



Understanding Chromosome & Gene Disorders

Duplications of 2q



rarechromo.org

Duplications of chromosome 2q

A duplication of 2q means that the cells in the body contain extra material from one of the body's 46 chromosomes – chromosome 2. For healthy development, chromosomes should have just the right amount of material – not too much and not too little.

Extra material is likely to disturb development but how obvious and serious the disturbance is depends on the amount of duplicated material, on which part of the chromosome is duplicated and on what genes are disturbed.

Chromosomes are the structures in the nucleus of the body's cells that carry genetic information. They carry this information in the form of genes that tell the body how to develop, grow and function. Chromosomes come in pairs, one from each parent, and are numbered 1 to 22 approximately from largest to smallest. So chromosome 2 is almost the largest chromosome. Most chromosomes have a short (p) arm (at the top in the diagram on the next page) and a long (q) arm (at the bottom in the diagram).

A duplication of 2q means that the extra material is from the long arm of chromosome 2. A duplication of 2q has also been called partial trisomy 2q.



Five years old
with a 2q13q23 duplication

Sources & references

The information in this leaflet is drawn from what is known about 60 people with a duplication of 2q. Thirty-one people have been described in the medical literature with a pure duplication of 2q without loss or gain of material from any other chromosome arm. The first-named author and publication date are given to allow you to look for the abstracts or original articles on the internet in PubMed. If you wish, you can obtain most articles from *Unique*. The leaflet also draws on *Unique's* database. When this leaflet was written in 2008, *Unique* had 29 members with a pure duplication of 2q.

Many more people have been described in the medical literature with loss or gain of material from another chromosome arm as well, usually as the result of a chromosome change known as a translocation. As these people do not show the effects of a 'pure' duplication, they are not considered here. *Unique* holds a list of these cases in the medical literature and karyotypes of those in *Unique*, available to members on request.

Reasons for diagnosis

We know why the chromosomes of 20 youngsters were tested and this shows two distinct groups of reasons. In eight cases, babies' small size at birth together with their unusual facial features and sometimes early feeding difficulties or need for special care alerted paediatricians to seek a diagnosis. In just one case, a significant birth defect (missing nasal spine)



Six years old
with a 2q13q22
duplication

was a contributory factor. In the other cases, delayed development was the main reason for testing chromosomes, in one case with disproportionate speech delay. Sometimes parents were first to notice anything amiss – the absence of a social smile at two months, no ‘stepping’ reflex – and in one case there was a 15- year gap between parents noticing delay and the diagnosis (Lukusa 1999; Barnicoat 1997; Matos 1997; Cooke 1995; Couturier 1977; Unique).

Looking at 2q

You can't see chromosomes with the naked eye, but if you stain them and magnify them under a microscope, you can see that each one has a distinctive pattern of light and dark bands. You can see these bands in the diagram, right. They are numbered outwards starting from the point where the short and long arms meet (the **centromere**) (marked in yellow). A low number such as q11 is close to the centromere. Material close to the centromere is called **proximal**.

A higher number such as q37 is close to the tip (the **telomere**). Material closer to the tip is called **distal**.

The karyotype

The results of genetic (genomic) testing are likely to be given to you by your geneticist or a genetic counsellor. They will talk you through the results and can also tell you more about the genes and chromosome material that have been deleted.

Depending on the test that was carried out, someone with a 2q duplication might have results that look like one of these examples:

46,XY,dup(2)(q21→q23).ish dup(2)(q21q23)(wcp2+) de novo

46 = The total number of chromosomes in your child's cells

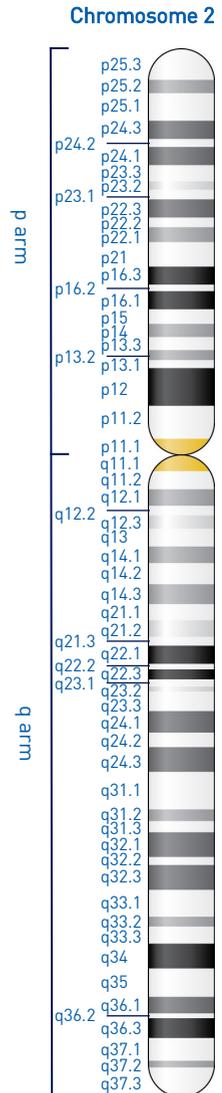
XY = The two sex chromosomes, XY for males; XX for females

dup = A duplication, or material has been repeated

(2) = The duplication consists of material from chromosome 2

(q21→q23) = The chromosome has broken in two places.

The first break is at q21 and the second break is at q23 so these are the ends of the duplicated section



.ish dup(2)(q21q23) = The diagnosis has been checked using a second technique known as FISH and the duplication from q21 to q23 confirmed
(wcp2+) = Using a technique known as whole chromosome painting, the extra material seen on the chromosome has been identified as coming from chromosome 2

de novo = The parents' chromosomes have been checked and no duplication or other abnormality found. The duplication has not been inherited.

The more commonly used test nowadays is called **chromosomal microarray (CMA)** and allows genomic DNA to be analysed in greater detail. An array test can detect very small duplications even when this diagnosis is not suspected. It will also identify a more precise position on the chromosome for the piece of DNA that has been duplicated.

arr[hg19] 2q12.2q13(107039678_111482522)x3 mat

arr = This result shows that the analysis used microarray technology.

[hg19] = Tells you which version of the human genome was used for comparison (see **Genome Assemblies** (blue box)).

2q12.2q13 = There is a DNA anomaly involving bands **2q12.2** to **q13**.

107039678_111482522 = The DNA anomaly is identified by its base pair numbers (the points where the change has occurred). This DNA anomaly lies between base pairs **107039678** and **111482522** (by taking the first number from the second, you can work out that this is 4,442,844 bp, or 4.4 Mb).

x3 = There is an extra copy (the normal copy number is two) so it is a duplication.

mat = The anomaly has been inherited from the mother (**mat**).

Genome Assemblies

The human genome project, an international effort to sequence the entire human genome and map all of its genes, was announced complete in 2003.

However, there were many gaps in the sequence and mapping data, and scientists have since been working continuously to identify the missing information. When new sequence information is identified, the base pair numbers of each chromosome change slightly and hence the numbers for individual genes and duplications can shift.

Each new version of the genome is often referred to as an 'assembly'. Every few years a new assembly is released. The genetic information you are given will be based on the Genome Reference Consortium (GRC) human (h) genome assembly that was the most up-to-date at the time the test was carried out. Therefore, you may see the DNA sequence referred to as hg19 (human genome 19) (on your child's genetic report it may also be referred to as GRCh37), which was released in 2009, or hg 18, which was released in 2006. The lower the hg number, the earlier the release.

The databases commonly used by clinical geneticists and *Unique* will soon move to a more recent assembly named GRCh38/hg38, which was released in 2013. Genetic reports will at some point also be altered, so genes and genetic changes may have new base pair numbers.

Is there a 2q duplication syndrome?

Chromosome 2 contains between 1200 and 1300 protein-coding genes so it's inevitable that people with different duplicated parts of the chromosome will be affected differently. Thus, it isn't easy to describe a specific 2q duplication phenotype, and many of the entries listed below have problems that are relatively common in other chromosomal disorders, such as low muscle tone, delays in development, failure to thrive and anomalies affecting the internal organs or the appearance of the hands and feet.

In addition to the chromosome 2 duplications, the genes on other chromosomes and environmental factors can also influence how people develop. This means that individuals with a 2q duplication can be as different from each other as they are similar. Overall we can't identify a clear enough pattern of similarities to say that there is a 2q duplication syndrome. It's possible that syndromes will in the future be identified for short duplicated segments of 2q but we can't be sure of this. Even if it is true, there will still be differences between individuals.

