

## Support and Information



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**Facebook page for chromosome 6: [www.facebook.com/groups/chromosome6](http://www.facebook.com/groups/chromosome6)**

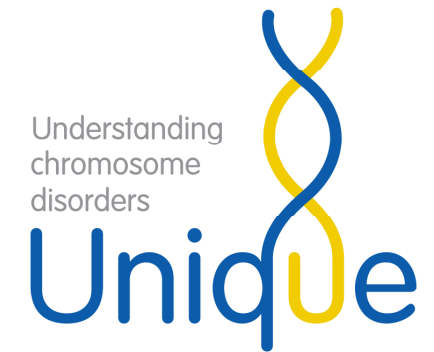
Unique lists external message boards and websites in order to be helpful to families looking for information and support. This does not imply that we endorse their content or have any responsibility for it.

This updated 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 Professor Hilde Van Esch, Centre for Human Genetics, Leuven, Belgium and by Unique's chief medical advisor, Professor Maj Hultén BSc PhD MD FRCPath, Professor of Reproductive Genetics, University of Warwick, UK. Version 2 (PM)

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# 6q deletions 6q13 to 6q14



## Sources & References

The information in this guide is drawn from what is known about a small number of people - just 23 - with a 6q13q14 deletion. Fifteen people have been described in varying detail in the 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 (www.ncbi.nlm.nih.gov/pubmed). There is a literature list on page 18. You can get articles marked **Free access** yourself on the internet. If you wish, you can obtain other articles from *Unique*. The guide also draws on *Unique*'s database. When this guide was written, *Unique* had seven members with a 6q13q14 deletion (McNeal 1977; Young 1985; Yamamoto 1986; Lonardo 1988; Rose 1992; Romie 1996; Hopkin 1997; Kumar 1997; Gershoni-Baruch 1996; Myers 2005; Lespinasse 2009; Van Esch 2010; *Unique*).

### Deletions on chromosome 6 between 6q13 and 6q14

A 6q deletion is a rare genetic disorder in which there is a tiny piece missing from one of the body's 46 chromosomes. This tiny piece is missing from virtually all the cells in the body that are needed for growth, development and healthy functioning.

The missing piece raises the risk of development and learning problems and specific connective tissue disorders.

Connective tissues are the structural parts of our body that hold the cells together. Connective tissue disorders that seem to be especially common include very loose joints, hernias and abnormal positioning of the feet.

Chromosomes are the structures inside the body's cells that carry DNA, the genetic information that tells the body how to develop and function. They come in pairs, one from each parent, and are numbered 1 to 22 approximately from largest to smallest. Each chromosome has a short (p) arm and a long (q) arm.

People with a 6q deletion between 6q13 and 6q14 have some DNA missing from one of their chromosome 6s.

### Looking at chromosome 6

#### Chromosome analysis

You can't see chromosomes with the naked eye, but if you stain them and magnify them under a high-powered microscope, you can see that each one has a distinctive pattern of light and dark bands. You can see these bands in the diagram of chromosome 6 on page 3. The bands are numbered outwards starting from the point where the short and long arms meet (the **centromere**).

A low number such as q11 is close to the centromere. A higher number such as q13 is a little further away from the centromere.

If you magnify the chromosomes to hundreds of times life size and look at them down a microscope, there may be a small piece visibly missing from the long arm of chromosome 6. This is called a **deletion**.

#### Microarrays and other technologies

The missing piece may be so tiny that even when the chromosome is magnified many hundreds of times it looks normal down a microscope. The missing piece can then only be found using a combination of different techniques including refined chromosome analysis and, increasingly, a technique known as chromosomal microarrays or array-CGH. Such a tiny missing piece of a chromosome is called a **microdeletion**.

Chromosomes are made up of DNA, which has a ladder-like structure, as you see in the diagram on page 3. Each 'rung' in the ladder links a pair of chemicals known as bases. The size of small deletions and microdeletions is often measured in pairs of bases,

### Medical articles

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- Yamamoto 1986: Deletion of Proximal 6q: A Clinical Report and Review of the Literature *American Journal of Medical Genetics* Volume 25 pages 467-471 Yamamoto Y *et al.*
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## How did this happen?

The great majority of 6q13q14 deletions occur out of the blue and on examination the parents have normal chromosomes. The genetic term for this is de novo (dn) (see page 3-4). Occasionally, one parent is found to have a change in their own chromosomes at 6q13 or 6q14 that makes them much more likely to have a child with this type of deletion. A blood test to check the parents' chromosomes will show what the situation is.

