome characterised by rapid, brief muscle contractions usually of the neck and upper arms with onset in first 25 years of life. The movement disorder does not necessarily progress or impact on the development of gross motor skills (Asmus 2007).

- “ He needs a back support as he still slumps when sitting. When walking, he is clumsy and wobbly and has a wide stride and a bouncing run with short steps - 7q21.2q22 deletion, 4 years
- “ He walks everywhere but needs regular rests as he can't walk far. He's unsure of his balance, and gets tired very quickly - 7q21.2q22.1 deletion, 6 years
- “ She loves her new wheelchair as she can operate it herself and thinks it funny to go off on her own to the sweet aisle in the supermarket! - 7q11.23q21.2 deletion, 7 years
- “ She wears insoles and can walk fine - 7q22.1q22.31 deletion, 15 years

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

Most children, though not all, experience quite considerable delay in controlling their hand use. As a broad generalisation, their skills match those of a child half their age. Recurring themes in parental reports are poor coordination, a weak hand grip, a delay in developing a pincer grip and holding objects, particularly in a child with very small hands. Small children find manipulating small objects such as buttons, poppers and zippers a challenge but with consistent training, adapted tools and verbal prompting many achieve feeding skills by mid childhood and dressing skills in late childhood or adolescence.

Undressing comes before dressing and finger foods before the use of cutlery. In *Unique*'s experience, children continue to need help and supervision to feed, dress and care for themselves throughout childhood.



Five years old
7q21.2q22.1 deletion

Intention myoclonus (myoclonus dystonia syndrome – MDS) has been described in a child with deletion at 7q21 probably due to deletion of the *SGCE* gene; it was treated successfully with clonazepam (DeBerardinis 2003). The jerks may be hardly visible at rest but are strongly aggravated by movements such as drawing and writing (see page 11).

In terms of self care, most youngsters achieve some collaborative independence in dressing, washing and personal care tasks. It may not be appropriate for parents to expect toileting to occur at the same age as other unaffected children and data from *Unique* suggest that while daytime bladder and bowel control may be achieved in some children with a slight to moderate delay (between three and four years), in many children control may not prove consistently possible (*Unique*).

“ She finds it difficult to complete a large 4-piece inset puzzle – she can identify the shape but cannot manipulate it into the hole. She isn’t yet able to trace over a line but will occasionally imitate a vertical one. She can wash her hands and hold a toothbrush to her mouth but not brush; she can undress by pulling her clothes down her body rather than over her head; she can undo zips but not do them up; and she can pull open poppers; can take off and put on her right sock and shoe but not the left one; and can take off her coat but not put it on - *microdeletion at 7q11.21, 3 years*

“ He can almost fully dress himself minus buttons, snaps and zippers and needs help with socks and shoes - *7q21.2q22 deletion, 4 years*

“ He will have a go at doing his teeth but has trouble maintaining his arm position (very poor muscles at shoulder level) so we usually complete - *7q21.2q22.1 deletion, 6 years*

Learning

In the medical literature there are reports of individuals with tiny microdeletions and no evidence of learning difficulties as children or adults (Wieland 2004; Asmus 2007). Apart from these very rare individuals, it is *Unique*’s experience that children will benefit from extra support with their learning. How much support is needed usually only becomes apparent over time, but as a general guide, it seems that children with a more proximal deletion between 7q11 and 7q21, larger than the typical Williams syndrome deletion, will need more support than children with a deletion at 7q21q22. *Unique* has family reports of children with difficulties that range from moderate to profound and reports from the medical literature show IQs between 57 and 71 (Young 1984; Allanson 1988; Fryns 1987; Nunes 1994; Gillar 1992; Wu 1999; *Unique*).



