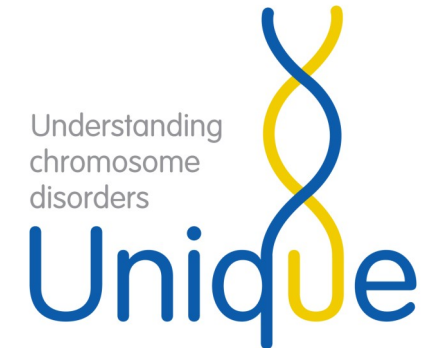


Can it happen again?

Where both parents have normal chromosomes, it is unlikely that another child will be born with a 1p36 deletion or any other chromosome disorder. Where a parent has a rearrangement of their chromosomes with a break at 1p36, the risk of having another affected child is higher.

If they wish, parents should have the opportunity to meet a clinical geneticist or genetic counsellor to discuss the 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) and amniocentesis to test the baby's chromosomes. Testing is very accurate, although not all of these tests are available in all parts of the world.



Inform Network Support



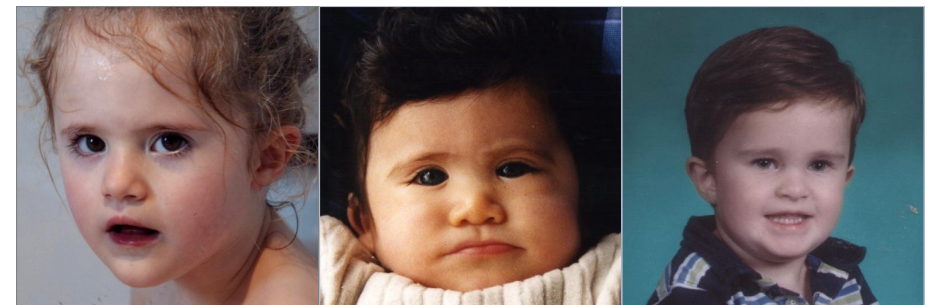
Rare Chromosome Disorder Support Group,
The Stables, Station Rd West, Oxted, Surrey. RH8 9EE
Tel: +44(0)1883 723356
info@rarechromo.org | www.rarechromo.org

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Please help us to help you!

1p36 deletion syndrome



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. It was compiled by Unique and reviewed by Dr Louise Brueton, Consultant Clinical Geneticist, Birmingham Women's Hospital, UK, Dr Mohnish Suri, Consultant Clinical Geneticist, University of Nottingham and by Professor Maj Hulten BSc, PhD, MD, FRCPath, Professor of Medical Genetics, University of Warwick, UK 2008, 2011, 2013

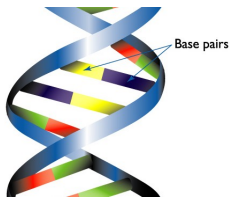
Version 2.3 (SW)

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1p36 deletion syndrome

1p36 deletion syndrome 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 1p36 deletion syndrome have lost a small but variable amount of genetic material from one of their 46 chromosomes.

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, and 22 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 (shown at the top in the diagram below) and a long (q) arm (the bottom part of the chromosome).



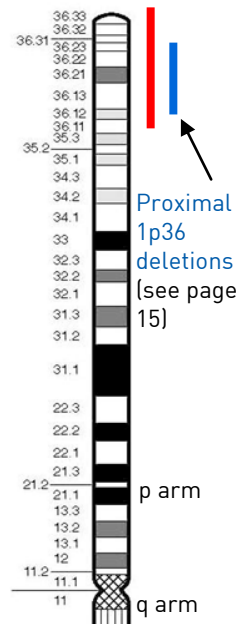
1 base pair = bp
1,000 base pairs = 1kb
1,000,000 base pairs = 1Mb

Chromosome 1 is the largest chromosome and represents about eight per cent of the total DNA in cells. Base pairs are the chemicals in DNA that form the ends of the 'rungs' of its ladder-like structure. For healthy development, chromosomes should contain just the right amount of material – not too much and not too little. People with 1p36 deletion syndrome have one intact chromosome 1, but the other is missing a tiny piece which affects their learning and physical development in relatively predictable ways. Most of the clinical difficulties are probably caused by the presence of only one copy (instead of the usual two) of a number of genes. However, a child's other genes and personality also help to determine future development, needs and achievements.

