Unique

7q36 deletions

Sources

The information in this leaflet is drawn from the published medical literature and from *Unique*'s database. At the time of compiling the information, *Unique* had 53 members with a 7q deletion, 35 of them with a simple deletion of 7q that did not involve any other chromosome.

Twenty members had a deletion of all or part of 7q36 and of these, eleven completed a detailed questionnaire in 2004/5.

References to information from *Unique* and the questionnaire are marked U.

Unique is extremely grateful to the families who took part in the survey.

Main features

No two children are affected in exactly the same way by a chromosome disorder. Your child may show features so mildly that you would hardly notice them or more obviously. Some people have no obvious features of a chromosome disorder at all and most *Unique* members were diagnosed not because of medical problems but because of developmental delay.
The features listed here have been described most often in medical publications and are most likely to make a difference to a child's health or development.

- Some difficulty with learning. This may be borderline, mild or more severe.
- Feeding problems.
- Floppiness (hypotonia).
- Underdevelopment of the middle of the face, showing for example as a single front tooth, close set eyes, marked narrowing or blockage of the back of the nose and throat (choanal atresia) or, more severely, a cleft lip.
- Underdevelopment affecting the head and sometimes the brain. The head can be very small (microcephaly).
- Malformations of the base of the spine (sacrum). Faults in the structure of the anus and rectum (bottom) may go along with this and there may be structural anomalies of the urinary system and /or kidneys.
- Anomalies of the sex organs (genitals) in boys.

References

The text contains references to articles published in the medical press. The first-named author and publication date are given to allow you to search for the abstracts or original articles on the internet in PubMed. If you wish, you can obtain abstracts and key articles from *Unique*.

Deletion sizes

Unique's survey included eleven members with a deletion of all or part of band 7q36 and nine people who had a larger deletion reaching to band 7q35, 34, 33 or 32. Where this is helpful, breakpoints are stated.

First signs

The signs at birth among *Unique's* eleven members with a specific deletion at 7q36 were quite varied and not particular to this disorder. They included slow feeding, a heart defect and, in one boy, a small head and loose scalp, out turned feet and slight anomalies of the sex organs. Two members showed more specific signs, including involvement of the kidneys and underdevelopment of the anus (the hole in the bottom). Three of *Unique*'s members were only identified in the toddler years because they showed delayed development. One mother with a deletion within band 7q36 developed completely normally, was perfectly healthy and was diagnosed only after the birth of an affected baby.

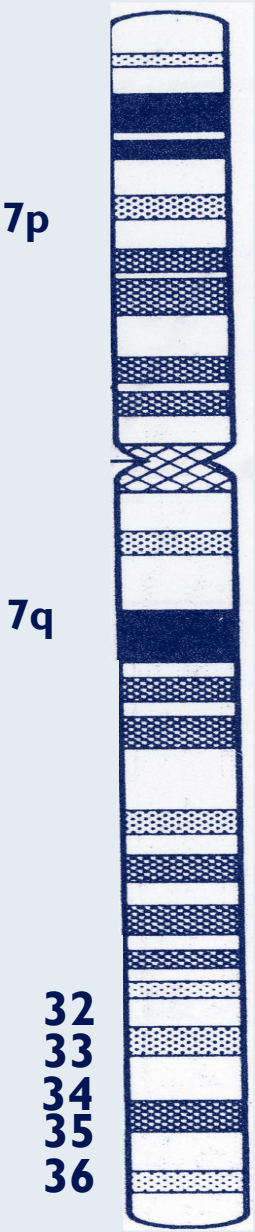
Diagnosis

To reach a diagnosis, a small sample of blood is taken, the white blood cells are grown and the chromosomes are separated from them. They are then stained with a dye that gives each one a typical pattern of light and dark bands. To diagnose 7q36 syndrome, the chromosomes need to be analysed using high resolution banding, a technique that allows fine bands to be seen and small missing pieces to be identified. Some deletions may still be invisible, however, giving a false result that all is normal, and a technique called FISH (fluorescent in situ hybridisation) is needed, using a probe that is specific to 7q36. This test is available at specialist genetic centres (Wang 1999; Horn 2004).

