14q11.2 deletions

This information guide is not a substitute for personal medical advice. Families should consult a medically qualified clinician in all matters relating to genetic diagnosis, management and health. Information on genetic changes is a very fast-moving field and while the information in this guide is believed to be the best available at the time of publication, some facts may later change. Unique does its best to keep abreast of changing information and to review its published guides as needed. It was compiled by Unique and reviewed by Jana Drábová, Division of Medical Cytogenetics, Department of Biology and Medical Genetics, Charles University 2nd Faculty of Medicine and University Hospital Motol, Prague, Czech Republic.

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14q11.2 deletions
A chromosome 14 deletion means that part of one of the body’s chromosomes (chromosome 14) has been lost or deleted. If the material that has been deleted contains important genes, learning 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 precisely the deletion is.

Genes and chromosomes
Our bodies are made up of billions of cells. Most of these cells contain a complete set of thousands of genes that act as instructions, controlling growth, development and how our bodies work. Inside human cells there is a nucleus where the genes are carried on microscopically small, thread-like structures called chromosomes which are made up of DNA.

Chromosomes come in pairs of different sizes and are numbered 1-22 from smallest to largest, roughly according to their size. In addition to these so-called autosomal chromosomes there are the sex chromosomes, X and Y. So a human cell has 46 chromosomes: 23 inherited from the mother and 23 inherited from the father, making two sets of 23 chromosomes. A girl will have two X chromosomes (XX) while a boy will have one X and one Y chromosome (XY).

Each chromosome has a short (p) arm (at the top in the diagram on this page) and a long (q) arm (at the bottom of the diagram). In a 14q deletion, material has been lost from the long arm of one chromosome 14. The other chromosome 14 is usually intact. The short arm of chromosome 14 contains no unique genes, so losing material from the short arm generally does no harm.

You can’t see chromosomes with the naked eye, but if you stain them and magnify their image with a computer or under a microscope, you can see that each one has a distinctive pattern of light and dark bands. The bands are numbered outwards from the point where the short arm meets the long arm, and in a 14q11.2 deletion, DNA has been lost from the band in the long arm numbered 11.2.

A small or very large piece of the chromosome can be missing. If the piece is visibly missing when the chromosomes are magnified it is called a deletion. If the missing piece is so small that the magnified chromosome looks normal, and it can only be found using enhanced techniques such as FISH or array CGH, it is called a microdeletion.

Genes

**HNRNPC**
14q11.2 21,209,135-21,269,478
Developmental delay has been found in children with deletions involving the **HNRNPC** gene [Cooper 2011].

**SUPT16H**
14q11.2 21,351,471-21,384,638
**SUPT16H** encodes so-called chromatin remodelling factors (enzymes which are involved in regulating the expression of other genes) which have been associated with the development of autism spectrum disorders and learning difficulties [Zahir 2007; Prontera 2014; Terrone 2014; Drabova 2015].

**CHD8**
14q11.2 21,385,193-21,437,297
Like **SUPT16H** (above), **CHD8** also encodes so-called chromatin remodelling factors (enzymes which are involved in regulating the expression of other genes) which have been associated with the development of autism spectrum disorders, learning difficulties and a large head, and there is a particularly strong link for **CHD8**. The presence of changes (mutations) within the **CHD8** gene has been shown to be linked with these problems. It is therefore strongly suggested that when the gene is partly or completely lost, as in a 14q11.2 deletion or microdeletion, similar problems will occur [Zahir 2007; O’Roak 2012; Bernier 2014; Prontera 2014; Terrone 2014; Drabova 2015].

**DAD1**
14q11.2 22,564,906-22,589,236
The **DAD1** gene, is involved in regulating apoptosis (cell death), has been suggested as a candidate gene responsible for the skin webbing found between toes and/or fingers in some people [Terrone 2014].

