

*Unique*

Support and Information

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This leaflet is not a substitute for personal medical advice. Families should consult a medically qualified clinician in all matters relating to genetic diagnosis, management and health. The information is believed to be the best available at the time of publication. It was compiled by *Unique* and reviewed by Professor Robert Hopkin, Division of Human Genetics, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio, USA and by Professor Maj Hulten BSc, PhD, MD, FRCPath, Professor of Medical Genetics, University of Warwick, UK. 2007.

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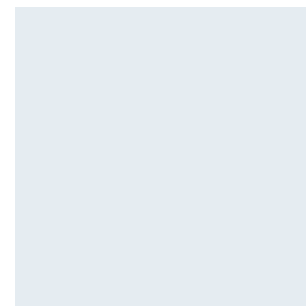
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Registered in England and Wales

Charity Number 1110661  
Company Number 5460413

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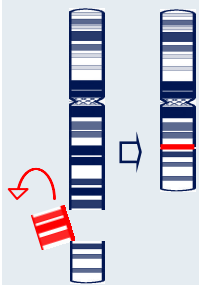
# 6q deletions from 6q23 to 6q24



## Sources & references

The information in this leaflet is drawn partly from medical publications. The first-named author and publication date are given to allow you to look for articles on the internet in PubMed.

The leaflet also draws on *Unique's* database. When this leaflet was written, *Unique* had 67 members with a 6q deletion, of whom 46 had a pure 6q deletion with no other chromosome involved.



**An interstitial deletion**

## Deletions from 6q23 or 6q24, interstitial or to the end of the chromosome

A chromosome 6q deletion means that part of one of the body's chromosomes has been lost or deleted. If the missing part contains important instructions for the body, learning difficulties or disability, developmental delay and health problems may occur. How serious these problems are depends on how much of the chromosome has been deleted and where the deletion is.

### Genes and chromosomes

Our bodies are made up of billions of cells. Most cells contain a complete set of genes. We have thousands of genes which act like a set of instructions, controlling our growth, development and how our bodies work.

Genes are carried on microscopically small, thread-like structures called chromosomes. We usually have 46 chromosomes, 23 inherited from our mother and 23 inherited from our father, so we have two sets of 23 chromosomes in 'pairs'. Chromosomes and genes are made up of a chemical substance called DNA.

Apart from two sex chromosomes (two Xs for a girl and an X and a Y for a boy), chromosomes are numbered 1 to 22, generally from largest to smallest. Each chromosome has a short (**p**) arm (at the top in the diagram) and a long (**q**) arm (at the bottom). In a 6q deletion, material has been lost from the long arm of one chromosome 6.

The chromosome may have broken in two places and the part between them is missing (an **interstitial** deletion) or it may have broken in one place and the part of the chromosome from the breakpoint to the end of the arm is missing (a **terminal** deletion).

You can't see chromosomes with the naked eye, but if you stain them and magnify their image under a microscope, you can see that each one has a distinctive pattern of light and dark bands. This leaflet tells you about interstitial deletions within bands 6q23-24 or terminal deletions with one breakpoint within these bands.

A small or much larger piece of the chromosome can be missing. If the piece is visibly missing when the chromosomes are magnified, it is called a **deletion**. The missing piece may be so tiny that it can only be found or characterised using more recently developed DNA-based techniques such as microarrays. It is then called a **microdeletion**.

## Speech and communication

Some delay in the development of speech and language is to be expected, but the extent of the delay is variable and probably reflects the level of cognitive ability. Due to incomplete descriptions in the medical literature, it is not possible to say whether all youngsters with a 6q23~q24 deletion will eventually acquire some speech but it is clear that some will.

“ He expresses himself by showing what he wants. ” - age 5

“ Speech is the area of development that is most affected. She had a hoarse and very quiet cry as a baby. After 3 years of speech therapy, she is able to communicate her basic needs vocally most of the time. Her first word (mom) was at 8 1/2 months, but she couldn't speak enough to express her needs until she was about 3 1/2 years old. Today she uses 3 word phrases, using only words she's been taught. I believe she actually understands less than she expresses. She has an auditory processing disorder. She has been taught to express her needs, because that was the main priority in speech therapy. She cannot, however, follow simple one-step commands unless they are heard on a daily basis. ” - age 5

“ He uses vocal noises, gestures, pushing, pulling and hitting his head to show displeasure. His receptive skills far outstrip his expressive skills. ” - age 8

## Learning

Some learning difficulties or disabilities are to be expected but it is unlikely to be possible to precisely predict the level of difficulty from the diagnosis or the karyotype.