Looking at 1p36

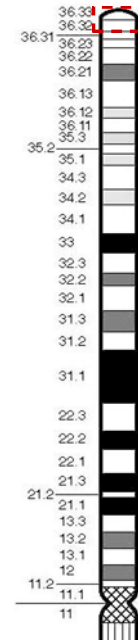
Chromosomes can't be seen with the naked eye, but if they are stained and magnified under a microscope it is possible to see that each one has a distinctive pattern of light and dark bands. By looking at your child's chromosomes in this way, it is possible to see the points where the chromosome has broken and to see what material is missing. However, because the amount of material missing is often quite small, in this type of routine analysis your child's chromosomes may have looked normal. Consequently there are certainly people with 1p36 deletion syndrome who have not yet been diagnosed. New, more sensitive, molecular techniques such as FISH testing or array comparative genomic hybridisation (array-CGH) may be necessary to confirm or detect 1p36 deletions.

1p36 deletion syndrome was described for the first time in the late 1990s, although the first case of a child with a deletion of 1p36 was published in 1981. The disorder is now believed to affect one in 5,000 newborn babies, making 1p36 deletion syndrome one of the most commonly observed chromosome deletion disorders. Most reports suggest that 1p36 deletions affect girls more often than boys – around 65 per cent of reported cases are girls. Unique families support this: 73 per cent of the children with 1p36 deletion syndrome are girls. The reasons for this are, as yet, not known (1, 2, 3, 4, U).

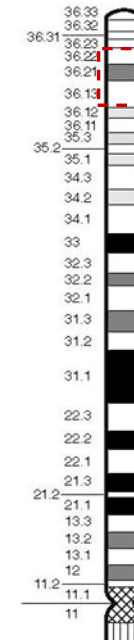


Chromosome 1

A small number of people have proximal interstitial deletions of 1p36 in which an internal part of 1p36 is missing but this very end portion of the chromosome (the "critical region"), and therefore the genes mentioned on page 14, are still present (see diagram below). Since these deletions are much rarer than deletions involving the end of the chromosome there are few published reports. However, a recent study suggested that these deletions result in slightly different characteristics. Hypotonia and developmental delay are still features, and the characteristic facial appearance is similar, but with arched (instead of straight) eyebrows. In addition, people with these deletions have hirsutism (excessive body hair) and the majority (5/6) have structural heart defects (11, 16).



(A) An example of a terminal deletion. The area marked by the red box is missing. The karyotype would be del(1)



(B) An example of a proximal interstitial deletion. The area marked by the red box is missing. The karyotype would be del(1)(p36.13p36.22)

With the increasing use of molecular techniques such as array-CGH and FISH in diagnosing 1p36 deletion syndrome the deleted region will be more accurately defined, and there will almost certainly be an increase in the number of people diagnosed. This will lead to a more accurate delineation of 1p36 deletion syndrome.

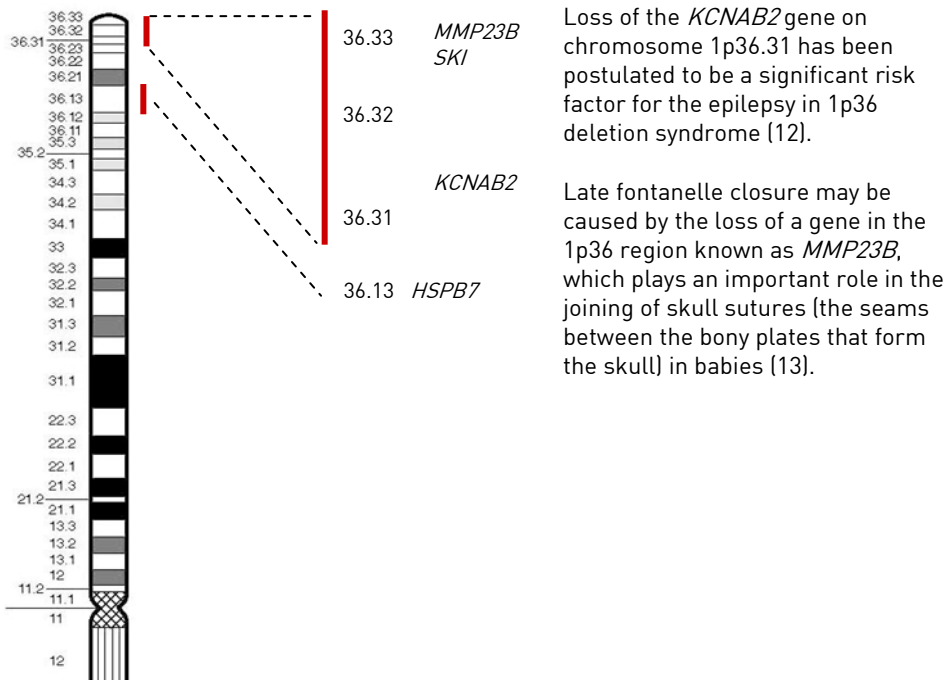
Why did it happen?