**MMP14**
14q11.2 122,836,532-22,847,599
Researchers have suggested that extreme obesity in a woman of 21 with a 14q11.2 deletion weighing 107.5kg (almost 17 stone, heavier than 95% of women) could be due to her having lost the **MMP14** gene [Terrone 2014].
A deletion close to the point on a chromosome where the short and long arms meet is called a **proximal** deletion.

Each band of each chromosome contains millions of **base pairs** of DNA. Base pairs are the chemicals in DNA that form the ends of the ‘rungs’ of its ladder-like structure. There are millions of base pairs in every chromosome. An array CGH test shows which base pairs and which genes are missing.

Your geneticist or genetic counsellor can tell you more about the genes and chromosome material that have been lost. You will be given the results of your child’s genetic test, which will tell you what is missing.

The deletion may be within the band numbered 14q11.2, or it may be larger, extending to neighbouring bands.

**Sources & references**

The information in this guide is drawn partly from the published medical literature. The first-named author and publication date are given to allow you to look for the abstracts or original articles on the internet in PubMed (www.ncbi.nlm.nih.gov/pubmed). Articles consulted include: Bisgaard 2006; Zahir 2007; Papa 2008; Mencarelli 2009; Cooper 2011; Torpyekes 2011; Allou 2012; Ellaway 2012; O’Roak 2012; Santen 2012; Perche 2013; Bernier, 2014; Prontera 2014; Terrone 2014; Drabova 2015. If you wish, you can obtain abstracts and most articles from Unique. The leaflet also draws on Unique’s database. When this leaflet was updated in 2016, Unique had 179 members with a 14q deletion, of whom 12 had a deletion involving 14q11.2 with no other chromosome involved.
Test results
Your child’s test results are likely to look like one of these examples.

\[ \text{del 14q11.2} \]
This tells you that the missing (\text{del} = \text{deletion}) material comes from the band of the long \text{(q)} arm of chromosome \text{14} that is numbered \text{11.2} (see diagram, page 2).

\[ \text{46,XY.ish del(14)(q11.2q13)de novo} \]
This result shows that the expected number of chromosomes \text{46} were found, and there was an \text{X} and a \text{Y} chromosome, so this is a boy or man. The test used the FISH technique (\text{ish}) and this showed that DNA was missing from chromosome \text{14} (\text{del(14)}). There were two breakpoints in chromosome \text{14}, one at \text{q11.2} and the other at \text{q13}, and the DNA was missing from between them. \text{de novo} means that the parents’ chromosomes have been checked, and this chromosome change is a new occurrence and has not been inherited from either the father or the mother. De novo is often shorted to \text{dn}.

\[ \text{arr[hg18] 14q11.2(19229020–19462732)x1 pat} \]
\text{arr} The analysis was by array (\text{arr}) comparative genomic hybridisation (\text{cgh})
\text{[hg18]} Human Genome build 18. 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. The current build is hg38.
\text{14q11.2} The chromosome involved is \text{14} and the position of the deletion is in band \text{q11.2}
\text{(19229020–19462732)} The base pairs between \text{19229020} and \text{19462732} have been shown to be deleted. Take the first long number from the second and you get \text{233,712} (0.234\text{Mb} or 234\text{kb}). This is the number of base pairs that are deleted.
\text{x1} means there is one copy of these base pairs, not two – one on each chromosome \text{14} – as you would normally expect.
\text{pat} means that the deletion has been inherited from the father; \text{mat} means that it was inherited from the mother.

Comparing your child’s genetic test results with others, both from the medical literature and within Unique, 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 test results. After all, each of us is unique.

Sleep
Among Unique children with a 14q11.2 deletion, 2 families report a sleep problem. In one child it is thought to be due to an underlying anxiety. In the other child, with a large 14q11.2q21 deletion, the cause is physical, in that he has sleep apnoea where he stops breathing for short spells.

“I can’t even begin to describe how she has contributed to our family. I am a better person every day because of her.”

“He has a wry smile and it is so heartwarming when he gives you that. He has made the family appreciate that being healthy is far better than being wealthy.”