“ Her memory is random, at best. She will occasionally remember things and surprise us, but she easily forgets what she is being taught. She will also learn something, know it for weeks, and then if it isn't mentioned for a couple of weeks she'll forget it. Her most able areas are her excellent rote skills and she learns music quickly. She learns well due to her desire to please. She recently learned about four or five sight words. ” - age 5

“ A mental age of half his real age. ” - age 5

“ He has profound learning disabilities but his memory is good, he is able to master toys he likes and is very determined for things he likes to do such as ball play and musical toys. ” - age 8

## Behaviour

“ He is tactile defensive in and around the mouth, does not want to grasp objects for more than a few seconds. He enjoys musical toys; balls; videos; music; playing with other children; and is very sociable. ” - age 8

“ She is inappropriately friendly with other children. She loves cats, music, TV, books, playing with kids, entertaining anybody who will watch or listen, and looking through drawers of very small toys. ” - age 5

“ She has sensory processing difficulties (for example, her food has to be cold, she can't tolerate any heat, she is a sensory seeker, crashing into people and things and standing on her head), she smells everything and has an oversensitive sense of smell, she can't tolerate the sunlight so she looks down at the ground outside, loud noises frighten her tremendously, she is terrified of crowds or busy environments and has temper tantrums typical of a 2 year old. ” - age 5

One baby was born with a cleft palate (a split in the roof of the mouth), needing surgical repair for feeding and speech development. Another baby had an umbilical hernia. This shows as a soft, skin-covered bulge at the umbilicus (navel, belly button) that contains a small piece of abdominal lining and sometimes part of the abdominal organs. A small hernia can be left to resolve naturally, while a large hernia may need surgical repair.

In babies with two copies of 6q24 on the chromosome 6 they inherit from their father, a temporary form of diabetes known as transient neonatal diabetes (TND) is sometimes seen. This has also been found in one baby with a 6q24 deletion but we do not yet know how common this may be (Diatloff-Zito 2007).

#### ■ Eyesight

In this small group, two babies had marked vision problems at birth but in each case they improved. In one case the baby, considered blind at birth, became able to see after successful heart surgery for Fallot's tetralogy. In the other case, eyesight improved so that by the age of four vision therapy was stopped. This child has structurally normal eyes but has additional problems with strabismus (squint).

#### Outlook

The outlook for any child is determined largely by their clinical problems. Generally, children were well but were vulnerable to respiratory infections and when ill became sicker than other children. One baby in this group, with the most severe brain malformation, died in the newborn period. One baby had persisting upper airway obstruction, with frequent breathing arrests during sleep; this was successfully treated by inserting a tracheostomy to allow direct flow of air and oxygen to the windpipe.

### Development

#### Sitting, moving: gross motor skills

Most children with a deletion in this area develop more slowly than other children, although a three-year-old girl with a 6q23.3~q24.2 deletion was developing normally. The extent and severity of delay among others is not yet known and it is unlikely that it can be predicted precisely from the karyotype. All children known to *Unique* were walking by five years, although their gait could be unusual (toe-walking), they might tire easily and need the support of a walker. Low muscle tone is common in babies and children with a chromosome disorder. This makes it harder for the child to move and is one of the causes of the delay in sitting, standing and walking that most children can expect.

#### Using their hands: fine motor and coordination skills

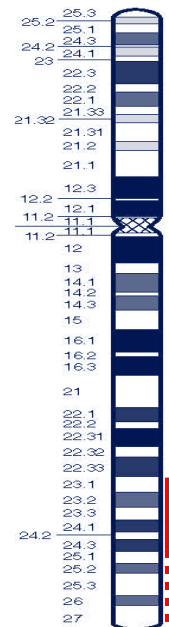
Hand and eye coordination skills such as holding a bottle and playing with small toys may not develop in line with gross motor skills. Overall, there is fairly consistent delay in hand use and fine motor skills. This delay means that early intervention by occupational therapy to stimulate hand use is vital.

“ At 5, she cannot open standard door knobs or pedal a bike. She tries to brush her teeth, but mostly chews on the toothbrush. She can undress herself, but she cannot dress herself. She needs help with pretty much everything.

“ At 8, he needs 100% care.

Toilet training is also late and was not yet complete in any of *Unique*'s members by 8.

### Chromosome 6



Your geneticist or genetic counsellor can tell you more about the chromosome material that has been lost. You will almost certainly be given a **karyotype**, a shorthand code for the image of your child's chromosome make-up that shows the points where the chromosome has broken and rejoined. Comparing your child's karyotype with others can 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 deletions. 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.

Some thirteen cases with a pure deletion in this area are described in this leaflet, at least ten from the medical literature and three members of *Unique*. Four babies have been described with a terminal deletion from 6q23 and two, with a possible third, with a deletion from 6q24. Three children have been described with a 6q23~q24 deletion, one of them a *Unique* member; two have been described with a 6q23~q25 deletion, one a *Unique* member. One child is described with a 6q24~q25 deletion. One girl with a 6q23.3~q24.2 deletion was developmentally normal at the age of three.

(Diatloff-Zito 2007; Kumar 1999; Sukumar 1999; Meng 1992; McLeod 1990; Shen-Schwarz 1989; Matkins 1987; Fryns 1986; Lozzio 1982; Goldberg 1980; Kueppers 1977; *Unique*)

#### Your baby at birth

Low birth weight was frequently signalled during pregnancy and one baby was induced at 38 weeks following stress tests. Apgar scores, rating babies' condition at birth on a scale of 0-10, were generally low and together with feeding difficulties, babies' appearance alerted medical staff to a possible underlying problem.

Range of birthweights at or near term: 5lb/2.268 kg to 8lb 13oz/4 kg.