Are there people with a 2q duplication who are healthy, have no major medical problems or birth defects and have developed normally?

There are certainly people who are healthy and whose development is only mildly or moderately affected. A brother: sister pair each with a duplication of the whole of band 2q31, with breakpoints at 2q24.3 and 2q32.1, were healthy and, albeit somewhat delayed, were in mainstream education at primary school age (Barnicoat 1997). Two children with a small duplication of the 2q36 bands, with breakpoints at 2q35 and 2q37.1 were healthy and showed mild to moderate delay (Hermesen 2005; Fritz 1999). A baby with a 2q33.1q35 duplication was progressing well and only mildly delayed at 16 months, with a small hole between the upper chambers of the heart (atrial septal defect, ASD) (Sebold 2005).

A 14-year-old girl inherited a tiny microduplication at 2q32.2 to 2q32.3 from her mother who was much more mildly affected and only diagnosed because her daughter showed more delay (Willatt 2008). This apart, at the time of publication we are not aware of people with duplications of material from 2q who have shown no developmental delay but it is certainly possible that there are others scarcely affected by a relatively small duplication who have never been identified or reported by the medical profession.

What is the outlook?

The outlook for any baby or child depends on how the duplication has disrupted early development in the womb. The most important effect is on the major internal organs, especially the heart, kidneys and brain. Historically, babies with heart defects have not thrived as well as those born

with a healthy heart but improvements in children's heart surgery and cardiac care mean that today's outlook is generally better than in the past. There are many healthy older teenagers and adults with particular duplications and you may wish to compare your child with others with the same duplication. It's important to remember that the same duplication can have different effects on different people and there will be differences, sometimes quite marked, between your child and others with an apparently similar karyotype. It is very important to see your child as an individual and not to rely on direct comparisons with others who appear to have the same karyotype. After all, each of us is unique.

Your baby at birth



Five minutes after delivery (left) and two days old (right) - with a 2q34qter duplication

Most babies are small and light at birth, regardless of the size or position of their duplication. In many cases, the small size and slow growth rate was noticed during pregnancy; this is especially true of babies with a proximal duplication, up to around band 2q23. Babies with a more distal duplication were more likely to be born following an apparently normal pregnancy. The average birth weight (of 44 babies) was 2.8kg (6lb 3oz), so on average, this group of babies was in the smallest 15 per cent of the newborn population. But there were marked differences between individual babies. While one baby in three was as small as the smallest five per cent, one in four was a perfectly normal size and weight for gestation. The babies who had grown well in the womb and were a good size at birth had quite different duplications in size and position, including some with proximal duplications and a group with duplications of different sizes between 2q23 and 2q32.

Range of birthweights at or near term: 1.81 kilos (4lb) to 4.25 kilos (9lb 6oz)

Babies' condition at birth varies. Some new babies are born with a reasonable Apgar score (a measure of general wellbeing on a scale of 0-10), feed adequately and raise no concerns. Others have low initial Apgar scores and may need resuscitation and some time in special care, possibly with

extra oxygen. Some babies have a difficult delivery or are delivered after an emergency Caesarean or an induction when their small size or slow growth rate is noticed. Some babies have a weak or inaudible cry. Generally speaking, new babies feed reluctantly or with difficulty and may fail to show a sucking reflex, so it is difficult to establish breastfeeding. When they do feed, they may have problems coordinating breathing and swallowing. In the early days they may be helped by being fed through a nasogastric tube threaded through the nose and down to the stomach. Some babies are sleepy and less active than you expect (you may have noticed the lack of activity during pregnancy). If this is not your first baby you may notice that their facial features are different from their brothers' and sisters'. It is possible that your baby will need to spend some time in special care. This is an anxious time for parents, as medical staff may now seek a cause for any problems and take a blood sample to examine the chromosomes.



At three weeks old
- with a 2q21.2q24.2 duplication

“ She fed well at breast and bottle and was breastfed for two months. Her appetite was good but she remained under weight - 2q11.2q21.3 duplication

“ I tried to give her 30cc of milk every 3 hours but much of the milk was lost. She has swallowing difficulties and oral aversions which resulted in gagging and aspirations when she was given anything by mouth. By four weeks she was diagnosed with failure to thrive and I learned to place a nasogastric tube to supplement her feeds - 2q13q23 duplication

What about birth defects?

Few babies were born with a major birth defect that contributed to the diagnosis. One baby with a 2q12q21 duplication was born with the nasal spine missing and choanal atresia (blockage of the nasal passages) requiring a composite bone graft and several later revisions to improve the appearance of the nose. Three babies were born with complex heart malformations (Matos 1997; Schumacher 1983; *Unique*).

Facial appearance

A large number of unusual facial features have been noted by geneticists in reports on babies and children with a 2q duplication. Your baby or child may have just one or two of these features or sometimes more and you may find that he or she looks more like others with a 2q duplication than like other members of your own family – or you may find that your baby looks just like the rest of the family. The unusual features are not specific to 2q duplications and are found in people with many other chromosome



21 months old
(2q13q22q duplication)

2 years 9 months old
(2q31q32 duplication)

4 years old
(2q35qter duplication)

10 years old
(2q33q35 duplication)

disorders. They include: a short, broad nose with a low nasal bridge; low set ears that may have an unusual shape or be tilted back (posteriorly rotated); eyes set wide apart (hypertelorism) that may have an up- or downsweep (up- or downslanting palpebral fissures) and may have shallow sockets (and so protrude) or be deep set; tiny skin folds at the inner corners of the eyes (epicanthic folds); a prominent or rounded forehead; a thin upper lip; a short neck; a small and sometimes receding lower jaw which may self-correct over time (micrognathia or retrognathia); and a long (occasionally flattened) groove between the nose and the upper lip (long philtrum).

In a substantial minority of cases, your baby's head may be unusually small (microcephaly) and unusual shapes have been reported, including trigonocephaly (a pointed shape) due to early fusion of parts of the skull (craniosynostosis), as well as a flattened occiput, brachycephaly (the head is short from front to back) and plagiocephaly (longer on one side from front to back or asymmetrical). Hairless skin patches on the crown of the head and small areas where the skin has not grown properly have also been reported (Dennis 1978; *Unique*).

Hands

Your baby's hands may have some slightly unusual features. Many of these features are not specific to babies or children with a 2q duplication but are also found in other chromosome disorders. The hands may be small; the fifth finger may curve inwards on one hand or both (fifth finger clinodactyly); there may be a single crease across the palm (transverse palmar crease). Fingers may be tapered or long and slender or else one finger or more may be unexpectedly short. Finger joints have been reported that either do not straighten or remain fixed in a straight position; in an adult contractures increased despite splinting. In two cases fingers have been partly joined together (syndactyly) and in one case there was an extra finger.

Thumbs too have been reported that do not straighten or remain 'tucked in' across the palms. In two cases thumbs have been described as thick or broad and in one case grew from closer to the wrist than usual. Nails have been described as hollowed, soft or underdeveloped and in one case the

hands smelled unusual after the nails were cut or after showering or washing. In two cases the palms were unusually red and the hands puffy. A minority of babies 'fisted' for longer than usual but outgrew this tendency. In *Unique's* experience, children cope well with their unusual hands but if necessary, finger or thumb positions can be corrected by splinting, although this is not always successful (Hermsen 2005; Slavotinek 2003; Riegel 2002; Fritz 1999; Lukusa 1999; Seidahmed 1999; Barnicoat 1997; Grammatico 1997; Matos 1997; Cooke 1995; Dahoun-Hadorn 1992; Yu 1982; Dennis 1978; Couturier 1977; *Unique*).