Notes
Autism

Many children with 14q11.2 deletions exhibit behaviours which indicate that they have an autistic spectrum disorder (ASD). This may be a key feature of a 14q11.2 microdeletion syndrome. ASDs are associated with impaired social skills, problems with communicating and a need to carry out repetitive and restrictive behaviours (obsessive-compulsive disorder [OCD]). A boy with a 14q11.2 deletion was very shy, avoided eye contact with strangers and had specific everyday rituals that he felt compelled to carry out (OCD) [Drabova 2015]. A four year old girl with repetitive movements and echolalia (speech repetition) underwent more formal testing using the Autism Diagnostic Observation Schedule (ADOS)-module 1 and the Childhood Autism Rating Scale (CARS). These tests look at areas such as the ability to communicate and interact socially. Both tests produced results suggesting an ASD. The diagnosis was confirmed by follow up tests at the age of 8 years [Prontera 2014]. ASD was also suspected in several other people with 14q11.2 deletions of varying sizes, including a 21 year old woman [Zahir 2007; Terrone 2014].

Among Unique families, no child with a 14q11.2 deletion has a formal diagnosis of autism, although three families report that their child has some characteristic features, such as social communication difficulties, some repetitive behaviours, and sensory hypersensitivities.

The Supt16h and CHD8 genes which are located on 14q11.2 belong to a class of genes that have been associated with ASD, with a particularly strong link for CHD8 (see Genes, page 18-19).

How did it happen?

A blood test to check both parents’ chromosomes allows parents to find out how the 14q11.2 deletion occurred.

Where both parents have been tested and have normal chromosomes, the deletion occurred in the child for the first time and was not inherited. Geneticists call this de novo. De novo 14q deletions are caused by a change that occurred when the parents’ sperm or egg cells formed, or possibly during the formation and copying of the early embryonic cells.

The great majority of 14q11.2 deletions are de novo. In a minority of cases where the microdeletion is very small, it may also be found in the mother or father. The parent would usually be unaffected by it, or only mildly affected.

Whatever the situation, there is nothing you, as a parent, did to cause the deletion, either before or during the pregnancy. Parents should feel reassured that no lifestyle change – environmental or dietary – would have prevented it from occurring.

Can it happen again?

In families where both parents have been tested and have normal chromosomes, the possibility of having another child with a 14q11.2 deletion is almost certainly no higher than anyone else’s.

So long as the parents have normal chromosomes, the extremely unusual sequence of events that led to a baby with a 14q11.2 deletion is very unlikely to happen again.

There is a remote possibility that a blood test would show normal chromosomes in both parents, but a few of their egg or sperm cells would still carry the 14q deletion. Geneticists call this germline mosaicism. It means that parents whose chromosomes are normal when their blood is tested can have more than one child with the deletion.

If either parent has a 14q11.2 microdeletion, there is a 50 per cent chance of passing it on and a 50 per cent chance of having normal chromosome 14s. The parent’s ability to look after a child is very likely to be related to their own degree of learning ability.

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; 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 these tests are available worldwide.
Can it be cured? How can it best be treated?
Unfortunately, there are no specific treatments at the moment to stop or reverse the progression of the effects of a 14q11.2 deletion. Managing the care of a child with a 14q11.2 deletion focuses on their individual symptoms, making the very most of their abilities. A dynamic team approach works best, with specialist input from developmental paediatricians, physiotherapists and occupational therapists. Psychosocial support for the families plays an important role.

Is there a 14q11.2 microdeletion syndrome?
Researchers believe there is a growing body of evidence for a specific 14q11.2 microdeletion syndrome (Zahir 2007; Prontera 2014; Terrone 2014; Drabova 2015). Some children’s facial appearance is strikingly similar and there are developmental and medical features that are common to many of them. There is a critical region within 14q11.2 where the genes CHD8 and SUPT16H are found. When these genes are lost, the features associated with 14q11.2 microdeletion syndrome are generally found (see Genes, pages 18-19)
When the deletion extends beyond the 14q11.2 band, the effects tend to be more marked and more complex (Prontera 2014; Terrone 2014; Drabova 2015).
Unique also publishes a guide to 14q12 deletions.

