

## Support and Information



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# 16q deletions

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 David Callen, Department of Medicine, Hanson Institute, University of Adelaide, Australia, and by Professor Maj Hultén BSc PhD MD FRCPATH, Professor of Reproductive Genetics, University of Warwick, UK 2007. Revised 06/2009; 09/2011. (PM)

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## Sources and references

The information in this leaflet is drawn partly from the published medical literature. The first-named author and publication date are given to allow you to look for the abstracts or original articles on the internet in PubMed. If you wish, you can obtain abstracts and articles from *Unique*. The leaflet also draws on *Unique*'s database. When this leaflet was revised in 2009, *Unique* had 21 members with a chromosome 16q deletion, of whom 120 had a pure 16q deletion with no other chromosome involved. Seven families completed a detailed questionnaire in 2006.

## 16q deletions

A chromosome 16 deletion is a rare genetic condition in which part of the genetic material is missing that makes up chromosome 16, one of the body's 46 chromosomes. Like most other chromosome disorders, this increases the risk of birth defects, developmental delay and learning difficulties. However, the likelihood of problems developing depends very much on what chromosome material is missing.

Chromosomes are the microscopically small structures in the nucleus of the body's cells that carry genetic information. Apart from the sex chromosomes (two Xs for a girl and an X and a Y for a boy), chromosomes are numbered 1 to 22 in pairs, roughly from largest to smallest. Each chromosome has a short (p) and a long (q) arm, so a 16q deletion means that material has been lost from the long arm. A large 16q deletion can also be called **monosomy 16q**.

The part of the arm that is close to the centromere, where the short and long arms meet, is called the **proximal** part and when material is lost from this area it is called a proximal deletion. When the deletion is closer to the end of the chromosome, it is termed **distal**. When there are two breakpoints that have rejoined, leaving a segment out, the deletion is called **interstitial**.

Where there is just one breakpoint before the end of the chromosome, the deletion is described as **terminal**, meaning that the end of the arm has been lost. Very small deletions from near the end of the arm of the chromosome are called **subtelomeric deletions**.

Your geneticist or genetic counsellor can tell you more about how much material has been lost. You will almost certainly be given a **karyotype**, a shorthand notation for your child's chromosome make-up, which will show the breakpoints in chromosome 16. Comparing your child's karyotype with others, both in the medical literature and within *Unique*, will help to build up a general picture of what to expect. But there will still be differences, sometimes quite marked, between your child and others with apparently similar karyotypes. It is very important to see your child as an individual and not to make direct comparisons with others with the same karyotype. After all, each of us is unique.

### ■ Cleft

Two babies were born with a cleft palate (a split in the roof of the mouth) and in one, the lip was split as well. A cleft lip and palate can be surgically reconstructed and feeding support is given in the meantime.

### ■ Joints and limbs

One *Unique* member developed an evolving spastic diplegia in early childhood, in which the muscles in all four limbs but mostly in the legs are constantly tense. Physiotherapy and serial casting have helped to control the tendency to toe-walk.

## Eyes and vision

Most youngsters have good eyesight and a normal eye structure. In two children a developmental defect known as a coloboma of the iris has been observed, giving the iris a keyhole-like appearance. In one child, cataracts formed on both eyes and comparison with a child with a ring 16 chromosome who also had cataracts has led to a suggestion of a cataract gene close to the end of 16q (He 2002).

## Sitting, moving: gross motor and fine skills

Children are likely to sit and become mobile later than typically developing children but with opportunity and where necessary physiotherapy and support, most are eventually successful. Underlying the delay in mobility is a frequent finding of low muscle tone (hypotonia). Additionally, there is some evidence that at least some children develop a stiffness in certain joints that further limits their mobility. The range of ages at which children first walked was between 16 months and six years.

Children are likely to need support learning the hand-eye coordination and control they need to feed themselves, to hold a bottle and to play with toys, as well as later to dress and write.

## Learning

Children will usually need support with their learning, but the extent is fairly varied. While the extent of delay in some children is considerable, others have only a moderate learning difficulty and are able to write their name. Where IQ has been characterized, it has been around 59, suggesting ability at the lower end of a mild disability. This appears to be particularly true where the deletion is more distal, covering band 16q23.

