Understanding chromosome disorders

Unique

Duplications of distal 14q

rarechromo.org

14q duplications

A chromosome 14 duplication is a rare condition caused by an extra segment of genetic material from one of the body's 46 chromosomes, resulting in extra copies of the genes present on that segment. The correct amount of genetic material is needed for normal growth and development. Extra genetic material is likely to result in some problems. However, the nature of the problems depends on the chromosome segment that is duplicated, the genes it contains and in some cases the parent of origin. So far over 730 genes have been identified on chromosome 14.

Genes and chromosomes

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

Genes are carried on microscopically small, thread-like structures called chromosomes. There are usually 46 chromosomes, 23 inherited from our mother and 23 inherited from our father, so we have two sets of 23 chromosomes in 'pairs'. Apart from two sex chromosomes (two Xs for a girl and an X and a Y for a boy) the chromosomes are numbered 1 to 22, generally from largest to smallest.

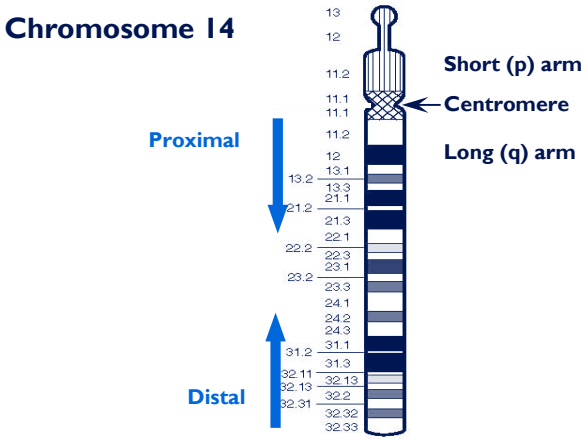
Each chromosome has a short arm (at the top in the diagram on the next page) called **p** from petit, the French word for small, and a long arm called **q** (at the bottom). The short (p) arm of chromosome 14 is very small and we believe that it can be duplicated without apparent harm. Extra genetic material from the long arm is expected to have more consequences as this part contains important genetic information.

Chromosomes are not visible with the naked eye, but after staining with a dye that produces a characteristic banding pattern can be seen when magnified under a microscope. The diagram on page 3 shows the bands of chromosome 14, numbered outwards starting from the **centromere** (the indented region of the chromosome that divides it into two arms). A low number, as in q11, is close to the centromere. Regions closer to the centromere are called **proximal**. A high number such as q32 is near the tip of the chromosome and is called **distal** as it is further away from the centromere.

The karyotype

Your genetic specialist can tell you more about what chromosome material has been lost. You will almost certainly be given a karyotype, a shorthand code that shows the bands where the chromosome has broken and rejoined. A band can contain many genes and depending on the technology used to find your child's chromosome duplication, the karyotype sometimes shows whether particular genes are duplicated or not. But you will usually need to ask your genetic specialist for a full explanation.

Your child's karyotype may look very like another person's, from *Unique* or in the medical literature, or it may look exactly the same. But even in people with the same karyotype, the chromosome may have broken at a different point within the same band. This is one important reason why people with apparently similar karyotypes do not all have the same problems or features. Individual differences can be quite marked and it is very important not to make direct comparisons between your child and others. After all, each of us is unique. But some features and health problems are similar in people with a 14q duplication. This leaflet describes the things that are similar.



Does it matter which parent the extra piece of 14q came from?

The extra piece of chromosome 14 comes either from the mother or the father and it is possible that the effects may be different depending which parent it comes from. This is due to a phenomenon known as **imprinting**, where certain parts of chromosomes have different effects depending on the parent of origin. The effect of imprinting on duplications of 14q would be to give the affected baby or child a single dose of genes from one parent and a double dose from the other parent. Certain genes on chromosome 14 are known to be imprinted and people with two 14q arms from their mother are very different from those with two 14q arms from their father (see *Unique*'s leaflet on **Uniparental disomy 14**).

Associations have been found between certain features of a 14q duplication and particular regions of the chromosome arm. Some evidence comes from six relatives in one family with a duplication of a small band within 14q31, who were apparently entirely normal except for one child with moderate developmental delay. The duplication was inherited from the mother, suggesting that this small maternally-inherited duplication of 14q31 may generally not be harmful. In another family with a different small duplication within band 14q31, the most severely affected child inherited the duplication from his mother, suggesting that in this family the effect was milder if the duplicated material was inherited from the father (*see* **Families with a duplication with no apparent effect**, page 5).

As you can see from this, the information about the effects of imprinting is still unfolding (Palmer 2006; Sutton 2002; Mignon-Ravix 2001; Georgiades 1998; Robin 1997).

Sources and references

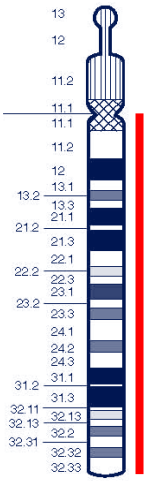
The information in this leaflet is drawn partly from the published medical literature. In many cases a detailed molecular analysis of the chromosome has not been carried out and the cases discussed often combine a duplication of 14q with a deletion or duplication of another chromosome, but at the moment it is the best information available.