Dn 6q13q14 deletions are caused by a mistake that occurs when the parents' sperm or egg cells are formed or else very shortly after conception, when a baby is made. In bands 6q13 and 6q14 there do not appear to be any particular hotspots or 'weak sites' where the chromosome is liable to break and re-join. This is one reason why there are individual differences between people with 6q13q14 deletions - they have different break points in the chromosome, with slightly larger or smaller missing sections.

Whether the deletion is inherited or dn, what is certain is that as a parent there is nothing you did to cause it and nothing you could have done would have prevented it from occurring in your child. 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?

Where both parents have normal chromosomes, it is unlikely that another child will be born with a 6q13q14 deletion or any other chromosome disorder. Where a parent has a rearrangement of their chromosomes with a break at 6q13 or 6q14, the risk of having another affected child is higher.

## Will my child with a 6q13q14 deletion have similarly affected children?

Some adults who themselves have a 6q13q14 deletion may form relationships and want to have children of their own. We have not known about the deletion for long enough to be certain if it affects fertility and it is possible that men at least will have fertility problems. However, a parent with a 6q13q14 deletion faces a raised risk of passing the deletion on that could be as high as 50 per cent.

called base pairs. Since each chromosome has millions of base pairs the numbers are very long. Often they are shortened, like this: one thousand base pairs can be shortened to 1 kb; one million base pairs can be shortened to 1Mb.

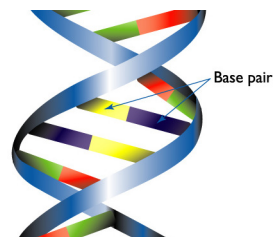
People with a deletion between 6q13 and 6q14 have different sizes of deletion. But all of them have lost a section about 3.7Mb - or 3,700,000 base pairs - long. This section includes 16 genes identified so far.

## The genetic test results

Your geneticist or genetic counsellor will give you your child's genetic test results. If the test used chromosomal microarrays, the result is likely to look something like this:

arr 6q13q14.1(74856944-76925922)x1

The analysis used microarray technology 6q13q14.1 The change is in chromosome 6, starting in band q13 and finishing in band q14.1 (74856944-76925922)x1 The base pairs between 74856944 (around 74.8 Mb) and 76925922 (around 76.9 Mb) have been shown to be missing. Take the first long number from the second and you get 2,068,978. This is the number of base pairs that are missing. This can be rounded to 2Mb. x1 means there is one copy of these base pairs, not two - one on each chromosome 6 - as you would expect.



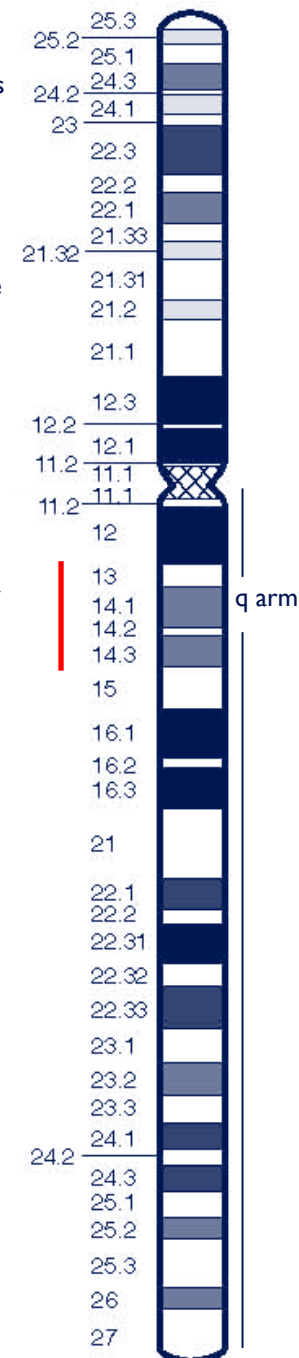
Bases are the chemicals in DNA that are linked in pairs to form the ends of the 'rungs' of its ladder-like structure. One thousand base pairs is often written as 1 kb. One million base pairs is often written as 1Mb.

Sometimes you will receive a report like the one below. This report is not so helpful, because it doesn't tell you as precisely how big the missing piece is.

