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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 Veronica Mando, John Hopkins University, USA and by Professor Maj Hultén BSc, PhD, MD, FRCPath, Professor of Medical Genetics, University of Warwick, UK.
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10q deletions: breakpoints in 10q25 or 10q26

A 10q25 or 10q26 deletion means that the cells of the body have a small but variable amount of genetic material missing from one of their 46 chromosomes – chromosome 10. For healthy development, chromosomes should contain just the right amount of genetic material (DNA) – not too much and not too little. Like most other chromosome disorders, having parts of chromosome 10 missing may increase the risk of birth defects, developmental delay and learning difficulties. However, the problems vary and depend very much on what and how much genetic material is missing.

Background on Chromosomes

Chromosomes are structures found in the nucleus of the body’s cells. Every chromosome contains hundreds to thousands of genes which may be thought of as individual instruction booklets (or recipes) that contain all the genetic information telling the body how to develop, grow and function. Chromosomes (and genes) usually come in pairs with one half of each chromosome pair being inherited from each parent. Humans have 23 pairs of chromosomes for a total of 46 individual chromosomes. Of these 46 chromosomes, two are the sex chromosomes that determine gender. Females have two X chromosomes and males have one X chromosome and one Y chromosome. The remaining 44 chromosomes are grouped in 22 pairs, numbered 1 to 22 approximately from the largest to the smallest in size. Each chromosome has a short or petit (p) arm (shown at the top in the diagram opposite) and a long (q) arm (the bottom part of the chromosome).

Chromosome Deletions

A sperm cell from the father and an egg cell from the mother each carries just one copy of each chromosome. When they join together they form a single cell that now carries two copies of each chromosome. This cell must make many copies of itself (and all the chromosomes and genetic material) in order to make all of the many cells that form during human growth and development. Sometimes during the formation of the egg or sperm cells or during this complicated copying and replication process, parts of the chromosomes can break off or become arranged differently from usual.

People with a 10q25 or 10q26 deletion have one intact chromosome 10, but a piece from the long arm of the other

It is important to remember that while identifying the gene(s) responsible for certain features of 10q deletion syndrome is interesting and may help guide future studies, it does not lead directly to immediate improved treatment. Additionally, even if the supposedly responsible gene is missing it does not always mean that the associated feature(s) will be present. Other genetic and environmental factors often have a role in determining the presence or absence of a particular feature.

Why did this happen?

A blood test to check both parents’ chromosomes is needed to find out why the 10q25 or 10q26 deletion occurred. In the majority of cases the 10q25/6 deletion occurred when both parents have normal chromosomes. The term that geneticists use for this is de novo (dn) which means ‘new’. De novo 10q25 and 10q26 deletions are caused by a change that occurred when the parents’ sperm or egg cells formed or possibly during formation and copying of the early cells after the egg and sperm joined.

Some 10q25 and 10q26 deletions are accompanied by a gain of material from another chromosome and are often the result of a rearrangement in one parent’s chromosomes. This is usually a rearrangement known as a balanced translocation in which material has swapped places between chromosomes. As no genetically important material has been lost or gained, the parent usually has no clinical or developmental problems, although they may have difficulties with fertility or childbearing. Balanced translocations involving one or more chromosomes are not rare: one person in 500 has one, making a total world population of over 13 million balanced translocation carriers.

Whether the deletion is inherited or de novo, what is certain is that as a parent there is nothing you did to cause the 10q25/6 deletion and nothing you could have done would have prevented it from occurring in your baby. No environmental, dietary or lifestyle factors are known to cause these chromosome changes. No one is to blame when this occurs and nobody is at fault.

Can it happen again?

The possibility of having another pregnancy with a 10q25/6 deletion depends on the parents’ chromosomes. If both parents have normal chromosomes when their blood cells are tested, the deletion is very unlikely to happen again. However, if either parent has a chromosome rearrangement or deletion involving 10q25 or 10q26, the possibility is greatly increased of having other affected pregnancies.

Parents should have the opportunity to meet a genetic counsellor to discuss their specific recurrence risks and options for prenatal and preimplantation genetic diagnosis (PGD). PGD requires the use of in vitro fertilisation and embryo biopsy, and only healthy embryos are transferred to the mother’s uterus. If the parents choose to conceive naturally, prenatal diagnosis options include chorionic villus sampling (CVS) and amniocentesis to test the baby’s chromosomes. Testing is generally very accurate, although not all of these tests are available in all parts of the world.
deleted that included the region distal to D10S1679, suggesting that this region is responsible for cardiac anomalies. However, one boy who had ambiguous genitalia had a deletion that did not include this proposed critical region for genital development and the authors of this paper proposed a second critical region for genital development within 10q25.3q26.13. Therefore it has been proposed that there are two critical regions for genital development on the long arm of chromosome 10 (Ogata 2000; Mardo 2008).

There are a number of genes located on 10q25/6 which may be responsible for certain features of a 10q25/6 deletion, but for the moment are just candidate or potential genes and more studies need to be undertaken to establish what role, if any, they play. The characteristic facial features have been postulated to be due to the loss of the fibroblast growth factor receptor-2 (FGFR2). FGFR2 is also highly expressed in the fetal female ovaries although its function in the developing gonad is not yet known. The EMX2 gene maps to 10q26.1 and has been shown to be critical for central nervous system and urogenital function. Mice that are missing this gene show a complete absence of kidneys, ureters, gonads and genital tracts (Irving 2003; Mardo 2008).

FGFR2

EMX2

Critical Regions:

Genital development

Urinary development

Cardiac anomalies

Genital development

Looking at 10q

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 that look like horizontal stripes. Bands 10q25 and 10q26 contains around 29.7 million base pairs. This sounds like a lot, but it is actually quite small and is less than 1 per cent of the DNA in each cell. Base pairs are the chemicals in DNA that form the ends of the ‘rungs’ of its ladder-like structure. By looking at your child’s chromosomes in this way, it is possible to see the point (or points) where the chromosome has broken and to see what material is missing, if the missing piece is large enough. 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 a 10q25/6 deletion who have not yet been diagnosed. New, more sensitive, molecular techniques such as fluorescent in situ hybridisation (FISH) testing or array comparative genomic hybridisation (array-CGH) may be necessary to confirm or detect 10q25 or 10q26 deletions.

