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15q duplications

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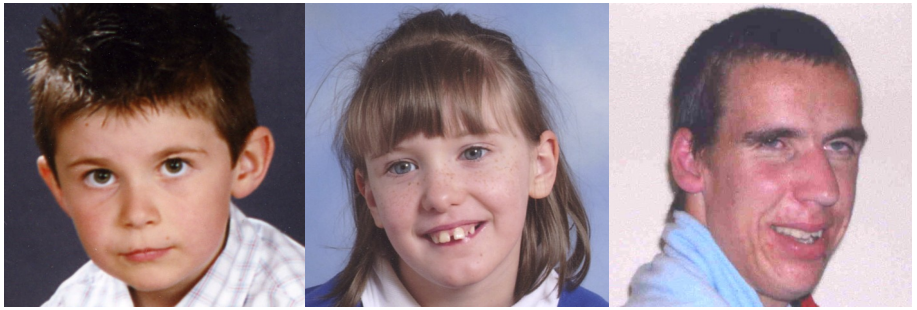


Version 2.1 2014

Rare Chromosome Disorder Support Group
Registered in England and Wales

Charity Number 1110661
Company Number 5460413

rarechromo.org

Sources and references

The information in this leaflet 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 (http://www.ncbi.nlm.nih.gov/pubmed). If you wish, you can obtain abstracts and articles from *Unique*.

The leaflet also draws on *Unique*'s database which contains regularly updated information that reveals how children and adults develop.

When this leaflet was revised in 2009, *Unique* had 83 members with a 15q duplication, of whom over12 had a pure 15q duplication other than the PWACR region (*see page 3*) that did not involve any other chromosome.

15q duplications

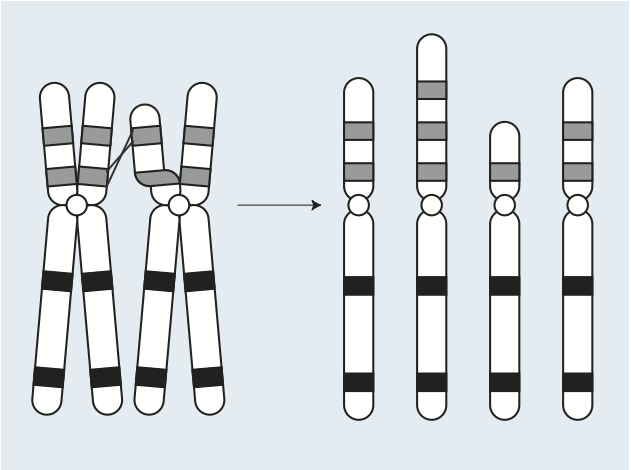
A chromosome 15 duplication is a rare genetic condition in which there is an extra copy of part of the genetic material that makes up one of the body's 46 chromosomes. A duplication is also called a **partial trisomy**. Like most other chromosome disorders, this increases the risk of birth defects, developmental delay and learning difficulties. However, the problems that can develop depend very much on what genetic material has been duplicated.

Chromosomes are the microscopically small structures in the nucleus of the body's cells that carry genetic information. They come in pairs, one inherited from the mother and one from the father and are numbered 1 to 22 approximately from largest to smallest, apart from the sex chromosomes (two Xs for a girl and an X and a Y for a boy).

Each chromosome has a short (p) arm and a long (q) arm. In chromosome 15 duplications, the p arm can generally be duplicated without harm, and any problems are caused by extra material from the q arm.

Chromosomes can be stained so that each has a distinctive pattern of light and dark bands when viewed at about 1000 times life size under a light microscope. You can see these bands in the diagram on the facing page. The bands are numbered outwards starting from the point where the short and long arms meet (the **centromere**). A low number such as q11 is close to the centromere and the part of the arm that is fairly close to the centromere is called the **proximal** part. A higher number such as q26 is closer to the end of the chromosome, in the part referred to as **distal**.

Your geneticist or genetic counsellor will tell you more about how much chromosome material has been duplicated and where the duplication has occurred. You will almost certainly be given a report of the **karyotype** (picture of the chromosomes), showing the breakpoints or a report of a molecular analysis such as array comparative genomic hybridisation, also known as microarrays. Comparing your child's karyotype with others, both in the medical literature and within *Unique*, will help to build up a general picture of what to expect from the duplication. But there will still be differences, sometimes quite marked, between your child and others with apparently similar duplications. It is very important to see your child as an individual and not to make direct comparisons with others with the same karyotype. After all, each of us is unique.