46,XY,del(6)(q13q14.2)

46 The number of chromosomes in your child's cells  
XY The two sex chromosomes: XX for females; XY for males  
del A deletion, or there is missing material  
(6) The deletion is from chromosome 6  
(q13q14.2) The chromosome has broken in two places, q13 and q14.2, and the material between them is missing.  
The report may show the letters dn. This is the short form of de novo, Latin for 'from the beginning'. This means that the parents have had their chromosomes in a blood sample checked and no

## Chromosome 6



change has been found at 6q13q14. The deletion is very unlikely to be inherited and has occurred for the first time in this family with this child. If the letters **pat** are given, then the deletion is inherited from the father. The letters **mat** mean that it's inherited from the mother.

### Are there people with a 6q13q14 microdeletion who have developed normally and have no health, learning or behaviour difficulties?

At the moment, everyone reported with a deletion in this part of chromosome 6 has needed some level of support with their development or learning. However, learning difficulties can be mild and at least one young adult known to *Unique* has acquired vocational accounting qualifications (Lespinasse 2009; *Unique*).

#### Most likely features

- Some slightly unusual facial features
- Marked joint laxity
- Hernias
- Developmental delay
- Hypotonia
- Motor delay
- Speech and language delay
- Foot deformities
- Undescended testicles in males

#### Some slightly unusual facial features

Babies, children and adults with a 6q13q14 deletion may have some facial features that are unexpected in their family but are seen in others with this chromosome deletion. The most commonly described feature is a long philtrum [groove between the nose and upper lip] that may be flattened out.

In babies and young children the upper lip is frequently thin, but can fill out with time. The eyes may slant slightly upwards and ears are typically large, with large lobes, and set low on the side of the head. There may be small skinfolds across the inner corners of the eyes [epicanthic folds], the nose is often short and upturned and the chin pointed (Kumar 1997; Lespinasse 2009; Van Esch 2010; *Unique*).

#### Marked joint laxity

Almost two thirds of reports on babies and young people with 6q13q14 deletions highlight that they have very flexible joints. Any joints in the body can be affected, both large [hips], medium [elbows, ankles] and small [fingers, thumbs]. A significant number of babies are born with developmental hip dysplasia, where the thigh bone can be readily moved out of its socket in the pelvis. Treatment involves stabilising the joint until it forms a stronger union, either by wearing a second nappy [diaper], a harness or splint or, for a time, a plaster cast.

Once children start walking - and due to this laxity they usually walk late - they will often be flat-footed. If necessary, they can wear insoles, special support boots or splints to correct the angle of the foot (Lespinasse 2009; Van Esch 2010; *Unique*).

“ Her wrists, ankles and hips are very loose. She moves her wrists a lot and in a resting position, her hands are always turned more than 90 degrees upwards - 13 months