The vast majority of 10q25 and 10q26 deletions are terminal. This means that the tip of the long arm of chromosome 10 is included in the deletion. However, some deletions are interstitial. This is where a piece of the long arm of chromosome 10 is missing, but the tip (and possibly more than just the tip) is still present. In the diagram of chromosome 10 on the right the bands are numbered outwards starting from where the short and long arms meet (the centromere). A low number, as in q11 in the long arm, is close to the centromere. Regions closer to the centromere are called proximal. A higher number, as in q26, is closer to the end of the chromosome. Regions closer to the end of the chromosome are called distal. A distal deletion of 10q refers to a copy is missing or deleted. Although the exact numbers and types of genes that are affected by the deletion are often not known, since some genes are missing there can be effects on a person’s learning and physical development. Therefore it is believed that most of the clinical difficulties are probably caused by having only one copy (instead of the usual two) of a number of genes.

We are still learning about the specific jobs or functions of the genes in these regions. Also, it is important to keep in mind that a child’s other genes, environment and unique personality also help to determine future development, needs and achievements.

The first published description of a person with a 10q25 or 10q26 deletion was in 1978. There have since been over 60 cases reported in the medical literature worldwide. The deletion occurs in equal frequency in males and females (Lewandowski 1978).

bp = base pair
kb = kilobase pair or 1000 base pairs
Mb = megabase pair or 1 million base pairs
deletion in the long arm of chromosome 10 within the bands 10q25 or 10q26. Hereafter in this leaflet these deletions will be referred to 10q25/6 deletions. However, these deletions are sometimes also known as 10q deletion syndrome or 10qter syndrome.

Results of the chromosome test
Your geneticist or genetic counsellor will be able to tell you about the point where the chromosome has broken in your child. You will almost certainly be given a karyotype which is shorthand notation for their chromosome make-up. With a 10q25/6 deletion, the results are likely to read something like one of the following examples:

46,XX,del(10)(q25.3)dn
46 The total number of chromosomes in your child’s cells
XX The two sex chromosomes, XY for males; XX for females
del A deletion, or material is missing
[10] The deletion is from chromosome 10
[q25.3] The chromosome has one breakpoint in band 10q25.3, and material from this position to the end of the chromosome is missing
dn The deletion occurred de novo (or as a “new event”). The parents’ chromosomes have been checked and no deletion or other chromosome change has been found at 10q25.3. The deletion is very unlikely to be inherited and has almost certainly occurred for the first time in this family with this child

arr[hg19]10q26.2q26.3(129,634,839-135,506,703)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
10q26.2q26.3 Chromosome 10 has two breakpoints, one in band 10q26.2 and one in band 10q26.3
129,634,839-135,506,703 The base pairs between 129,634,839 and 135,506,703 have been shown to be deleted. Take the first long number from the second and you get 5,871,864 (5.88Mb or 588kb). 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 10 as expected

Most common features
Every person with a 10q25/6 deletion is unique and so each person will have different medical and developmental concerns. Additionally, no one person will have all of the features listed in this leaflet. However, a number of common features have emerged:

- Growth delay both in the womb and after birth
- Feeding difficulties
- Hypotonia (floppiness or unusually low muscle tone) in newborn babies
- Variable disabilities in learning and motor development. Children will often need

Ongoing research involving 10q25/6
The features of a 10q25/6 deletion are likely to be a result of the loss of a number of different genes found in this region. The size of the deleted region found in those with 10q25/6 deletions varies widely ranging from a small interstitial deletion to much larger ones. However, there is a wide variation of features, even within families where the same deletion is shared. There have been attempts to try to correlate the size of the 10q25/6 deletion with severity, but no strong correlation has been found.

Nonetheless a number of studies have attempted to correlate the size of the deletions and the presence or absence of certain features. A number of authors have suggested that a more proximal deletion of 10q leads to more significant congenital abnormalities, particularly where it involves 10q25 although this has not been substantiated by subsequent studies or data at Unique. One study suggested a correlation between the size of the deletion and the severity of growth retardation and presence of microcephaly, but this has been disputed by several other studies and evidence at Unique [Wulfberg 1989; Petersen 1998; Irving 2003; Courtens 2006; Unique].

However, the increasing use of molecular techniques such as FISH and array-CGH in the research laboratory enables more accurate definition of the breakpoints. This, in turn, enables researchers to study more accurately which parts of the chromosome are missing and attempt to correlate certain regions with the different clinical features of the condition. Indeed, a number of recent studies have attempted to correlate the clinical features in people with a 10q deletion with the part of the chromosome they have missing in order to define a critical region of 10q that is responsible for the features of 10q deletions, and to help to narrow down the regions and/or genes responsible.

Since behavioural problems seem to be a common feature affecting those with a 10q25/6 deletion a number of studies have attempted to identify the gene(s) responsible. One study observed hyperactivity in a person with a small terminal 10q deletion and this region contains four possible candidate genes for the behavioural problems: C-terminal binding protein 2 (CTBP2) which codes for two distinct proteins, one of which regulates the expression of other genes, the other of which is a component of synapses (junctions through which the neurons of the central nervous system signal to each other); adrenergic beta-1 receptor (ADRB1) which codes for a protein which mediates the physiological effects of adrenalin (a stress hormone); dihydropyrimidinase-like 4 (DPYSL4) which is thought to have a function in neuronal differentiation and Calcyan (or DRD1IP) which codes for a dopamine receptor-interacting protein, and dopamine, acting through receptors, acts as a transmitter in neural circuits which mediates learning and memory. However, there is a recent report of a girl with severe behavioural issues who did not have the genes CTBP2 or ADRB1 deleted. Further studies are needed to ascertain which, if any, of these genes play a part in the behavioural problems seen in children with a 10q25/6 deletion [see diagram on page 22] [Petit 1998; Courtens 2006].