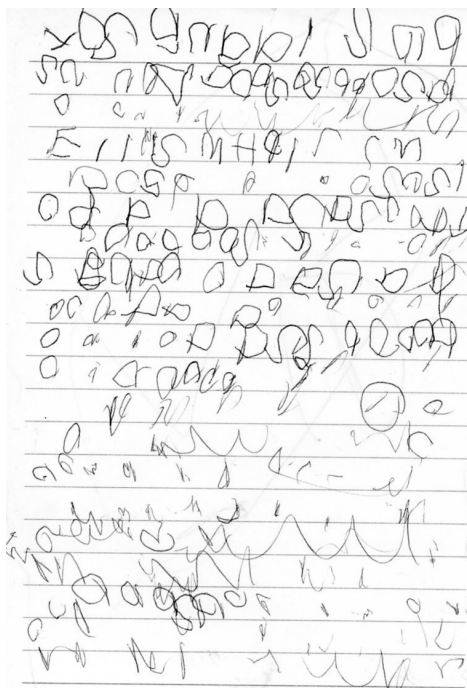
Six years old
7q21.2q22.1 deletion

It's important to remember that youngsters with a learning disability are capable of considerable depth and complexity in their learning and may well acquire some reading and writing skills. This appears to be especially likely among those with a 7q21q22 deletion.

“ She has an excellent visual memory for places such as family or friends' homes but is unable to understand or remember such things as colours. She learns a lot through singing and enjoys listening to music and looking at books but cannot read. She holds a pen or pencil very well but just scribbles - *microdeletion at 7q11.21, 3 years*

“ He is at a 36-month level in all areas. His strengths are music, his personality, friendliness and liking to learn. His memory not very good but is improving. He loves new things and gets excited by them – and learns more when it's fun! - *7q21.2q22 deletion, 4 years*

“ He is a low achiever academically, in the bottom few of his year group but progressing slowly. He can count reliably to 10 and recognise 20+ letters. He can use a computer keyboard to type his name and is good with a mouse. He has a good visual memory for places, but doesn't grasp more academic things. He can recognise the names of all the children in his class. He is helped by determination, is happy to try new things and laughs at himself if things go wrong – to a certain extent! He can write his first name and draw a face but mainly scribbles and squiggles. He attends a mainstream school with full 1:1 support including playtimes; attends literacy and numeracy small group support groups, a separate speech group and will do extra activities for gross motor skills and coordination and for fine motor skills - *7q21.2q22.1 deletion, 6 years*



“ He needs visual clues and can read a few frequent words (mum, dad, no) and can trace over words but not write letters independently - *7q21.12q21.2 or 7q21.2q22.1 deletion, 11 years*

“ She can use a computer. And loves YouTube wrestlers. Her most able areas are comprehension and being very caring with less able children. She learns best with good routines; loves school; and talks to her toy cars as if they were her best imaginary friends. She looks at books on animals and cars and Mary Queen of Scots. She has a poor writing technique but likes drawing, painting and expressing herself – and has a photographic memory for her cars – all of which have names - *7q22.1q22.31 deletion, 15 years*

This level of achievement will not be possible for all. A number of adults known to *Unique* do not read or write. There is variability in other underlying skills as well: many children, but not all, have a good memory, especially for visual material; most children, but again not all, have reasonable powers of attention; many respond well to a reward system of learning and to learning made fun. It is true that some youngsters will need extensive support and skilled 1:1 teaching to develop and maintain the skills they need for daily living. It is important for any family with a child with a 7q deletion to approach their learning ability with an open mind, to 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.

Speech and communication

Some information on speech and communication is available on 28 children and adults but while information from *Unique* is more detailed, in the medical literature the information is generally more limited. It shows that while speech is very significantly delayed and may remain limited or not emerge at all among those with a proximal 7q11q21 deletion, in general those with a more distal deletion acquire more language and some speak quite fluently. However, even among those with a more distal deletion, speech and language development may remain severely delayed and no recognisable words may emerge (Klep de Pater 1979; Gibson 1982; Young 1984; Mizugishi 1998; Wu 1999; Morimoto 2003; Tzschach 2007; *Unique*).

Youngsters use a wide variety of methods to communicate their feelings and needs, including gestures, facial expressions, vocal sounds, pictures, objects of reference and signing systems. Among those with a proximal 7q11q21 deletion, signing and other communication systems can be quite advanced and either supplement or lead on to speech. Speech sounds are not always clear and in some cases may be transposed. Where speech does emerge, more often among those with a more distal deletion, first words are typically heard between two and four years of age. Singing is a useful activity for some children (*Unique*).