One way that a deletion and a duplication could theoretically arise during the formation of egg or sperm cells. On the left are two matching chromosomes, each split to the centromere and ready to pair and exchange segments. The shaded bars show similar sequences of DNA in the chromosome that enable correct pairing. But just above the centromere mispairing has occurred. When the chromosomes separate (right), the mispairing has given rise to two normal and two abnormal chromosomes, one with a deletion and one with a duplication.

How did the chromosome disorder occur?

Chromosome disorders are usually passed down in the sperm and egg cells. This is part of a natural process and as a parent there is nothing you can do to control it. Children from all parts of the world and from all types of background have chromosome 15q duplications. No environmental, dietary or lifestyle factors are known to cause them. So there is nothing you did before you were pregnant or during pregnancy that caused this to occur and there is nothing you could have done to prevent it.

A chromosome 15q duplication can occur as a result of rearrangements in one parent's chromosomes or it can happen out of the blue when parents have entirely normal chromosomes. A blood test to check the parents' chromosomes will show what the situation is.

If the check reveals a structural rearrangement of one of the parents' chromosomes, this is usually balanced so that all the chromosome material is present, and the parent is then almost always healthy.

When the parents' chromosomes are normal, the child's chromosome make-up is called a *de novo* (*dn*) rearrangement. There are a number of ways in which *de novo* 15q duplications can arise. The diagram on the facing page shows just one theoretical way in which a duplication can arise on a chromosome.

Could it happen again?

Where both parents have normal chromosomes, it is unlikely that another child will be born with a 15q duplication. If a test shows that either parent has a chromosome rearrangement involving 15q, the chances of further affected pregnancies with similar or occasionally different abnormalities are increased. Once the family translocation has been characterised, it will be possible to diagnose an unbalanced chromosome arrangement prenatally. Other family members should also be tested in case they, too, are carriers of the balanced form of the rearrangement.

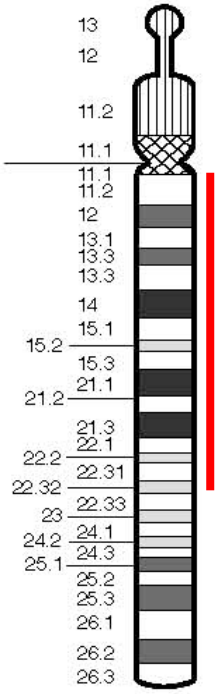
Occasionally one parent may be found to have two types of cell in their body, one with normal chromosomes and one with the same rearrangement as the child. This is known as mosaicism and the parent is most often more mildly affected than the child.

A clinical geneticist or genetic counsellor will give individual guidance for your family.

Duplications of 15q11q13

The most common duplication of proximal 15q involves the 15q11q13 region including a segment with its own name - PWACR, meaning Prader-Willi and Angelman Critical Region. It is called the PWACR region because losing one copy (as in individuals with a 15q deletion of this region) causes either Prader-Willi syndrome or Angelman syndrome. The effects of this common duplication are described in *Unique*'s leaflet on Idic 15. The duplications described in this leaflet may include this region but if they do they extend beyond it.

Proximal duplications of 15q: from the tip of the short arm as far as 15q21/22



More than eighteen individuals with a pure duplication in this area not involving any other chromosome are described, at least thirteen in the medical literature and six members of *Unique* (Akahoshi 2001; Schroer 1998; Elcioglu 1997; Herweijer 1988; Veenema 1984; Herr 1983; Anneren 1982; Power 1977; Cohen 1975; *Unique*).

This small number means that large proximal duplications of more than 15q11q13 seem to be really quite rare. Some of the duplications include the short (p) arm, but that should make no difference. Most of the individuals described have slightly different breakpoints and some of the duplications appear to be genuinely unique. Two cases are included from the medical literature with breakpoints further down the long arm at 15q15q24 (Han 1999) and 15q22q24 (Dhaliwal 1990).

The red line shows roughly where the duplication is.
Pages with red bars by the page number are about proximal duplications of 15q

At birth

Eight weeks old

Babies have generally been born at full term after an uneventful pregnancy, with a reasonable weight (ranging from 3.7kg/ 8lb 3oz to 2.67kg/ 5lb 14oz) and have had high Apgar scores of between 8-10 (a measure of wellbeing at birth on a scale of 0-10). In two cases mothers noticed less fetal movement than in their other pregnancies and both babies were unusually floppy after birth (they had low muscle tone, hypotonia). Two babies had respiratory problems at birth, and needed additional oxygen in the newborn period.