The frequent association between 10q deletions and urogenital anomalies suggests the presence of a gene or genes for urogenital development on 10q25/6. In the light of this one group conducted a study to try to identify this gene or genes by looking at ten people with a deletion of 10q26, five of whom had a pure deletion and five of whom had involvement of another chromosome. They proposed that a gene responsible for urinary development was located in a region distal to D10S5186 (see diagram), and a gene responsible for genital development was located in a region distal to D10S5124 located within 10q26. They also noted that all of the people with cardiac anomalies had a region...
Adults with a 10q25/6 deletion

Unique has seven adult members between the ages of 18 and 28 years. A 20-year-old man with an interstitial deletion has moderate to severe learning difficulties, ADHD and speaks in two to three word sentences. He walks on his toes but does trampolining, swimming and dancing. He is friendly and very active and lives in a group home with five others. An 18-year-old girl with a 10q26 deletion left a special educational school last year. She learned to read around the age of 5 years old. She has ADHD and challenging behaviour, but loves books, children’s TV shows and arts and crafts. She lives at home with her family and needs support when out and about. She goes to a day centre for some days a week and does supported voluntary work. A 23-year-old woman with a 10q26.1 deletion left school at 16 years of age and can read and write. She loves music, reading magazines and doing word-search puzzles and has basic computer literacy. She has been diagnosed with ADHD and is currently living in a low security hospital due to her challenging behaviour. A 23-year-old woman with a 10q26.3 deletion has learning difficulties. She is able to drive and helps out on the farm where she lives (Unique).

Growing up with a 10q26 deletion

A number of adults have been reported in the published medical literature. One family had six members with a 10q26.2 terminal deletion with the oldest, 63 years old, who attended mainstream school and worked as a supermarket shelf-stacker. She passed the deletion on to three daughters. One daughter, 38 years old at the time of the report, attended mainstream school but did not achieve any examinations and worked in a food factory and supervised junior staff. The second daughter (37 years old) attended mainstream school and worked in a factory as a packer; she had no behavioural problems but was said to be accident-prone and sustained a number of fractures. The third daughter (19 years old) had moderate learning difficulties and attended a special school. Her behaviour was occasionally disruptive and she was described as being very active. A 40-year-old woman, who passed the 10q26.2 deletion on to a daughter, left school without obtaining any examinations and worked in catering. A 48-year-old man has severe learning problems and short stature [McCandless 2000; Irving 2003].

Does the breakpoint matter?

The size of the deleted region found in those with 10q deletions varies widely, ranging from a small interstitial deletion to much larger ones. In the published medical literature there are eight individuals with an interstitial deletion, ten individuals with a terminal deletion with a break in q25 and 47 with a break in q26. Unique has 13 members with an interstitial deletion, five with a break in q25 and 44 with a break in q26 (see below). However, there is a wide variation of features, even within families where the same deletion is shared. The clinical features in people who have smaller terminal deletions are mainly the same as in people with larger deletions suggesting that the features are due to the deletion of the very distal part of chromosome 10q. Additionally, there are cases of those with a larger deletion who are affected relatively mildly without any major birth anomalies. Having said that, the two individuals who are the most mildly affected and only discovered the deletion after they passed it on to their children, both had small terminal deletions with breakpoints in 10q26.2 (see Ongoing research into 10q25/6 deletions) (Irving 2003; Unique).

Breakpoints in Unique families

Bracketed numbers show numbers of families on the Unique database [2009]. These breakpoints are recorded for members of Unique with a ‘pure’ terminal 10q25/26 deletion.

10q25.2 - qter [3]
10q25.3 - qter [2]
10q26 - qter [7]
10q26.1 - qter [16]
10q26.11 - qter [2]
10q26.2 - qter [6]
10q26.3 - qter [13]

These are the breakpoints recorded for members of Unique with interstitial deletions.

10q25.1q26.1 [1]
10q25.2q26.1 [1]
10q25.2q26.11 [11]
10q25.2q26.13 [2]
10q26q26 [1]
10q26.13q26.3 [3]
10q26.2q26.3 [3]
10q26.3q26.3 [1]

Support with learning although the amount of support needed by each child will vary

- Squint (strabismus)
- Kidney and/or urinary tract anomalies
- Heart conditions, though the majority of reported cases are minor and often resolve naturally without surgical intervention
- Microcephaly (an unusually small head)
- Genital anomalies, most commonly cryptorchidism (undescended testes) in boys
- Characteristic facial features
Are there people with a 10q25/6 deletion who are healthy, have no major medical problems or birth defects and have developed normally?

In a few people (all with deletions in the 10q26.2 band nearer the end of the chromosome), the deletion appears to have a more mild effect. A 40-year-old woman with mildly asymmetrical ears only discovered that she carried a 10q26.2 deletion after her 9-year-old daughter was found to have a 10q26.2 deletion. A 63-year-old woman and two of her daughters (37 and 38 years) all of whom had a 10q26.2 deletion all attended mainstream school and were in full-time employment (Irving 2003).

What is the outlook?

There are some older reports in the literature of neonatal death, most commonly due to severe cardiac problems. Progress in the management of cardiac disease has improved the prognosis of babies with cardiac anomalies. For children with no serious heart or other organ problems, lifespan should not be significantly affected (Mulcahy 1982; Taysi 1982; Wulfsberg 1989; Unique).

While the outlook depends on a child’s individual progress it is likely that most children with a 10q25/6 deletion will continue to need support throughout their lives.

Pregnancy and birth

Many mothers carrying babies with 10q25/6 deletions experienced no pregnancy problems, had a normal delivery and only discovered their baby was affected after the birth. However, pregnancy complications are not uncommon in mothers carrying a baby with a 10q25/6 deletion. Of the 41 families who have told us about their pregnancy experiences, eight babies were small for gestational age or were described as having intrauterine growth retardation (IUGR). This is a term used to describe babies whose growth in the womb has slowed resulting in babies that are smaller than expected for the number of weeks of pregnancy. Six babies showed little fetal movement while in the womb. A number of parents also had unusual findings when undergoing ultrasound scans: two babies had a two vessel umbilical cord; a kidney anomaly was detected in one baby; increased fluid around the baby was seen in two pregnancies; ureteral reflux was detected in one baby; and one baby was diagnosed with hydronephrosis. There are also two cases in the published medical literature in which urinary tract anomalies were detected on prenatal scans (Scigliano 2004; Unique).