Understanding is consistently better retained than expression, both for speech and for signing, with some non-verbal children able to carry out one-step and more complex requests.

- “ Her words not always very clear, for example, she says puc, meaning cup. She speaks in single words but also ‘sings’, using intonation. She seems to understand more than she can express - *microdeletion at 7q11.21, 3 years*
- “ His speech is slow, monotone, slurred and at times difficult to understand. However, he uses four-word phrases and short sentences and understands more than he can express. It is hard for him to find the words he wants to use and he has difficulty with certain consonants and putting letters together correctly - *7q21.2q22 deletion, 4 years*
- “ He communicates with speech and has a good understanding if you are clear and concise and he is feeling compliant. He tends to use stock phrases and is quite fluent but not clear, with difficulties with l, f and th sounds. Although he can say consonants individually, he tends to miss them off the start and end of words - *7q21.2q22.1 deletion, 6 years*

- “ She signs and uses a picture exchange system board and can construct three-word sentences but misses out the first letter of every word. She makes up names for objects she can't pronounce - 7q11.23q21.2 deletion, 7 years
- “ He uses basic, simple, repetitive sentences. He finds information recall difficult as he has memory problems; and has basic understanding but needs instructions or questions to be short and simple - 7q21.12q21, 11 years
- “ Her speech can be hard to understand for people unfamiliar with her. Her comprehension is good; she understands what is being said or asked of her. She has a limited vocabulary and uses 2-3 word phrases, yes or no – or she blanks you, like any other teenager. She finds it difficult to finish words - 7q22.1q22.31 deletion, 15 years

Generally the development of speech and language appears to reflect the child's cognitive abilities. Progress is slowed overall, with first words emerging late and not all children acquiring more complex speech patterns. Children who have not yet acquired speech can communicate well using gestures and signing. Among those without speech, communication devices are popular and some use is made of sign language as well as gestures, facial expressions and picture symbols.

Behaviour

Unique has fairly detailed information on the behaviour of 16 children with a 7q deletion. There are also brief descriptions of some children in the medical literature (Pfeiffer 1984; Gillar 1992; Wu 1999; *Unique*). The number is too small for a definitive picture to emerge but the remarks that follow may give families helpful insights.

Families most often mention unusual behaviours with some features of atypical autism including lack of empathy, stereotypic behaviours and a need for repetitive routines. Other frequent features include immaturity, demanding adult attention, intermittently challenging behaviour (hitting, spitting, slapping, biting, hair pulling, temper tantrums, tearing clothes, self injury) often when bored or understimulated and frustration due to underdeveloped communication skills. Some children are easily overexcited and need a carefully modulated environment. These behaviours usually sit alongside delight in the company of others, especially adults, as well as polite, sweet behaviours and a sense of humour, sometimes with unpredictable switching between the two faces. Many children are friendly, sometimes inappropriately, and need danger protection. A low attention threshold and frequent flitting between activities is often seen, with some children diagnosed with hyperactivity or attention deficit hyperactivity disorder and treated with medication. Hyperactivity can be mild (getting over-excited) or extreme. Many affected youngsters have had behaviour plans, behaviour therapy, psychological training or taken medication. Parents may initially resist treatment with medication but frequently find that it does help their child to concentrate for longer and achieve a more consistent routine.

Overall, most children and adults behave well when they are appropriately supported with firm and consistent behaviour techniques (time out, reward charts) and positive reinforcement of their good behaviours and even children who can be challenging at times can also be calm, quiet and lovely.

Children enjoy music (with a fast beat) and musical toys, books, computers, animals, outdoor activities and playing with adults, especially being the centre of attention. Reactions to other children are less predictable and they may be wary of them. Common interests among older children frequently also include social activities.