#### Appearance

Doctors may notice in a baby what are known as 'dysmorphic features' which may or may not be obvious to a parent. Most of these are facial features with no impact on health.

Some of the most common features are seen in many babies and children with a chromosome disorder, while others are more specific to a 6q deletion. The most common features seen in young babies include a small chin and lower jaw, with the jaw possibly offset backwards, tiny skinfolds across the inner corners of the eyes, ears set lower than usual and sometimes unusually formed or tilted backwards, a short neck, sometimes with loose skin, thin lips, particularly the upper lip, a prominent or broad bridge to the nose, small eyes, a small nose with a bulbous tip, an asymmetrical face and tiny holes on the cheek in front of the ears. One child has an unusually small mouth and her teeth are crowded.

## Feeding

Many babies with a chromosome disorder have initial feeding difficulties and it is probable that babies with a 6q23~q24 deletion will too. The three *Unique* members had feeding difficulties as newborn babies and two had long-lasting problems and required feeding by gastrostomy tube direct to the stomach. One child graduated to feeding by mouth at two years, but an eight-year-old was still fed mainly by gastrostomy.

Babies are likely to have difficulty establishing feeding. They may show no interest, be unable to suck effectively or to coordinate sucking with swallowing. In some babies the problems are mild and temporary and it may be possible to breastfeed but many need long-term support. Once they move on to solids, children may have difficulty with lumpy foods and need their feeds pureed. They may also have difficulty moving food from the front to the back of the mouth.

Gastro oesophageal reflux (GORD, GERD), where the stomach contents return up the food pipe, affected at least one baby. Reflux raises a baby's risk of inhaling food contents and setting up 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 and counteract any acidity. 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 baby is sufficiently mature to tolerate feeding by mouth.

*“ She was only able to drink out of the old fashioned rubber-type nipples. She couldn't get any formula out of silicone nipples. ” - 6q23.3q24.2 deletion*

*“ Fed by gastrostomy tube to 2 years. Since then successfully orally fed. ” - 6q23q25 deletion*

*“ Still fed mainly by g-tube. ” - 6q24q26 deletion, at 8 years*

## Growth

Babies and children with a 6q23~q24 deletion can be tall, medium or short for their age, but the limited evidence shows that most commonly they are short. Their growth rate may not follow the curves on a growth chart, as shown by the example below. There is a very limited amount of evidence that suggests that some children have a tendency to become plump around the stomach and abdomen.

*“ She was short for the first year of her life. Then she was on the 50<sup>th</sup> centile until she turned three, which is when she began dropping down centiles, stopping at the tenth centile, where she has stayed for one year now. ” - 6q23.3q24.2 deletion, at 5 years*

## Hands and feet

Minor anomalies of the hands and feet are relatively common in children with chromosome disorders. These may just be cosmetic or they may make it harder for the child to use their hands or to walk. In this group, babies have been described with short and sometimes chubby (babyish) hands and feet, tapered or very flexible fingers and small nails. A baby with a large terminal deletion with a breakpoint at 6q23 or q24 had small, unbendable fourth and fifth fingers.

## Medical concerns

	Numbers affected
■ Minor genital anomalies	4/9 boys
■ Heart condition	6/13
■ Structural anomalies of brain	4/13
■ Imperforate anus	2/13
■ Vision problems at birth	2/13

### ■ Genital anomalies

Four out of nine boys in this group had undescended testicles or very small genitalia. The testes descend during fetal life from 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 on the need for surgery. One boy had retractile testes, which can be brought down into the scrotum but may then retract again.

### ■ Heart

Defects in the structure of the heart were found in six of the thirteen babies. Anomalies include a hole between the two lower (pumping) chambers of the heart (ventricular septal defect/ VSD) and two more complex problems. One baby was born with an atrioventricular canal (AV canal/AVC), a complex defect that involves several abnormal heart structures, including a hole between the upper heart chambers (atrial septal defect), a VSD and incorrectly formed valves separating the upper and lower chambers. Two babies were born with the complex anomaly known as tetralogy of Fallot. In both babies successful surgery was carried out.

### ■ Head and brain

Head size among babies and children with a 6q23~q24 deletion may be unusually small (microcephaly), normal or large. Some children also have an unusually shaped head. A baby with an unusual head size or shape may have investigative tests and in four children with a 6q23~q24 deletion these showed unusual features. In two babies the broad band of nerve fibres linking the two sides of the brain (corpus callosum) was missing and two further babies had anomalies associated with a failure of the forebrain to divide properly into two separate hemispheres. Saying what findings such as these are likely to mean for an individual child is the role of a paediatric neurologist.

### ■ Other concerns

Two babies were born with an imperforate anus, where the opening at the end of the rectum or anus is absent, so stools cannot leave the body normally. This is caused by improper development of the baby's rectum and anus and can be corrected by surgery. One baby was born with a diaphragmatic hernia, where the muscular wall separating the heart and lungs from the contents of the abdomen develops with a gap. Part of the bowel, stomach or liver take up space in the chest, depriving the lungs of room to develop properly. Early surgery is needed with respiratory support.