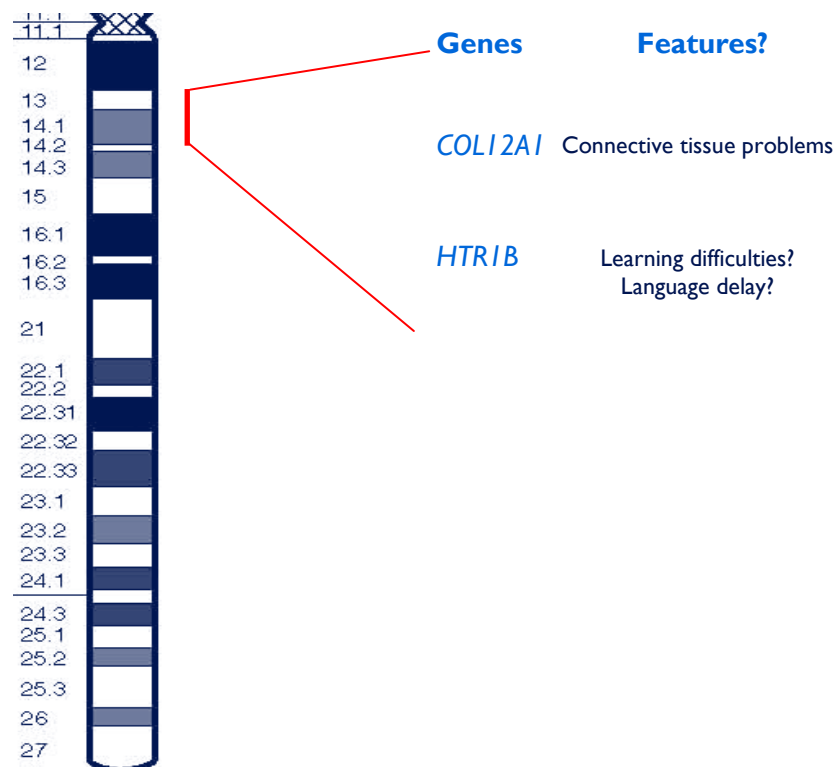
#### Genes

People with the classic 6q13q14 microdeletion are usually missing one copy of 16 known genes covering a length of around 3.7Mb of the DNA in the chromosome. The function of some of these genes is not yet known, but losing one copy of some of these genes has been suggested as the possible cause for certain symptoms (Van Esch 2010).

*COL12A1* may be the underlying cause of the connective tissue problems. This gene encodes the instructions for the correct development of a type of collagen that is found in many connective tissues (Van Esch 2010).

*HTR1B* Possibly at root of learning difficulties and language delay. The *HTR1B* gene is also known as *5HT-1B* (Lespinasse 2009).

Identifying the gene or genes responsible for certain features of a 6q13q14 deletion may interest researchers and doing so may help to guide future studies, but it does not lead directly to immediate improved treatment. Even if one copy of the supposedly responsible gene is missing, the associated feature[s] will not necessarily be present. Other genetic and environmental factors are often important as well.



Shy, timid but more confident with social interactions with age. Temper tantrums with head banging and some hand flapping when younger, abated by 5-6 years. Continued improvement now: friendly, tentative, shy - 8 years

Bursts of hyperactivity. Rare aggressive/ disruptive outbursts. Overfriendly, hypersociable, extreme empathy. Appeared sensitive, easily anxious, intensely emotionally reactive, with trend to retreat from interaction and remain inhibited.

Fluctuating attention - 10 years

Timid but friendly - 13 years

(Yamamoto 1986; Kumar 1997; Lespinasse 2009; *Unique*).

“ She is timid, has difficulty with relationships, anxiety and is hypersensitive and extremely anxious in an insensitive environment [shows as crying, sleep difficulties]. She lives somewhat in her own world. Some autistic traits, but autism has not been diagnosed. She would love to have friends but her immaturity makes relationships with her peers difficult and she has few subjects of conversation. She gets on well with younger teenage girls and is very loving - 24 years

“ Typically, she is shy with others but is starting to be more social. She usually answers questions with a nod for Yes or No and then hides in me. If she is comfortable with someone, she may speak and show them, for example, her favourite shoes. She receives Applied Behavior Analysis [ABA] behaviour therapy through Autism Intervention Services, working on her behaviour, independence and speech: wonderful! She is loving and smart and so happy despite all of the challenges she has faced - 4¾ years

“ She is especially sensitive to other children and likes to watch, touch and laugh at them. She also likes to hold hands with other children, and always touches her brother when he sits next to her - 13 months



“ At her two month check up, her doctor noticed she could not move her head to the left (torticollis) and that her right hip dislocated easily. She wore a Pavlik harness to stabilise her hip from 3 to 7 months and today is fine - 4¾ years

“ She has long flexible fingers and the joints in her legs were loose until adolescence. You can still see it today when she sits with her legs in a W but it never caused her a problem and she didn't need any splints or other supports. Her joints just stabilised over time - 24 years

#### ■ Hernias

Almost two thirds of babies and children with a 6q13q14 deletion are known to have had a hernia, which is a protrusion of an organ out of the part of the body where it is normally situated. Most common is an umbilical hernia, which shows as an abnormal bulge that can be seen or felt at the umbilicus [navel, belly button]. The hernia develops when a small opening in the abdominal muscles that allows the umbilical cord to pass through does not close after birth. Part of the lining of the abdomen, part of the intestine and sometimes fluid from the abdomen passes through the opening, causing the hernia. Many umbilical hernias close naturally by the age of three or four but a very large hernia or one that stays open after this age can be closed surgically.

Also quite common is an inguinal hernia. This shows as a bulge in the area where the lower abdomen meets the upper thigh (the groin). The cause is that an opening in the lower part of the wall of the abdomen that is open during fetal life but closes before birth does not in fact close. The remaining opening may be small, only allowing fluid through, or it may be large enough for something such as a loop of the intestine to get stuck in it. An inguinal hernia should always be assessed by your child's doctors and your child may need surgery to repair it.