Only one family known to Unique discovered the 10q25.2q26.13 deletion before their baby was born. An amniocentesis was performed after a nuchal scan showed an increase in fluid at the back of the neck. There are two examples in the medical literature of prenatal diagnosis of a 10q25/6 deletion performed in one case for advanced maternal age and in the second after IUGR and heart anomalies were detected during an ultrasound scan. The parents, in both cases, chose not to continue with the pregnancy (Chung 1998; Kerher-Sawatzki 2005; Unique).

Growing up with a 10q26.1 deletion

Sleep

The majority of children go to bed easily at bedtime and sleep well. However, sleep problems affect some children. Some children find it hard to settle at bedtime and consequently fall asleep late. For some this means they struggle to get up in the morning and are tired the next day; others seem to have a diminished need for sleep, sometimes only needing six hours per night (Mehta 1987; Unique).

- **He is difficult to settle when he is tired and can take up to an hour or more to settle at bedtime and will cry for no reason** – 2 years
- **Bedtimes are tricky as she only settles well about seven days per month. Often it is 11pm before she goes to sleep and then she is so tired at school the next day** – 7½ years

Puberty and Fertility

There is limited information available on puberty in both males and females with 10q25/6 deletions. The evidence at Unique is that puberty proceeds as normal at the usual age. However, puberty began early, at 8 years of age, for one girl (Unique).

To date there are two families in the medical literature who have passed a 10q deletion on to their children. One family has six members with the deletion, ranging in age from 3 years to 63 years. A 63-year-old woman passed the deletion on to three daughters, one of whom passed the deletion on to a son and a daughter. The other family consists of a 40-year-old woman who passed a 10q26.2 deletion on to a 9-year-old daughter. One Unique boy inherited a 10q26.3 deletion from his mother (Irving 2003; Unique).
literature and at Unique of children who are unaware of danger (Schraender-Stumpel 1991; Petit 1998; Courtens 2006; Unique).

Over 50 per cent of those who took part in the Unique survey reported that their children had an increased tolerance to pain, often not noticing when they had been quite badly hurt (Unique).

Additionally, there is a higher percentage within the autistic spectrum that has been reported both in the published medical literature and in a number of Unique children. Some children do not have a diagnosis of autistic spectrum disorder (ASD) but show some autistic tendencies or traits. The autistic tendencies that have been noted include failing to recognise social cues, rarely crying and repeating movements like head shaking or wringing their fingers (Unique).

“Everyone loves him. He has a great personality and loves to say ‘Hi’ and ‘Bye’ to everyone. He is very easygoing and rarely cries” – 2½ years

“He has a warm heart and is warm and funny” – 3 years

“She is not a particularly naughty child and has no challenging behaviour. She has on one occasion shown inappropriate friendliness to a stranger in the park, so this needs watching. She is sometimes shy in new situations and can be quite clingy” – 4 years

“She works hard for everything and is determined” – 4 years

“She has been diagnosed with sensory issues, including auditory sensitivity, oral seeking and sensitivity, and she has problems regulating sensory input. She has also been diagnosed with obsessive compulsive disorder (OCD) and autism. She doesn’t like to see anyone hurt and loves to share” – 5 years

“She has challenging behaviour and can be difficult when tired. She has ADHD and is unable to sit and focus for a period of time at school” – 7 years

“She has just started to be disruptive at school” – 7½ years

“She is a very lovely little person. She loves all the family and she is permanently telling them so! She is very sociable and likes to say ‘Hello’ to everybody – 8½ years

“He is very social and likes to be with his friends. He picks (almost compulsively) at threads (on the hem of a T-shirt or socks)” – 9 years

“He is always happy and everyone loves his cheerful character. He can be impulsive and likes to get his own way” – 9 years

“He was usually calm until 2½ years and then was very difficult (agitated, always in opposition, always testing the limits) until 6 years. It is now much better. She shows inappropriate friendliness with adults she doesn’t know – 10 years

“She is very affectionate and caring” – 10 years

“Her behaviour is quite abusive. She swears, bites, pinches and back chats. But she is loving all of the time” – 11 years

“He is extremely social and is very loving and emotional” – 20 years

Newborn

Many babies with 10q25/6 deletions need help to establish breathing or experience spells of apnoea (pauses in breathing) and some may need extra oxygen within the newborn period. Reflexes (such as the startle reflex) may not be normal and in particular your baby may show a very weak sucking ability. Babies are sometimes exceptionally sleepy. Typically babies with a 10q25/6 deletion have a very faint cry or do not cry audibly (Wulfsberg 1989; Leonard 1999; Shapiro 1995; Piccione 2008; Unique).

Growth and feeding

Babies are often, but not always, small and underweight at birth. Regardless of the breakpoint, birth weights recorded at Unique show a considerable variation with an average of 2.94 kilos (6lb 8oz). Around a third of the Unique babies had a low birth weight (below 2.6 kilos or 5 lb 12oz) at term (Unique).

Range of birthweights at Unique (at or near term):

1.814 kilos (3lb 16oz) to 4.11 kilos (9lb 1oz)

One study reports that 40 per cent of babies have growth delay at birth but 75 per cent are described as being growth delayed later in babyhood or childhood (Wulfsberg 1989).

Feeding difficulties are a major area of concern for families, particularly as babies usually start out small and underweight. The hypotonia that is common in babies with a 10q25/6 deletion can lead to difficulties with sucking and swallowing, and/or latching onto the breast. Babies with a cleft or high palate can also find the action of sucking and swallowing difficult. Many babies have a small appetite and struggle to finish a feed. Fifteen of the 29 mothers surveyed by Unique attempted to breastfeed their babies, although only four established successful breastfeeding. However, a number of babies were bottle-fed expressed milk. Seven out of 39 Unique babies benefited from a temporary nasogastric tube (NG-tube, passed up the nose and down the throat). As some of these babies matured enough to suck effectively, the NG-tube could be removed and breast or bottle feeding established.