Sleep problems are common but not universal: young children may find falling asleep difficult and use self stimulatory activities (head banging, shaking, repetitive movements) before dropping off. Sleep disturbance occurs and in some children is caused in part by obstructive sleep apnoea and eased by the removal of enlarged tonsils and adenoids. In other children diagnosis of seizure activity and taking antiepileptic medication has eased sleep difficulties. Other children respond to antihistamine medication or melatonin. *Unique's* experience is that it is important for the family's wellbeing to seek a cause for sleep disturbance and have a staged management programme that includes support for the parents and respite care.

“ She lies on the floor and arches her back, kicking her right leg and holding her left hand up. She likes being upside down, even holding her head back when walking along. She likes rocking her head from side to side or back and forth. She is frightened of loud or unexplained noises but fascinated by lights or fans and seeks them out in new places. She likes to ‘feel’ things with her nose or eyelashes. She gets frightened of young children, especially if they get too close but is fascinated by adults and not worried by strangers - 3 years

“ She is friendly and kind but gets tired and grumpy at the end of the day - 4 years

“ He likes to be around others, but has some difficulty talking and sharing with other children and can become too rough in play when excited - 4 years

“ We love her to bits but she is very full on all the time – extremely loud and violent. We cope using time out and reward charts. She interacts variably with others: she can be lovely one minute, then screaming, kicking, hitting herself or her mother and biting the next - 7 years

“ Due to lack of concentration he doesn't play with anything for long and constantly seeks adult help and attention; he doesn't like to do anything on his own. He is very much a flitter and finds it hard to stick with one activity. He doesn't make friends easily but is very popular with adults. He orders other children around in a very loud voice but has a great sense of humour and loves being the centre of attention - 8 years

“ A change in routine can lead to challenging behaviour. She can be shy when buying things as she knows her speech is poor. She was quite shy but is growing more confident and starting to come out of her shell - 15 years

Health matters

■ Seizures

Seizures are common in children with a 7q proximal interstitial deletion, especially those with a large 7q11q21/2 deletion. There are frequent reports in the medical literature and among *Unique* members, 7/8 of those with a large 7q11q21/2 deletion were affected as well as 8/13 of those with a smaller deletion between 7q21 and 7q22. It has been suggested that seizures are associated with a deletion from 7q21, but *Unique* has experience of seizures occurring where the deletion is limited to 7q22 and there are a number of reports of children with a typical microdeletion for Williams syndrome at 7q11.23 who had infantile spasms (Mizugishi 1998; Morimoto 2003; *Unique*).

Infantile spasms have been specifically suggested as caused by a gene in 7q11.23q21.1. Infantile spasms are also known as West syndrome and are a disorder of the developing nervous system that begins in the first year of life. They are characterised by flexion jerks of the neck, trunk and the extremities lasting a few seconds and occurring in clusters of throughout the day. A distinctive pattern (hypsarrythmia) is seen on EEG in 2/3 cases. They are usually treated with vigabatrin, prednisolone or ACTH (adrenocorticotrophic hormone). Approximately 50-60% of children go on to develop other seizure types. In one case the infantile spasms were successfully treated with thyrotropin-releasing hormone (TRH) analogue (Morimoto 2003).

Apart from infantile spasms, other seizure types have occurred: absence seizures (a brief loss of awareness); febrile convulsions (seizures only triggered by a sudden rise in body temperature); myoclonic seizures (rapid, jerky contractions, especially in arms and legs); and tonic-clonic seizures (stiffness, followed by jerking or twitching). Seizures are reasonably well controlled with medication and in a few cases children have outgrown them (Young 1984; Fryns 1987; Allanson 1988; Fagan 1989; Zackowski 1990; Gillar 1992; Kahler 1995; McElveen 1995; Mizugishi 1998; Wu 1999; Morimoto 2003; Tzschach 2007; Marshall 2008; *Unique*).