*She can write her name and draw a basic person ” - 16q22.2q23.2 deletion, age 7*

## Speech and communication

Speech appears to be delayed in line with a child's learning disability. After an initial delay, words have first emerged between one and three years and progress to two-word phrases and short phrases has been steady, if slow so that children starting school are speaking in short phrases. Difficulties with articulation are likely to persist, sometimes making understanding outside a small group of familiar people difficult. Regular speech and language therapy is helpful.

## Behaviour

There is not enough evidence to suggest a specific pattern of behaviour. Children with autistic-like behaviour or unusual behaviour under stress have been reported, but not within *Unique*.



suture. Where the deletion is close to the end of 16q, the forehead may instead be broad. In order of frequency, the other typical facial features are upslanting eyes, ears that are either prominent, have a crumpled top or other unusual folding pattern and may be low set or oddly rotated; a broad, flat bridge to the nose; a large soft spot on the top of the head (anterior fontanelle) that may be slow to close; a short neck; widely spaced and sometimes deepset eyes.

### Hands and feet

Minor, usually non-functional anomalies of the hands and feet are relatively common in children with chromosome disorders. The most common feature seen in this group are fingers held in a bent position.

Unusual features seen in the feet include broad big toes and overlapping toes. The foot may be held at an unusual angle and club foot (talipes) requiring correction by physiotherapy, casting and sometimes surgery is fairly common. In one baby the soles of the feet were curved like the underside of a rocker.

## Medical concerns

### Heart

Most babies and children have a healthily functioning heart. In a small number of babies, a heart defect has been found but there has been little similarity between the problems. In one child a hole was found between the two lower chambers (a ventricular septal defect/ VSD); one baby had pulmonary atresia (a missing or blocked valve at the entrance to the pulmonary artery that blocks blood flow to the lungs. The blood cannot be pumped to the lungs from the right ventricle as it should); another had aortic stenosis (obstruction to blood flow from the left ventricle to the aorta) and Wolff Parkinson White syndrome (an abnormal heart rhythm caused by an extra conduction pathway between the upper and lower chambers of the heart). In another baby, there was coarctation of aorta, a narrowing of the main blood vessel leaving the heart to take oxygen-rich blood to the body.

In general, babies born with a heart condition have not fared as well as babies born with a healthy heart and where babies have died, this has occurred almost exclusively among those with a heart condition.

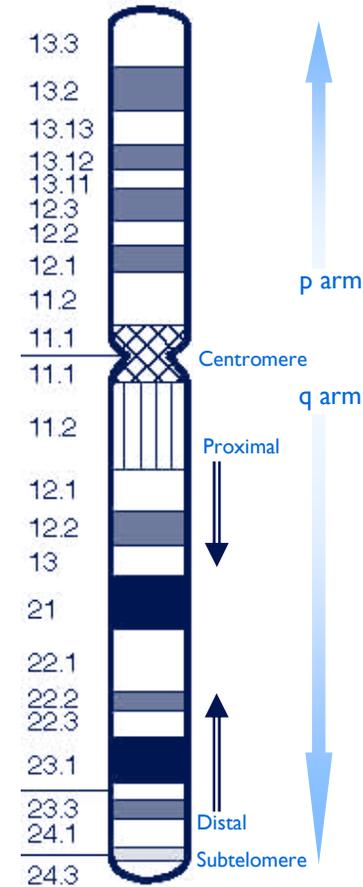
### Minor genital anomalies

Children with chromosome disorders, in particular boys, are more liable to be born with minor genital anomalies than other children. In this group, 2/4 boys had testicles undescended at birth. The testes descend during fetal life from a position just below the kidneys at the back of the abdomen. If one or both testicles remain undescended, a decision will be taken whether to bring them down surgically.

### Kidneys

Most children have been born with perfectly normal kidneys. In one child one kidney was missing and a further baby had unspecified kidney anomalies.

## How did the deletion arise?



Chromosome 16

Some 16q deletions occur out of the blue. The genetic term for this is *de novo* (*dn*). Others are the result of a rearrangement in one parent's chromosomes. A blood test to check the parents' chromosomes will show what the situation is.