Both parents of a child with a 1p36 deletion should have their own chromosomes tested, although 90 - 95 per cent will have normal chromosomes. The chromosome break is then said to have occurred out of the blue (*de novo*). In the remaining families, one parent usually has a balanced rearrangement of their own chromosomes which has become unbalanced when eggs or sperm were created. In both situations, there is nothing you can do to stop this, just as there are no environmental, dietary or lifestyle factors known to cause it. So there is nothing that either parent did before or during pregnancy that caused the deletion to occur and equally nothing could have been done to prevent it.

Potential genes involved in 1p36 deletion syndrome

Perhaps more significant than the size of the missing piece is the location of the part of the chromosome that is missing. In most cases, the part of chromosome 1 that is missing is the end of the chromosome and this region has been shown to be the critical region for most of the characteristics of 1p36 deletion syndrome (10).

There have been attempts to correlate the part of chromosome 1p36 that is missing with specific characteristics of 1p36 deletion syndrome (10, 11). However, this has proved to be extremely difficult since the size of deletions is so variable. Added to this, the end of the short arm of chromosome 1 (band 1p36.3, shown on the diagram below) is the part most commonly missing and is very gene-rich, making identification of specific genes involved in particular features very difficult. Even so, a few genes have been suggested as possible candidates for some of the features of 1p36 deletion syndrome.



Chromosome 1

Studies suggest that the *SKI* gene, located at the end of 1p36.33 is likely to contribute to the cleft palate seen in some people with 1p36 deletion syndrome. In this study, all the patients with a cleft palate had this gene missing. However, it should be noted that many people for whom this gene was deleted did not have a cleft palate, suggesting that other genes or factors also play a role (14).

Recent studies have identified the gene *HSPB7* located in band 1p36.13 as being a risk factor for the cardiomyopathy seen in some people with 1p36 deletion syndrome (15).

Results of the chromosome test

Most people have a pure terminal deletion (no other chromosome is involved). However, among Unique members seven per cent of children with 1p36 deletion syndrome have the involvement of an additional chromosome, usually a duplication of material from another chromosome.

Your geneticist or genetic counsellor will be able to tell you about the points where the chromosome has broken in your child. You will almost certainly be given a karyotype for your child, which is shorthand notation for their chromosome make-up. With a 1p36 deletion, the karyotype is likely to read something like one of the following examples:

46,XY,ish del(1)(p36.3)de novo

46	The total number of chromosomes in your child's cells
XY	The two sex chromosomes, XY for males; XX for females
.ish	The analysis was by FISH
del	A deletion, or material is missing
(1)	The deletion is from chromosome 1
(p36.3)	The chromosome has one breakpoint in the band 1p36.3, from this position to the end of the chromosome is missing. This is called a terminal deletion. If the portion of the chromosome that is missing is internal to the chromosome (interstitial) then two breakpoints will be specified (e.g. p36.22p36.33)
de novo	The parents' chromosomes have been checked and no deletion found at 1p36. The deletion is very unlikely to be inherited and has occurred for the first time in this family with this child

arr[hg19] 1p36.33p36.22(2,171,936 -10,198,956)x1

arr	The analysis was by array-CGH
hg19	Human Genome build 19. This is the reference DNA sequence that the base pair numbers refer to. As more information about the human genome is found, new "builds" of the genome are made and the base pair numbers may be adjusted
1p36.33p36.22	Chromosome 1 has two breakpoints, one in the band 1p36.22, and one in band 1p36.33
2,171,936 -10,198,956	The base pairs between 2,171,936 and 10,198,956 have been shown to be deleted. Take the first long number from the second and you get 8,027,020 (8.03Mb or 803kb). This is the number of base pairs that are deleted
x1	means there is one copy of these base pairs, not two – one on each chromosome 1 – as you would normally expect

Sources and references

To date, there have been over 100 published cases of 1p36 deletion syndrome and Unique has 74 affected families ranging in age from 1 year to 34 years. In addition to people described in the medical literature, this review draws on information from two surveys of members of Unique conducted in 2003 and winter 2007/2008, referenced U. Articles from the medical literature are referenced by a number. If you wish, you can obtain a full list of these articles from Unique.

Most likely features

The effects of 1p36 deletion syndrome vary between individuals. There have been two recent formal studies of children with a 1p36 deletion, one with 60 children (5) and one with 134 (6). Children will not necessarily have all of these features but they have been found to be the most common.