Pregnancy

For most people in the *Unique* series, pregnancy was unremarkable and nothing unusual was detected during routine antenatal screening. However, two mothers noted low levels of amniotic fluid, two babies were diagnosed with growth delay, one being induced at 37 weeks, and one baby was less active than expected. Premature birth may be common: of six babies with a deletion

Chromosome 7



confined to 7q36, two were born prematurely, one at 32 weeks, another four weeks early. Among five babies with a deletion extending beyond band 36, one arrived five weeks early, while another was born four weeks late (U). Prematurity as early as 30 weeks has been described in the medical literature in a severely affected baby. The medical literature also suggests that there are signs that may be evident during pregnancy: growth delay and a notably small head (microcephaly) are common and in babies where the effects on the face, the brain, the base of the spine or the kidneys and urinary system are severe, anomalies would be identifiable during pregnancy and probably at the mid-pregnancy ultrasound scan (Frints 1998; Wang 1999).

Newborn

The information about what to expect in the newborn period comes chiefly from the *Unique* experience, as the medical literature focuses on clinical problems. Among the babies with a small deletion within band 7q36, most problems in the first days of life related to feeding. Babies with larger deletions (extending as far as 7q32) were more likely to have more problems with breathing as well and tended to have slightly lower Apgar scores (standardised score from 0 to 10 of a baby's wellbeing at birth).

Most babies were small for dates and families found that their babies were extremely reluctant and slow to feed. No babies in the *Unique* series were able to breastfeed from birth without help. One baby fed with the help of nipple shields, another breastfed lying down and choked frequently but others took milk from bottles (with a teat for premature babies), from a syringe or a naso-gastric tube (a soft tube passed down the nose to the stomach). Babies with larger deletions frequently needed help with breathing (oxygen through a headbox, masked ventilation) and three out of five spent some time in special care.

Babies were typically unusually floppy (hypotonic) at birth and most had a weak cry. However, there were no specific signs of a chromosome disorder in most babies in the *Unique* series. One boy had unusual genital features (a curved penis and hypospadias, where the hole for urine is on the underside of the penis instead of at the end), but otherwise unusual features were subtle.

The *Unique* series may have been unusually mildly affected, because 7q36 deletions can cause the defects of the brain, mouth and palate and the lower back and spine listed in Main features that will be apparent at birth.

What about growth?

Like many other children with chromosome disorders, some babies with 7q36 deletions are born small for dates and grow slowly, remaining very short as children and as adults. However, this pattern is not universal, and although the medical literature states that short stature is the norm for someone with a 7q36 deletion, *Unique* members show that some children are of average or above average height. Short stature was more likely in children with larger deletions extending beyond band 7q36. The picture is more varied in children with a deletion that only affects 7q36 and while some children were of average or above average height, others were very small.

Unique's information on eventual adult height is limited, but one young man with a 7q34 deletion reached his adult height of four feet ten inches (147 centimetres) at the age of 13 and now weighs six stone four pounds (40 kg). Most children in the *Unique* sample were also thin (Horn 2004; U).

What about food and eating?

It seems that difficulties with feeding are extremely common. All families known to *Unique* have reported difficulties in the early months and for most these have persisted throughout childhood and in some cases into adulthood. Those babies who appear to be most mildly affected are either reluctant to feed from the breast and feed extremely slowly, at a rate of an ounce (25ml) of milk an hour. One baby with a small deletion within the 7q36 band fed for very short spells and was 'very distractible'. Some babies found latching onto the breast or sucking through a standard teat too difficult and either needed adapted (premature baby) teats or a nipple shield. Some babies outgrew this need and were successfully breastfed for many months. Most families reported that their babies were born with an immature sucking and swallowing reflex and those in whom the reflex was less well developed were fed breast milk or adapted formula by syringe or tube at first. A small number of children have needed to be fed through a gastrostomy tube direct into the stomach, but this is not necessary for most. Most families also reported frequent

Families say …

" *Even at five years old, Megan still prefers food which isn't too thick or lumpy and tends to swallow before she has chewed properly and then chokes* - del(7) (q36).

" *At 19, Andrew does not seem to know hunger and has difficulty swallowing and chewing. He only eats soft food such as cereals or custard and never eats meat, fruit or vegetables. Even though we have tried many occupational therapy guidelines, he will not feed himself* - del (7) (q34).

choking, gagging and vomiting, which lasted beyond the baby months. Families were able to introduce solid foods from four months but with a delay in chewing, babies needed food pureed or mashed for longer than other weaning babies, often well into childhood or longer (Young 1984; U).