Hands and feet

Various minor anomalies of the hands and feet are relatively common in children with chromosome disorders. In children with a15q duplication, these have been usually no more than cosmetic. Unusual features observed include large hands, shortened or incurving fifth fingers, long, clenched or bent fingers, short or ingrowing nails on one or more fingers, webbed toes or toes that override each other and long, narrow hands and feet with prominent big toes. One boy with a prominent, overriding big toe had it straightened. One girl who was particularly severely affected also had rocker bottom feet (the sole was curved like a rocker on a chair) and shortened bones in the foot leading to the second toe.

Spine

In most babies the spine appeared healthy and normal, but two babies with a duplication from the tip of the short arm to 15q22 had a pit at the base of the spine. A sacral dimple (dimple or hole in the skin just above the crease between the buttocks) may be shallow so you can see the base, but stools can collect there before your child is toilet trained, so keeping it clean and protected is important. A sacral pit may be deep and even connect to the spinal canal or the colon. If there is any concern about this, your baby's spine will be imaged, usually with ultrasound or an MRI scan.

Minor anomalies of the **genitals** and the bottom area are seen fairly often in babies with a chromosome disorder, especially in boys. In this group, four out of nine baby boys were born either with undescended testicles, requiring monitoring or later surgical correction, an unusually small scrotum or a small or crooked penis. Most girls had a normal genital area, but in one the anus was unusually far forward. When this occurs, it is important to pay careful attention to hygiene during nappy changes to protect against urinary tract infections.

Development

The young child has delayed development, walking independently at 28 months and then with a somewhat wide gait. At 5 years, he has poor coordination and is not yet toilet trained but is partly able to dress himself. He has a severe learning difficulty although he is good on a computer and has excellent mouse skills. His understanding is far ahead of his speech but he supplements his few words with gestures, some signing and picture exchanges as well as intonation. He is anxious and extremely shy by nature. His aunt's level of learning difficulty is described as moderate.

By contrast, neither the adult brother nor sister was suspected of having a chromosome disorder until well into adulthood. Both attended their local mainstream (regular) school and achieved average or somewhat below average grades across the full range of academic subjects, with a weakness in mathematics and consistently higher grades for effort than for achievement, as well as higher marks on continuous assessment than in examinations. Both left school at the age of 16 and since then the sister has worked continuously as a clerical assistant while her brother worked for 14 years as a university gardener. They live independent of their parents and the sister has bought her own flat.

The disposition of the brother is easy-going and sociable. He enjoys socialising, helping others and music. His sister had difficulties mixing with other children from primary school age, has shown some autistic traits and has been successfully treated for obsessive compulsive disorder and occasional depression. In adult life she has also developed intermittent but recurrent dizzy spells. She is regularly monitored by a psychiatrist but functions well in the workplace and leads a full, structured social life despite her natural tendency to social isolation.

Both brother and sister have normal mobility, although the sister has a stiff-legged and flat-footed gait, a late effect of the unusual foot position (talipes) she was born with and that was treated with casting. Both have minor difficulties with coordination with, for example, zips and changing light bulbs. The brother considers his reactions too slow for him to learn to drive. As an adult, he developed a tremor in his right hand.

Health

Neither of the brother: sister pair has any major health concerns or difficulties with hearing or eyesight. The sister was born with a squint (strabismus) in the right eye, which was eventually corrected at nine years in a two-stage operation. The brother had a sacral dimple at birth.

The young child is also in good general health at five years. However, he has a single kidney and is regularly screened for a type of kidney cancer called Wilm's tumour. He developed a bone tumour known as an osteochondroma which was successfully removed. He has also had a hernia repaired and has nystagmus (uncontrolled eye movements), a squint and wears glasses for close work. He has had grommets (aeration tubes) inserted to relieve glue ear but has no other hearing loss. His adult teeth have emerged early, starting to come through at four years. His aunt has a horseshoe kidney (where the bottom points of the two usually separate kidneys are joined, creating a U (horseshoe) shape). She also has a permanent hearing loss in both ears.

" He has a beautiful smile and a generally easy-going, placid nature. He is very loving.