Most common features of microdeletions of chromosome 14q11.2
- Developmental delay/learning difficulties
- Hypotonia (low muscle tone)
- Macrocephaly (an unusually large head)
- Autism spectrum disorder
- Typical facial appearance including ears that stick out (prominent), a small lower jaw (micrognathia) and widely-spaced eyes (hypertelorism) (Zahir 2007; Prontera 2014; Terrone 2014; Drabova 2015; Decipher database; ISCA database; Unique)

Pregnancy
In the medical literature the majority of pregnancies were described as uneventful and went to term (Zahir 2007; Prontera 2014; Terrone 2014; Drabova 2015). Most pregnancies at Unique went to term and any problems were only noted after the delivery but one baby with a large deletion extending to 14q13 was delivered at almost 35 weeks after early separation of the placenta and concerns over possible shortage of amniotic fluid (oligohydramnios). Two further babies were born at 37 weeks.

At birth
The range of normal birth weight in babies without chromosome anomalies is 2.5 kg (5lb 8oz) to 5kg (11lb). Average birth weight in babies without a chromosome anomaly is 3.4 kg (7lb 8 oz). Expected head size in baby boys

Behaviour and sensory issues
Children and babies with a 14q11.2 deletion are described as generally easy-going and happy. Some had tooth grinding (Zahir 2007; Allou 2012). Several children have been described as having autistic-like features, such as hand-wrunging and repetitively opening and closing doors, and one child who is otherwise mildly affected has shown social communication delays (Prontera 2014). One child had poor social interaction for all her first year but had improved and acquired some imitative play skills by school age (Zahir 2007; Fonseca 2012) (see Autism, page 16).
Sensory hypersensitivities have been seen in some children (Unique).

“He has a lot of trouble in social situations. He is very shy and hides and it takes him a long time to get comfortable. He has trouble communicating and interacting with other children. He is still unsure of himself in all that he does. He has a very hard time with tactile activities. Touching different textures is very difficult for him. These are all still issues we are dealing with although he has been improving: it seems that warm up time has decreased and he is starting to initiate play and interaction with peers.” 14q11.2 deletion, 5 years

“He remains quite placid in nature but enjoys interaction with his family. He has still never had a tantrum and rarely cries. He is still anxious about new situations and some sounds and sights such as shadows and reflections. He often asks the same question repeatedly even when given an answer. He has had episodes of strange movements (torso stretching, strange eye movements) which have been diagnosed as stereotypical movements. He has an aversion to lying on his back and refuses to lie down for a nappy change away from home due to extreme anxiety. He has always been fearful of being moved without being in control of the movement and so does not tolerate rough and tumble play or going on a swing.” 14q11.2 deletion, 5½ years

“I would describe her as having very little self-awareness in terms of her appearance (messy face, twisted clothing, etc). She needs lots of reminders. She also has unusual phobias, and at 14 she still has sensory issues: she likes to fidget and roll things in her hands. She has a concerning high pain tolerance. For example, we recently discovered a very severely infected ingrown toenail that she hadn’t said anything about. Most children would have been in a great deal of discomfort and when I asked her why she didn’t tell me, she said “I don’t know. It didn’t really hurt”. That’s just one example. She never really complains about anything.” 14q11.2 deletion, 14 years
One child with a microdeletion at 14q11.2 was talking well at four years, and a child of nearly 5 spoke some single words. Another child successfully learned limited sign language to help him communicate. A teenager of 14 with a tiny microdeletion was talking, although his speech was unclear. At Unique, the three children we know are talking have a small deletion within the 14q11.2 band. They started to say recognisable words between 18 months and the age of 3, and some learned signing to support their language development (Zahir 2007; Prontera 2014; Drabova 2015; Unique).