This persisting pattern of feeding difficulties means that in *Unique*'s view, problems should be anticipated and families should be offered proactive feeding support by the speech and occupational therapy services as well as any specialist feeding service available.

Speech and communication

All children in the *Unique* series experienced some speech delay but the range of eventual use of language was very broad. In general, children showed a strong wish to communicate so that where speech and language did not emerge, children communicated using a rich variety of other means.

While there was a general trend to greater speech and language problems in children with larger deletions, this was not consistent and some children with large deletions communicated well with speech. In general, children with deletions limited to 7q36 seemed to have less difficulty acquiring fluent speech and some used a wide vocabulary with complex syntax, though again this pattern was not entirely consistent.

Speech and language skills continued to develop for longer than in other children and families reported that language improved even in the late teen years.

Typically, a child's understanding outstrips the ability to express himself but in one or two instances, children achieved a fluency that belied their understanding.

Some people with a 7q36 deletion have narrowed structures in the mid face, mouth, nose and throat areas. This can result in a high palate and affect the quality of sounds, typically making speech nasal. Additionally, many children with poor muscle control in the face and tongue have difficulty forming particular speech sounds.

Effects on learning

The range of effects on learning is varied. *Unique* has one member with a small deletion within band 36 who is unaffected, although her daughter with apparently the same deletion has a moderate learning difficulty.

In others, the effects vary from causing a mild to severe learning difficulty, with a possible trend towards less difficulty when the deletion is smaller. No formal research has been conducted into the particular learning skills or obstacles for children with a 7q36 deletion, so this evidence rests on *Unique*'s experience.

Most children have a generally pleasant social nature that helps them to make the best of their learning opportunities and a sense of humour that enhances their personal relationships. Many families speak of their child's good or very good memory, with a highly developed aural memory (music, lyrics).

School reports note curiosity and an eagerness to discover how things work. In terms of formal academic skills, most children learn to read, although word recognition may be very limited and writing and computer use restricted, particularly in those with larger deletions extending to 7q33 or 7q32.

Schools

Unique's families show that children with larger 7q36 deletions are most likely to be placed in a school for children with special learning needs, while those with smaller deletions start their education receiving special provision in a mainstream school,

Families say …

- *Hale said his first word at 14 months and by two had a wide vocabulary of over 100 words. He cannot understand a lot but uses big words in 6 to10 word sentences, at one thought per sentence. He can repeat a long conversation he has heard without understanding what he is saying. He speaks fast and not very clearly so he has a few problems with pronunciation.* Hale, age 5, has a 7q36.2 deletion.
- *Saffron, 7, uses social language and has no problems with the sounds of speech but does not understand logic and cannot interpret stories.* Saffron's has a 7q36 deletion.
- *Melissa taps, pulls, gestures, vocalises, makes good eye contact and follows well.* Melissa, 8, has a deletion from band 7q32.
- *At 9, Erin's vocabulary is expanding enormously, she is trying new words and using long, complete sentences.* Erin has a deletion from band 7q32.
- *Jessica can understand everything and can say 'Mum' but has difficulty with the sounds of speech. She uses a range of methods including Makaton signing and a computer-based communication device.* Jessica, age 9, has a 7q33 deletion.
- *Lukas has articulation problems but is understood most of the time. He has a bilateral lisp, a long tongue and mismatched jaws that make certain blends and sounds difficult, if not impossible. He can use long sentences but his grammar is not usually correct.* Lukas, age 13, has a deletion within 7q36.
- *If we don't understand Andrew, he persists and tries other ways to make us understand. His speech is hypernasal, he has no* s *or* f *and has problems with words ending in* g. Andrew, age 19, has a 7q34 deletion.

although they may switch into the special needs sector later on. All children except one have a formal assessment of their learning needs supported by a statement, record or individual education plan.

Speech therapy

Every child known to *Unique*, however mildly affected, has received speech therapy to address social and communication skills, sound production, muscle tone, language structure, understanding and sequential memory as well as feeding issues. Children have received very varying amounts of therapy so it is impossible to draw any conclusions about what approaches have been most effective.