Feet

Some babies with a 2q duplication are born with feet of an unusual size or position. Feet may be small and narrow, particularly if the duplication is proximal, or they may be large, broad or long and this is more common when the duplication is distal. There may occasionally be specific features such as a prominent heel or an unusually high or flat arch. The big toes may be somewhat broad, large or long and other toes may occasionally curl under or over the neighbouring toe. One case of a baby with an extra sixth toe has been reported and two cases of webbed toes. In one child the middle three toes were fixed in a bent position. Toenails have been described as small or so underdeveloped as to be virtually absent, abnormally formed or very rounded, regardless of the size or position of the duplication. An adult with a 2q21.2q24.2 duplication has developed osteoporosis in the feet, treated with calcium supplements. Many of these features will not affect walking, although a child with very flat feet may need special footwear or arch supports and babies with curling toes may benefit from soft splints to straighten them. A small minority of babies (6/59) have been born with their feet held at an unusual angle or club foot (talipes equinovarus). Treatment for an abnormal foot or walking position is individually tailored and aims to straighten the foot so that it can grow and develop normally. First-line treatment is non-surgical and may include manipulation, casting, taping, physiotherapy and splinting, followed by bracing to prevent relapse. Ankle or foot supports are often prescribed, as well as special footwear. Surgery and sometimes splinting are considered if non-surgical treatments are not completely successful. The foot position may relapse as the child grows and develops, making further surgery necessary (Slavotinek 2003; Riegel 2002; Bird 2001; Fritz 1999; Seidahmed 1999; Grammatico 1997; Matos 1997; Cooke 1995; Romain 1994; Dahoun-Hadorn 1992; Ramer 1990; Moller 1984; Schumacher 1983; Dennis 1978; Couturier 1977; *Unique*).

“ Her right foot curves a little but it flexes back, so should self-correct. She wears 'Sure Step' foot braces for low tone - 2q33q37.3 duplication, 18 months

“ Her feet are so small that she wears shoes for a baby aged 18-24 months 2q31q32 duplication, 3 years

“ The soles, like the palms, are more pink than the rest of her body
2q12q23 duplication, 3 years

“ She has severe bilateral pes planus (severe pes valgus foot deformities with midfoot breakdown) and tight heel cords that have been treated once with Botox injections. She wears braces on her feet with shoes – this helps to correct her feet into a neutral position and prevent further damage as she grows. The bones in her three middle toes on both feet have fused into a contracted position. There is no specific treatment but she may need foot surgery in the future - *2q13q23 duplication, 16 years*

Minor genital anomalies

Minor anomalies of the genital system are not unusual in the general population and appear to be slightly more common among babies and children, especially boys, with a chromosome disorder. In this group, 13/29 boys were affected. One or both testicles may not have descended into the scrotum by birth. Treatment for undescended testicles (cryptorchidism) depends on the suspected cause but whatever it is, 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. Some boys (5/29) are born with hypospadias, where the hole that is normally at the end of the penis is located on the underside instead. Other reported anomalies were a very small penis and a shawl scrotum (where the scrotum is higher than normal and the penis is wrapped within the scrotal fold). One boy was found to have an open processus vaginalis (a channel linking the abdominal cavity with the scrotum that usually closes around the time of birth. If it stays open, fluid can gather in the scrotum, causing a hydrocele).

The genitalia are usually less often affected in girls but in this group there were 7/31 reports of minor anomalies, none needing treatment. Reports included swollen, protruding labia; ‘untidy’ appearance; a prominent clitoris and a urethra tucked inside the vagina. A baby diagnosed before birth was found to have underdeveloped genitals and a further baby with a 2q21q33 duplication had small, unformed labia, an unformed vagina and a bicornuate uterus. In one girl the vagina and anus were unusually close, so that extra care with hygiene is needed at nappy changes (Shim 2004; Riegel 2002; Bird 2001; Fritz 1999; Matos 1997; Cooke 1995; Marchese 1984; Schumacher 1983; Dennis 1978; Couturier 1977; *Unique*).

Feeding

Many newborn babies have difficulties establishing feeding and some of these are documented in medical literature (Fritz 1999; Seidahmed 1999; Cooke 1995). But feeding difficulties are not universal – at least one *Unique*



At one year old - with a 2q34qter duplication

baby breastfed well, although she remained underweight – and in all six/19 babies were successfully breastfed, although some fed in very small quantities and extremely slowly. Some babies found breastfeeding too much even with a nipple shield and thrived better on breast milk given from bottles with teats suitable for premature babies or those with a cleft palate.

Beyond the newborn period, *Unique* has information on feeding histories from 19 children. These show a range of challenges, the most common being failure to gain weight, managed by high-energy feed supplements, feeding by naso-gastric tube or, in two instances, by gastrostomy feeding direct to the stomach.

Unique data show that some babies and children have gastro oesophageal reflux (where feeds and stomach contents return into the food passage and are often vomited or may be inhaled, causing chest infections, known as aspiration pneumonia) but this has generally been well controlled by giving feeds slowly, positioning a baby semi-upright for feeds and where necessary raising the head end of the bed for sleeping. If these measures are not enough, prescribed medications or anti-reflux milk are usually enough to keep feeds down. Reflux may resolve but it can be persistent: one 30-year-old is still affected. Weaning may present problems, with many families reporting reluctance to take lumpy food, to chew or to accept anything but a narrow range of tastes and textures. Reluctance to chew can be especially persistent and was repeatedly seen in adults.

Early appetite problems largely resolved in older children and adults; one seven-year-old child was liable to stuff his mouth until he vomited. Constipation was seen in four children or adults but usually responds to increased fluid, fibre or prescribed medication.

Palate (roof of the mouth)

An unusually high palate is common in babies and children with a 2q duplication, reported in around one third of cases. A high palate can make latching on and sucking more difficult and some babies make better progress with a nipple shield or, if bottle fed, with a variable-flow teat or one specially adapted for premature babies. After weaning, solids may become lodged in the palate; regular sips of drink can help to prevent this (Slavotinek 2003; Fritz 1999; Seidahmed 1999; Grammatico 1997; Ramer 1990; Marchese 1984; Yu 1982; *Unique*).

A cleft (split) in the palate has been reported twice with a cleft lip as well in one case (Riegel 2002; Lanman 1986). This is caused by an error in fusion when the fetus is forming in the first three months of pregnancy. A cleft palate causes difficulties both in feeding and in speech production. Surgical repair of the palate eases these difficulties and may eliminate them altogether.

“ She is very finicky and prefers food with little texture. She has ‘oral sensory integration issues’, cannot bite food and has difficulty chewing it. She needs a large amount of food in her mouth to register its presence and hoards food in her cheeks - *2q31q32 duplication, 3 years*

“ She had severe reflux from birth, which was treated with medication. Finally we discovered that when her constipation is under control, so is her reflux - *2q11.2q21.3 duplication, 8 years*

“ She had severe feeding difficulties when she was a baby. She had swallowing problems including aspirating and a strong oral aversion which resulted in gagging and vomiting. We fed her orally from a bottle any amount she would take, then supplemented the remainder through her gastrostomy tube. She had frequent aspirations and developed pneumonia several times. It was recommended that we stop all oral feedings due to the aspirating but we chose to continue to offer some foods for the variety of tastes and textures. As a baby and young child, she strongly disliked anything that was sweet such as fruit or cookies. She had a preference instead for spicy and sour foods. Her absolute favourite for many years was tomato juice and cheese. As she grew we continued to offer a wide variety of foods and as time went by she accepted more different types of food. We continued to give her supplemental feedings of PediaSure through her gastrostomy tube for about 10 years. Now at age 16 she eats a wide variety of foods, although spicy still tends to be a favourite. She is able to feed herself with a fork and spoon if the food is cut into bite size pieces. She drinks from a regular cup or straw. She had her gastrostomy removed at age 10. Occasionally we still see a gagging reaction to a food that she finds undesirable - *2q13q23 duplication, 16 years*