One child has also been reported with a hiatus hernia, a protrusion of the stomach into the chest cavity through the hole for the food passage [oesophagus] (McNeal 1977; Young 1985; Lonardo 1988; Rose 1992; Romie 1996; Gershoni-Baruch 1996; Hopkin 1997; Myers 2005; Lespinasse 2009; Van Esch 2010; *Unique*).

#### ■ Delayed development

Developmental delay is a feature of a 6q13q14 deletion. It is usually apparent in the first year of life as babies fail to reach their developmental milestones and by the time children are diagnosed and formally assessed, they are often some months behind in their development. The delay is especially obvious in their body control [motor skills] but also in communicating with speech and language. Once children start to receive therapies [physiotherapy, occupational therapy, speech and language therapy, as well as early intervention], they often show catch-up, making encouraging progress (McNeal 1977; Gershoni-Baruch 1996; Romie 1996; Myers 2005; Lespinasse 2009; *Unique*).

“ Her development exploded when she was 3½ and first took steps on her own. She is still behind in fine and gross motor skills and most of all in speech - 4¾ years

“ She had global developmental delay and had to be taught how to reach her milestones [crawling, getting up, doing exercises to improve her tone (kinesiotherapy), walking, keeping her balance, riding a bike]. Homeopathy and osteopathy also helped her a lot. Her fine motor skills have overall improved, although she still has difficulty with manual tasks [organisation, cutting, scissors] - 24 years

## ■ Hypotonia

The great majority of babies are born with very low muscle tone. They feel floppy to hold and when they lie on their backs, their legs splay, rather than curling up. This low tone [hypotonia] may affect the whole body or just part of it and it makes learning to sit and become mobile much harder and more tiring. Babies and young children should have access to early physiotherapy to improve their muscle tone. While the low tone does have a significant impact on the age at which children learn to sit up and walk, the evidence from *Unique* is that children eventually overcome many of these difficulties, although walking may remain more tiring for them than for other people (Yamamoto 1986; Gershoni-Baruch 1996; Romie 1996; Hopkin 1997; Myers 2005; Lespinasse 2009; Van Esch 2010; *Unique*).

“ She has power in her limbs but cannot control head, neck or body and requires physiotherapy and many kinds of seating support – pillows, a special chair and a bath support. The support gives her comfort; and she is stimulated gradually in different positions - 13 months

“ She’s no longer floppy - 4¾ years

“ She still tires easily - 24 years

## ■ Motor delay, exacerbated by foot position anomalies

All reports show some degree of delay in reaching the milestones of sitting and walking. The amount of delay varies quite a lot but all babies and children benefit from early intervention with physiotherapy and exercises to improve their muscle tone and some need body support [such as a lycra suit] or leg or ankle splints or support boots. There is a suggestion that children with larger deletions face more delay in reaching their motor milestones.

Much of the delay is due to the low muscle tone which improves but can persist into childhood, making climbing, running and walking for long distances difficult and tiring. Very flexible joints mean that children often prefer to sit with their legs in a W and may slouch when sitting. Other underlying causes of the delay include unstable joints, in particular hip joints.

## Head control

When you hold a typical healthy baby’s hands and pull him or her to sitting, by six weeks they can often hold their head steady for a second. Babies with a 6q13q14 deletion will reach this stage later. *Unique* families tell us that individual babies have been able to hold their head steady in a supported sitting position and lift it from the floor when lying prone from around 6 months. They will also be late to turn or lift their head from lying and to hold their head still without wobbling when cradled in a sitting position. If you hold your baby tummy down on your forearm, their head will drop forward for longer than in a typically-developing baby. Just when a baby with a 6q13q14 deletion will acquire head control will depend partly on their innate abilities but also on the amount of ‘tummy time’ and therapy they receive.

## Rolling

A typically-developing baby will often have discovered how to roll from his tummy to his back during his fifth month and from back to tummy a month or so later. In a baby with a 6q13q14 deletion, these rolling skills will develop later - from experience, between 9 and 15 months - and the baby often needs help and lots of practice.

child had fibromatosis colli, a neck muscle lesion often linked with wry neck and related to breech or forceps delivery (McNeal 1977; Van Esch 2010; *Unique*).