When the breakpoint lies at 15q25 or 15q26 and there is a duplication of the end of the chromosome, babies have commonly been unusually large at birth with a very large head and in some cases have shown early fusion of one or more of the seamlines between the bony plates that come together to form the skull (craniosynostosis). There is currently some uncertainty over the causative gene for this craniosynostosis.

Babies have been typically 49cm (19") to 59cm (23") long at birth and weighed between 3.3kg (7lb 4oz) and 5kg (11lb). While growth tailed off in some children, some adults remain tall, with heights varying between 1.78m (5'10") and 2.1m (6'11"). The additional height observed in some children is attributed to duplication or disruption of the *IGF1R* gene at 15q26.3.

A spinal curvature is sometimes found as is a chest deformity and while most babies are born with a healthy, normal heart, around 30 per cent have a heart condition and a somewhat smaller number have a kidney disorder.

Many children have long, thin and sometimes tapering fingers, sometimes held in a bent position and most seem to have a typical facial appearance with a long, triangular face, eyes that slant downwards and unusual ears placed low on the side of the head. A recent suggestion has been made that a duplication from 15q25.2 may contribute to autism (Tatton Brown 2006; Bonati 2005; Faivre 2002; Zollino 1999).

When there is an interstitial duplication between15q24 and 15q26.3

Individuals differ from each other, but common features have included hooded eyelids (ptosis), developmental delay and small size (Roggenbuck 2004).

A brief description follows of three members of *Unique* and a relative of one, described in the medical literature, who have a pure duplication of 15q with a breakpoint at 15q26.1.

Three adults and a child with a pure duplication of 15q26.1

It seems to be extremely rare for a pure duplication of the end of chromosome 15q to occur. *Unique* has three affected members from two families, a brother and sister in their thirties and forties and a young child of pre-school age and a further adult, the aunt of the child, who has been described in the medical literature (Tatton Brown 2006; *Unique*).

Growth

The child is very tall for his age, in the highest 0.4 per cent of the population for height, and also has a large head. At five years, he was wearing clothes to fit a 9/10-year-old. All three adults are also tall, but the growth pattern of the brother: sister pair has been different. While ninety-five per cent of babies are born measuring between 46cm /18" and 56cm/22", the girl was very long at birth (61cm/24"), while her brother was born an average length. The girl reached an adult height of 1.78m/5'10", while her brother had a marked teenage growth spurt and as an adult is 1.9m /6'3" tall. The weight distribution between the two has also been different, with the girl (a very long baby) weighing 3.345kg /7lb 6oz at birth and 76kg /12 stone as an adult, giving a healthy body mass index of 24. Her brother, by contrast, was born shorter but heavier, at 3.713kg/8lb 3oz, and has grown into a very thin adult.

Appearance

There may be little sign in the facial appearance of many children with a proximal 15q duplication of any underlying disorder. Doctors may notice what are known as 'dysmorphic features' which may or may not be obvious to a parent. Most of these are facial features of little or no importance to the child but they can help doctors to reach the correct diagnosis.

There is no typical pattern of features, but those seen most commonly include eyes that slant downwards, a small chin and lower jaw, tiny skinfolds across the inner corner of the eyes, unusually placed or shaped ears, eyes that are spaced far apart and a short neck. Some babies and children may also be unusually fair or dark for their family, with light or dark eyes and blond or dark hair as well as skin colour. This is thought to be due to the presence of an extra copy of a particular gene (*P* gene, located on chromosome 15 at 15q11.2q13, close to the distal end of the PWACR) which plays a role in pigmentation.

Feeding

Although two babies breastfed and gained weight steadily with no difficulty, and a further baby also breastfed well after initial difficulties as a newborn, some babies can be expected to have difficulty establishing feeding. They may be unable to suck effectively or to coordinate the actions of sucking with swallowing. Typically the problems will be mild and temporary but some babies will need long-term support feeding through a nasogastric tube.

Gastro oesophageal reflux (GORD, GERD), where the stomach contents return up the food pipe, is fairly common in babies with a chromosome disorder and affected at least one baby in this group. Reflux raises a baby's risk of inhaling food contents and setting up an infection in the lungs known as aspiration pneumonia. Reflux can be eased by careful semi-upright positioning during and after feeds, sleeping in a prescribed sleep chair rather than a bed, raising the head end of the baby's cot and if necessary by prescribed medication that helps to keep the feed within the stomach and counteract any acidity. Babies who have continuing problems can have a surgical procedure called a fundoplication to improve the action of the valve at the junction of the food pipe and stomach. Where feeding and reflux problems are persistent, a gastrostomy tube (PEG, button) can be inserted to allow direct feeding into the stomach until the baby is sufficiently mature to tolerate feeding by mouth.