A further four babies who initially benefited from temporary NG-tubes later needed gastrostomy tubes (a G-tube, feeding direct into the stomach) in order to meet their nutritional needs (Unique).
Hypotonia can also affect their food passage and contribute to gastro-oesophageal (GO) reflux (in which feeds return readily up the food passage). In the Unique survey, almost a third of babies had reflux. This can generally be well controlled by giving feeds slowly, positioning a baby semi-upright for feeds and where necessary raising the head of the end of the bed for sleeping. Feed thickeners and prescribed medicines to inhibit gastric acid may control reflux. If these measures are not enough, some babies benefit from a fundoplication, a surgical operation to improve the valve action between the stomach and food passage [Unique].

Some older babies and toddlers have trouble chewing and can choke or gag on lumps in food so may continue to eat puréed food for longer than their peers and the start of finger feeding may be delayed. Parents have found that modifying the texture of foods by grating, mincing, chopping or adding sauces to foods can help to overcome these problems. Children often continue to be slow, fussy eaters although some children develop large appetites and a love of food. As a result of these feeding difficulties a number of families have consulted a dietitian [Unique].

However, a 3-year-old had no feeding problems and a 2-year-old is described as ‘always a good eater’. Another who had problems sucking as a baby had no feeding problems at age 2 years. A 17-year-old has a good appetite and loves vegetables! [Unique].

- She is still a poor eater and only likes certain foods, especially milk, pudding and porridge " – 7 years
- She was fed with a NG-tube for the first year and a half but kept pulling it out so it was decided she needed a G-tube which she used for six years until she started going to special school, where she learned to eat by mouth both by imitation of the other kids and because she received speech therapies that helped her to eat by mouth. The G-tube was removed last year " – 8½ years
- He had a weak suck. We tried breastfeeding for quite some time and were not successful. He was bottle fed expressed breast milk for 4 months” – now 9 years

**Appearance**

Children with 10q25/6 deletions sometimes have facial features in common. Typically, babies have a small head (microcephaly) with a broad nasal bridge with a beaked or prominent nose. They may have a triangular and sometimes asymmetrical face with unusually-formed, low set ears. They may have deep set eyes or widely spaced eyes (hypertelorism) or there may be an extra fold of skin covering the inner corner of the eye (epicanthic folds). They often have a thin bow shaped upper lip with a small, receding lower jaw (micrognathia). A short neck which is sometimes webbed is also common. However, many children look little different compared to other children and may closely resemble their siblings or parents [Unique].

- Digestion
  One problem is chronic constipation which affects almost half of Unique children. Dietary changes and/or medication can help to manage the problem [Unique].

- Other concerns
  A broad chest with wide-spaced nipples has been reported in as many as 30 per cent of those with a 10q25/6 deletion [Wulfsberg 1989].

  Both umbilical and inguinal hernias have also been reported in small number of people. A hernia is a lump that results from a part of the intestine slipping through a weakness in the abdominal wall. An umbilical hernia is a soft, skin-covered bulge at the belly button (umbilicus) that can look bigger when the baby strains or cries. The bulge contains a small piece of abdominal lining and sometimes part of the abdominal organs. It is caused by incomplete closure of the ring of muscle that the umbilical cord passed through in early life. An inguinal hernia, a bulge containing part of the bowel, is located in the lower abdomen (Petit 1998; Lukusa and Fryns 2002; Scigliano 2004).

**Behaviour**

Children with a 10q25/6 deletion are typically happy, sociable, loving and affectionate. A number of families describe their children as particularly empathetic. However, a significant number of children – although not all – show a similar pattern of behavioural difficulties. One study reported behavioural problems in over half of those children with a 10q25/6 deletion. The behavioural problems can be wide ranging. Typically children display sudden and extreme changes of behaviour, with outbursts of aggressiveness and destructive behaviour. This behaviour can be directed at themselves and others and include hair pulling, hitting, biting and kicking. A small minority have been known to be self-destructive or self-harm. They can be abusive, swearing at others. They are often easily frustrated and can be impulsive. They tend to be hyperactive with poor concentration, a short attention span and are easily distracted, all of which can make learning more challenging. Six of the 29 (21 per cent) who took part in the 2008 survey have been diagnosed with attention deficit hyperactivity disorder (ADHD) which is characterised by restlessness and a short attention span. Those diagnosed with ADHD include children with interstitial deletions, deletions in 10q26.1 and 10q26.3. Many families report that their children are overly affectionate and show inappropriate friendliness. A small number of reports in the medical literature suggest that behaviour can worsen in the pre-pubertal years. Behavioural management techniques have helped many families, but for some children medication has been shown to be the only effective treatment. Other strategies employed by families include a low sugar diet with no food dyes [see the Unique leaflet on Behaviour] (Petit 1998; Lukusa and Fryns 2000; Irving 2003; Courten 2006; Unique).

Sensory issues affect some children. They may display tactile sensitivity, disliking the touch of certain objects or textures, and/or oral hypersensitivity. Two Unique children have a heightened body awareness; one has a weighted blanket when asleep and wears a weighted vest for part of the day; the other wears a weighted bag at times. Around half of those surveyed had sensitive hearing and were hypersensitive to noise, although some children outgrew this. There are also descriptions in both the published medical
Palate
A cleft palate (opening in the roof of the mouth resulting from the palate not forming correctly during development) has been reported to affect some children with a 10q25/6 deletion. The evidence at Unique is that clefts affected 13 per cent (4/30) of those who participated in the survey regardless of the breakpoint. Cleft palates have also been reported in four cases in the published medical literature (Mulcahy 1982; Shapiro 1985; Petersen 1998; Scigliano 2004; Unique).

A number of children (3/29), all with breakpoints in 10q26.3, are reported to have a high palate (Unique).

Both cleft and high palates can contribute to the early feeding difficulties seen in children. A cleft or high palate may also make speech more difficult.