The speech of one child suggested autism (see Autism, page 16), when she exhibited echolalia, repeating phrases and words without meaning (Prontera 2014).

Where the deletion extends beyond 14q11.2, there is an increased possibility that the child will not learn to speak, and will use other means to communicate such as vocal sounds, signing and assistive communication devices.

"Mild social communication delays." 14q11.2 deletion, 14 years

"At 2½, he had never babbled and had only a few sounds. His understanding was really developing though, and he understood more than he could show and could follow instructions related to his routine.

"He began to copy some Makaton signs at 2½ and understood that he needed to use his hands if asked to sign something.

"At 3½ he was starting to try to copy everything. He still had great difficulty in making different sounds and most of his words began with g or n. He rarely formed a sound involving the front of his mouth. By now he had names for all the family members.

"By 5½, he had made excellent progress. In a familiar environment with close family he is now able to speak in full sentences. His sound formation is improving but he still makes many sounds at the back of his mouth. However, even at home he still finds direct questions difficult and will only answer with ‘I don’t know’. He does not speak when in a group or with unfamiliar people. He also has a limited range of facial expressions which makes it difficult to interpret his needs.” 14q11.2 deletion, 5½ years

"He only finally started putting a couple of words together around his third birthday. Now he is starting to speak in short sentences or statements. When he does speak he is very quiet and has trouble with eye contact. He is getting better with speech but still seems to have anxiety with speaking to adults in school. His school speech therapist said that he has many characteristics of children with selective mutism. He still struggles with multi-step directions and needs longer than others to process questions and requests.” 14q11.2 deletion, 5 years

"Apart from crying and laughing, he makes very few different sounds.” 14q11.2q21 deletion, 4 years

A wide range in the birth weight, length and head circumference has been observed, but the great majority of babies fell within the normal range. In the medical literature, babies with a 14q11.2 microdeletion ranged in weight from 4950g/10 lb 15oz to 2650g/5lb 13oz. Length at birth varied from 54cm (21 inches) to 48cm (19 inches). The range in head circumference is from 38cm (15 inches) to 32cm (13 inches) (Zahir 2007; Prontera 2014; Terrone 2014; Drabova 2015). At Unique most babies with a small deletion limited to 14q11.2 weighed very close to the population average - 3.42 kg (7lb 9oz). For babies with a larger 14q11.2 deletion, average birth weight was above the population average at 3.7 kg (8lb 3oz).

For some babies, no problems were reported in the newborn period. One baby had respiratory distress, and two structural heart problems that needed surgical correction; another baby also had breathing problems and needed tube feeding (Zahir 2007). Another had seizures caused by a low blood sugar (Drabova 2015).

The Unique babies’ condition varied: most seemed to be healthy without medical concerns, but one needed resuscitation, one had difficulty establishing feeding, and one was in a poor condition after an induction before term because of a failing placenta.

Feeding
Feeding difficulties are common, with some babies finding it hard to latch on to the breast and even struggling with a bottle. The Unique series shows that breastfeeding was exceptional. With age, feeding improves but families need support and difficulties can persist. Some babies have low muscle tone in the face, making sucking and later chewing more difficult. Swallowing may also present a challenge. The most affected babies, in Unique’s experience those with large 14q11.2 deletions extending to 14q13 or 14q21, need feeding through the nose (tube) or direct to the stomach (gastrostomy) for some time.

The good news is that children can get over their feeding difficulties and be eating family foods by school age or even earlier.

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Gastro oesophageal reflux (GORD, GERD), where the stomach contents return up the food passage, is common and while often improving with age, can be troublesome and persist into childhood. It can affect babies and children whatever the position or size of their deletion. Reflux raises a baby’s risk of inhaling feeds and causing an infection in the lungs known as aspiration pneumonia. Reflux can be eased by careful semi-upright positioning during and after feeds, sleeping in a prescribed sleep chair rather than a bed, raising the
head end of the baby’s cot and if necessary by prescribed medication that helps to keep the feed within the stomach. Babies who have continuing problems can have a fundoplication, a surgical procedure to improve the action of the valve between the food passage [oesophagus] and the stomach.