“ He has a good appetite but burns off a lot of energy and only chews food minimally so has a restricted diet to reduce the risk of choking. As a baby he had a good rooting reflex but was unable to draw milk and was diagnosed with failure to thrive at five weeks. He was then tube fed and though we tried to continue breastfeeding we resorted to a squeeze bottle to ensure he had sufficient intake - *2q21.2q24.2 duplication, 22 years*

“ Some difficulty in establishing breastfeeding. She was bottle fed from four weeks, but remained reluctant to feed. By a year, she was taking milk and juice from a beaker and solids if there were few lumps. Overall, she was a ‘lazy feeder’. But as an adult, you can’t stop her eating. Food is her great motivation! - *2q12q21 duplication, 27 years*

“ He was holding and using a feeder cup by a year. He showed no problem

taking a bottle but it was much more difficult when he went onto solids and as an adult he still has a lot of problems with eating and drinking, using it as a means to get his own way so we need to be very firm with him - *2q23q24.2 duplication, 30 years*

Growth

The majority of children and adults with a 2q duplication are unusually short and small for their family. The exceptions to this general rule include a child with a 2q21q31 duplication with a birth weight of 3.7kg (8lb 3oz) who had no feeding difficulties and was of average height at 10 years; a brother-sister pair with a 2q24.3q32.1 duplication with birth weights of 4kg or more; brothers with a 2q32.1q35 duplication and normal if below average birth weights and a toddler with a 2q33q37 duplication and normal birth weight. Some children are of below average height but within normal limits for the child population while others are exceptionally small. While some children maintain their growth rate on a percentile chart, in others the growth rate falls off over time.

The characteristic build for a child with a 2q duplication is both short and slender, with weight also below what is expected. However, there are children who are relatively plump.

Adults are also on the short side, although they are not typically exceptionally short, with heights for men ranging from 160cm (5'3") to 175cm (5'9") and heights for women ranging from 142cm (4'8") and 154cm (5'1"). Build among adults varies, with some adults becoming plump, while others remain in proportion and others remain slender (Hermesen 2005; Slavotinek 2003; Fritz 1999; Lukusa 1999; Glass 1998; Barnicoat 1997; Cooke 1995; Romain 1994; Ramer 1990; Dennis 1978; *Unique*).



At seven weeks old
- with a 2q13q23
duplication

“ Short and skinny; ‘pins’ for arms and legs -
2q13q22 duplication, 7 years

“ She looks like a 2-year-old - *2q11.2q21.3
duplication, 9 years*

“ She is very short for her age. Her height was below the tenth centile, dropping to below the third, she had no pubertal growth spurt and stayed a slim build until her late teens or early 20s when her weight increased. Today she is very active and eats well but is overweight with a protruding stomach and finds that trying to lose weight is difficult - *2q33q35 duplication, 32 years*

Growing up with a 2q duplication



**At three weeks;
nine months;
15 months; 7 years;
10 years; 21 years**
(left to right, top to bottom)
- with a 2q21.2q24.2
duplication



**At one day old;
one year old; two years;
two years;
three years old**
(left to right, top to bottom)
- with a 2q34qter
duplication



Development: sitting, moving, walking (gross motor skills)

Delay is typical in reaching the developmental 'milestones' of sitting, becoming mobile and walking. This means that your baby will make progress, generally following the expected developmental sequence, but progress will come slower than in other children. How much slower depends chiefly on your baby's innate abilities, but also on opportunities, on stimulation and to some extent on therapeutic interventions. It is hard to predict eventual mobility, but while in some it is virtually normal and gross motor skills are an area of particular ability, others may need a wheelchair long term. There appears to be little correspondence between the breakpoints in the chromosome, the size of the duplication and the support that a child will need with mobility. Individuals with very similar duplications have quite different eventual mobility levels (Sebold 2005; Fritz 1999; Seidahmed 1999; Romain 1994; *Unique*).

From *Unique's* experience, babies learned to roll over between three and 12 months, to sit without support between seven months and seven years, to become mobile between 10 months and four years and to walk, perhaps with some support, between 15 months and seven years. Not all babies crawled: some shuffled on their bottoms, scooted or slid along. Walking may remain unsteady for a long while after it is first achieved and most adults with a 2q duplication have an unusual gait. Your child may walk with their feet wide apart to improve their balance, they may find uneven surfaces a particular challenge and a buggy or wheelchair may be needed for outdoors or for long expeditions for a long while. Once on their feet, a few children rapidly acquire skills such as climbing stairs, running, skipping and hopping, but this is not possible for all.



At 9 months - with a 2q21.2q24.2 duplication

At twelve months and at 4 years - with a 2q31q35 duplication

At 8 years - with a 2q12q23 duplication

“ She first climbed stairs at 2½ and walked alone at three. She still struggles with walking; her balance is not very good and she holds her hand in front or holds onto walls and objects to improve her balance. She also still has difficulty moving between surfaces - 2q31q32 duplication, 3 years

“ She started walking at 4 years and could climb stairs by 5. We used a pushchair until she was nine but today she is very mobile, can walk for miles and practises running - *2q21q31 duplication, 10 years*

“ At the age of 12, she walks with pronation (her ankles lean inward) and a slight toe drag but she gets around on foot up and down stairs, tricycles and runs. She has upper body floppiness and wears supports for her feet and ankles. For longer walks and trips we use a wheelchair - *2q12q23 duplication*

“ At 16, she is independent in walking over most surfaces, although we usually hold her hand or arm when she is going up or down kerbs or walking on rough, uneven or icy surfaces. She is able to go up and down stairs independently if there is a hand rail. She has an odd run where she leans forward and goose steps. When sitting on the floor she usually sits cross-legged. She is able to pull her chair out at the table and sit down by herself but needs assistance moving closer to the table. She can jump with both feet to clear the ground. She enjoys riding an adaptive bicycle or tricycle - *2q13q23 duplication*

“ She can walk short distances alone and sometimes chooses to crawl. She cannot climb stairs, W-sits on the floor and cannot stand from sitting without help – she pulls up on furniture. Her mobility is getting harder due to scoliosis and her problems with hips and ankles. She may not be able to walk when she is older. For outings and travel she uses a wheelchair - *2q34q27 duplication, 17 years*

“ He can walk about the house with help from someone else - *2q23q24.2 duplication, 30 years*

One of the causes of the delay in mobility is a low muscle tone (hypotonia). This makes a child or baby feel floppy to handle and generally improves and may resolve with maturity, physiotherapy and exercises. In some children, muscle tone increases, so that muscles remain unable to stretch. Many children show a mixture of low and high body tone.

“ An exceptional climber, with great balance - *2q11.2q21.3 duplication, 8 years*

“ He had low tone as baby and wore adduction bandages on his legs for hypotonia. To encourage balance when learning to walk we used stretchy straps through his overalls shoulder straps (like a puppet). As an adult he has high tone in his arms and legs - *2q21.2q24.2 duplication, 22 years*

“ He enjoys playing football for his local special needs team - *2q12q21 duplication, 26 years*

“ He was a very floppy baby and could not hold his head up at all but overcame this with a lot of help by three years old - *2q23q24.2 duplication, 30 years*

Development: hand use, coordination (fine motor skills) and self care



Seven years old
(2q21.2q24.2
duplication)

Most children, though not all, experience quite considerable delay in controlling their hand use. As a broad generalisation, their skills match those of a child half their age. Recurring themes in parental reports are sensory integration issues, a weak hand grip, a delay in holding objects and motor apraxia. Small children find manipulating small objects such as buttons, poppers and zippers a challenge but with consistent training and verbal prompting many achieve feeding skills by mid childhood and dressing skills in late childhood or adolescence. In *Unique's* experience, children continue to need help to feed, dress and care for themselves throughout childhood and even as adults. However, some adults achieve reasonable

independence in self care. The exception to this general picture is a child with a very small duplication within the 2q37 band who reached his developmental milestones on time in early childhood despite weakness in fine motor skills.