Breathing
Breathing problems can affect children with 10q25/6 deletions. Around a third of all babies, regardless of the breakpoint, had respiratory distress at birth (see Newborn). Some babies need resuscitation or intubation at birth but subsequently manage to breathe normally, although some require ventilation for up to six months. Three Unique children had frequent respiratory tract infections, although one outgrew the problems at around 8 years of age. Two children known to Unique suffered from aspiration pneumonia, where there is inhalation of something from either the stomach or the oral airway leading to inflammation of the lungs. Asthma and severe bronchiolitis (inflammation of the small airways in the lungs) have also been reported (Scigliano 2004; Unique).

Teeth
Generally speaking, children with chromosome disorders appear to have somewhat more dental problems than their peers. A number of Unique children have teeth that are slow to erupt, whereas others acquired adult (permanent) teeth early. One Unique child had deciduous (milk) teeth that lacked enamel and one child required regular dental cleaning due to excessive plaque build-up. A small minority of children have a hypsensitve mouth (see Behaviour) resulting in an aversion to brushing teeth and visiting to the dentist; one child requires a hospital visit for dental treatment (Unique).

Spine
A small proportion (around 20 per cent in the Unique survey and about the same proportion in the published medical literature) have scoliosis (curvature of the spine). In most cases the scoliosis is mild and has not, at present, required surgery. One Unique child had damage to the nerve endings in the base of her spine resulting in a lack of bladder and bowel control requiring catheterisation every four to six hours. In another Unique child the fluid sac at the base of the spine is larger than is usual (Turleau 1979; Waggoner 1999; Lukusa and Fryns 2000; Lukusa 2002; Scigliano 2004; Unique).

Learning
Learning difficulties and intellectual disabilities are common in children with a 10q25/6 deletion, with most children moderately affected and a small minority severely affected. As always, there is individual variation, and a few children have mild, borderline or even no learning difficulties. However, most children will need support and benefit from early intervention programmes and may thrive best in a special learning environment. Around half of Unique children attend mainstream school, often receiving some learning support or 1:1 help in the classroom with the other half benefiting from a special education school (Unique).

Many children learn to read and write. The Unique experience is those who master reading start to recognise words between the ages of 4 and 8 years (with an average of 5½ years). Those mastering writing start forming letters between the ages of 4 and 10 years (with an average of 5½ years). For some children, hypotonia can make writing or drawing difficult and many children find using a keyboard to write easier than a pencil or pen. This level of achievement is not possible for all children and a number do not master reading or writing, although some can recognise their own name and make simple drawings. Children generally have a good memory. A number of children are hyperactive or described as being easily distractible or having a short attention span which can make learning more of a challenge (see Behaviour). Children with 10q25/6 deletions seem to share a love of music and singing (Unique).

- He has a good memory and it is only necessary to show him how to use a toy once and he knows how to turn it on/off. He loves music and has a lovely, bubbly, cheeky personality “ – 2 years
- He knows all the colours and body parts very well. He can stack blocks, use shape sorters and do simple puzzles “ – 2½ years
- She has a great memory, can read three letter words and some others. She has problems drawing pictures and writing. She writes most letters but at angles, disconnected and sloppy “ – 5 years
- She reads well and has an excellent memory although she has poor focus. She needs a quiet area where not much is happening in order to learn, otherwise she becomes overwhelmed and too excited “ – 4 years
- She learned to read at 5-6 years and reads short sentence books with help. She does not choose to read alone. She has an excellent memory “ – 7½ years
- He achieves at or above his grade level in all academic subjects and has an excellent memory. He has an excellent ear for music and plays the piano. He reads everything! He had a touch screen computer from the age of 2 years and became comfortable with it so that he can use the keyboard and computer to complete assignments even though his handwriting is not legible “ – 9 years
- She has a very good memory and is very good at maths. She reads any book she is given! She is in mainstream school with 1:1 support “ – 9½ years
- She loves music and has a great rhythm. She has an excellent memory and learned to read at 6 years. It took some time to understand maths “ – 10 years
- She has a fantastic memory. She can read some simple words (cat, milk, mum, dad, go, to, and, the, up “ – 11 years
Speech and communication

Many children with a 10q25/26 deletion learn to speak well. However, babies tend to cry very little and some do not cry audibly until 18 to 24 months. Speech too is almost always delayed with first words emerging between the ages of two and six years. Some children continue to have articulation difficulties, with consonant sounds often proving more difficult, and/or their speech may sound ‘slurred’. Many children use sign language, PECs (picture exchange communication system) and/or computer-based approaches to help to communicate their needs and wants. Often, as speech is mastered, they find they no longer have need of these aids. Evidence in the literature, which is also backed up at Unique, suggests that many children have better receptive language than expressive language: they understand more than they can express. Many children continue to have articulation difficulties, with consonant sounds often proving more difficult, and/or they may stutter or have ‘slurred’ speech. Speech therapy has proved extremely beneficial to many children and many can go on to speak in complex sentences and have a very large vocabulary, although the articulation difficulties may remain. There is a very small minority of children known to Unique who do not master language and continue to use gestures, facial expressions and vocal noises to indicate their needs and express their feelings (Teyssier 1992; Lukusa 2000; Piccione 2008; Unique).

There are many reasons for the speech delay, including the link between the ability to learn and the ability to speak. The hypotonia experienced by many children results in weakness in the mouth muscles which in addition to insufficient sucking, can also affect the development of speech. Those with a cleft or high palate may also have specific difficulty with certain sounds (Unique).

“He currently knows about 150 signs and his vocalisation is improving a lot” – 2½ years
“An evaluation showed her to be above average in comprehension and use of language, however, it is selective” – 4 years
“She has always been very keen to communicate and uses a combination of signing and speech and gestures. She is now using more speech than noises but has to be reminded often to use words” – 4 years
“She doesn’t use words but she points, cries and looks at pictures to communicate” – 4 years
“He has fluent speech now but this was acquired late and needed therapy. He initially experienced some processing delay but now speaks in long sentences using polysyllabic words” – 4 years
“She said a few words at 2 years but did not progress further until 6½ years and has improved since. She now speaks in sentences and is generally understood by everyone.”
“She used to use signing but stopped as she began talking” – 7½ years
“He uses very developed speech but still has significant articulation difficulties” – 9 years

Feet

The feet of those with a 10q25/6 deletion are often not perfectly formed. Evidence from the literature and Unique suggests that almost half of children have a foot anomaly. A number of children have joined toes (syndactyly), usually involving the second and third toes. Other anomalies include talipes (clubfoot), overlapping toes, flat feet, feet that turn inwards, hammer toes (where one or more toes is permanently bent), and sandal gap (an increased gap between the first and second toe). Some children who have clubfoot may need surgery to correct the unusual positioning of their feet, although for other children plaster and splints may be sufficient. Generally the foot anomalies may mean that children require special insoles or inserts in their shoes or special supportive footwear (Lewandowski 1978; Wulfsberg 1989; Leonard 1999; Waggoner 1999; Irving 2003; Unique).