■ Kidneys

Among babies with a 7q11q22 deletion, a variety of anomalies of the structure, positioning and functioning of the kidneys has been reported. In one baby the kidneys were small but worked well, another had a duplex kidney, where all or part of the kidney or its drainage system forms in duplicate. Sometimes this causes no problems but it can make urinary tract infections more likely and these can cause chronic damage to the kidneys. One child had an obstruction where the urine flows from the kidneys to the tube that leads to the bladder (ureteropelvic junction obstruction). One child had kidney reflux and recurrent urinary infections. This is caused by backflow from the bladder, allowing urine to flow back into the ureters and even as far as the kidneys. This increases the risk of developing kidney infections that over time can cause damage and scarring to the kidneys. The first line of treatment is usually low-dose antibiotic treatment, which may give a child the opportunity to outgrow the reflux (Gibson 1982; Fryns 1985; Allanson 1988; *Unique*).

■ Other conditions

There are individual reports of conditions affecting people with a 7q deletion that may or may not be caused by the deletion. These include: missing adrenal glands; congenital hypothyroidism; thrombocytopenia (reduced number of platelets in blood); panhypopituitarism (inability of pituitary gland to produce enough hormones); choanal atresia (blockage of the nasal passages) (Fryns 1985; Fagan 1989; *Unique*).

■ Happy and healthy?

“The most frequent complaint among *Unique* families is repeated respiratory infections. These often start in early infancy and in many cases are linked with reflux and silent aspiration (see [Feeding](#)). With frequent infection, the tonsils and adenoids may become enlarged and risk affecting breathing while asleep. Many children gradually outgrow this tendency to infection, but in some the infections remain frequent and are controlled by continuous low-dose antibiotics.

“Happy, healthy and growing in confidence as she goes through adolescence - 15 years

■ Brain

Specific lesions of the brain may develop in adulthood if the *KRIT1* gene at 7q21.2 is lost (see Gene research, page 22) (Tzschach 2007).

■ Eyesight

Many people with a 7q proximal interstitial deletion have normal eyesight. Others have been reported with a vision problem of varying severity. This can be a simple astigmatism, when the cornea, the clear cover over the iris and pupil, is abnormally curved, making objects appear blurred. Or it can be more serious, with changes to the structures at the back of the eye that are likely to cause a degree of permanent vision impairment or cortical blindness, with visual systems in the brain that do not consistently understand or interpret what the eyes see. In one case, the pupil of one eye was missing and was markedly misshapen in the other.

Short sight can occur – in one case causing effective blindness, as can long sight and a squint (strabismus), looking inwards, outwards, up or down. The main effects of a squint are that the person will usually have one eye which is stronger than the other. Treatment depends on the cause but can include patching the stronger eye, exercises, glasses to correct a refractive error such as long sight and surgery to realign the muscles that hold the eye in place. Nystagmus, an uncontrolled movement of the eyes back and forth, usually associated with reduced vision, has also occurred as has ptosis of one eye or both. This is a drooping of the upper eyelid so the eye is not fully open. Children tilt their heads back to see properly. If it interferes with vision, the eyelid can be raised surgically. Where eyesight is significantly impaired in both eyes, children should have access to support services and vision teaching (Klep de Pater 1979; Allanson 1988; Chitayat 1988; Tajara 1989; Wu 1999; Manguoglu 2005; Tzschach 2007; *Unique*).

“Very light sensitive. She wears tinted glasses & baseball caps - 7q22.1q22.31 deletion

■ Hearing

A temporary or permanent hearing loss is relatively common among babies and children with a 7q proximal interstitial deletion. A temporary hearing loss is caused most often by a build-up of fluid behind the eardrum, sometimes as a result of repeated ear infections. This type of so-called conductive hearing loss can be relieved by inserting grommets (ear tubes) into the eardrum to aerate the middle ear. In some children the degree of loss is so great that hearing aids are also needed for a time.

A temporary hearing loss may be caused by immaturity, where a hearing test shows that sounds are reaching the brain but a baby or young child fails to respond to them. Some improvement may then occur as the child matures.