## Pregnancy and birth

Pregnancy was generally uncomplicated and babies were born at or near term. However, six babies presented breech [feet first] and were delivered by Caesarean section. A seventh baby had fibromatosis colli, a neck muscle lesion associated with breech or forceps delivery.

The breech presentation may be due to babies’ low muscle tone and thus a predictable risk factor to bear in mind at delivery. Low muscle tone was noted in most but not all babies and feeding difficulties were prominent in many (Young 1985; Lonardo 1988; Gershoni-Baruch 1996; Romie 1996; Kumar 1997; Van Esch 2010; *Unique*).

## Other issues

**Heart** Two babies were born with a persistent ductus arteriosus [PDA]. This is a channel between the aorta and the pulmonary artery that takes blood from the heart to the lungs and usually closes shortly after birth. When it stays open, the lungs receive more blood than they should and the heart has to work too hard. It can be closed if necessary using minimally invasive surgery. One baby was born with a small hole between the two upper chambers of the heart and one with a hole between the two lower chambers: treatment under the care of a cardiologist depends on the size of the hole and how much it affects the child (Yamamoto 1986; Lonardo 1988; Rose 1992; Kumar 1997).

**Spine** A girl with a 6q13q14 deletion has a minor syringomyelia [formation of a fluid-filled area within the spinal cord] (*Unique*).

**Palate** One baby with a 6q13q15 deletion was born with a cleft palate, repaired when he was a year old (Yamamoto 1986).

## Hearing

Among a total of 22 babies, children and adults with a 6q13q14 deletion, there is just one report of a baby with a significant permanent hearing loss. As far as is known, others had normal hearing. There are two reports of hypersensitive hearing (Romie 1996; Van Esch 2010; *Unique*).

## Self care

*Unique* is almost the only source of information on how children with a 6q13q14 deletion acquire self care skills. Their fine motor difficulties present a challenge in terms of washing and dressing but there is quite a broad range of outcomes. A child of almost 5 years can dress herself with minimal assistance but needs help bathing and brushing her teeth. The age at which children are toilet trained again shows a range: from 3 to 7 years, according to *Unique* records (Kumar 1997; *Unique*).

## Behaviour

No-one has studied the behaviour of people with a 6q13q14 deletion yet to see if there are common features. What we know about behaviour comes from reports in the medical literature and *Unique*. One notable feature among *Unique* members is a high rate of diagnosis of autism or autistic features. Some reports follow.

## Eyesight

More than half of the babies, children and adults we know about with a 6q13q14 deletion have a strabismus [squint] affecting one eye or both. The crossed eye can look inwards, outwards, up or down. The main effects of a strabismus are that usually the person will have one eye which is stronger than the other. This is because the brain has to give priority to one eye over the other with the result that the weaker one does not 'learn' to see as well as the stronger one. Treatment of strabismus depends on the cause but can include patching the stronger eye, exercises, glasses to correct a refractive error such as long sight and surgery to realign the muscles that hold the eye in place.

Six/19 people have nystagmus, a jerky movement of the eyes that can be caused by a problem with the eye or the visual pathway from the eye to the brain. It is found more commonly in children with chromosome disorders. The effects vary from person to person but vision is almost always affected. Although nystagmus cannot be cured, your child will be referred to an ophthalmologist and there are several treatments that can help. Two/19 people have an additional eyesight problem. These include short and long sight and difficulties with depth perception (Young 1985; Lonardo 1988; Rose 1992; Gershoni-Baruch 1996; Myers 2005; Kumar 1997; Romie 1996; Van Esch 2010; *Unique*).

“ Her strabismus is controlled with glasses but shows when she is tired or has been working at a computer screen. She sees an orthoptist every two years, and has had 10-15 sessions to re-align her eyes - 24 years

## Spine

Six/19 children are known to have a significant curvature of the spine, probably caused by the underlying low muscle tone. The direction of curve varied: inwards [lordosis]; outwards [kyphosis]; or sideways [scoliosis] (McNeal 1977; Young 1985; Yamamoto 1986; Van Esch 2010; *Unique*).