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.

You can also obtain abstracts and articles from *Unique*.

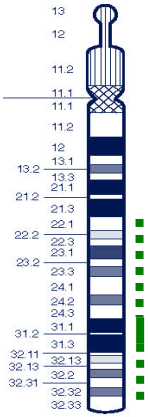
The leaflet also draws on *Unique*'s database. When this leaflet was written, *Unique* had 44 members with a chromosome 14q duplication, of whom 24 had a pure 14q duplication. Eighteen families completed a detailed questionnaire in 2006.

Complete duplication (trisomy) of 14q



It is possible for a baby to be conceived with an entire additional long arm of chromosome 14. This occurs most often when one parent carries a Robertsonian translocation, in which the long arm of chromosome 14 is fused with the long arm of another chromosome, most frequently chromosome 13 or, in descending order of frequency, with chromosome 21, 15, 22 or 14. However, pregnancy loss is the norm and babies with a complete extra 14q do not generally survive to birth. Of those babies who do survive, the overwhelming majority have some cells with the normal number of chromosomes and some with the extra 14q. This is known as mosaic trisomy 14. The problems faced by children with mosaic trisomy 14 tend to be more severe than the problems faced by children with a partial duplication and include growth and developmental delay, unusual facial features (a broad, upturned nose, abnormally formed or placed ears, a small lower jaw and a short neck), congenital heart disease and, in boys, minor genital anomalies. This leaflet considers duplications of part of chromosome 14q. Large duplications between 14q22 and 14q32 are considered as well as duplications that extend as far as 14q13 proximally and, distally, include the end of the long arm.

Large duplications between 14q22 and 14q32



Some eight cases have been reported in the medical literature, including one report where more than one family member was affected, as well as members of *Unique* with smaller duplications within bands 14q31 and q32. In addition, there have been reports of at least twelve relatives from three families with a small duplication of band 14q31 or a larger duplication from 14q24.3 to 14q31 with no apparent effect on development (Palmer 2006; Mignon-Ravix 2001; Robin 1997; North 1995; Rivera 1992; Gilgenkrantz 1990/2; Mikelsaar 1987; Sobel 1984; Nikolis 1983; Orye 1983; *Unique*).

Duplication within bands14q22~24 to 14q32

The reports of people with a duplicated segment from 14q22~24 to 14q32 include a 29-year-old and his nephew (Rivera 1992; Gilgenkrantz 1990/2; Mikelsaar 1987; Sobel 1984; Nikolis 1983; Orye 1983). Features were generally not very specific but included a low birth weight (range 2.25kg /4lb 15oz to 2.9kg/ 6lb 6oz); in some cases short height in childhood; developmental delay; speech delay and learning difficulties. Reported health problems have been quite serious and have included a heart problem for two babies (in one case a ventricular septal defect (VSD), a hole between the lower chambers of the heart). Specific treatment for VSD is determined individually as a small hole may close spontaneously but a larger VSD usually needs surgical repair. One child was severely affected, with posterior urethral valves (obstruction of the valves that let urine flow out from the bladder) and kidney failure as well as underdevelopment of the lungs. Vision may be affected as well as hearing, including a temporary impairment due

to glue ear. A further child (with a duplication of 14q22q24.3) had blocked nasal passages requiring corrective surgery (choanal atresia), an immune deficiency, a large VSD and genital anomalies (North 1995). In this group, two babies died, one at four months and one at 10 months.

In some cases, the hands had slightly unusual features, including a single palm crease, short or tapered fingers; two babies with a 14q24q32 duplication had a similar pattern of long thumbs and middle fingers overlapped by adjoining fingers. Two children were born with their feet in the talipes equinovarus position (clubfeet), in which the foot points downwards and inwards, requiring correction, usually with surgery.

Focusing on the individuals with a slightly smaller duplication between 14q23.3 and 14q32.3, the effects were generally milder, with a lesser degree of general developmental delay. In terms of mobility, from the information available, rolling over was achieved around 6-7 months, sitting around nine to 15 months, independent mobility around the first birthday and walking late in the second year of life. However, walking was not possible for all and the child with a 14q22q24.3 duplication was neither walking nor talking yet at four and a half years.

Smaller duplication within bands 14q31 to 14q32

From the limited information available at *Unique*, two major clinical problems emerged. One child with a duplication within band 14q32 developed absence seizures which were controlled with anti-epileptic medication. Another child was born with short eyelids that made it impossible for her to close her eyes. This condition, seen in others with a 14q duplication, requires surgical correction, after which vision appears to develop normally (*see* **Hayleigh**, *pages 12-13).*

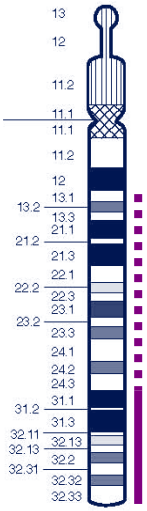
Development was also affected, with moderate delays in mobility, low muscle tone (hypotonia) and walking achieved in the second or third years. There is no specific information on fine motor skills, but one child showed marked difficulty in holding a pencil to write at seven years. Reading ages suggest that these children started to read at 6 to 8 years, having been speaking from three to four years. They succeeded in becoming clean and dry by day around four years (*Unique*).