Babies and children with a 7q deletion that includes 7q21.2q22.1 are at risk for a permanent hearing loss. This does not mean that everyone with this deletion is hearing impaired: data from *Unique* show that around half its members are affected, while the others have normal hearing. This does mean, however, that any baby or child found to have a deletion in this area should have hearing screening until their ability to hear has been positively shown. Where a permanent hearing loss is found, aids may be worn and a cochlear implant considered to enhance hearing potential. One child given a unilateral cochlear implant was speaking in three-word sentences by the age of nine (Haberlandt 2001; Fukushima 2003; Wieland 2004; Courtens 2005; Asmus 2007; Tzschach 2007; *Unique*).

“Significant hearing loss; she wore aids until she was 13. Her hearing then improved so she now no longer needs aids. No medical reason was given - 7q22.1q22.31 deletion

■ Teeth

Generally speaking, children with chromosome disorders appear to have more dental problems than others. Information on 16 children and adults shows a wide variety of problems, some due to imperfect dental formation, others due to irregular placement within the mouth and others to difficulties with diet and dental hygiene.

Some children are highly orally defensive and resist having their teeth brushed or inspected by a dentist; severe decay and discoloration of both primary and adult teeth has been seen and one 10-year-old had all his teeth extracted as a last resort (Young 1984; Nunes 1994; *Unique*). Two children had very small primary teeth, with adult teeth no bigger; another child had conical canines; others had defective enamel. Teeth may erupt early or late; primary teeth may fail to drop out when adult teeth come in, needing surgical removal. In addition, accidents occur fairly frequently in which front teeth can be chipped or knocked out.

It is suggested that dental defects form part of a syndrome involving deletion of part or all of 7q21 and this is reinforced by finding an unusual rate of caries in an individual with a tiny microdeletion at 7q21.3 but otherwise normal development, apart from some features specific to 7q deletions (Klep de Pater 1979; Nunes 1994; McElveen 1995; Wu 1999; Haberlandt 2001; Morimoto 2003; Courtens 2005; Asmus 2007; *Unique*).

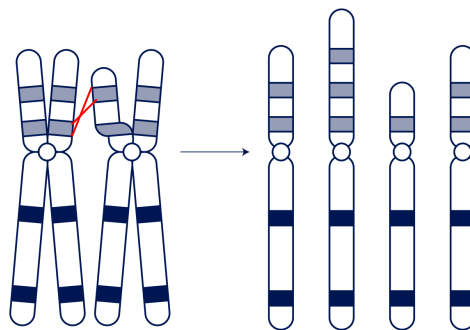
This adds up to a picture of youngsters and adults needing high quality, probably special care dentistry. Despite this, some youngsters have strong, healthy teeth.

How did the chromosome deletion occur?

A blood test to check both parents' chromosomes is needed to find out why the 7q deletion occurred in the child. Most 7q interstitial deletions occur when both parents have normal chromosomes. The term that geneticists use for this is *de novo* (dn), meaning 'new'. De novo 7q deletions are caused by a sporadic mistake that is thought to occur when the parents' sperm or egg cells are formed or around the time of conception. The underlying mechanism is not quite clear although 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.

When a sperm cell from the father and egg cell from the mother first join together, each carries just one copy of each chromosome. Together they form a single cell that now carries two copies of each chromosome. This cell must make many copies of itself (and all the chromosomes and genetic material) in order to make all of the many cells that form during human development. Sometimes during the formation of the egg or sperm cells or during this complicated copying and replication process, parts of the chromosomes can break off or become arranged differently than usual. People with a 7q deletion have one intact chromosome 7, but a piece from the long arm of the other copy is missing.

One possible way in which a deletion might occur is by a mismatch between chromosomes. This works as follows: at one point in the formation of the sperm or egg cells, all the chromosomes including the two chromosome 7s pair up and swap segments. To pair up precisely, each chromosome 'recognises' matching or near-matching DNA sequences on its partner chromosome. However, throughout the chromosomes there are many DNA sequences that are so similar that it is thought that mispairing can occur. Although no-one has ever seen this happen, it is believed that when the next step, the exchange of genetic material known as 'crossing over' occurs, it is unequal, looping out or doubling up a length of the chromosome. This process is shown in the diagram below, with mismatching leading to a deletion or a duplication in the short (p) arm of the chromosome.