Some babies feed reasonably well but fail to gain weight as desired. They are then usually given supplementary or calorie-enriched feeds. Two *Unique* families have reported persistent diarrhoea and in one case there is a possibility of malabsorption.

Growing

Children, adolescents and adults with a 15q duplication can be extremely short, short, average or tall. The most typical body build appears to be thin or very thin.

Medical concerns

Seizures

Around half the children with a proximal 15q duplication have developed seizures. Seizures are known to have started between babyhood and 15 years but it is not yet known whether adults too may develop seizures. Imaging of the head and brain typically reveals no abnormalities, but an electroencephalogram has usually confirmed abnormal activity in the brain. In at least some children the seizures are hard to control and at least one child has had vagal nerve stimulation (VNS). In VNS, a battery-powered device similar to a pacemaker is implanted under the skin, delivering mild electrical stimulation to the brain via the vagus nerve. Therapy can reduce the severity and frequency of seizures in some patients. However, VNS has only become widespread within the past few years, especially among younger children, and it is too early to judge its success. Recovery may take months or even a year and it is possible that the epilepsy might have improved spontaneously.

Spinal curvature

A marked spinal curve has developed in a minority of children. One adult with an inverted duplication of 15q13.3q21.3 developed a kyphosis, an excessive outward curve of the spine in the upper back area. Treatment of a spinal curvature is tailored to the individual and may include observation, physiotherapy, exercises, bracing and possibly surgery.

Other medical concerns

Most children with a 15q proximal duplication have been generally healthy. However, families have reported difficulties in getting over the common upper respiratory tract infections of childhood, with invariable weight loss when ill. One child with a duplication between 15q11q15 has a diagnosis of combined variable immunodeficiency disorder.

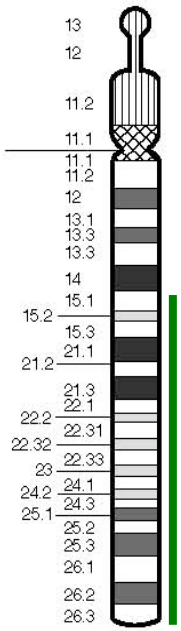
Babies with more distal 15q duplications are at risk of congenital heart disease. In this group, all babies were born with a healthy heart apart from two babies with a duplication that extended as far as 15q24. One of these had an unspecified heart condition, while the other was born with a patent foramen ovale (PFO). This is an opening between the two upper chambers of the heart that does not close soon after birth, as expected. When it remains open, this allows extra blood to pass from the left to the right side of the heart.

Outlook

The outlook for any child is determined largely by their clinical problems rather than their specific karyotype. Apart from the infections described above, children with a 15q duplication have been generally healthy and the oldest person known with the duplication was 46 years old.

Distal duplications of 15q

Many children and adults with a duplication of part of this area have been described in the medical literature and general conclusions drawn about the effects. However, very few people have been found to have a pure duplication. Breakpoints vary and while some individuals have an interstitial duplication (with two breakpoints), others have a duplication of the end of the chromosome. This means that the general conclusions that follow below about the effects of a distal 15q duplication need to be read with caution.



The green line shows roughly the extent of distal duplications. Pages with green bars by the page number are about distal duplications of 15q

The effects described below are considered to be typical. Individuals do vary and the appearance of any feature in this list does not mean that your child will be affected.

When the breakpoint lies between 15q15 and 15q24 and there is a duplication of the end of the chromosome, the most common features are considered to be a degree of developmental delay and learning disability; unusual fingers or toes; an unusually shaped chest and usually minor anomalies in the genital area. Between two thirds and three quarters of babies have been born a normal weight and size but their growth has then slowed down, usually leading to short eventual height. Heart conditions may occur and the head may be abnormally small. More than half of children have also had a spinal curvature and also low muscle tone, so they feel floppy to hold. Around a half have had seizures and most have had some fairly subtle facial anomalies including a pointed chin, a prominent nose, an asymmetrical face, unusual ears and eyes that slant downwards (Faivre 2002; Zollino 1999; Chandler 1997).