Whole body movements

Almost everyone in the *Unique* series was somewhat delayed in starting to sit, crawl and walk but the range of eventual mobility was extremely wide. The exceptions were the mother-daughter pair with the same small deletion within 7q36 who experienced no delay in gross motor development. In general children with larger deletions seem more likely to have markedly delayed development of their mobility skills, to have muscular

Families and schools say …

7q36 plus: children with a larger deletion

" *Melissa enjoys coming to school and often kicks her legs and makes happy sounds as she comes into class. She joins in with all curriculum areas with great enthusiasm and has a very inquisitive nature. This is particularly apparent when she is crawling where she will investigate contents of boxes and bags. Melissa has a lovely sense of humour and there are often times in the day when she starts to giggle. This can be linked to a noise of a toy or a physical activity, but sometimes we just don't know what! Melissa has been developing the strength in her pincer grip and can use a three-fingered grip* - del(7)(q32qter), age 8.

" *Erin has developed a degree of word recognition, although she is not able to read. She has been able to write her name in capitals (backwards) since the age of 9 and use a keyboard and mouse from the age of 8. Her determination, enthusiasm and her eagerness to learn and show off her new skills help her to learn* - del(7)(q32qter), age of 9.

" *Jessica recognises her own name and favourite words (like 'Scoobydoo') and although she cannot write, she tries with a switch* - del(7)(q33), age 9.

" *Andrew can write his own name in very large letters, although he usually misses out the 'n'or 'd'. He likes to use a keyboard but does not form words. He can read individual words from packets and instructions from packets and tins using visual clues. He can count with help. With his excellent memory, he talks about events that happened years ago, starting 'Remember Mum' and then he proceeds with the conversation* - del(7)(q34), close to school leaving age.

Families and schools say …

7q36: people with deletions at the end of the long arm of chromosome 7

“ *Hale is very good at music and remembers hundreds of songs. In most other areas he is delayed and though he knows his letters he cannot read yet. He can draw an O and an H* - del(7)(q36.2), age 5.

“ *Megan is very musical and will hum lots of recognisable tunes. She has a good memory and being very strong willed and determined helps her to learn* - del(7)(q36), age 5.

“ *Amy is a concrete learner with a very good memory, excellent at remembering people's names and the lyrics to music. She knows the letters of the alphabet and their sounds and started to read early readers at 6½. She can write her own and her sister's name and can use a keyboard and has good mouse control for playing computer games* - del(7)(q36.1q36.3), age 6½.

“ *Saffron reads basic words and has been writing her name and short common words from age 7. Her memory is not her strength but she learns well through pictures* - del(7)(q36), age 7.

“ *Hannaa has difficulty reading and expressing sounds, but she started to read at 7 years and to write at 6. She is very good at art* - del(7)(q36q36), age 10.

“ *L is developmentally at a 5 or 6 year level. He started to read when he was 9, using a sight reading programme (Edmark) and can now read more than 112 words by sight but does not yet know the full alphabet. He can print his name and copy part of his address and can use a computer. He has good visual discrimination* - del(7)(q36.1->q36.3), age 13.

floppiness (hypotonia) and to need supports and walking aids. However, the pattern is not consistent and at least one child with a large deletion from 7q32 is active and sporty, kicking a ball with accuracy, throwing balls and a Frisbee and playing swingball to develop hand-eye co-ordination.

Children in whom the lower spinal area (sacrum) is affected by the deletion may have specific difficulties with mobility and balance, making them clumsy, particularly when they move quickly. However, in the *Unique* series, only one child has sacral agenesis (failure of the lower spine to develop, see below) and he is mobile if somewhat clumsy at the age of 5. What is uncertain is whether minor effects of the development of the caudal area subtly affect children's mobility.

On average, children started to roll over between four and 12 months, sat alone between 10 and 20 months, crawled or commando crawled between their first and second birthdays, walked alone between

Families say …

" *Andrew used to walk with his hands outstretched and still holds them bent up from the elbows with his hands facing down. He has an uneven footfall and a wide gait and walks to the right. When he is outside, he likes to arms. He enjoys water and swimming and in the last two or three years has started to kick a ball with his right foot. He likes to dance on the spot and plays basketball but has a short activity span* – age 19.