What is certain is that as a parent there is nothing you did to cause the 7q deletion and nothing you could have done to prevent it. No environmental, dietary or lifestyle factors are known to cause these chromosome changes. No one is to blame when this occurs and nobody is at fault.



Can it happen again?

The possibility of having another pregnancy with a 7q deletion depends on the parents' chromosomes. When both parents have normal chromosomes, the deletion is very unlikely to happen again.

If either parent has a chromosome change involving 7q, the possibility is 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 for prenatal and preimplantation genetic diagnosis (PGD). 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) or 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 7q deletion have similarly affected children?

There is at least one case in the medical literature of a mother with a tiny microdeletion at 7q11.21 who was unaffected by it herself but passed it on to her daughter (Caselli 2007). *Unique* is not otherwise aware of anyone with a 7q deletion who has passed it on and is not aware of any cases reported in the medical literature. However, as advances in technology, especially the use of microarrays, uncover smaller microdeletions, the possibility will increase of discovering families where the deletion has been passed from generation to generation. Theoretically, someone with the deletion would have a 50% chance of passing it on and a 50% chance of having an unaffected child.

Potential genes involved in proximal interstitial deletions of 7q

Chromosome 7 has been estimated to contain around 1150 genes, that is, 4-6 per cent of the total number of genes in the human genome. The major features of proximal interstitial 7q deletions are likely to be caused by having lost one or more of these genes, acting singly or together.

The increasing use of sensitive molecular techniques such as array-CGH (microarrays) and FISH has led to more accurate definition of breakpoints in people with a 7q deletion. This, in turn, has enabled researchers to study which parts of the chromosome correlate with the different clinical features. Indeed, a number of recent studies have tried to correlate certain clinical features in people with a 7q deletion with the missing part of the chromosome in order to help to narrow down the genes responsible.

There is currently active research interest in the proximal regions of chromosome 7, with a growing number of published case reports of individuals with tiny microdeletions showing just one or two features typical of a 7q deletion. This suggests that many of the expected features of a 7q deletion are caused by having lost specific genes (Asmus 2007).

Another probably relevant factor is which parent the deleted chromosome came from. Parts of chromosome 7 have different effects, depending on whether they come from the mother or the father. This is technically known as imprinting. However, only the most recent cases reported in the medical literature record which parent the deleted chromosome came from and so we don't yet know enough to draw clear conclusions.

It is important to remember that while identifying the gene(s) responsible for certain features is interesting, it does not lead directly to immediate improved treatment. Also, even if the supposedly responsible gene is missing, it does not always mean that the associated feature(s) will be present. Other genetic and environmental factors often have a role in determining the presence or absence of a particular feature.

The *ELN* gene at 7q11.23 provides instructions for making a protein called elastin. This is an important component of the connective tissues that support the body's joints and organs. One copy of the gene is lost in people with Williams syndrome and anyone with a larger or smaller deletion covering the stretch of 7q11.23 whose absence causes Williams syndrome. The effects are commonly a narrowing of the blood vessel that takes blood from the heart to the rest of the body (aorta – supravalvular aortic stenosis, SVAS). It can also affect other blood vessels. It's also believed to be at the root of other features of Williams syndrome such as joint problems and loose skin.

Where the *SGCE* gene at 7q21.3 is deleted from the chromosome 7 inherited from the father (and less often from the mother), there is a raised risk of myoclonus dystonia, a syndrome characterised by rapid, brief muscle contractions usually of the neck and upper arms with onset in first 25 years of life. The contractions are made worse by purposeful movements, last less than a second and are generally not accompanied by EEG changes. The jerks may be hardly visible at rest but are strongly aggravated by movements such as drawing and writing. Generally they are harmless, but control with standard anti-epileptic and other prescribed medication may be tried (DeBerardinis 2003; Asmus 2007).