Hands

Many children with 10q25/6 deletions have unusual hands including large hands, an in-curving little finger (clinodactyly), single palmar crease, extra palmar crease, underdeveloped or concave nails, long fingers or fingers that are fused together (syndactyly). In general, the hand anomalies do not greatly affect the function of the hands, although they can lead to problems with fine motor skills. A number of Unique children have high muscle tone (hypertonia) in their hands which can lead to problems with fine motor skills and make using sign language more challenging. One Unique child has no finger pads and one has stiff joints in her hands and can no longer make a ‘fist’ (Mehta 1987; Wulfsberg 1989; Petit 1998; Waggoner 1999; Lukusa 2002; Irving 2003; Scigliano 2004; Motoyama 2008; Unique).

Genital anomalies

Minor anomalies of the genitals are common in babies with chromosome disorders, most often affecting boys. The most common problem is cryptorchidism (undescended testes) which affects over 80 per cent of boys with a 10q25/6 deletion. The testicles can be brought down by a straightforward surgical operation if they do not descend of their own accord in time. Micropenis (a small penis) and an imperforate anus (a malformed, blind anus) have also been observed. The published medical literature reports ambiguous male genitalia in two boys (one with an interstitial deletion and one with a 10q25.3 deletion) and complete male to female sex reversal has been observed in two males, one with a 10q25 deletion and one with a 10q26 deletion (Mehta 1987; Wilkie 1993; Tanabe 1999; Irving 2003; Mardo 2008; Unique).

Girls may also have minor genital anomalies, although these are much less common. The most frequent genital anomaly in girls is underdeveloped labia (Rooney 1989; Ogata 2000; Unique).
- Vision
A squint (strabismus), where one or both eyes can turn inwards, outwards or upwards, is the most common vision problem noted by researchers and by almost all Unique families. Many squints are convergent (the eyes cross) and many children need surgery to re-align the eyes. Evidence in the published medical literature suggests that squints are more common in those with a subtelomeric deletion with breakpoints in 10q26.2 or 10q26.3 than those with more proximal breakpoints in 10q25 or 10q26.1, however, evidence at Unique does not support this with over 80 per cent of all children affected regardless of breakpoint [Waggoner 1999; Scigliano 2004; Unique]. Other problems reported were long sight, short sight and astigmatism (the cornea, the clear cover over the iris and pupil, is abnormally curved resulting in blurred vision). These problems are often mild and can be corrected with glasses. Blocked tear ducts have also been reported in three Unique children and in one published report [Lukusa 2002; Courten 2006; Unique].

A number of other problems have been reported in only one child. One child in the medical literature was reported to have hypoplastic optic discs; one had nystagmus (rapid, uncontrolled eye movements); one Unique child had a cortical visual impairment (the visual systems of the brain do not consistently understand or interpret what the eyes see) and another had monocular vision (where each eye is used separately as opposed to the usual binocular vision where the eyes work together) [Waggoner 1999; Courten 2006; Unique].

- Hearing
More than half of Unique children surveyed reported excessively sensitive or acute hearing and an exaggerated response to loud noises. Some children appear to outgrow this problem although for others it remains a problem [Unique]. Hearing impairment is common in children with chromosome disorders and has been reported in almost a third of Unique children with this deletion. The most common cause of hearing impairment is glue ear, where there is a build-up of fluid in the middle ear. Glue ear usually resolves as children get older and the ear tubes widen and become more vertical resulting in improved drainage of the middle ear. Therefore, any hearing loss caused by glue ear is usually temporary. However, persistent fluid in the middle ear and glue ear can reduce a child’s hearing at a time that is critical for speech and language development. Therefore, while glue ear persists, many children will need a grommet (a small ventilation tube) inserted into the eardrum. Hearing loss has also been reported in the published medical literature, albeit infrequently [Wulfsberg 1989; Petersen 1998; Mardo 2008; Unique].

“He has sensitive hearing. He hears everything – aeroplanes from inside the house, heaters turning on and off” – 2½ years

“He talks very fluently now although used sign language initially. He still finds certain sounds difficult but he can be understood and ‘talks the hind legs off a donkey!’” – 9 years

“She communicates well. She still has speech problems but speaks in 5/6 word phrases although sometimes not in the correct order” – 9½ years

“She talks but pronounces words differently; she says ‘ralad’ instead of salad and ‘tamel’ instead of towel” – 11 years

“She speaks in sentences and uses signs, but she is hard for new people to understand” – 18 years

Development: sitting, moving, walking (gross motor skills)
Children with a 10q25/6 deletion are typically slow to reach their developmental motor milestones. The Unique experience is that babies start to roll between 3 months and 15 months (average 7 months); sit between 6 months and 4½ years (average 19 months) and crawl between 9 months and 2½ years (average 16 months). Some children, however, do not crawl but instead move around by bottom shuffling. Independent walking was mastered between 14 months and 6 years (average 2½ years). Some children need support (such as a standing frame, walking frame, support boots, a supportive Lycra ‘second skin’ and/or leg braces) while learning to walk. Most children go on to walk, climb stairs and run, although they can be unsteady with poor balance and co-ordination. Many children walk with a wide gait and trip easily [Petersen 1998; Scigliano 2004; Unique].