“ She had significant kyphosis as a child, less obvious later. This was treated with occupational therapy and exercises and in later life with posture exercises and swimming - 24 years

## Kidneys

One girl with a 6q13q14 deletion has urology problems leading to very frequent urinary infections and kidney reflux, necessitating reimplantation of the tubes [ureters] leading from the kidneys to the bladder and a vesicostomy [a drainage channel from the bladder to just below the umbilicus] to protect the kidneys from damage. A girl with a larger 6q11q15 deletion also needed the ureters implanted to control kidney reflux and urinary infections and a further girl with a 6q13q15 deletion had persistent kidney reflux despite reimplantation of the ureters. Three babies were born with asymmetrically placed kidneys and one was born with small kidneys. In all, 6/19 children had kidney issues and in three these caused significant clinical problems (McNeal 1977; Yamamoto 1986; Gershoni-Baruch 1996; Romie 1996; Van Esch 2010; *Unique*).

## Neck

Two babies had 'wry neck', a condition also known as torticollis, in which the head tilts towards one shoulder and the chin rotates towards the opposite shoulder. A third

## Sitting

While a typically-developing baby can usually sit unsupported for a few seconds by four months, babies with a 6q13q14 deletion are unlikely to be able to sit alone before their second year, although there are exceptions. From experience, they sit between 10 and 17 months but one child of more than 2½ years still was not able to sit upright.

## Moving around

While a typically-developing baby will often get onto all fours ready to crawl by six months, some babies with a 6q13q14 deletion find other ways to get mobile such as scooting or bottom-shuffling. Most toddlers started to move around during their second year, although one child only started to move around after his second birthday.

## Walking

While typically-developing babies are walking in their second year, there is a very wide range of ages at which a child with a 6q13q14 deletion learns to walk - from 19 months to 6 years.

One factor is that babies are frequently born with their feet held in an odd position - turned out or in, up or down - or they have flat feet with no arch. Eight/14 children are known to have one or more of a variety of foot position anomalies, including heels that turn outwards, club feet, claw feet with a very high arch, in-turned feet and tight ankle tendons. Most of these problems have been treated with physiotherapy, stretching and strengthening exercises, shoe supports and splints but surgery and casting may be needed.

It can be a long time before walking is steady and children stop falling over but children's walking keeps on improving with age and practice. All the same, at least two children continued to walk on the edges of their feet, causing hard calluses to develop. Many children need splints or leg supports at first (Young 1985; Yamamoto 1986; Romie 1996; Gershoni-Baruch 1996; Hopkin 1997; Kumar 1997; Myers 2005; Lespinasse 2009; Van Esch 2010; *Unique*).

“ She can lift her legs up in the air now and almost roll over. She is much more comfortable than she was and likes to play, usually lying on her back and watching people around her, as she has trouble balancing her head. She enjoys playing with toys hanging above her [playgym] so they don't roll away - 13 months

“ She sits well now but does not like crossing her legs and prefers to stick them out. She tries to 'W'-sit with her knees bent and feet out, but this is discouraged. She is now walking independently without any supports or aids and can walk very well for any distance. She is just starting to jump, likes to climb stairs, slide down slides and throw a ball - 4¾ years

“ She stands with hunched shoulders, a slightly humped back and a protruding stomach due to her continuing lack of tone. She still has problems walking on a difficult surface such as a slope, or on stony or slippery ground. Above all she is uncertain on a slope and holds her arms out for balance. It is hard or impossible for her to go for a walk on uneven ground – she has a terror of falling and lacks balance and confidence. She enjoys swimming, cycling and walking on even ground - 24 years

## ■ Speech and language delay

Speech and language are usually delayed. The delay usually affects both understanding and talking but not always to the same degree. While most children understand more than they can say, sometimes as much as a typically developing child, at least one child talks well but has more difficulty understanding. There has been a suggestion that children with larger 6q13q14 deletions are more severely affected but there is marked individual variation and information from *Unique* shows strong speech and language skills in some children with relatively large deletions.

Social contact does not appear to be affected, so babies smile responsively at around the expected age of 2 months or a little later. However, while most toddlers are producing words in the months after their first birthday, it may be the second or even third birthday before you hear recognisable words from a child with a 6q13q14 deletion and for some children even this may not be possible. Vocabulary will increase but not necessarily at the pace you expect in a typically-developing child. One child of 2 years and 10 months had a working vocabulary of around 50 words but this is not possible for all. Joining words into phrases is also delayed, with a child of 3½ years still using single words and signs and a 13-year-old child still using mostly 2-word phrases. But there is quite a lot of individual variation. Some children talk slowly.