In terms of self care, most youngsters achieve a quite high level of collaborative independence in dressing, washing and personal care tasks. It may not be appropriate for parents to expect toileting to occur at the same age as other unaffected children. Data from *Unique* suggest that in some children daytime bladder and bowel control may be achieved with a slight to moderate delay (between 30 months and 4 years), in others toilet timing is most successful, while in others control may not prove consistently possible (Sebold 2005; Riegel 2002; Cooke 1995; *Unique*).

“ At 3, she is at a 12-18 month level. Sensory integration issues mean she does not like to hold certain objects in her hands. We are working on incorporating textures such as rice, beans, corns and playdough into her therapies. She has difficulty in feeding herself due to a lack of coordination and will not allow her teeth to be brushed due to sensory integration issues - 2q31q32 duplication

“ She held her own bottle at nine months and has just learned to hold a pencil correctly and to cut but is not yet able to do snaps or buttons. She is dry during the day and wears pull-ups at night; can dress herself but needs help with shorts; and can brush her teeth with help - 2q35qter duplication, 4 years

“ He has no difficulty holding his bottle or toys but cannot use cutlery. He can remove his shoes, socks, trousers and nappy – but not to order - 2q31q35 duplication, 4 years

“ She plays with simple toys, uses a switch but cannot grasp - 2q13q22 duplication, 7 years

“ She holds her spoon and fork correctly now having learned using ABA techniques which showed her the correct way and rewarded her when she did it correctly. It took years but she’s finally doing it right. She’s also making tremendous progress with brushing teeth and dressing. With the help of ABA, she can do most steps with just verbal prompts - 2q11.2q21.3 duplication, 8 years

“ Her fine motor skills are quite limited. Her little finger sticks up when drinking from a cup; she uses a sippy cup but with a lot of incentives can use an ordinary cup. She can scribble, zip zippers, do puzzles with small tab holders, open doors, push buttons and use a computer mouse and keyboard. She still needs help with all her personal care: she can partially brush her teeth but is orally defensive so needs someone else to do it. She cannot dress herself but helps to put on her shirt and pulls up her - 2q12q23 duplication, 12 years

“ He can wash and dress himself and is very able: he has his own house key and is responsible for it. He can make his own tea and coffee, prepare a cold meal on his own and a hot meal when supervised by a carer, though he still holds cutlery and a pen awkwardly - 2q12q21 duplication, 26 years

“ He has motor apraxia but over time and with practice was able to perform skills independently - 2q11.2q21 duplication, 29 years

“ He couldn’t hold anything for a long time but with a lot of help he overcame this. He was holding and using a feeder cup by around 12 months but toys took a lot longer and even today he does not like using his hands - 2q23q24.2 duplication, 29 years

“ She was assessed as performing at a 5½ month level at 12 months. By 4 years she could build a tower of 8 bricks but was unable to copy a bridge and was not yet drawing a man, which is something that most 3-year-olds can do. Today, she can take care of her personal care herself but needs prompting - 2q33q35 duplication, 32 years

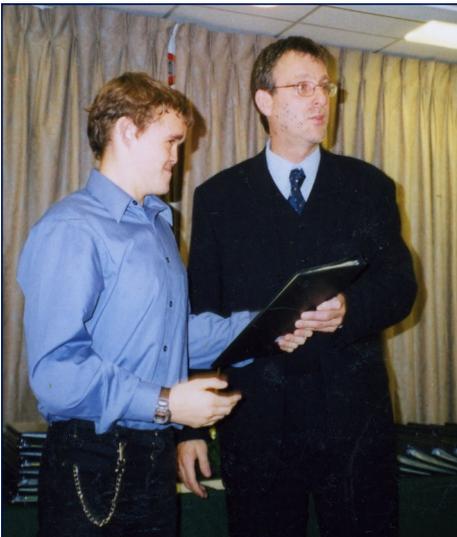
Learning

It is *Unique’s* experience that children will benefit from some extra support with their learning. How much support is needed usually only becomes apparent over time, and not enough experience has yet built up in youngsters with a 2q duplication to make reliable predictions. There are a number of reports in medical literature of school age children with a mild level of learning difficulty, some in mainstream education (Glass 1998; Barnicoat 1997; Cooke 1995; Gardner 1994). *Unique* has family reports of children and adults with difficulties that range from moderate to profound. It’s important to remember that youngsters with a learning disability are capable of considerable depth and complexity in their learning and may well learn some reading and writing skills.

“ She has a moderate to severe learning disability and started both reading and writing at 8 years. As an adult, she reads books for 5-7-year olds and

writes 6-8 word sentences. She also plays card games (Pairs, Uno, rummy) without help. She's a member of a drama and dance group; and she is a good cook, reading recipes and magazines, picking out words she knows and attempting those she doesn't - *2q12q21 duplication, 27 years*

“ Her level of learning difficulty is mild to moderate and she attended a mainstream school, reading from 6 years and writing from 5. As an adult, she has good keyboard skills; she can touch type; she is great at reading and spelling; reads magazines and books at a 10 year old level (e.g. Babysitter club books) and enjoys copying out the lyrics of songs - *2q33q35 duplication, 32 years*



19 years old - with a 2q12q21 duplication

This level of achievement will not be possible for all. A number of adults known to *Unique* do not read or write. There is variability in other underlying skills as well: many children, but not all, have an excellent memory; most children, but again not all, have reasonable powers of attention; most respond well to a reward system of learning. It is true that some youngsters will need extensive support and skilled 1:1 teaching to develop and maintain the skills they need for daily living. It is important for any family with a child with a 2q duplication to approach their learning ability with an open mind, to ensure that she or he is regularly and thoroughly

assessed and placed in a calm, stimulating and supportive learning environment where his or her strengths and abilities are recognised and built upon and weaknesses minimised.

“ She has memorised the alphabet and numbers, can count to 50 and can continue if she stops partway. She loves books and can find a favourite picture or poem in a book; she tears paper but has never torn a paper book and is very particular about how they are handled. She is very observant and we are very proud of how her brain seems to be functioning - *2q31q32 duplication, 3 years*

“ She functions at around a 2 year level and has a full scale IQ of 40. Learning a new concept is slow but is usually retained and her memory can be very good. She is able to use a switch device or touch screen computer with help and can colour, scribble and draw circles. She attends a Life Skills classroom with close to 1:1 staffing. Three afternoons a week she 'works'

sorting, cleaning equipment and shredding paper at a preschool facility - *2q13q23 duplication, 16 years*

“ He has a good memory for people and is very social so he learns in the company of people he likes. He studies the pages of popular entertainment industry magazines but cannot read or write - *2q21.2q24.2 duplication, 22 years*

“ He cannot read or write but he has a memory like an elephant and acute powers of observation. His strengths are social interaction and language - *2q11.2q21 duplication, 29 years*

Speech and communication



At one month and at three years old - with a 2q34qter duplication



Some information on speech and communication is available on 33 children and adults but while information from *Unique* is detailed, in the medical literature the information is sketchy. It shows that around half have acquired useful speech

and some children and adults speak fluently (*Unique*). Out of eight people over 16, four speak well, and in two of them speech is a particular strength; two have very limited speech; and two rely on signing, gesture, vocal noises and communication devices to express their needs. Understanding is consistently better retained than expression, both for speech and for signing, with non-verbal children able to carry out one-step and even more complex requests.