Sleep

There is some evidence from *Unique* that many children have sleep difficulties. Families have found sleep training programmes and firm, reassuring bedtime regimes helpful as well as medication with melatonin, although the evidence base for this treatment remains controversial.

Therapies

In addition to physiotherapy, occupational therapy and speech therapy, families have reported success with the following therapeutic approaches:

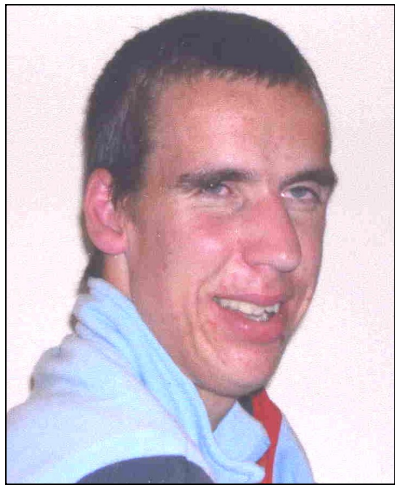
- Riding for the disabled from 4 years to improve balance, strengthen joints and improve language
- Craniosacral therapy from 2 years to improvement physical movement
- Bobath therapy to improve gross motor skills. Bobath therapy uses a holistic approach to give children the experience of normal movement by enabling them to respond actively to specialised handling
- Vojta therapy to stimulate movement, originally designed for children with cerebral palsy

Growing up and independence

Children tend to be late in acquiring self care skills and will usually always need some help and supervision. They are also late to be toilet trained, although there is a very wide range in this, from children who are trained at three years to others still not trained at 13 years.

This suggests a picture in which children will usually need ongoing supervision throughout their lives.

In terms of puberty, there is a mixed picture, with one boy experiencing precocious puberty at 10 years, a girl going through normal puberty at 12 years and other teenagers experiencing puberty delay.



“ At 25 years old, he lives with his family but attends voluntary run day centres. He has an active social life, enjoying special Olympics, cycling, chatting, shopping, the local club for people with special needs, and dancing in shows. His best friends are his family and people at the day centres and clubs. ”

Eyesight

Children usually have structurally normal eyes but a minority have a squint (strabismus) requiring treatment with exercises, patching, glasses or surgery. However, one girl with a duplication from the tip of the short arm to 15q22 was found to have cataracts forming and abnormalities at the back of the eye making her effectively blind. Other families' comments include:

“ She was investigated by an orthoptist due to her abnormal head posture: she stands still, her head on one side, looking out of the sides of her eyes. No problems were found ” - *11 years*

“ He has poor vision in his right eye and a moderate right convergent squint but he manages well ” - *adult*

Hearing

A hearing assessment is important for all children whether or not they have a chromosome disorder. In this group, most children seem to have good hearing, although a failure to respond may at first be interpreted as a failure to hear. A hearing impairment has been described in one or two individuals.

Teeth

Dental problems are common in children with chromosome disorders for many reasons. The underlying development of the structures of the face may be abnormal and this will affect the development of the teeth; differences in feeding and mouthing experiences also affect tooth development. Some children do not tolerate a toothbrush or dental treatment. There is evidence from *Unique* families that both baby and permanent teeth may emerge very early or late and that milk teeth may need to be removed under general anaesthetic.

“ He lost his front teeth at 2 years because he was always falling on them. ”

“ He teethed early, the bottom teeth came through at 3.5 months, the top ones at 4.5 months. As an adult, some baby teeth are still in place and some adult teeth never came through. One tooth is divided, with a common root. ”

Sitting, moving: gross motor skills

Babies and children with a proximal 15q duplication typically face some delay in reaching their mobility milestones but there is a lot of individual variation. An early delay in rolling over and sitting alone without support is often the first sign that anything is wrong. Most children develop more slowly than normal and do eventually walk, run, climb and even cycle and swim, but this may not be possible for all. Babies have mastered independent sitting between six months and two years; they have become mobile between 14 and 24 months and walked between 18 months and three and a half years. Initially, their style of walking may be unusual or unsteady in part because the hip and leg joints may be loose or unusually tight and some children wear supporting boots to steady their ankles.

Underlying some of the delay in mobility is a low muscle tone, making a baby or child feel unusually floppy to hold and making their joints very flexible. The presence of hypotonia is variable, but most babies and children have been affected.