*De novo* 16q deletions are caused by a mistake that occurs when the parents' sperm or egg cells are formed. When egg and sperm cells are formed, the two members of each pair of chromosomes normally line up together and then break and recombine to create new chromosomes that contain different combinations of the genes transmitted by the grandparents to the parents of the child. The recombining can occasionally take place between the wrong broken ends, and you can imagine how this could lead to a 16q deletion, but this is still a theory as nobody has ever seen it happen.

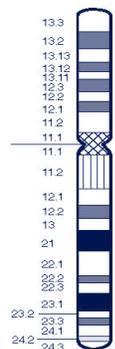
Recombining is part of a natural process and as a parent there is nothing you can do to change or control it. Children from all parts of the world and from all types of background have 16q deletions. No environmental, dietary or lifestyle factors are known to cause them. So there is nothing that either parent did before or during pregnancy that caused the deletion and equally nothing could have been done to prevent it.

## Could it happen again?

The possibility that a couple will have another pregnancy affected by a 16q deletion depends on their chromosomes. If both parents have normal chromosomes, the 16q deletion in the child has in all probability occurred as a chance event, in which case the child's karyotype will be marked *de novo* or *dn*. It is then very unlikely to happen again.

If a test shows that either parent has a chromosome rearrangement involving 16q, the chances of further affected pregnancies with similar or occasionally different abnormalities are high. Once the family translocation has been characterised, it will be possible to diagnose an unbalanced chromosome arrangement prenatally. Other family members should also be tested in case they, too, are carriers of the balanced form of the rearrangement. A clinical geneticist or genetic counsellor will give precise guidance.

## Proximal deletions between 16q11 and 16q13



The region of 16q near the centromere known as 16q11 contains only genetically inactive material. Losses from this region are not expected to have any effect on the individual. Deletions with an effect only start from band 16q12.1. Deletions vary in size and the advent of sensitive molecular ways of looking at chromosomes has led to the identification of tiny microdeletions, with the possible emergence of a new microdeletion syndrome at 16q11.2q12.2. The oldest person described was 18 years old (Ballif 2008; Borozdin 2006; Doco-Fenzy 1994; Callen 1993; Schuffenhauer 1992; Krauss 1987; Hoo 1985; Elder 1984; *Unique*).

The **red line** shows roughly where the deletion is.

Pages with **red bars** by the page number are about proximal deletions.

## Pregnancy and birth



**One month old**

Three out of eight pregnancies were considered completely normal; in the fourth, there was spotting and decreased fetal movement; in the fifth, severe cramping started at 25 weeks but resolved of its own accord; in the sixth, the baby's growth rate tailed off at 35 weeks; in another, slight spotting occurred in the seventh month; and in the eighth the baby was noted to be small by mid-pregnancy. Twin girls, each with the 16q deletion, were born at

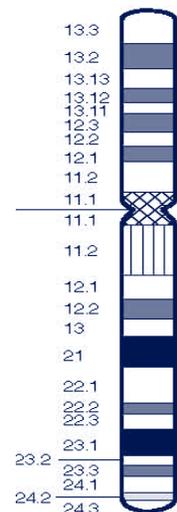
35 weeks. Babies born between 36 and 42 weeks weighed between 3.345kg (7lb 6oz) and 2.1kg (4lb 10oz). The two heaviest babies were *Unique* members; there may therefore be under-reporting of babies with a normal weight. While one baby was slow to cry and breathe, most others were in good condition, although some were unusually floppy due to hypotonia (low muscle tone).

## Feeding

Many babies with a proximal 16q deletion have had marked initial feeding difficulties. An inability to suck as well as uncoordinated swallowing have led to great difficulties putting on weight. Failure to thrive is common. Reflux (return of the stomach contents up the food passage) is very common and brings with it a risk of inflammation of the food passage (oesophagitis) and inhalation of feeds. While mild reflux may be controlled by careful feeding in an upright position, sleeping with the head end of the cot or bed raised and if necessary with medication, surgery may be needed to improve the action of the valve between the food passage and the stomach. The most common operation for this is a Nissen fundoplication. Some babies have been fed successfully directly into the stomach through a tube (a gastrostomy). High-energy milks help to maintain calorie intake.

Although this picture of ongoing feeding difficulty is common, and in one child continued to difficulties handling different food textures, it is not universal; at least one *Unique* member has fed normally from birth and as a teenager eats a reasonably normal variety of foods.