- Developmental delay
- Children need support with learning. The amount of support needed by each child will vary, although most benefit from attending a special school
- Hypotonia (floppiness), especially in babies, but this may persist
- Feeding difficulties
- Seizures
- Cardiomyopathy (disease of the heart muscle) and minor heart defects
- Hearing loss and vision defects
- A large soft spot (fontanelle) at birth that is slow to close

How might a 1p36 deletion alter a child's ability to learn?

All children studied so far have shown some degree of learning disability, usually in the moderate to severe range. It has been suggested that children with the very smallest deletions have milder difficulties. Unique's membership does not appear to confirm this but until everyone has an up-to-date chromosome analysis confirmed at least by a FISH test, we cannot be certain. Studies of the specific learning needs of children with 1p36 deletions are urgently needed.

Parents observe that the most important single influence on a child's ability to learn is seizure control. Children are reported to regress or to fail to make progress while seizures are uncontrolled. Concerns over the sedating effects of anticonvulsant medication have led some families to try non-pharmacological means of seizure control but there are no studies to show the effectiveness of this approach (1, 7, U).

Many parents report that the most effective learning strategies include music, lights, visual learning and books, especially tactile ones. Patience, repetition and lots of praise and encouragement are important. Some children have found a touch screen computer a useful learning aid. Some children learn to draw simple lines and shapes, read and write. Parents note that many children have good memories, particularly for faces and places (U).

“Robbie can recognise the numbers 0 through to 10 and simple shapes” - 3 years

“Sophia has an excellent memory with a good memory for spellings. She began reading at reception class at school at age 5. She can also now write and loves new words” - 6½ years

“Bebhinn loves music and has an incredible innate beat/rhythm (demonstrated by movement of her right arm only)” - 10½ years

“She cannot read but can recognise about 15 words. She loves books. She can draw a passable square, triangle or circle Her geographical memory is very good” - 20 years

What is the outlook?

It is difficult to predict the long-term outlook for an individual child. There is only one study to date in which the natural history of 1p36 deletion syndrome has been investigated with a follow-up spanning 18 years. This reported a gradual acquisition of adaptive behaviours (where inappropriate or unconstructive behaviour is replaced by more constructive behaviour), improved social interaction and attainment of gross motor and fine motor skills. An improvement in communication skills and verbal comprehension was also seen, however, Unique's experience has been that children will normally need lifelong care and medical support and will at best achieve only limited independence. Parental experience suggests that a small minority of children achieve toilet timing or toilet training. Many can help get themselves dressed by pushing their arms through sleeves and a few learn to undress but almost all need a carer for dressing. Some children are able to brush their teeth and wash their hands and faces, although the majority need help with these tasks (5, U).

“Laura still wears nappies at night. She can dress herself with varying degrees of accuracy but cannot put on a bra and her shoes are often on the wrong feet!” - 20 years

Growing up with 1p36 deletion syndrome:



2 years



11 years



20 years

What causes 1p36 deletion syndrome?

Children inherit one copy of each of the 23 chromosomes from each parent, giving 46 chromosomes in each cell. In 1p36 deletion syndrome, the end of the short arm of one of the two chromosome 1s has been lost. Breakpoints differ, with most clustering between 1p36.13 and 1p36.33, so people have different-sized pieces of chromosome missing. The deletion in some people is 10 times larger than in others. In general children with larger deletions with more genes missing are believed to be more severely affected, but there is no straightforward link between genes and effects. Indeed, one study found no correlation between the size of the deletion and the number of features that children had (6). Even children with small deletions can have most of the features of 1p36 deletion syndrome. However, it seems that for certain features, for example seizures and sensorineural hearing loss, a larger deletion appears to cause more severe effects (10).

restraints or a chewable object attached to their child's clothes to be helpful. Head banging and hitting their own head is less common. Parents suggest that these traits may be linked to a high pain threshold. There have been some reports of autistic behaviours in children with 1p36 deletion syndrome, although this is rare among Unique families with only one of the surveyed children diagnosed with autism (1, 5, U).

Many parents report that children with challenging behaviour have responded well to standard discipline techniques such as ignoring unwanted behaviour and rewarding them with cuddles and attention when they stop. Other parents explain that keeping a daily routine where the child understands what happens and when can help children to feel safe and secure (U).