Constipation is common, and is particularly associated with 14q12 deletions, so is most likely to affect babies and children with a large 14q11.2 deletion. Many children need to take daily laxatives [Unique].

“Poor sucking skills. Fed by gastrostomy tube.” 14q11.2q21 deletion, 13 months

“One of the biggest problems is his eating. At around 14 months he started regressing in his eating habits and stopped eating table food. Over time he has stopped eating most foods and rarely gains a new one. He does not eat fruits, vegetables or protein. He only eats soft or crunchy foods that dissolve easily in his mouth. He seems to have a lot of trouble biting and chewing and has very low muscle tone in his mouth and face.” 14q11.2 deletion, 5 years

“He was very difficult to feed at birth because he was sleepy and had polycythemia [a high red blood cell count]. He had no idea how to feed and seemed to have no sucking reflex. We persevered with breast feeding and although it was never easy, managed for about 10 months. At 2½, he ate brilliantly and had no swallowing difficulties. At 3½, he was feeding himself really well, could use a fork and spoon properly, and could bite into a wide range of foods, but regularly overfilled his mouth. Two years on, he still has a good appetite, but he still needs everything chopped to bite-size pieces.” 14q11.2 deletion, 5½ years

Hypotonia
An unusually low muscle tone, so that the baby or child feels floppy to handle, is common in 14q deletions involving 14q11.2 as in many other chromosome disorders. The degree of hypotonia may be mild and may resolve over time, but it may be more marked. Babies with hypotonia tend to lie with their arms and legs loosely outstretched instead of bent at the knee or elbow. When held under the arms, their bodies easily slip through the hands. In one baby, head control only evolved by 6 months (Zahir 2007; Terrone 2014). Every Unique family with a child with a 14q11.2 deletion who told us about their child’s muscle tone reported hypotonia.

Babies and children with hypotonia benefit from early intervention with physiotherapy.

“He had poor head control as a baby, and general poor tone of his core muscles for the first 6 months. At 3½, his muscle tone was still low but he managed brilliantly, walking quite confidently indoors and occasionally trying to run. At 5½, his muscle tone is still low. His ankles are still very flexible and he still needs to wear Piedro [support] boots with inserts to stabilise his ankles and stop his feet from rolling inwards too much. He has recently started to be able to perform a jump.” 14q11.2 deletion, 5½ years

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Learning
We only have limited information relating to learning, but it is clear that children with a 14q11.2 deletion are likely to need educational support. The level of support varies, and evidence suggests that the larger the deletion, the greater the probability of more marked learning difficulties (Santen 2012).

One boy with a 14q11.2 deletion attended a mainstream school from the age of 8 years, but was transferred to a special school after one year. When assessed at the age of 14 years he had mild learning difficulties, with an IQ estimated at 50 – 55 (Drabova 2015). Similarly, a 21 year old woman had an IQ of 45 (Terrone 2014), and an 8 year old girl had an IQ of 76 (Prontera 2014).

Among Unique children, all had or were suspected to need some support with learning. Children attended both mainstream schools with extra help, or special schools better suited to their needs.

“He has settled very well. He is able to recognize about 15 letters and the numbers 0–9.” 14q11.2 deletion, 5½ years

“She has a fantastic memory recall for dates and places and events. She really likes school. She does really well in math and science.” 14q11.2 deletion, 14 years

Speech and communication
Generally, speech and language reflect the level of learning disability and children with greater learning difficulties appear to use less speech. Understanding is also affected but children generally understand more than they can express. Many children with a limited 14q11.2 deletion will develop speech, but it may not be clear or fluent.
Teeth
At the age of 20 months a boy with a 14q11.2 deletion was found to have accelerated teeth maturation and already had 17 teeth; however, when he was re-examined at the age of 9 years his milk teeth had not been replaced by permanent teeth and he needed treatment to correct overcrowding. A 10 year old girl with a similar microdeletion had unusually large central incisors (front teeth) and required a brace (Prontera 2014; Drabova 2015). Three out of 4 Unique families who completed a survey in 2016 mentioned dental abnormalities. These included severe crowding and weak enamel (at 14 years) and small, but well-formed teeth (at 4 years).