## Distal interstitial deletions between 16q21 and 16q24



The information on this group is drawn from a group of around thirteen cases described in the medical literature, as well as a *Unique* member. The deletions vary in size with the proximal breakpoint between 16q21 and 16q23.1 and the distal breakpoint between 16q22.1 and 16q24.2. Generally speaking, where the deletion is more distal, children have been less severely affected (Monaghan 1997; Werner 1997; Callen 1993; Fujiwara 1992; Natt 1989; Cooke 1987; McDonald 1987; Natt 1987; Rivera 1985; Fryns 1977; *Unique*).

The **purple line** shows roughly where the deletion is. Pages with **purple bars** by the page numbers are about distal deletions.

## Pregnancy and birth

Pregnancy has rarely been described but where it has, it has appeared to be generally normal, although in one case there was excess amniotic fluid and two babies were born prematurely, one in fetal distress. Babies have been delivered between 34 and 41 weeks, with most babies born at term. Birth weights at term have been low, although the range has been from 3.741kg (8lb 4oz) to 2kg (4lb 7oz).

## Feeding

It seems likely that many babies will need support with feeding in the early days after birth. Typically, a baby may not be able to suck strongly enough to meet their own nutritional needs and without active support, they may lose weight and be classified as 'failure to thrive' babies. Some babies have been fed initially by nasogastric tube.

*She wasn't interested in sucking, so the hospital 'forced' her to use a dummy while she slept to encourage a sucking action. She became interested in feeding at about four weeks and was then bottle fed " - 16q22.2q23.2 deletion*

## Growth

Children with a distal interstitial deletion may be short or average for their age. While many babies fail to thrive and are short for their age, height and growth in others with a 16q22q23 deletion has been recorded as average.

## Appearance

There may be little sign in the appearance of a baby or child of the underlying disorder although doctors may notice 'dysmorphic features'.

The most typical feature is a prominent and usually high forehead on which you may see a vertical central ridge marking the fusion of the seam known as the metopic

## Outlook

A child's outlook depends largely on their clinical problems. Children without major organ abnormalities have reached adulthood while those who died had complex heart anomalies.

## Hearing

In most of the reports in the medical literature, no information was collected on hearing. However, two *Unique* members have a hearing impairment requiring aids and a profound permanent deafness has been observed in at least one other child.

## Eyesight

Information on vision has not been collected consistently. In two people a squint (strabismus) has been observed; in one, an astigmatism; and in a 21 year-old cataracts.

## Sitting, moving: gross motor skills



Children are likely to sit and to become mobile later than typically developing children but with opportunity, physiotherapy and support, most do eventually walk. There is considerable variation between children, but mobility tends to remain restricted. Underlying some of the mobility problems is low muscle tone (hypotonia), as well as the joint problems already described. The range of ages at which babies first rolled over was five to 20 months; sitting has been achieved between nine months and three years; walking between 28 months and six years. Most children have needed support and regular input from physiotherapy to make these achievements.

## Using their hands: fine motor and coordination skills

Children are also likely to need support learning the hand-eye coordination and control they need to feed themselves, to hold a bottle and to play with toys, as well as later to help with dressing.

## Learning

Children will usually need support with their learning, and they may need considerable support. Individuals will vary, but the evidence from *Unique* and the medical literature suggests that a severe learning disability is most typical and special education is usually appropriate.

“ He can use switches and likes to play on a keyboard making sounds. He has a very good memory. His strengths are his ability to learn from observation and problem solving for his own ends ” – 17 years

## Speech and communication

Speech appears to be delayed in line with a child's learning disability, so there will be marked variation between individuals. While some children have been using words and speech from the age of three years, this is not possible for all. Other youngsters rely on a range of means to communicate their needs and wishes, including gesture, vocal noises, facial expression and assistive communicative devices.

## Growth

A typical baby is small for dates and where height has been recorded later, children have usually been short for their age and sometimes extremely short. However, children have usually been proportionately small – ‘harmonious’ – and shown a steady, if slow gain in weight and height. One *Unique* member with a deletion from 16q11.2 to q13 is a teenager of average height and build; he was one of the heaviest babies in this group at birth. A 13-year-old was also of average height for his age.