Speech quality can be affected, with one child of 2½ years described as having a high-pitched voice and nasal tone and a child of 4¾ years having difficulty with *k* sounds. Children benefit from early speech and language therapy and when there is a delay in producing words, learning to sign helps to support the development of speech. Talking and understanding continues to improve throughout childhood and into adulthood (Yamamoto 1986; Romie 1996; Gershoni-Baruch 1996; Hopkin 1997; Kumar 1997; Myers 2005; Lespinasse 2009; Van Esch 2010; *Unique*).

“ At 5 months, she said *mama* and babbled a lot, but then at some point she went silent again. By 3½ she had a 10-20 word vocabulary but relied on signing and gestures to communicate most of the time. Now she signs, uses gestures and speaks, using single words and 2-3 word phrases. She is very intelligent and can follow multiple-step directions, so she understands a lot more than she can express - 4¾ years

“ She was babbling at a year and saying her first words at 2. As a young child, she used vocal noises, crying, signing and gestures to communicate and gradually learned to speak. As an adult, she has some gaps in her vocabulary and some difficulties with understanding due to her attitude, lack of attention and vocabulary gaps. She needs clear precise instructions. But overall she expresses herself appropriately, and can hold a normal adult conversation with a slightly limited vocabulary - 24 years

## ■ Undescended testicles in males

It has been suggested that baby boys with a 6q13q14 deletion are especially likely to be born with one testicle or both undescended. Some baby boys are born with both testicles already in the scrotum, so this feature does not affect all. Undescended testicles are also found quite commonly in the general population of newborn baby boys and even more commonly among baby boys with a chromosome disorder. So it's not clear yet whether this is a feature of a 6q13q14 deletion or a more general finding. Treatment for undescended testicles depends on the suspected cause but whatever the

cause, treatment is usually needed if the testicles do not descend naturally in time. If a hormone problem is suspected to be the cause, a short course of hormone treatment may be suggested. Otherwise, or if hormone treatment does not work, the testicles can be brought down in a short operation under general anaesthetic called an orchidopexy (Rose 1992; Gershoni-Baruch 1996; Hopkin 1997; Kumar 1997; Van Esch 2010).

## Other features

### Cognitive delay

All children and adults we know about with a 6q13q14 deletion have needed some support with their learning. The amount of support has varied a great deal and the range of learning outcomes is very broad. At least one child has attended a mainstream [regular] school, continuing into higher education leading to vocational qualifications in accounting, while others have generally attended schools where the teaching was more specifically focused on their needs. Some children are assessed as having a 'mild' learning difficulty, while others have a more obvious level of difficulty and need more support. Where IQs [intelligence quotients] have been measured, they have ranged from 23 to 70 and likely even higher.

Generally speaking, children's performance is affected by their delay in fine motor skills due to their low muscle tone and loose joints. Mark making, drawing and writing are subject to particular delay and these children may find touch screens or keyboards much easier to manipulate. There has been no specific study of thinking skills in children with a 6q13q14 deletion, but one child was said to have a thinking process that was 'somewhat difficult to follow with abrupt changes of topic.' One child was able to write a few simple letters at the age of 13; another was starting to read at seven, knew all his colours, played computer games and understood simple addition and subtraction (Yamamoto 1986; Kumar 1997; Lespinasse 2009; *Unique*).

“ She has a very good memory: likes to 'write' names and use letters to spell names and memorises how to spell them quickly. She learns quickly but sometimes loses what she has learned and regresses. She is driven on by her own determination, a desire to do what others do and natural curiosity. She recognises her own name, can write a capital H and draw a circle - 4¾ years

“ She attended a mainstream school but was obviously different from the other children. Learning to speak, write and to think reflectively were slow and difficult for her; she started reading and writing at 7. But she has an excellent memory and learns best number work and any rule-based area of learning such as grammar and multiplication tables. Years have passed and she has studied with considerable courage, but it has not been easy. She has successfully sat vocational tests and is studying for French national vocational qualifications (brevet de technicien supérieur) in accounting. However, she has a slow learning curve and has needed 2 extra years for the course. She has difficulty finding her way around the town, has difficulty with the course (it goes too fast, she listens but can't think and take notes at the same time), intellectually she tires faster than other students. Driving a car is another source of difficulties: she has problems analysing situations as they arise and reaching decisions. She is also not creative. She can draw a house, person or flowers but nothing more. She writes slowly, so has difficulty taking notes, but uses a computer with no problems at all - 24 years