Spine
A girl of 13 was diagnosed with a moderate progressive spinal curve (scoliosis), with muscle weakness in her hips and legs contributory factors. She has a very unusual stance and gait (Unique).

Development
Sitting, moving - gross motor skills
Babies and children with a 14q11.2 deletion are likely to be a little slow in reaching their developmental `milestones' of sitting, moving and walking. Most children have low muscle tone, which can make it harder to learn to control the body. One boy was reported to have delayed motor milestones at the age of 6 months, but at later follow up no further delay was reported. Other children were walking by 20-26 months. Among Unique children, two were sitting by 6 and 9 months, and three started walking between 18-22 months. Two others, one with a large 14q11.2q21 deletion, were still unable to sit with support or to walk at 22 months and 4 years. A girl of 4½ had the physical abilities of a child of 2 to 3. An adult walked with her feet well apart, and tended to stumble and fall (Zahir 2007; Prontera 2014; Terrone 2014; Drabova 2015).

He has trouble with balance, both gross and fine motor skills, and motor planning. This has improved with the last 3 years of physical therapy, swimming, tumbling and yoga, but he is still not as stable as other children his age. He is starting to run a little better and faster but still not as smoothly as other typical children.” 14q11.2 deletion, 5 years

In all instances, early physiotherapy input is important to assess babies’ needs for therapy and equipment and to guide families to stimulate early activity.

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. A child who is late to hold his head steady may still reach for toys. A child of 4½ had moderate delay, with the fine motor skills of a 3-4 year old (Zahir 2007). Where there is a delay early intervention by occupational therapy to stimulate hand use is vital.

Head
The range of outcomes for babies with head and brain anomalies associated with a 14q11.2 deletion is quite broad; your child’s neurologist or paediatrician is best placed to interpret what they are likely to mean.

Reports in the medical literature suggest that microdeletions involving 14q11.2 are often associated with macrocephaly, where the head is larger than would be expected. The head circumference seems to become proportionally larger with age and has been found to be on the 97th centile or above, meaning that the baby’s head is as large or larger than 97% of the population. This is not however always the case: one child was born with a relatively small head, as small as the lowest 10% of the population (Zahir 2007; Prontera 2014; Terrone 2014; Drabova 2015).

The evidence for a large head at Unique is much less clear. Expected head size in baby boys ranges from 31.5cm (12 inches) to 39cm (15 inches), and in baby girls from 32cm (13 inches) to 38 cm (15 inches).

One baby was born with a head circumference at the top limit of the normal range, but by the age of 14 her head was normal-sized. Other babies and children had smaller than average heads, although one boy with a very large 14q11.2q21 deletion had a large head but a small brain. In one child with a deletion within the 14q11.2 band, the corpus callosum, the band of nerve fibres linking the two sides of the brain, was almost completely missing (See also Seizures, page 11) (Unique).

Appearance
There may be little sign in the appearance of some babies and children with a 14q11.2 deletion of the underlying disorder. Doctors may notice what are known as dysmorphic features which are not always obvious to a parent. Each baby is an individual and some have almost no features considered 'typical'. Common facial characteristics include widely spaced eyes with high arched eyebrows and epicanthal folds (where the skin fold of the upper eyelid covers the inner corner of the eye); a broad, flat nasal bridge and short nose; a long groove between the nose and upper lip; an obvious ‘Cupid’s bow’ on the upper lip and a full lower lip. Children with ‘pointy’ or low set ears have also been described. One baby with a large 14q11.2 q21.1 deletion had a triangular face and a prominent chin. Other facial features mentioned by Unique families include a large lower jaw and a slightly broad face, short slits for the eyes, unusual ear lobes, a small mouth and a small lower jaw (Zahir 2007; Terrone 2014; Drabova 2015; Unique).