## Appearance

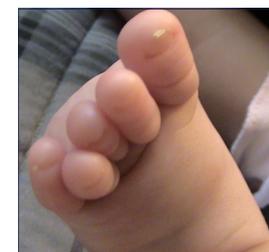
There may be little sign in the appearance of a newborn baby of the underlying disorder. Doctors may notice what are known as ‘dysmorphic features’ which may or may not be obvious to a parent. Most of these are facial features of no consequence to the baby.

The most typical features in babies and young children include prominent ears that may also be set low on the side of the head and may have an odd shape, most typically with a crumpled top or other abnormal folding; a high or prominent forehead on which a vertical ridge may be visible in the centre (metopic ridge); a short neck that may be broad; a flat, wide nasal bridge; slanted eyes, more often upwards than downwards; a small chin and lower jaw that may be set back against the upper jaw, giving the face a triangular appearance; a large soft spot (anterior fontanelle) that is slow to close.

In *Unique's* experience the only unusual facial feature which parents sought to correct was prominent ears. In two *Unique* children odd-shaped ears were the only unusual facial feature.

## Hands and feet

Minor, non-functional anomalies of the hands and feet are relatively common in children with chromosome disorders. Some typical features are unusually short fingers or an incurved fifth finger. In children and adolescents with a proximal 16q deletion, thumbs with a third joint have been seen, as well as an extra finger and unusually long fingers. Typical anomalies of the feet include overlapping or webbed toes and a degree of malposition of the foot, requiring physiotherapy or casting and sometimes surgery to straighten it. Additionally, in this group, three children had very broad big toes, one had ‘rocker bottom’ feet (the soles were curved like a rocker), one had short big toes, two had a wide ‘sandal gap’ between the first and second toes and two had very long, narrow feet with long toes. One child has been described with one foot longer than the other; a child with a leg length difference of over two centimeters (an inch).



## Medical concerns

As a group, children with a proximal 16q deletion have been healthy and have not had major birth defects. However, one child with heart problems and severe failure to thrive died at the age of 18 months. One child with a deletion of 16q11.2q12.2 had a cleft palate.

### ■ Townes-Brocks syndrome

This syndrome (TBS) usually results from mutations in the *SALL1* gene at 16q12.1. The key features are thumbs with an extra joint, a closed anus, hearing loss (see below) and unusually formed ears. Occasionally, loss of the *SALL1* gene can cause features of TBS, although they appear to be milder than in cases caused by mutations. Where the deletion removes more than the *SALL1* gene, the risk increases that the deletion will have an impact on learning ability (Borozdin 2006).

### ■ Genitals

Children with chromosome disorders, in particular boys, are more liable to be born with minor genital anomalies than other children. In this group, every boy was affected and girls were not. Some boys had testicles that were undescended at birth. The testes descend during fetal life from a position just below the kidneys at the back of the abdomen to reach the scrotum, usually before birth. If one or both testicles remain undescended, a decision will be taken whether to bring them down surgically and anchor them in the scrotum. One boy had hypospadias, where the hole usually at the end of the penis is on the underside and one had chordee, where the penis curves downwards. Both of these conditions can be corrected surgically. Two boys were born with the anus placed further forward than normal (anterior anus). This does not usually require treatment although it does call for stricter hygiene than usual.

### ■ Hearing

Five children in this group are known to have had a degree of hearing impairment and in at least two children this was permanent, while a further child wore hearing aids. The most common cause of temporary hearing loss in young children is glue ear, caused by a build-up of fluid behind the ear drum, and treatable if necessary by inserting tiny tubes (grommets) into the tympanic membrane to equalise air pressure inside and outside the middle ear. Glue ear is at least as common in children with chromosome disorders as those without and it is particularly important to treat it.

### ■ Infections

Two *Unique* children have had frequent chest infections, leading to a diagnosis of asthma but there is no evidence that other infections are any more frequent than in other children. Children with a 16q deletion are especially vulnerable to chest infections because of the high rate of gastro oesophageal reflux, putting them at risk of inhaling part of their feeds and causing aspiration pneumonia.