These are families' comments on their child's mobility:

" Probably double jointed as she can get herself into very unusual positions " - *duplication of 15q11.2q14*

" He moves around well and is always very careful but he is slow and quite ungainly because of his size " - *duplication of 15q13.3q21.3*

Using their hands: fine motor and coordination skills

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

Snapshots of what children were achieving at different ages:

At 6 years - Can hold a toothbrush but not brush thoroughly yet; can dress himself but not his socks; can turn a computer on and off and change games and DVDs but feels more comfortable with an adult standing by. He can eat with a fork but prefers fingers; good at holding felt tips, cups, glasses; cannot cut his own food - *duplication of 15q11q14*

At 9 years – Needs help brushing his teeth; sometimes needs help with his jacket and shoes; needs help washing and brushing his hair - *duplication of 15q13q15*

At 11 years - Can hold a spoon but usually with her whole hand round the handle. Holds a cup but often drops it - *duplication of 15q11.2q14*

At 14 years – Has specific problems with coordination of fine motor tasks such as writing or oromotor tasks such as speech production. Very clumsy writing (dyspraxia) - *duplication of 15q13.3q21.3*

Speech and communication

Some delay in the emergence of speech and language is to be expected, and while the extent of the delay is variable and partly reflects the level of cognitive ability, most children experience a severe delay and some children do not acquire speech. There is evidence that in some cases oromotor apraxia affects children's ability to produce the sounds of speech. Evidence from at least one family shows that the development of epilepsy can have a detrimental effect on speech and language, with skills lost after seizures develop. In general children appear to understand more than they can say; at least one child showed good understanding but limited speech in two languages spoken at home.

The *Unique* series of children shows very much better speech and language than the cases described in the medical literature. Before speech emerges, children generally communicate by gestures, vocalisations and in some cases by signing. The evidence is that children have spoken their first words between the ages of two and four years but some children have first used words much later than this. Some children learn best by singing and in general find one-syllable words easiest to acquire. Progress in developing a vocabulary is usually slow and it may be some years before two-word phrases emerge or are used frequently.

Learning

A child with a proximal 15q duplication can be expected to have some learning difficulties or disabilities and it seems most likely that children will have a difficulty in the moderate to severe range. Reports in the medical literature suggest an IQ in the 25-50 range with some children learning to read and write in the upper primary school years, but reports from *Unique* illustrate the variety between individuals and children's particular strengths. Specific difficulties with fine motor control may make hand control for writing especially difficult.

At 6 years – His strong point is computer skills; he is extremely good at working with the mouse and finding the logic of the game; and keeps trying until he succeeds. He started playing computer games at 4.5 years and loves it! He has an extremely good memory and great patience with computer games and toys but not when he doesn't want to be patient. He is good at visual tasks; but cannot read yet. He loves to paint and draw and has been able to draw since he was 2; he can draw straight lines & circles - *duplication of 15q11q14*

At 9 years – He knows all his letters and loves to count numbers. He has a very good memory and good receptive language skills - *duplication of 15q13q15*

At 11 years – She can remember song words and music but not for example where she lives or how old she is. She does not read but will hold a pencil and draw lines with support. She has a sensory processing difficulty and difficulties discriminating tactile information and auditory information as well as concentrating in a noisy environment; distressed by loud noises - *duplication of 15q11.2q14*

As an adult – He reads books made for him, signs, notices and small pieces in the newspaper and writes short sentences - *duplication of 15q13.3q21.3*

Behaviour

The evidence is that as babies, many children are quiet and unresponsive. It is not yet known whether any typical behaviours develop in childhood, but there are some reports of children with autistic features and behaviours. Some children have a high level of activity and a short attention span. Many children enjoy music and singing. A high pain threshold is typical. One child developed anxiety episodes, especially in new places. A number of children have been described as warm and loving.

Age 6 - He is extremely loving and caring. He is a quiet and calm child when he is in his secure surroundings. He loves contact with adults, loves to play on his computer, watch cartoons, listen to music, and shows great care for animals - *duplication of 15q11q14*

Age 9 - He's very warm and fond – and sensitive! He likes to kiss. He's cute. He likes poems and remembers them. He likes singing, pets, cats and dogs; some children's TV programmes; and being at the seaside - *duplication of 15q13q15*

Age 11 - A very loving child who has brought a great deal of joy into our lives. Also I think a very happy child - *duplication of 15q11.2q14*

Adult - Generally very happy and placid but can get frustrated if people don't understand him. No autism - *duplication of 15q13.3q21.3*