“Shaunna is a complete joy! She asks for nothing except to be loved and hugged”
- 18 months

“Ameeliah is a very happy little girl who is very strong and is proving everyone wrong”
- 2 years, 4 months

“Robbie is very loving and cuddly. Everyone who meets him loves him straight away. He is warm and sociable and makes everyone laugh” - 3½ years

“Sophie loves music of any kind, playing with her dog and horses. She is very demanding. She will bite and has in the past self-harmed (by head butting cot). She is generally a very good natured girl and rarely cries or whines. She can be clumsy when tired. Exceptionally shy when meeting new people and hates change. Very much likes routine” - 3 years, 8 months

“Matthew is generally happy, but needs to be kept in a happy atmosphere. If he gets upset, it is hard to bring him round” - 4½ years

“Sophia can be stroppy and used to get quite violent before she could express herself with language. Much happier now than as a baby or toddler” - 6½ years

“Patrick loves TV, cooking, mowing the lawn and hoovering and he is now beginning to cuddle. But he has challenging behaviour especially when out or in the car. He often refuses to do as asked and reacts aggressively by hitting, pinching or kicking other people. Very active” - 10 years

“Holly is a very good girl and doesn't have any behavioural problems” - 11 years

“Megan can be very shy with people she doesn't know. She can exhibit some very challenging behaviour when she doesn't get her own way and can be overly affectionate at times” - 11½ years

Sleep problems

Some children with 1p36 deletion syndrome have sleep problems. The most common is multiple wakings during the night, but most children are able to fall back to sleep on their own. However, some children find it extremely hard to settle themselves and are up for long periods during the night. Sleep medication is used in some cases. Children and adults for whom disturbed nights are common will often need to nap during the day. Night-time seizures can also cause sleep disturbances (U).

How might 1p36 deletion affect my child's ability to communicate?

Among Unique families, babies first smiled between one and 15 months; the average age was just over four months. Many children with a 1p36 deletion are skilful communicators of emotion, using expression, vocal noises, gestures and body movements as well as copying the actions of others. For example, an open mouth for a kiss, open arms for a cuddle, rotating the body to show unhappiness, pointing and gesturing. Children show emotions by laughing, giggling, squealing, screaming, wailing or whining.

Delayed or absent speech has been reported in 98 per cent of children. From around 3 years, some master a signing system, although for those with persistent hypotonia this can be difficult. Some children use a few words, and a minority of children may develop some complex speech. Speech and language therapy has helped some children enormously. Three of the 25 Unique children surveyed can make simple three or four word sentences.

For many children, receptive language is markedly better than their expressive language skills – they understand far more than they are able to express (6, 7, 8, U).



3 years



3½ years

“Chloe communicates by looking and pulling things towards her when she wants something and pushing away when she's had enough. By vocalising she can tell us when she's cross or upset. She giggles and shrieks with delight when she is happy” - 4 years

“Helen has no difficulty communicating her needs, wants and emotions because of her ability to sign” - 4½ years

“Megan can speak in sentences. Not everyone would understand her and at times we (her parents) have difficulty. However, she can make her needs clear. At times she still uses signs” - 11½ years

How can a 1p36 deletion affect a child's development and mobility?

Babies with 1p36 deletion syndrome have a characteristic pattern of motor development. In their second year many start to roll, at first onto their side but eventually from back to stomach. Among 18 Unique babies, the average age at which rolling started was 13 months, with a range of six to 24 months. For most toddlers, rolling, twisting and wriggling remained the favourite way to move until they became strong enough to sit. Head control started to improve in the second and third years and some babies could pull to sit if supported. Sitting independently was achieved among Unique children at an average age of 24 months, with a range of 9 months to 5½ years. Most babies never crawl, typically rolling or bottom-shuffling instead. However, swimming is popular as well as therapeutic and many children swim and start other activities (such as adapted

activities (such as adapted horse riding) before they walk. Standing and walking are skills that children with 1p36 deletion syndrome find especially challenging, often despite years of practice and training in standing frames and walkers and using ankle/foot orthotics. But there is a great range in the age at which children start to walk – from one year, 5 months to eight years, with an average of three years and 10 months. Children often



4 years

continue to need help climbing stairs, getting in and out of bed and the bath. Once mobile, some children go on to run, climb, dance and even ski. However, walking may not prove possible for all. A small number do not master sitting unaided and require the use of special supportive seating. The floppiness (low muscle tone or hypotonia) that is one cause of this severe motor delay is usually obvious from birth, affects nine out of 10 babies, and gradually improves with age and physiotherapy. A number of families also reported a lack of balance in their children (5, U).