18 months and four and a half years, ran between two and eight years and climbed stairs from the age of three. However, two members, both with large deletions, were not walking at 8 or 9 years.

Therapies

All *Unique* families who gave detailed information were offered physiotherapy (physical therapy) to improve their child's mobility skills, balance, strength and co-ordination. For most children physiotherapy was needed from babyhood until at least the late years of primary school. Outcomes were variable but generally satisfactory.

Using their hands

Most children have shown delay in learning to use their hands for everyday activities such as feeding and dressing themselves, computer activities or play. The typical picture is one of delay in co-ordination, with extra difficulties with muscle weakness (hypotonia) for some children. Children are markedly delayed in starting to feed themselves and in handling pencils for writing and are generally more successful earlier with keyboard writing. Older children who have mastered dressing themselves can rarely cope with fastenings such as zips and buttons.

In general there does not seem to be any feature specific to the 7q36 deletion that contributes to the general delay in fine motor control. However, one boy with a 7q34 deletion has a missing joint at the base of his thumb and a slight tremor in his right arm.

The great majority of children were provided with occupational therapy (OT) services or access to pre-school portage in early childhood up to age 5 to 7.

Most parents felt that OT was helpful although it did not eradicate the problems and one family said it was specifically unhelpful.

Skin colour

It has been suggested that children with a 7q36 deletion may have a different skin colour to the rest of their family. One quarter of *Unique* families have confirmed this observation and in each case, the child with the 7q36 deletion has a lighter skin colour than the rest of the family.

Puberty

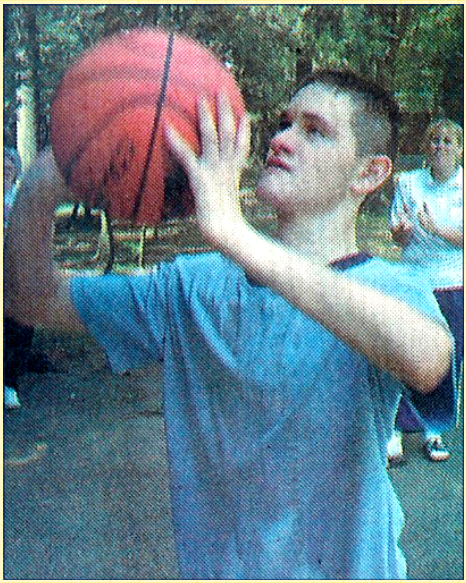
The evidence from *Unique*'s small sample is that puberty may be early but proceeds normally. In two boys, the first signs of puberty emerged at 11 and 12 (compared with 13 in their brothers) and one girl was diagnosed with premature sexual development at the age of 6.

Medical concerns

Holoprosencephaly (HPE)

The absence of the so-called Sonic Hedgehog *(SHH)* gene at 7q36 is associated with a developmental disorder called holoprosencephaly, also known as HPE. This affects the brain and often the central part of the face as well. Its effects can range from being scarcely noticeable to very severe. A mild form of HPE might show as a single central front tooth or other abnormalities of the teeth in the upper jaw, as an extremely small head (microcephaly), close set eyes, narrow nasal and throat passages or cleft palate and absence of the sense of smell. In its most severe form, the brain fails to develop into two halves (hemispheres) with serious effects on its function. Many children with HPE associated with a terminal 7q deletion only show minimal signs, most characteristically microcephaly, and these may only become evident after birth (Benzacken 1997; Horn 2004; U).

If your child's chromosome test shows that the *SHH* gene is missing, your child should be offered imaging of the brain, usually a CT or magnetic resonance imaging (MRI) scan. *Unique*'s experience among its membership is that only one child was found to have any abnormalities of the brain, although the great majority of children had microcephaly (an unusually small head and



Summer camp, 12 years old, deletion 7q36.1-36.3

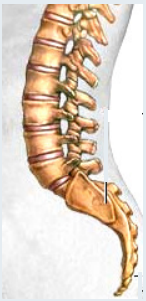
brain). The child with an unusual brain structure has since developed especially well considering the size of the chromosome deletion.
One child in the *Unique* series also has a cleft palate (roof of the mouth) and three more have a remarkably high palate. This feature is common among all children with chromosome disorders and can affect speech (making it more nasal), hearing (fluid in the middle ear and glue ear is common) and feeding.