“ He has a great intent to communicate but lacks the tools. He has good receptive language but little expressive language - *2q21.2q24.2 duplication, 22 years*

“ His speech continues to improve even at the age of 29. He can talk in complete sentences, asks questions and converses on the phone. His understanding is better than his speech but he can express his ideas - *2q11.2q21 duplication, 29 years*

There is no obvious association between the size or position of the 2q duplication and the level of speech acquisition and generally the development of speech and language appears to reflect the child's cognitive abilities. Progress is slowed overall, with first words emerging late, between the ages of 12 months and seven years, and some but not all children acquiring more complex speech patterns. Some children showed

disproportionate delay in speech and language (Fritz 1999; Lukusa 1999). Around half the children over eight have not yet acquired speech, but communicate well using gestures and signing. Among those without speech, communication devices are popular and some use is made of sign language as well as gestures, facial expressions and picture symbols.

Some children have difficulty making particular sounds of speech, particularly certain consonants such as *c*, *k*, *v*, *g* and the final *y* sound (*Unique*).

“ She doesn’t speak but uses vocal noises or stands at the table if she’s hungry or turns away if she isn’t interested - *2q13q22 duplication, 7 years*

“ She is non verbal but uses a springboard at school and picture exchange at home in a notebook. She also uses gestures and several signs (more, please, yes, no). Her expression is based on simple needs and activities; she doesn’t understand feelings or illnesses. She also squeals, squeaks and hums well - *2q12q23 duplication, 12 years*

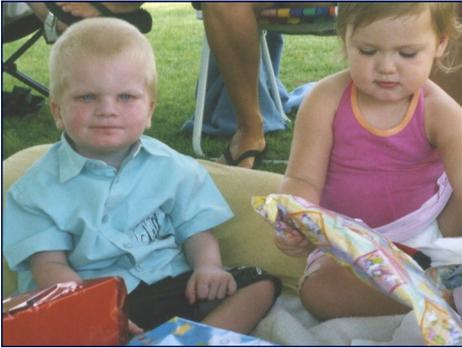
“ She is very good with visual symbols and logos like McDonalds and Tesco etc. - *2q34q37 duplication, 17 years*

“ He speaks well with a fair vocabulary considering his hearing problems. Some words are mispronounced but otherwise he communicates well and understands most things if he hears and listens properly. He uses long sentences but has difficulty with *or* and *r* sounds - *2q12q21 duplication, 26 years*

Behaviour

Unique has fairly detailed information on the behaviour of 16 children and nine adults with a 2q duplication. There are also brief descriptions of seven children and two adults in the medical literature (Riegel 2002; Lukusa 1999; Glass 1998; Barnicoat 1997; Cooke 1995; Dahoun-Hadorn 1992; Mu 1984). This is too small a number for a definitive picture to emerge but the remarks that follow may give families helpful insights.

Families most frequently mention that their children are happy and have good social interactions, more so with adults than with children, although in individual cases these may be late to develop and some children can become overwhelmed by a large social group and prefer individual contact. Other children and adults have autistic behaviours (repetitive play; difficulty changing routines) and may dislike close physical contact, although this tendency lessens with maturity and children learn to respond to love and physical affection. Some explore with their mouths and eat unintended objects. Older children and adults are generally caring, expressing concern at others’ distress, but some adults and children can be boisterous with others, wanting to claim the social limelight, or invade their space and need careful social skills teaching to avoid confrontation. A few children lack a sense of danger; a small number have an obsessive disorder (nail-picking,



At two years old -
with a 2q31q35 duplication

curbed by taping nails). Hyperactivity is commonly mentioned, and can be mild (getting overexcited) or extreme, as is a short concentration span and most affected youngsters have had psychological training or taken medication to cope with this. Some children have a fiery temper (most obvious at puberty) and some can be destructive, hitting, banging, smacking, biting and pulling hair, but this behaviour lessens in time.

Two related adults have been described with a 2q11.2q21.1 duplication who developed major psychiatric disorders in young adulthood (at 23 and 31 years) (Glass 1998). None of the nine adults known to *Unique* has developed any major psychiatric disorder but overall, six adults have received medication to help manage their behaviour.

Many youngsters are described as caring and have a good sense of humour although they do not always know when to stop. Children enjoy music (especially with a fast beat) and musical toys, books, computers, animals, outdoor activities like swinging, walking, playing in water and playing with adults. Adults enjoy music, listening to the radio or watching television, sports activities such as football, swimming, dancing, yoga and being sociable as well as collecting, computer-based activities and shopping.

Overall, most children and adults behave well when they are appropriately supported and even children who can be challenging at times can also be calm, quiet and lovely.

Sleep problems are common and around half the group take melatonin, as well as other medications, including clonidine, chloral hydrate and Vallergran.

Puberty

Unique has information on puberty in seven young women with a 2q duplication and three young men. Among the young men, secondary sexual characteristics developed and puberty progressed as expected at a normal age of 13-14 years. Two of the three young men developed difficult behaviours and one developed over-demonstrative sexual behaviour towards family and carers.

Five of the young women went through puberty as expected but one girl with a 2q34q37 duplication had a protracted puberty with six years between the start and finish and another young woman with a 2q33q35 duplication never underwent puberty. In four cases periods are described as scant or irregular. Five young women showed marked mood swings, with an increase in

Growing up with a 2q duplication



At seven weeks;
five years;
16 years;
with family
(left to right, top
to bottom)
- with a 2q13q23
duplication



At one year, two years; three years;
three years; and four years (left to
right, top to bottom)
- with a 2q31q35 duplication

unpredictable, aggressive or difficult behaviour. Seizure activity increased in two young women and was triggered by puberty in a third. In one case a spinal curvature became much more marked at puberty (Glass 1998; *Unique*).

Health matters

■ Kidneys

The most frequent health concern in babies, and to a lesser extent in adults with a 2q duplication, is a kidney and/or urinary tract problem. This ranges in severity from infrequent urinary tract infections to kidney failure requiring dialysis or transplant. However, an adult with a single, small, abnormal kidney who eventually required dialysis and transplant has two relatives with normal chromosomes and a single kidney; her brother who shares her chromosome complement has no kidney problems. Although kidney or urinary tract problems are common, four-fifths of people have no problems. Nonetheless, precautionary imaging of the kidneys and urinary system is advised.

Functional problems include various grades of vesicoureteric reflux, a condition where the valve between the bladder and the ureters is not working properly, urine from the bladder can flow back into the ureters and, depending on the severity, as far as the kidneys. This increases the risk of developing kidney infections that over time can damage and scar the kidneys. Reflux can be graded from 1 to 5. The higher the grade, the more severe the reflux. While most children with grades 1-3 reflux do not need intense therapy as the reflux usually resolves on its own, children with grade 4 or 5 reflux may need surgical intervention to prevent the reverse flow of urine to the kidneys. The first line of treatment is usually low-dose antibiotic treatment, which may give a child the opportunity to outgrow the reflux.

The structural defects include a single kidney; a pelvic kidney which is not in the normal position in the upper back but has failed to move up from the lower abdomen before birth; a horseshoe kidney, where the bottom points of the two usually separate kidneys are joined, creating a U (horseshoe) shape; small kidneys; narrowing and/or displacement of the ureters leading from the kidneys to the bladder; and enlarged kidneys (hydronephrosis) (Slavotinek 2003; Bird 2001; Seidahmed 1999; Glass 1998; Matos 1997; Ramer 1990; Marchese 1984; Moller 1984; Schumacher 1983; *Unique*).