“Looks perfectly normal.”
Heart
One baby was born with a hole between the upper chambers of the heart (atrial septal defect/ ASD) which closed naturally without treatment (Prontera 2014) and another with a hole between the lower heart chambers (ventricular septal defect/ VSD) that again closed naturally and a large PDA, needing surgical correction in the newborn period (Zahir 2007).

Hands and feet
Minor, non-functional anomalies of the hands and feet are relatively common in children with chromosome disorders.

A common feature of many chromosome disorders including 14q11.2 deletions is cutaneous syndactyly (when the skin of two or more toes – often the second and third toes - or fingers is fused together) and clinodactyly (when the toes and/or fingers are curved inwards) [Zahir 2007; Terrone 2014; Unique]. These anomalies rarely cause problems and do not generally need treatment. The DAD1 gene (see Genes, pages 18-19) has been suggested as a candidate gene responsible for the skin webbing (Terrone 2014).

Other anomalies have been described in only one or two people: a boy with unusually large hands and feet and a girl with prominent digit pads (the soft tissue covering the tips of the fingers) as well as a woman with small hands and tapering fingers [Prontera 2014; Terrone 2014; Drabova 2015]. Flat feet are relatively common in children with chromosome disorders and occur in those with a 14q11.2 deletion (Zahir 2007; Drabova 2015; Unique). They are generally related to low muscle tone, but should be assessed, and if necessary your child can be prescribed shoe inserts or supportive footwear. Other features include prominent heels (Zahir 2007; Unique) and ingrowing toe nails (Unique).

Growth and weight gain
A range of birth weights, lengths and head circumferences has been reported [see At birth, pages 6-7], and reports in the medical literature suggest that children with 14q11.2 deletions are usually of average or above average height. The evidence from Unique is mixed, as some children are not tall for their age, while others are.

At the age of 21 years one woman weighed 107.5kg (almost 17 stone, heavier than 95% of women) and it was suggested that there was a risk of putting on too much weight, but again the evidence for overweight at Unique is mixed. See Genes, pages 18-19.

Seizures
Apart from seizures in a newborn caused by a low blood sugar (Drabova 2015) seizures have not been frequently reported in the medical literature. They are however common among Unique children with a 14q11.2 deletion, affecting 5/11, especially when the deletion extends to 14q13 or 14q21. Seizure types include absence seizures and infantile spasms (clusters of brief periods of movement of the neck, trunk, or legs that last for a few seconds and start before the age of 6 months). Generally seizures are well controlled with anti-epileptic medication. Seizures are specifically associated with deletions involving 14q12 (Bisgaard 2006; Papa 2008; Mencarelli 2009; Torgeykes 2011; Allou 2012; Ellaway 2012; Perche 2013), and so children with 14q11.2 deletions extending over the 14q12 band may be more at risk. They are also more common when there is a brain anomaly such as a missing corpus callosum (the band of nerve fibres that links the left and right sides of the brain).

Eyesight
Various problems with eyesight have been found in people with 14q11.2 deletions, usually minor and correctable with glasses. A boy of 15½ years was longsighted, and had semi-drooping eyelids (Drabova 2015). A child of almost 2½ had a squint (strabismus) and long sight (Zahir 2007). Among Unique members, two children with a larger 14q11.2q13 deletion had a squint. A delay in vision development was found in one of these children, as well as in a child with a 14q11.2q21 deletion. When the optic nerves were examined, they were found in one child of 5 to be extremely large and swollen (Unique), and a woman of 21 years was found to have an underdeveloped optic disc which was also pale. This is a sign of optic nerve damage; however, the transmission of electrical signals by the optic nerve was normal (Terrone 2014).