“Chloe’s no.1 favourite is time in the hydrotherapy pool” - 4 years

“Amy taught herself to sit using a rocking motion until she was upright” - 10 years

“Laura can sit, walk, run, dance, prance, and sit on a horse when led” - 20 years

Hand-eye co-ordination and dexterity (fine motor skills)

Fine motor skills can also be seriously affected, making holding objects such as toys, cutlery and cups very difficult. Achieving milestones such as holding a cup or spoon are therefore often delayed, with many children needing special cutlery and cups. Older children may find holding pencils and pens difficult. Poor fine motor skills can also make mastering sign language more challenging. Parents report that with occupational therapy and play activities these skills can improve significantly. Some of the Unique children, however, seem to be spared and have good fine motor skills, mastering finger feeding and other skills on a par with their friends and classmates.

“Ameeliah has excellent hand co-ordination. She finger feeds and uses a spoon and a beaker” - 2 years, 4 months

“Sophia’s fine motor skills were quite poor to start with, but after lots of work they are now quite good” - 6½ years

Appearance

Children with a 1p36 deletion have a distinctive, if subtle facial appearance: typically, a small head (microcephaly), large, rounded forehead (frontal bossing), a small, pointed chin, low set and unusually formed ears, eyes set in well defined sockets under straight eyebrows and a flat nasal bridge.



4 years

Digestive Disorders

Digestive conditions are not a recognised feature of 1p36 deletions, but one child developed pyloric stenosis (an obstructed outlet from stomach to intestines) which can be corrected with an operation, and one has Crohn’s disease (an inflammatory disease of the intestines). However, many of the Unique children suffer from constipation (see [Growth and Feeding](#)) (U).

Hands and feet

Small hands and feet are common in children with 1p36 deletion syndrome. A number of other hand anomalies have been described including one or both hands with a single palm crease (instead of the usual two), fingers and/or toes with either one crease or three creases (instead of the usual two), and incurving fingers (clinodactyly), most frequently the 5th finger. Some families reported clenched fists in young children, which can be a sign of neurological compromise or damage. Daily exercises and sensory play proved successful in helping the hands to open. Unusual features affecting the feet have also been reported, including flat feet, talipes (clubbed feet) and overlapping toes. A number of children wear supportive footwear, orthotics or splints to help overcome these problems (5, U).

Palate

Cleft palate or lip has been reported variously in between five and 17 per cent of children. Likewise, five per cent of Unique children surveyed had a cleft lip/palate which was repaired surgically. More common in the Unique survey was a high palate which affected 32 per cent of children. Both cleft and high palates can contribute to the early feeding difficulties seen in children. A high palate may make speech and making the sounds of speech more difficult (4, 5, U).

Behaviour

In general, children with a 1p36 deletion are placid and affectionate. However, they are as vulnerable to frustration as other children with a communication difficulty and temper tantrums and aggression can present carers with challenges. Behavioural problems have been reported in as many as 50 per cent of children and the evidence from Unique seems to back up this figure (5, 8, U).

The behavioural issues are wide-ranging. A number of children are extremely shy in new situations and have difficulty making eye contact, especially with people they don’t know. Conversely, others can be overly affectionate, including with strangers (U).

Evidence from Unique suggests that sensory difficulties can be problematic for some children. This can be tactile defensiveness, where children are sensitive to touch (with some children finding it hard to have their hands and/or feet touched or their hair washed and brushed) or sensitivity to certain textures. Occupational therapy can be extremely beneficial for those with tactile defensiveness, with some families using a therapy of brushing the skin with a surgical brush (U).

Some children go through a long phase of chewing or biting their own hands, arms and wrists, and occasionally other people’s, usually when in pain, tired, frustrated or frightened but on occasion for no obvious reason. This can be hard to stop without actual physical intervention, although some parents have found arm splints that act as

■ Spine

Children with marked hypotonia are sometimes prone to develop a spinal curve, such as kyphosis (forwards curve) or scoliosis (sideways curve). The literature reports scoliosis in 16 per cent of children, whereas in the Unique survey 30 per cent of children had spinal curvature. A small number have needed surgery to correct the curvature, whereas for others posture management such as a spinal brace or jacket, good seating and a sleep system (a special bed which offers support for the spine and keeps the child in a good position during sleep) have been necessary. Physiotherapy has also been effective for some children (4, 5, U).

■ Thyroid

Studies have indicated that around one child in five has been found to have a low thyroid hormone level (hypothyroidism) and to need thyroxine replacement and it is suggested that all children should be monitored for thyroid function. However, the Unique experience is that while many children are monitored for thyroid activity, only one of the 25 surveyed children has been found to have hypothyroidism (5, 6, U).