Sacral defects

Your child should have a pelvic X-ray or other imaging when a 7q36 deletion is diagnosed because the development of the base of the spine can be affected. The *HLXB9* homeobox gene (sited between the sonic hedgehog gene and the telomere (tip) of the chromosome) affects the development of tissues that have their origin in the tail bud of the embryo. The absence of the *HLXB9* gene on its own can cause a condition known as Currarino syndrome (caudal regression syndrome or hereditary sacral agenesis) in which the lowest bones of the sacrum at the base of the spine and the coccyx (the lowest element of the backbone) fail to form properly. In children with a larger 7q36 deletion other tissues that develop from the embryonic tail bud may also be involved, including the anus (the hole for the bottom), the rectum, the genital system, the urinary tract and the bladder.

Apart from the absence of the lower bones in the sacrum, the most common features are chronic constipation, the growth of a cyst, fatty lump or other mass near the sacrum and the development of a meningocele, a spina bifida-like defect on the inner aspect of the spine. Kidney and urinary tract problems affect around one person in three and a smaller number develop a bowel obstruction as babies or have a tethered spinal cord. The involvement of the spinal cord raises the risk of meningitis and structural defects in the anus and rectum can lead to infections. The severity of symptoms varies enormously, even between family members, and one third of all people with this syndrome and many *Unique* members have no obvious signs. In fact many people with missing sacral bones remain undiagnosed in the absence of other problems, although secondary effects such as severe constipation and urinary tract infections are common (Wang 1999; Belloni 2000; Lynch 2000; Horn 2004; U).

The sacrum is a shield-shaped bony structure at the base of the backbone and joined to the coccyx or tail bone.



Kidneys, bladder and urinary tract

Your child should have an ultrasound scan of the renal system, particularly if they develop a urinary tract infection. This will ensure that any unusual formations of the kidneys, fistulae (unexpected channels) between the intestines and the urinary system, obstructions or urinary reflux (where the urine flows back towards the kidneys instead of out from the bladder) are detected and if necessary antibiotics given to protect against infections that could scar the kidneys.

The types of anomalies that have been found in children with 7q3 deletions include constrictions of the tubes connecting the kidneys with the bladder and swelling of the tubes caused by a constriction further downstream. As urinary tract infections are relatively common in children with 7q3 deletions, it is important to be alert for them. The symptoms of urinary infections are vague in very young children but any baby with an unexplained fever or more than usual listlessness should be seen by a doctor (Lurie 1990).

Constipation

Many children with chromosome disorders have constipation, in part because they often eat and drink small quantities and also because they tend to be less active than other children. Constipation in the *Unique* series of children with 7q36 deletions is not very much more common than among other children with chromosome disorders but it can be both severe and persistent and a high proportion of children need regular prescribed laxative medication. A few children with constrictions in the rectum and anus need dilatation, a procedure to stretch the tube taking waste matter to the outside world, and some children need this repeatedly. Evacuation is also needed commonly, where the contents of the bowel are emptied.

Toilet training

Children may be particularly late to become dry in the daytime and at night. A condition known as neurogenic (or neuropathic) bladder – where the bladder does not function properly and cannot be emptied normally - has been shown to be linked with 7q3 deletions. In some children the sensation of bladder fullness may be impaired. While some children achieve day dryness by

the age of 6 or 7, night wetting can persist into the teenage years (Wang 1999; U).

Genital area (boys)

Slight defects of the penis and genitals are fairly common in boys with chromosome disorders and also in those with regular chromosomes. The problems noted in boys with a 7q36 deletion do not affect all boys and apart from a very small penis that may be curved are almost all quite easily correctable with fairly simple surgery. The hole that is usually at the end of the penis may be found on the underside (hypospadias) and one or both testicles may not come down as expected into the scrotum. The immediate consequence at birth is that a boy with hypospadias should not be circumcised as the foreskin is used in the repair of hypospadias and resiting of the hole (Bernstein 1980; Warburg 1995; U).