### ■ Other concerns

Two sisters, each with a 16q deletion, each had small kidneys, but this has not been seen in other youngsters. One child was born with a hole between the lower chambers of the heart (VSD, ventricular septal defect) and one child had bicuspid instead of tricuspid valves at the exit points from the heart. This means that each valve had two flaps of tissue instead of three. Some people have this anomaly without it ever being diagnosed. It may not need treatment or surgical repair may become necessary. A child with a microdeletion at 16q12.1 was born with a hole between the two upper heart chambers and a patent ductus

Two babies with a 16q13q22 deletion were born with a single, small kidney or a single malfunctioning, cystic kidney.

### ■ Heart

Most babies and children have a healthily functioning heart. In a small number, a variety of heart problems has been found. In one child a hole was found between the two lower chambers (a ventricular septal defect/ VSD), which closed of its own accord. In another there was a VSD and a hole between the upper chambers, as well as an unusually formed valve. In two further babies, a complex developmental defect known as an atrioventricular canal (AV canal/AVC endocardial cushion defect) was found. In this condition, there is a large hole in the middle of the heart between the two upper chambers (atria), the two lower chambers (ventricles) and a single atrioventricular valve instead of two separate valves on either side of the heart. The large hole allows too much blood to flow to the lungs and needs surgical repair. Another child developed right heart failure at four months, which worsened until she died at 19 months.

### ■ Brain

The experience of *Unique* and in the medical literature is that the great majority of babies have normal, intact brain development. In two babies described in the medical literature, an enlargement of the fluid-filled ventricles within the brain has been seen and in one of these babies there was a defect in the skull, allowing the membranes encasing the brain and some of the brain tissue to protrude, while in the other there was an enlarged space between the membranes covering the brain within the skull. The defect was successfully surgically repaired.

### ■ Seizures

The experience of *Unique* and in the medical literature is that seizures are not typical and the great majority of babies and children have been seizure-free. Two babies have been described in the medical literature, in one case with generalised seizures from two months and in the other case a single seizure occurred at 18 months.

### ■ Hernias

In two boys an inguinal hernia (in the groin) occurred on one side or both. This involves part of the bowel protruding 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. This usually needs surgical repair, but is normally a small operation.

### ■ Limbs and joints

In some babies and children, certain joints may not have a full range of movement. Children have been observed to have knees and elbows that could not be fully straightened. In one *Unique* member, flexed knees were treated with injections of botulinum toxin to help to prevent permanent contraction of the joints.

Hip problems have been observed in two *Unique* members. In one, Perthes disease was diagnosed; this is an abnormality of the hip in which the ball and socket joint becomes irregular and flat after a temporary loss of blood flow. For treatment, stress on the hip is reduced but if the hip becomes too stiff or starts to come out of the socket, reconstructive surgery may be needed. Another child was kept under observation after one hip was found to be easily dislocatable. Another child had unusually lax joints.

marking the fusion of the seam known as the metopic suture, widely spaced eyes and sometimes a broad, flat bridge to the nose. Less commonly, the chin and lower jaw may be small and recessed, giving the face a triangular shape.

### Hands and feet

Minor, usually non-functional anomalies of the hands and feet are relatively common in children with chromosome disorders. There does not appear to be any particular pattern in this group, but unusual hand features seen include small hands, clubbed fingers (the fingers have a rounded end with no angle between the nail bed and the finger), bent or clenched fingers, a fifth finger with a missing joint, broad thumbs, an additional finger and a single palm crease.

Unusual features seen in the feet suggest a more recognisable pattern, with very broad big toes and overlapping of the other toes seen most often. Feet may also be small and the nails underdeveloped. Less commonly, two or more toes may be webbed. The feet may be held at an unusual angle.

Many of these features are cosmetic, but a range of treatments is available for positional abnormalities of the feet, including stretching, splinting, physiotherapy, casting and surgery.

### Medical concerns

The nature of the evidence about most youngsters with an interstitial 16q deletion makes it very difficult to be certain what the major medical concerns are for this group. Descriptions in medical journals are usually episodic and frequently describe babies, with scant or no information on later health.

#### ■ Minor genital anomalies

Children with chromosome disorders, in particular boys, are more liable to be born with minor genital anomalies than other children. In this group, five out of six boys were certainly affected. Most commonly, boys had testicles that were undescended at birth and one boy had a small scrotum. The testes descend during fetal life from a position just below the kidneys at the back of the abdomen to reach the scrotum, usually before birth. If one or both testicles remain undescended, a decision will be taken whether to bring them down surgically and anchor them in the scrotum.