■ Genital area

A variety of genitourinary disorders have been reported. Minor anomalies of the genitals are common in babies with chromosome disorders, most often affecting boys. According to one report, 25 per cent of children with 1p36 deletions are affected, having problems such as undescended testes (cryptorchidism), and underdeveloped scrotum and genitalia in boys. The Unique survey revealed that 50 per cent of boys have small genitals and 38 per cent have undescended testes (which can be brought down by a straightforward surgical procedure).

■ Puberty

There are very few reports on adolescents, but it seems that in either sex puberty may start early. Other reports suggest that some children never become fully sexually mature adults. Amongst the Unique families, puberty took place in girls most often between the ages of 9 and 11 years (1, 5, 7, U).

■ Kidneys

A few children have been reported with kidney defects. Among Unique members these include kidney reflux, a single kidney, an accumulation of calcium in one kidney and kidney stones (5, U).

■ Infections

Two thirds of Unique's children with a 1p36 deletion suffer from recurrent infections whose range and nature suggest some degree of immune compromise. Fourteen children have had repeated pneumonias and four contracted meningitis. Chest infections, colds and gastroenteritis are all common, often longer lasting than in typically developing children. However, many families report that as children get older (over the age of 4 or 5 years) they are no longer as susceptible to infections and are in good general health (U).

“ He has a permanently snotty nose during winter. It takes him a long time to get over infections. As he gets older and stronger, he appears to be in better health ” - 3½ years

Growth and Feeding

Some children, but not all, are very small for their age. Some babies are born short and grow slowly so that small size can be a marked feature of a 1p36 deletion (U).

Feeding problems are common in newborn babies. Two-thirds of babies in one study either sucked too weakly to meet their nutritional needs or had difficulties co-ordinating sucking with swallowing. Swallowing studies have shown dysfunction in almost three quarters of babies and swallowing difficulties and choking mean that both breast or bottle feeds can take a long time (10). Fourteen of the 25 mothers surveyed by Unique attempted breastfeeding but due to the difficulties encountered only five succeeded, although a number of parents fed their children expressed breast milk with a spoon or bottle. Some babies have benefited from a temporary nasogastric (NG-tube, passed up the nose and down the throat) or gastrostomy tube (a G-tube, feeding direct into the stomach). Gastro-oesophageal reflux (in which feeds return readily up the food passage) and vomiting are also common in babies and young children. In the Unique survey, over 70 per cent of babies had reflux. Feed thickeners and prescribed medicines to inhibit gastric acid may control reflux but some babies benefit from a fundoplication, a surgical operation to improve the valve action between the stomach and food passage (U).

Among Unique members, many feeding problems eased by the second year, with babies typically eating mashed and pureed food, although weak sucking and swallowing difficulties continued to create problems with drinking (U).

Sixty-one per cent of Unique families surveyed reported constipation, occasionally very severe. Apart from standard prescribed and/or over-the-counter laxatives, one family reported success with adding ground linseed to food. Others have found dietary changes such as increased fibre and wholegrain intake and reducing dairy intake to be successful. One family supplements their child's diet with mineral oil and another with one tablespoon per day of olive oil. Any dietary changes should be undertaken with the support and guidance of a dietician (U).

Conversely, some children (around 20 per cent in the Unique survey) develop hyperphagia (an abnormally increased appetite) and may become obese (1, U).

“ Megan has always been in the bottom 10 centile for height and, since the age of about 4, has been in the top percentile for weight ” - 11½ years

What are the medical concerns?

Children with 1p36 deletions have a variety of treatable medical problems. Left untreated, these can compound the child's difficulties.

■ Heart

Studies suggest that heart (cardiac) problems occur in around 44 per cent of children. Approximately 30 per cent of the heart problems were cardiomyopathy, where the heart is enlarged and doesn't pump as strongly as it should, and around 70 per cent had structural defects. Cardiomyopathy may require medication but may also gradually improve over time. In the Unique survey, 54 per cent of children had cardiac problems. Most cardiac problems are comparatively minor and resolve either on their own or with medical treatment, without surgery. The most frequent problems are persistence of prenatal cardiac structures - patent foramen ovale (PFO) or patent ductus arteriosus

(PDA). For around half of those Unique children with PDA, the defect corrected itself within several months of birth. For the remainder, the PDA was closed either by surgical ligation (where the open channel is closed either with stitches or cut and cauterised) or by cardiac catheterisation (where a coil or plug, deployed using a catheter, is used to block the bloodflow). Atrial septal defect (ASD) and ventricular septal defect (VSD) are also common, with the holes often closing themselves without surgical intervention. Also reported by Unique families and in the published literature are Ebstein's anomaly (reported in two Unique children) and Fallot's tetralogy (in one Unique child). (5, 6, U).