Jaws and teeth

A very mild degree of holoprosencephaly (page 12) can result in a narrow upper jaw, a very high arched palate (roof of the mouth) and, typically, a single central tooth or other defects in the upper row of teeth with the bottom teeth affected much more rarely. The *Unique* series of children showed a great variety of dental problems, including mismatched jaws, uneven dental growth, a cusped front tooth, fusion of the front four teeth, extreme crowding and a single root giving rise to two separate deciduous (milk) teeth, as well as early and late eruption of first teeth. Additionally, one child had extreme decay and by the age of 19 had only eleven remaining teeth (Horn 2004; U).

Cold hands and feet

More than half of *Unique* families surveyed reported that their child typically has extremely cold extremities, especially hands. While this may result from a low level of activity in some children, in *Unique*'s experience it is an unusual finding and suggests that families should be alert to the possibility.

Many children with chromosome disorders have unusually formed toes, thumbs or fingers. Some people with 7q36 deletions may have webbed toes, particularly the second and third toes, or toes that curl or overlap and need to be straightened. Two families reported that their child has a

very large big toe and in one child the thumbs are affected as well. Another child is missing the lowest joint on his thumbs. Three families also reported flat feet.

Joints

Loose and easily dislocatable joints are a common feature in children with a chromosome disorder, especially those with hypotonia (floppy muscles) and were reported by almost half of *Unique* 7q36 deletion families surveyed. Hips, shoulders, ankles, elbows and fingers were affected but only one child had developmental hip dysplasia severe enough to need treatment. Some children with flexible ankle joints have needed orthotic supports (DAFOs) but families of older children have reported an improvement with time and most children have not needed any special treatment or surgery.

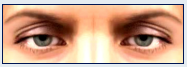
Heart

Around one person in five with a 7q36 deletion is born with a heart problem. These have included ventricular septal defects (VSDs, holes between the pumping chambers of the heart) and anomalies of the blood vessels leading to and from the heart. In *Unique,* three families have reported a VSD, one had a double outlet right ventricle (a complex anomaly of blood flow from the ventricles) while another child had a cyst on the left ventricle. Small holes may well close up naturally in time but in two *Unique* children surgery was needed. Both children are healthy and thriving after surgery (Tiller 1988; U).

Eyes and vision

Ptosis

Over half of all children with a 7q36 deletion are reported to have a hooded upper eyelid (ptosis) on one or both eyes and this was reported in over one third of *Unique* families. However, the eyelid was not so low as to obscure vision and no children known to *Unique* have needed a surgical operation to raise the lid. It has been suggested that ptosis may be a sign of minimal HPE. There is one child described in the medical literature in whom the ptosis was accompanied by blepharophimosis and epicanthus inversus (the opening for the eyes is small and a bridge of skin covers the inner corner) (Warburg 1995; Horn 2004; U).



Squint

Squint (strabismus) occurs commonly in children with chromosome disorders and is reported by one quarter of U*nique* 7q36 deletion families, in two cases needing surgical correction.

Long sight

Half of *Unique*'s families report that their child is sufficiently long sighted to need correction, although younger children are typically loath to wear the glasses prescribed for them!

Structural anomalies of the eye

Optic nerve coloboma and a severe microphthalmus and large retinal coloboma, causing congenital blindness, have been described in a child with 7q34qter. A coloboma is a developmental defect (Taysi 1982; Reynolds 1984).

Behaviour

The overall impression of children with a 7q36 deletion is that they are pleasant, sociable people and this puts them at an advantage at school and later in life in their placements.

Some families comment that their child gets on better with adults than with other children and many note that their child is withdrawn in an unfamiliar environment.

Families also note a strong streak of stubbornness that can develop into challenging behaviour.