Among both boys and girls, the anus may be sited unusually far forward and this was found in three babies. This does not usually cause problems, but in girls in particular especial care is needed with hygiene.

#### ■ Infections

The evidence from *Unique* and to a lesser extent from the medical literature is that children are very vulnerable to infection as babies and young children. There is no evidence of an underlying immune dysfunction, but the high rate of reflux (see **Feeding**) puts them at risk of developing chest infections.

#### ■ Kidneys and urinary tract

Most babies and children had two healthy, normally functioning kidneys. However, since a small number of babies have been born with a kidney anomaly, babies and children with an interstitial 16q deletion may expect the kidneys and urinary tract to be scanned.

arteriosus, left from fetal circulation, but both of these resolved before her first birthday. A six-year-old boy with a 16q12.1q12.2 deletion developed seizures but they were well controlled with medication. Both children were diagnosed with a low thyroid level but were effectively treated with thyroid replacement.

#### ■ Vision

Information on vision is not available in the published reports. Among *Unique* members, four had a squint (strabismus), one child had severe myopia (short sight), and one had an astigmatism (abnormal curve of the front of the eye).

### Sitting, moving: gross motor skills

Hypotonia (low muscle tone) is a significant feature of a proximal 16q deletion, may be apparent from birth and causes a delay in children becoming mobile. Typically, children's joints are extremely mobile, so they need supporting and even splinting in the early stages of learning to walk. Children are likely to reach their developmental milestones later than typically developing children but with opportunity and where necessary physiotherapy and support, it appears that most are eventually successful. The range of ages at which babies first rolled over was between six months and three years; typically, they walked around two years although a boy with a 16q11.2q13 deletion walked alone before his first birthday, a 26-month-old girl had not yet started to walk and a boy with a 16q12.1q12.2 microdeletion walked at three years.

### Using their hands: fine motor and co-ordination skills

The hypotonia that affects mobility also affects children's ability to use their hands to feed themselves, to dress and at school. Children are likely to need support learning the hand-eye co-ordination and control they need to feed themselves, hold a bottle and play with toys, as well as later to dress and write. The extent of delay appears quite variable, with two children achieving most self care tasks, albeit with delay, but this is not possible for all.

### Learning

Children with a proximal 16q deletion will usually need support with their learning, but the extent appears to be varied, ranging from a borderline or mild learning difficulty and inclusion in a mainstream (regular) school curriculum to more pronounced learning disabilities and special education. One child with a 16q12.1q13 deletion was reading and writing by the age of 6 and had age-appropriate computer skills. Another child with a small deletion within the 12.1 band is scoring at age-appropriate level at the age of five. Two children with a 16q12.1q12.2 microdeletion were assessed as having a moderate degree of delay. Another child with a 16q11.2q13 deletion was not reading but had savant general knowledge. Two children showed an excellent memory and one had evident musical talent, with perfect pitch and rhythm. A borderline learning difficulty can be harder to accommodate within the education system than a child with a more severe learning disability for whom special education is obviously needed. At least one *Unique* member has had many changes of educational setting in an attempt to find a suitable educational, social and behavioural placement.



“Very bright: understands most everything!”  
5 years

## Speech and communication

Speech appears to be delayed in line with a child's learning disability and the hypotonia that affects mobility will almost certainly affect the muscles of the mouth and face as well. The evidence from both the medical literature and *Unique* is that after an initial delay, during which some children benefit from learning to sign, first words often appear between two and four years and speech complexity steadily increases so that by school age speech is the child's main means of communication rather than signing, gesture or facial expression. One child with a small deletion in band 16q12.1 first started to talk at the age of five. At the same time, the gap between understanding and expression lessens, diminishing children's frustration at not being able to express themselves. Children appear to retain difficulties in making some of the sounds of speech and benefit from ongoing speech and language therapy.

The level of fluency suggested here may not be achievable for all children and one 13-year-old with a 16q12.1q12.2 microdeletion was not yet using words to communicate.