11½ years

Some terms explained:

Patent foramen ovale Opening between the two upper chambers of the heart does not close soon after birth, as expected

Patent ductus arteriosus Failure of the ductus arteriosus (channel between the aorta and the pulmonary artery that takes blood to the lungs) to close

Atrial septal defect There is a hole in the muscular wall between the two filling parts of the heart (atria)

Ventricular septal defect There is a hole in the wall between the two pumping chambers of the heart (ventricles)

Ebstein's anomaly Congenital heart defect affecting the right side of the heart. The tricuspid valve that controls blood flow from the top chamber (atrium) to the bottom (ventricle) is too low down. This makes the top chamber too big and the bottom chamber too small. The valve may also be leaky, letting blood that should be in the ventricle leak back into the atrium

Fallot's tetralogy Two chief things: the artery that takes the blood to the lungs has an unusually narrow entrance (pulmonary stenosis), and there is also a ventricular septal defect (VSD)

■ Hearing

Hearing loss affects around two thirds of people with 1p36 deletion syndrome. It can vary from mild loss at various frequencies to severe loss at all frequencies. There is evidence that the loss is progressive in some children, so an annual hearing check is recommended. The hearing loss can be sensorineural (caused by damage to the inner ear or to the nerve used for hearing) or conductive (associated with the function of the outer or middle ear). Sensorineural hearing loss is permanent and is usually treated with hearing aids, or for those more severely affected, cochlear implants. The conductive hearing loss is temporary and due to glue ear (a build up of fluid in the middle ear). Glue ear resolves itself as children get older and the ear tubes widen resulting in improved drainage of the middle ear. However, while glue ear persists, many children will need grommets (a small ventilation tube) inserted into the ear. Alternatively, hearing aids may be used for the duration of the glue ear. Among Unique families, eight out of 14 children with hearing loss had conductive deafness (4, U).

■ Vision

Vision problems are very common and variable. Around 80 per cent of children have been found to have some vision defect. The problems can be due to the structure and function of the eyes, or problems with the brain processing the information received from the eyes. In the Unique survey, the most common problem affecting the eye itself was strabismus (squint), affecting around half of the children. Other eye problems that have been found include optic disc atrophy, short or long sightedness, nystagmus, photosensitivity (photophobia), cataracts and astigmatism. Glasses can help or correct a number of these problems, and for those with photosensitivity, photochromic glasses have helped enormously. In addition to problems with the eye itself, some children suffer from cortical visual impairment, where the visual systems of the brain do not consistently understand or interpret what the eyes see. Whatever the cause of the vision impairment, the problems can be severe; one of the 25 Unique children is registered partially sighted, and one is registered blind. In addition, recent reports suggest that between half and two thirds of children are visually inattentive and unable to fix or follow movements (5, 6, U).

Some terms explained:

Optic disc atrophy The optic disc is the part of the optic nerve that exists at the back of the eyeball, carrying information from the retina, the photographic film of the eye, to the brain. In optic disc atrophy, it is pale or has undergone some sort of degenerative change

Strabismus is a squint or lazy eye. The crossed eye can look inwards, outwards, up or down

Amblyopia Reduced vision (usually in a lazy eye). For many possible reasons, the brain prefers one eye, reducing the vision in the other eye

Nystagmus Rapid involuntary (wobbly) eye movements

Photosensitivity/photophobia Excessive sensitivity or intolerance to light

Astigmatism The cornea (the clear cover over the iris and pupil) is abnormally curved. The effect on vision is to make objects appear blurred. Sometimes the brain can compensate for astigmatism although it may be too strong for this to happen without the aid of glasses

■ Seizures

Seizures affect around half to three quarters of all the children. Onset of seizures ranged in the Unique survey from birth to 3 years (the medical literature cites seizures starting from 4 days of age to 7 years). Some families report just one or two seizures in babies that never recur. For most children the seizures are relatively well controlled with medication. There are some children, however, for whom their epilepsy is extremely difficult to control, despite multiple medications. In two of the Unique families, the seizures evolved into Lennox-Gastaut syndrome, an uncommon form of epilepsy that is difficult to treat. With the support of their child's neurologist, some parents have tried alternative approaches such as a ketogenic diet (high fat, low protein and carbohydrate, only to be followed under medical supervision), vitamin B6 supplements and homeopathic remedies (5, 9, U).