There are several reasons for these motor delays including hypotonia that affects around a third of children with a 10q25/6 deletion. A few children have increased muscle tone (hypertonia) or varying muscle tone (hypotonia in some parts of the body and hypertonia in others). Hypotonia often improves as children mature; nonetheless, early physiotherapy and occupational therapy can be beneficial. Some children find it hard to fully straighten their elbows or knees and this can make walking and physical activities difficult. Physical activities enjoyed by some children at Unique include swimming, riding a tricycle, bicycle or scooter, playing football, trampolining, ballet, skiing and dancing [Mehta 1987; Wulfsberg 1989; Leonard 1999; Tanabe 1999; Waggoner 1999; Unique].

“He lacks some of the physical skills of his peers but can swim and has generally advanced rapidly with support and therapy” – 4 years

“She is very active. When she was young she took a while to walk and never crawled but you can’t stop her now!” – 9½ years
Development: hand-eye co-ordination and dexterity (fine motor skills) and self care

Hypotonia and hypertonia can also affect fine motor skills in children with a 10q25/6 deletion and they may take longer to reach for and grab toys and hold a bottle or cup. This can lead to delays in children being able to self-feed, dress themselves (zips and buttons can be especially problematic) and hold a pen to write or draw. Special chunky cutlery, cups with handles and cutting up food have helped some children. For those children who have problems holding and controlling a writing implement, mastering a keyboard or touch screen computer can often be easier. A small number of children have been reported with hyperreflexia; overactive reflexes which can result in twitching and can also affect fine motor skills. Many children have occupational therapy in order to help improve these skills [Gorinati 1989; Petersen 1998; Leonard 1999; Waggoner 1999; Unique].

As a result of these difficulties, children are likely to continue to need help with dressing and undressing. They will also require assistance in tasks such as brushing teeth and washing. Toilet training is also likely to be affected. The information at Unique shows that consistent toilet training was mastered between 2 years and 8½ years (average just over 4 years). However this level of training has not been possible for all children with some children achieving bowel and bladder control during the day but not at night. One child was toilet trained during the day at 8 years old but regressed at 17 years and is now doubly incontinent and another was fully toilet trained at 5 years old but regressed when her baby sister arrived (Unique).

“ She was completely toilet trained by 3½ years. She dressed herself by the age of 3 years. She now needs help with brushing her teeth and washing her hair but can wash her own hands ” ~ 4 years

“ He has very poor fine motor skills and is a very messy eater and writer ” ~ 9 years

Medical concerns

Kidneys and urinary tract

Unusual features of the kidneys and urinary tract appear to be common in children with 10q25/6 deletions and your baby may have a renal scan. Almost a third (10/36) of those surveyed by Unique had a kidney anomaly, a figure which is backed up by the medical literature [13/47 had a kidney or urinary tract anomaly]. Among the problems reported at Unique and/or in the published medical literature are anomalies where the ureters [the tubes that carry urine from the kidneys] enter the bladder; an obstruction in the valves that let urine flow out from the bladder; underdeveloped [small] kidneys or enlarged kidneys (hydronephrosis); a duplex kidney and kidney vesico-ureteral reflux [where the urine flows upwards from the bladder back up to the kidney, potentially damaging the kidneys]. For those affected by kidney reflux, ureteral re-implantation may be necessary. This surgical procedure is performed when the ureters do not join the bladder in the correct place which can cause kidney reflux. The procedure disconnects the ureters from the bladder and reconnects them in the correct place. Urinary tract infections are also common, affecting around a quarter of those surveyed by Unique [Scigliano 2004; Courtens 2006; Motoyama 2008; Unique].

Heart conditions

Heart (cardiac) conditions have been reported to affect up to half of all babies born with a 10q25 or 26 deletion. The most common conditions seen in Unique children were persistence of prenatal cardiac structures such as persistent ductus arteriosus [PDA; where the channel between the aorta and the pulmonary artery that takes blood to the lungs fails to close after birth] which often resolves without the need for surgical intervention, although surgery was necessary for three children. Holes between the upper or lower chambers of the heart (ventricular septal defects [VSD] or atrial septal defects [ASD]) have also been reported. Again, in many children these defects heal (close) naturally without surgery. Four children had an innocent heart murmur; two had mitral valve prolapse (one or both flaps of the valve are enlarged) and one had a bicuspid aortic valve (the valve that regulates blood flow from the left ventricle into the aorta has two flaps instead of the usual three) but the heart function was normal [Unique].

More rarely, and not seen in any Unique children, complex heart conditions have been found including Fallot’s tetralogy [involving both a VSD and pulmonary stenosis] that required surgical correction, and a hypoplastic left heart [Wulfsberg 1989; Petit 1998; Ogata 2000].

Heart conditions occur irrespective of breakpoints affecting those with breakpoints in 10q25 and 10q26 although there is some evidence that severe cardiac defects are less common in those with a subtelomeric [just above the telomere at the end of the chromosome] deletion [in 10q26.2 or 10q26.3] [Courtens 2006].

Circulation

Around 25 per cent of Unique families who took part in the survey reported that their child had a low body temperature or has difficulty maintaining the temperature in their hands and feet. Families have told us that their child’s hands and feet are often very cold and can turn a blue/purple colour at times, with the problem frequently worse after periods of inactivity such as upon waking in the morning. One child who suffered cold hands and feet before she was fully mobile was no longer affected after she started to walk and become more active. Another Unique child’s circulation seemed to be improving as she grew older [Unique].

Seizures

Seizures are not a major feature of 10q25/6 deletions. One in five of those who took part in the Unique survey suffered from at least one seizure, however many children only had one or few seizures and outgrew them. A number of other children’s seizures are well controlled by medication, although two children out of 36 have seizures that have not been completely controlled by medication. The published medical literature also describes a small number of children who suffer from seizures and one study suggests that seizures are more common in those with a subtelomeric deletion. The study reports 31 per cent of those with a subtelomeric deletion had seizures whereas seizures were only sporadically described in those with a larger deletion. The evidence at Unique does not back this up: seizures appear to affect those with small or large deletions with equal frequency [Wulfsberg 1989; Waggoner 1999; Lukusa and Fryns 2000; Lukusa 2002; Irving 2003; Courtens 2006; Piccione 2008; Unique].