## Behaviour

There is no pattern of behaviour specific to proximal 16q deletions. If anything, children are described as socially adept. In the years before language becomes easier to manipulate, some children may be prone to tantrums and apparently immature behaviour, but once fluent language emerges, this behaviour usually fades. One child developed a range of challenging behaviours when exposed to a mainstream school environment and persisting social difficulties in relating to his classmates. A child with a 16q12.1q12.2 microdeletion was diagnosed with autism at the age of three and a half because of difficulties with social interaction and by 13 still was not speaking and had repeated, stereotypic behaviours.

“ People think that because he has a rare condition he must have a behaviour problem and treat him like he does. I have more of a problem with people's attitudes than with him. ”

## Independence

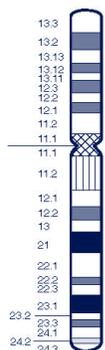
A girl of 15 years with a 16q11q12.1 deletion was able to carry out many aspects of personal care and household tasks. She was toilet trained at 2 years but at 15 years still wet the bed between one and three times a week.

## Interstitial deletions between 16q12 and 16q22

The information on this group is drawn from around 15 cases described in the medical literature, as well as four *Unique* members. Deletions vary in size with the proximal breakpoint at 16q12 to 16q13 and the distal breakpoint between 16q21 and 16q22.

The effects are extremely variable. Individuals and related family members with a deletion of band 16q21 between 16q13 and 16q22 have been described in which there was no apparent effect (Hand 2000; Callen 1993; Witt 1988) while others with an apparently similar deletion have been affected as described below (Hand 2000; Chen 1998; Callen 1993; Carter 1992; Edelhoff 1991; Casamassima 1990; Naritomi 1988; Witt 1988; Lin 1983; Fryns 1981; *Unique*).

The **green line** shows roughly where the deletion is. Pages with **green bars** by the page number are about deletions between 16q12 and 16q22.



## Pregnancy and birth

Pregnancy has rarely been described but has appeared to be generally normal, as has the baby's delivery. Babies have been delivered between 34 weeks and term and birth weights at term have been low, ranging from 3.06kg (6lb 12oz) to 2.73kg (6lb).

## Feeding

It seems likely that babies will usually need considerable support with feeding. At birth they may not be able to suck or to coordinate the actions of sucking, swallowing and breathing or to meet their own nutritional needs and they may need tube feeding or direct feeding with a gastrostomy. In some babies the feeding difficulties are heightened by the presence of a recessed lower jaw and in some cases by a split (cleft) in the roof of the mouth (palate). In one *Unique* member, feeding problems were exacerbated by a narrowing of the food passage, which required surgical correction. Even with feeding support, babies may grow very slowly and be marked as 'failure to thrive' babies.

Gastro oesophageal reflux (GORD, GERD), where the stomach contents return up the food pipe, may occur. Reflux raises a baby's risk of inhaling feeds and causing an infection in the lungs known as aspiration pneumonia. Reflux can be eased by careful semi-upright positioning during and after feeds, sleeping in a prescribed sleep chair rather than a bed, raising the head end of the baby's cot and if necessary by prescribed medication that helps to keep the feed within the stomach. Babies who have continuing problems can have a surgical procedure called a fundoplication to improve the action of the valve at the junction of the food pipe and stomach.

Where feeding and reflux problems are persistent, a gastrostomy tube (PEG, button) can be inserted to allow direct feeding into the stomach until the child is sufficiently mature to tolerate feeding by mouth. Constipation is also common and many children need to take daily laxatives.

## Growth

Typically, babies are born short and light and continue to grow slowly, with their weight and height at or below the lowest curves on a growth chart. In two cases, teenagers of 15 to 17 years have been as tall as 10 to 11-year-old children.

## Appearance

There may be little sign in the appearance of a baby or child of the underlying disorder. Doctors may notice what are known as 'dysmorphic features'; most of these are facial features of no consequence to the baby but they do help doctors to reach the correct diagnosis.

By far the most typical feature is an abnormality of the ears, which are either prominent, have a crumpled top or other unusual folding pattern and may be placed low on the sides of the head or oddly rotated. In order of frequency, the other typical facial features are a very short neck that may also be broad, a large soft spot on the top of the head (anterior fontanelle) that may be very slow to close, as may the seam between the bony plates of the skull, a high forehead on which you may see a vertical central ridge



**16q12.1q22 deletion:  
birth to 16 years**