Families say …

- *A would describe himself as happy, moody, shy, cheerful, pleasant, tender hearted, sensitive, aggressive and nervous. He gets angry if he does not get his own way and spits, swears, signs, kicks, hits and bangs doors. He has a very pleasant nature most of the time but is not very sociable. He only likes adult company and has huge problems going into strange situations. At first he is shy but is fine providing people smile at him. Anyone who has a frown or a sad face makes him worried. We have been told over the past few years that A is on the autistic spectrum. He has amazing memory recall and latches onto things such as hedge cutters or lawn mowers and puts his hands up to his eyes or ears when excited and trembles with excitement. He stares at the hair on people's head or their legs when he knows them well and makes a strange contentment noise* – A, age 19.
- *L is a very happy, caring child who loves everyone and thinks everyone loves him. He has mild obsessive/ compulsive tendencies, some repetitive behaviour, a 45-second attention span and a very high pain threshold. He started on Ritalin at 3, switched to Concerta, then Adderall and is now unmedicated but his focus has improved greatly* – L, age 13.
- *H sometimes has very challenging behaviour, and has obsessions with clothes and games* – H, age 10.
- *J gets frustrated when she is unable to communicate and may pinch, bite and pull hair (her own and others). She hates being put in her car seat or buggy and will fight everything* – J, age 9.
- *M is placid and content if she is well but can have challenging behaviour with unfamiliar people* - M, age 8.
- *A can be overfriendly towards strangers so always has adult supervision* – A, age 6.
- *M can be very loving and affectionate but is very determined and can cry and scream when not allowed to do what she has in mind. She has just started to bite* - M, age 5.
- *H is pleasant but has a bad temper. He has poor social skills and attaches to adults he does not know* – H, age 5.
- *D is very pleasant and sociable, a joy to take anywhere for any amount of time* – D, age 3.

Can it happen again?

The possibility of having another child affected by a 7q3 deletion depends on the results of the chromosome tests on the parents. When you are ready to think about another pregnancy, you should be able to discuss this with your genetics service and weigh up the pros and cons of prenatal diagnosis.

Most often, the chromosomes of both parents are normal. It is then most likely that the 7q3 deletion occurred by chance either during the cell divisions that created the sperm or egg that went to form the child or early in cell division after conception (when a baby is made).

If the test shows that either parent has a rearrangement of their own chromosomes, they have a significantly raised risk of having another affected child.

There is a very distant possibility that in some people the deletion occurred during the formation of the cells that later give rise to the egg or sperm. This can result in a condition termed gonadal mosaicism – there are both normal and abnormal cell lines - and when it occurs, there is a tiny possibility that parents with apparently normal chromosomes from a blood test could have another affected pregnancy.

A case has been reported of a mother with a deletion so tiny it was not visible under a microscope who passed it on to her son. The mother had minimal signs of HPE while in the baby there was a facial cleft (Wilson 2005).

Causes

Changes to the structure of chromosomes such as 21q deletions occur most often during the cell divisions that lead to the creation of eggs or sperm. Each arm of each of the 46 chromosomes first splits lengthwise into two strands that are held together at the centromere, the point where the short and long arms meet. The chromosomes then arrange themselves in 23 pairs, with pairs lying alongside each other apart from the sex chromosomes X and Y which attach to each other primarily at one end

The chromosome pairs ‘recognise’ each because they are similar. However, where the DNA of the chromosome is very similar to the DNA at another point on the chromosome, the pairs of chromosomes may not align

correctly. Segments of DNA are then exchanged in a process known as crossing-over (recombination) with the chromosome strands held together at the crossing points (known as chiasmata). Deletions almost certainly arise during this process when the chromosomes line up incorrectly. Then an unequal cross-over means that a piece of chromosome can be looped out and lost (interstitial deletion) or lost from the end of the chromosome that then heals over (terminal deletion).

These rearrangements occur in chromosomes as part of evolution. They affect children from all parts of the world and from all types of background. They also happen naturally in plants and animals. So there is no reason to suggest that your lifestyle caused the rearrangement.

Chromosome disorders can occur as a result of rearrangements in one parent's own chromosomes or they can happen out of the blue, so the child with the chromosome disorder is the first person in the family with rearranged chromosomes. The only way to know if the disorder is inherited or not (when it is called *de novo*) is for the parents' chromosomes to be checked and the results explained by a geneticist or genetic counsellor.

In some cases the check reveals a structural rearrangement of the parents' own chromosomes, but one that is balanced so that all the chromosome material is present, and the parents are then almost always entirely healthy. Occasionally the rearrangement will be the same as in the child, and again the parent may be healthy.

6 years old, 7q36.1-36.3 deletion

Unique

Support and Information

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This leaflet 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. The information is believed to be the best available at the time of publication. The genetic content was verified by Professor Jean-Pierre Fryns, Center for Human Genetics, Leuven, Belgium and by *Unique*'s chief medical advisor Professor Maj Hulten, Professor of Medical Genetics, University of Warwick, 2005.

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Charity Number 1110661
Company Number 5460413