■ Heart

Most babies with a 2q duplication were born with a healthy heart: 13/60 were born with a heart defect. It's hard to be certain quite how the 2q duplication affects heart development since no parts of the chromosome arm were particularly associated with heart defects and some duplications had inconsistent effects, with heart defects in some but not in others.

In 10 cases, the defects were treatable or did not need treatment, but three babies had defects that proved incompatible with life (Matos 1997;

Schumacher 1983; *Unique*).

One child with a probable duplication between 2q11.2 and 2q13 has malfunctioning valves and takes protective antibiotics for dental work. A child with a 2q11.2q21.3 duplication has a 'redundant aorta', also commonly found in the general population. Two babies with 2q21q33 duplications were born with quite different but severe and complex heart defects (Matos 1997; Schumacher 1983). A baby with a 2q13q23 duplication had a 'massively enlarged' heart at two months that led to congestive heart failure, for which she was treated with diuretics; however, by nine months, the heart resumed its natural size and at 15 she has no ongoing problems. A child with a 2q31q32 duplication has a hole between the upper chambers of the heart (atrial septal defect; ASD) and a leaky aortic valve. She tires easily and may need corrective surgery. A baby with a duplication between 2q33 and the tip of the chromosome had two holes between the upper heart chambers. Small holes, usually between the upper chambers, and sometimes in association with other defects, were also found in babies with partly overlapping duplications in the 2q33q37 region (Sebold 2005; Bird 2001; *Unique*). A small hole between the lower heart chambers (ventricular septal defect; VSD) did not affect a child with a 2q35qter duplication and needed no treatment.

■ Seizures

Most babies, children and adults with a 2q duplication have not experienced seizures.

A small minority (9/60) have had fits but in most cases have either outgrown them or the seizures have not recurred. Seizures have been of different types (partial complex, generalized absence and tonic-clonic seizures) and have generally been well controlled with standard anti-epileptic medications. Onset has ranged from birth to 16 years and remission from three years to 15 years. Electroencephalogram (EEG) recordings have been sometimes but not consistently abnormal. Brain imaging showed a variety of abnormalities in four cases.

In one girl with a 2q13q23 duplication and a partial complex seizure disorder, in whom a change of hand dominance followed one tonic-clonic seizure at the age of five, fits virtually ceased following the introduction of the combined oral contraceptive (Enpresse) to control her periods at 15 years. Only three of the nine are known to still be experiencing seizures. One of these is a girl with a 2q12q23 duplication whose frequent seizures cause her to be labelled medically fragile. Another is a girl with a 2q34q37 duplication whose seizures developed from febrile convulsions and who has a suspected diagnosis of photosensitive epilepsy (Riegel 2002; *Unique*).

■ General health and wellbeing

Most children and adults with a 2q duplication enjoy good or excellent health. Specific health concerns affect no more than two or at most three individuals

and so are probably not directly linked to the 2q duplication. Hernias have been identified in babies and children with a 2q13q23 duplication (umbilical and inguinal) and both 2q21.2q24.2 and 2q24.2q31 duplications (both inguinal). In an [inguinal hernia](#), part of the bowel loops through an opening in the inguinal canal. In fetal development, the testes descend into the scrotum through this opening which usually then closes. If it fails to close, or re-opens, part of the intestine can bulge through. The hernia usually appears as a swelling in the groin or enlargement of the scrotum. An inguinal hernia usually needs surgical repair. An [umbilical hernia](#) shows as an abnormal bulge at the umbilicus (belly button). It develops when an 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 but a very large hernia or one that stays open can be closed surgically.

Two related young adults with a 2q11.2q21.1 duplication developed insulin-dependent [diabetes](#), but this has not been seen in others with similar or overlapping duplications. A young man with a 2q21.2q24.2 duplication had a haemangioma (a benign overgrowth of blood vessels) removed from the bladder.

One adult has developed osteoporosis, leading to a hip replacement, and another has had multiple fractures of both small and large bones, although scans have shown his bone density to be normal.

A variety of respiratory problems have been described: a young child and an adult have reactive airways disease (asthma); one baby with a floppy larynx and wind pipe (laryngomalacia, tracheomalacia) who also developed heart failure needed a tracheostomy (a tube inserted into the wind pipe to allow oxygen and air to reach the lungs) and after developing respiratory distress, extra oxygen. By one year the oxygen could be withdrawn and by two years the tracheostomy was removed. Another baby with a 2q21q33 duplication was born with small lungs and probable atelectasis (failure of the lungs to expand) and a further child with a 2q31q32 duplication has lung disease for which she is treated with asthma medication.

[Infections](#) in babies and young children are common regardless of chromosome make-up and five individuals with a 2q12q23 duplication, a 2q21.1q24.2 duplication, a 2q31q33 duplication, a 2q32q37 duplication or a 2q34q37 duplication had frequent episodes of chest infections or [pneumonia](#), the first also having frequent gastrointestinal upsets. An adult with a 2q33q35 duplication had two bouts of pleurisy and has occasional asthma. Others have had frequent sinus infections. As a generalisation, children with chromosome disorders can become quite ill with infections and may need early hospitalisation for support with feeding and fluid intake. [Ear infections](#) are very common in young children and have been noted in one child with a 2q31q33 duplication.

A child with a 2q11.2q21 duplication had frequent [abdominal migraines](#) between the ages of 6-13; another child with a 2q31q32 duplication developed them at 3 years. Allergies are common in the general population and occur in this group as well. Two young children are reported to have [eczema](#), controlled with skin creams; an adult with a 2q11.2q21 duplication has [seasonal allergies](#), treated with loratadine (Claritin) (Sebold 2005; Slavotinek 2003; Seidahmed 1999; Glass 1998; Schumacher 1983; *Unique*).

■ [Eyesight](#)

Around half the people with a 2q duplication have normal eyesight. Others (27/60) have been reported with a sight problem of varying severity, from adults who need glasses for reading to others who are registered blind. Eighteen/60 are shortsighted or have a squint (strabismus). The main effects of a squint are that the person will usually have one eye which is stronger than the other. Treatment 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. Long sight is less common, but has been reported three times, once in association with a squint. Four children had nystagmus, an uncontrolled movement of the eyes back and forth, usually associated with reduced vision. One child was reported with glaucoma, involving damage to the optic nerve, and was successfully treated by surgery known as goniotomy to relieve eye pressure. One child had underdeveloped tear ducts, needing surgical correction, and another had missing tear ducts. One child had a coloboma of the iris, a developmental defect. One child had slow conduction of signals along the optic nerve (Hermsen 2005; Riegel 2002; Bird 2001; Barnicoat 1997; Cooke 1995; Mu 1984; *Unique*).

“[He lacks depth perception with a downward gaze as one eye strays up and out, resulting in difficulty managing steps - 2q21.2q24.2 duplication, 22 years](#)

■ [Hearing](#)

Most children and adults with a 2q duplication have normal hearing. Some individuals (18/60) have had a transient or more permanent hearing impairment in one ear or both, but this is not necessarily connected with the 2q duplication. Thirteen children have experienced a conductive hearing loss, where a build-up of fluid behind the ear drum, very narrow ear canals or both have stopped sound waves from reaching the inner ear. If persistent, this temporary, fluctuating form of deafness is usually treated by inserting tiny plastic tubes into the ear drum to aerate it. Five further children or adults have shown evidence of a permanent form of deafness and wear aids to enable them to hear. Three children are reported to have an unusual ear structure: in two cases, the ear canals are very narrow and one child has an extra lining to his ear, but normal hearing. This child is especially sensitive to high-pitched tones (Sebold 2005; Shim 2004; Slavotinek 2003; Riegel 2002; Barnicoat 1997; *Unique*).