The *KRIT1* gene (also known as the *CCM1* gene) at 7q21.2 is associated with a condition known as cerebral cavernous malformations. These are abnormal collections of small blood vessels. The *KRIT1* gene provides instructions for making a protein that probably plays an important role in the formation of blood vessels, especially tiny capillaries, during

the development of an embryo. It may also be involved in creating the blood-brain barrier between capillary walls and the surrounding tissues in the brain (Asmus 2007; Tzschach 2007).

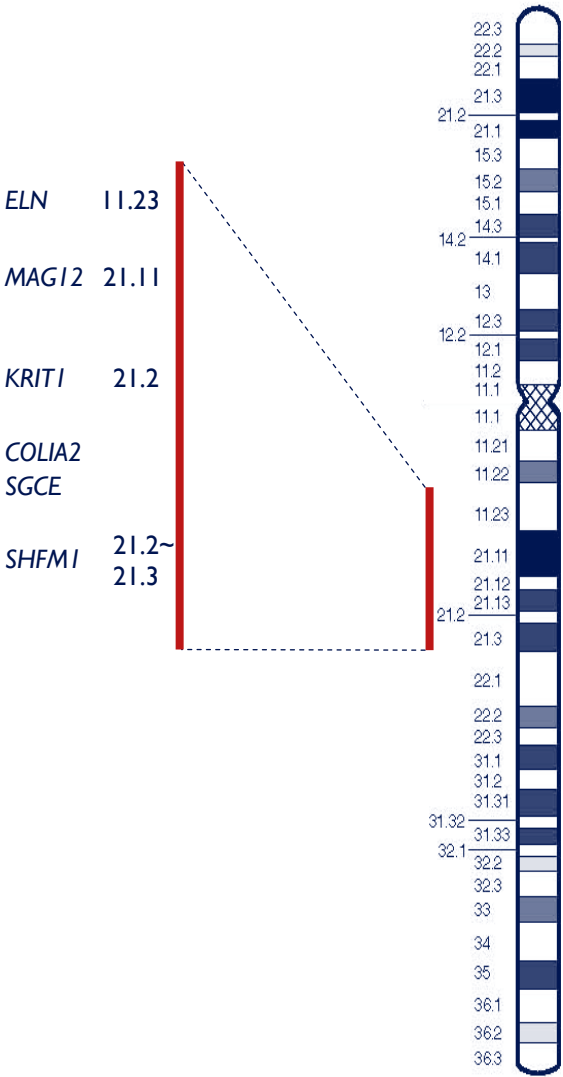
Three genes have been identified as possible candidates for the split hand-foot defect that some people with a 7q21q22 deletion show.

Occurring at the site known as Split hand-foot malformation 1 (SHFMI) at 7q21.2q21.3, the genes are known as *SHFMI*, *DLX6* and *DLX5*. Their role in limb development is still a matter for debate as it appears that all three need to be lost or moved away from chromosome 7 for the hands or feet to be affected. Some additional factor may be needed, as some people who lose all three genes have normal hands and feet (Tackels-Horne 2001; Wieland 2004; Asmus 2007; Bernardini 2007; Tzschach 2007).

As well as limb development, these three genes may play a role in the development of the inner ear, causing a particular malformation known as Mondini dysplasia, and hearing loss (Tackels-Horne 2001; Fukushima 2003; Wieland 2004; Courtens 2005; Tzschach 2007).

Infantile spasms have been specifically suggested as caused by a gene in 7q21. The *MAGI2* gene has been identified as a candidate gene. However, it is still possible to have infantile spasms with this gene intact and also to have lost this gene without apparently developing the spasms (Marshall 2008).

The *COL1A2* gene at 7q22.1 has been suggested as a candidate gene for abnormal dental development such as hypodontia, where people are born with fewer than the regular number of adult teeth (Asmus 2007).



Support and Information



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info@rarechromo.org | 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 Please help us to help you!

Facebook group for 7q deletions and duplications:

www.facebook.com/groups/493223084038489

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 guide was compiled by Unique and reviewed by Dr Steve Scherer, Centre for Applied Genomics, Hospital for Sick Children, Toronto, Canada and by Professor Maj Hultén, BSc, PhD, MD, FRCPath, Professor of Medical Genetics, University of Warwick, 2009.

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