“ My daughter was suspected to have a mild to moderate hearing loss but this was probably due to attention difficulties - *2q13q23 duplication, 16 years*

“ My daughter has had bouts of dizziness since 2000 that are possibly labyrinthitis - *2q33q35 duplication, 32 years*

■ Teeth

Generally speaking, children with chromosome disorders appear to have more dental problems than others. Information on 21 children and adults in the group shows that four children have a very narrow (lower) jaw and may need teeth removed due to overcrowding or braced due to irregular placement. Four individuals have teeth that are noticeably small, in one case with a size mismatch between the upper and lower jaws, and may be widely spaced or have small/shallow roots; two others have teeth of an unusual shape. In two cases, teeth emerged unusually early (one baby had a single tooth at birth), while in one child primary teeth emerged in an unusual order, with a single tooth at first in the upper and lower jaw and in two others all or some of the primary teeth were late to emerge; in another child primary teeth did not fall out before secondary teeth came in. One child had underbite due to a mismatch between the upper and lower jaw. Two adolescents have gaps in their permanent teeth or missing wisdom teeth. Some children are very orally defensive and resist having their teeth brushed; severe decay of the primary teeth has been seen in four cases. Accidents occur fairly frequently in which front teeth are chipped or knocked out (Hermesen 2005; Slavotinek 2003; Riegel 2002; Fritz 1999; Barnicoat 1997; Yu 1982; Couturier 1977; *Unique*).

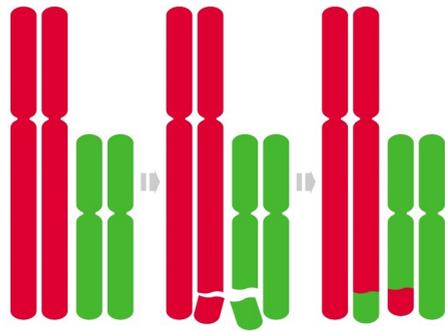
This adds up to a picture of youngsters and adults needing high quality, probably special care dentistry. But some youngsters have strong healthy teeth.

“ Spectacularly good! No decay; all teeth present bar the wisdom teeth at the age of 22, with very good placement. One front upper tooth was unfortunately knocked out due to a fall from a bus

How did the chromosome duplication occur?

A blood test to check both parents' chromosomes is needed to find out why the 2q duplication occurred in the child. Some 2q duplications are accompanied by a loss of material from another chromosome and are the result of a rearrangement in one parent's chromosomes. This is usually a rearrangement known as a **balanced translocation** in which material has swapped places between chromosomes (see diagram, page 29). As no material has been lost or gained, the parent usually has no major clinical or developmental problems, although they may have difficulties with fertility or childbearing. Balanced translocations involving one or more chromosomes are not rare: one person in 500 has one, making a total world population of over 13 million balanced translocation carriers.

Some 2q duplications occur when both parents have normal chromosomes. The term that geneticists use for this is *de novo* (dn). *De novo* 2q duplications are caused by a change that occurred when the parents' sperm or egg cells were formed. The underlying mechanism is not quite clear although we know that chromosomes must break and rejoin in quite a complex process when egg and sperm cells are formed but this only occasionally leads to problems.



A balanced translocation: material has swapped places between chromosomes

One possible way in which duplications might occur is by a mismatch between chromosomes. This works as follows: at one point in the formation of the sperm or egg cells, all the chromosomes including the two chromosome 2s pair up and swap segments. To pair up precisely, each chromosome 'recognises' matching or near-matching DNA sequences on its partner chromosome. However, throughout the chromosomes there are many DNA sequences that are so similar that it is thought that mispairing can occur. No-one has ever seen this happen, but it is believed that when the next step, the exchange of genetic material known as 'crossing over', occurs it is unequal, looping out or doubling up part of the chromosome.

What is certain is that as a parent there is nothing you did to cause the 2q duplication and nothing you could have done to prevent it. No environmental, dietary or lifestyle factors are known to cause these chromosome changes. They are no-one's fault.

Could my child with a 2q duplication have similarly affected children?

Unique has member families where a 2q duplication has been inherited from a parent and there are other cases in medical literature. The precise duplication varies, but includes families where a 2q11q13 duplication, 2q13 duplication and 2q21.2 duplication has been passed from generation to generation. Theoretically, someone with the duplication would have a 50% (1 in 2) chance of passing it on and a 50% (1 in 2) chance of having an unaffected child.

Can it happen again?

The possibility that a couple will have another pregnancy affected by a 2q duplication depends on their chromosomes. Where both parents are found to have "normal" chromosomes, it is very unlikely that another child will be

born with a 2q duplication or any other chromosome disorder. Very rarely (less than 1%), both parents have normal chromosomes by a blood test, but a few of their egg or sperm cells carry a chromosomal change. This is called germline mosaicism and it means that parents whose chromosomes appear normal when their blood is tested can have more than one child with the duplication.

If either parent has a chromosome rearrangement involving 2q, the possibility would be increased of having further affected pregnancies. However, the effect on that child's development, health and behaviour cannot be reliably predicted.

If they wish, parents should have the opportunity to meet a genetic counsellor or doctor to discuss in more detail what the implications are for having a baby. They will help you to decide whether or not you are interested in having any of the chromosome tests that may be available to you before or during pregnancy. If you are eligible and decide to have any of these tests, they will organise these for you. They can also arrange to give you the results and will be able to organise any necessary follow up support. Please refer to *Unique's* leaflet '[Planning your next child](#)' for detailed information about these tests.



Brother (three years old) & sister (two years old): the sister has a 'de novo' 2q21q31 duplication



Brother & sister: both have a 2q12q21 duplication and their mother has a balanced translocation with part of 2q inserted into chromosome 11

Adults with a 2q duplication



He lives with four other young men with very high support needs but still has lots of parental involvement. He likes his house, music, family pictures on DVD, fashion magazines with women, going out with Mum and his day program

and enjoys other adults' company.

21 yrs, with a 2q21.2q24.2 duplication



When she was 25, she moved into a Rudolf Steiner community with two carers and two friends. She enjoys her new social life and has become more independent and as well as joining a theatre group, for two days a week helps in the

kitchen and waits at table in their organic café.

27 yrs, with a 2q12q21 duplication



She has a daily carer and lives in a group home run by social services. The move was very easy and she enjoys it. She also swims, shops, watches soaps on TV and attends a social club for special needs.

23 yrs, with a 2q duplication (unspecified)



He lives in a group home and works in a sheltered workshop. He will always have limitations and require supervision for many of his needs but he is an able-bodied man

who attends synagogue weekly, goes to monthly dances and attends a college evening class. He swims regularly and participates in the Special Olympics.

29 yrs, with an inverted 2q11.2q21 duplication



He works part-time in a charity shop, has his own home and lives with his fiancée. A carer comes in at the main mealtime. He spends his spare time shopping, watching TV and at the sports club - and dreams of being a footballer!

25 yrs, with a 2q12q21 duplication



She works in an office one morning a week and in a workshop on the other four days. She is very sociable, attends church and loves music. Her behaviour is great when she is well supported but she

doesn't like plans being changed. She has a wonderful sense of humour and is very caring and loving.

32 years old, with a 2q33q35 duplication

Inform Network Support



Understanding Chromosome & Gene Disorders

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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 Dr Anne Slavotinek, clinical geneticist, University of California, San Francisco, US and by Professor MajHulten BSc, PhD, MD, FRCPath, Professor of Medical Genetics, University of Warwick, UK 2008. (PM)

V1.1 2021 (CA)

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