Families with a duplication with no apparent effect

In one family, six members carried the same duplication of band 14q31, inherited from their mother, in five cases without any apparent effect on development or growth. In a sixth family member the duplication probably played no role in his developmental delay (Mignon-Ravix 2001). In a further family, four members carried a small duplication of part of band 14q31. Individual family members had a variety of problems, including developmental delay and cataracts, but since one family member with the duplication was clinically and developmentally normal, the tiny duplication found was probably not the cause of the problems (Palmer 2006). In one father: daughter pair with a duplication of 14q24.3q31, the father was unaffected and the daughter mildly so (Robin 1997).

A possible explanation for some of these findings is that the duplication may exert a different effect, depending on the parent of origin (*see* **Does it matter which parent the extra piece of 14q came from?** page 3).

Large duplications of the end of the long arm: starting from 14q13 to 14q24.3



Some eleven babies and a pregnancy have been described in the medical literature and *Unique* has three members with a pure duplication of the long arm of chromosome 14q starting between 14q13 and 14q24.3. This amounts to a duplication of between one third and two thirds of the long arm of the chromosome. Although in many cases, the duplication occurs together with a deletion or duplication from a different chromosome, only individuals with a pure duplication have been described here or individuals with a combined duplication involving the short arm of chromosome 13, 14, 15, 21 or 22, which would not be expected to affect the outcome. Individual stories of *Unique* members with a 14q duplication combined with a deletion or further duplication then follow.

Generally speaking, *Unique*'s experience is that its members fare better than the depictions in the medical literature suggest (Ohtake 1994; Duckett 1990; Nakamura 1990; Gilgenkrantz 1990/1; McCorquodale 1985; Kaiser 1984; Sklower 1984; Atkin 1983; Cohen 1983; Georgmaneanu 1981; Pfeiffer 1978; Fryns 1977; Trunca 1977; Weinstein 1977; *Unique*).

Out of eight pregnancies, two ended in a preterm birth. Birth weights for the term babies ranged from an underweight 1.83kg (4lb 1oz) to 3.8kg (8lb 6oz), a higher than average weight for a newborn. Many babies grew into short children.

Sadly, many babies have had major medical problems to overcome, particularly heart defects or anomalies of the great vessels, which occurred in seven of the fourteen. In the medical literature, a variety of other serious problems has been seen, including a large hernia in the diaphragm that separates the contents of the abdomen from the chest, small kidneys with multiple cysts and absence of the corpus callosum (the broad band of nerve fibres that connects the two hemispheres of the brain) and seizures. Additionally four babies including two girls had an anomaly in the genital area and at least one had a severe visual defect. Sadly, two babies died in the early months of life; two *Unique* members with the 14q duplication combined with a deletion or duplication of a different chromosome also died, in each case from the consequences of a respiratory infection.

Minor anomalies of both hands and feet and particular facial features are common in babies and children with a chromosome disorder but are chiefly of interest to families when they affect the way a child can function. In babies with large 14q duplications, incurving of the fifth finger and overlapping fingers and toes have been seen and one baby had talipes calcaneovalgus (clubfeet), a positional deformity in which the feet point outwards and downwards. Among the unusual facial features observed were a prominent forehead, a prominent nose, a small chin and lower jaw, unusual ears, a protruding upper lip, a high forehead, fontanelles (soft spots on top of the head) that were slow to close, downslanting, widely spaced eyes and possibly sparse hair growth. The palate may be unusually high or narrow. A very unusual finding in one baby is a developmental defect of the lower eyelids, making it difficult or impossible for the eyes

to close and for which surgical correction is needed. This defect has also been seen in two *Unique* members with small terminal duplications of 14q (Gilgenkrantz 1990, *see* **Hayleigh**, pages 12-3).

Most babies either had hypotonia (low muscle tone, making them feel floppy to hold) or a mixture of hypotonia and hypertonia, increased muscle tone. Development was delayed and babies have needed considerable support to achieve developmental milestones such as sitting.

Information on the later development of children with a large distal 14q duplication is limited, but one young man with a large duplication from 14q21 as well as a small deletion from the end of the short arm of chromosome 3 (breakpoint at 3p25) was described at the age of 27. In his case, he had gone through puberty normally, but ten years later than expected.

Andrew

Andrew has a deletion from the end of the long arm of chromosome 1, with a breakpoint at 1q44 and a duplication of around one third of the long arm of chromosome 14, with a breakpoint at 14q24.3.


Age 2

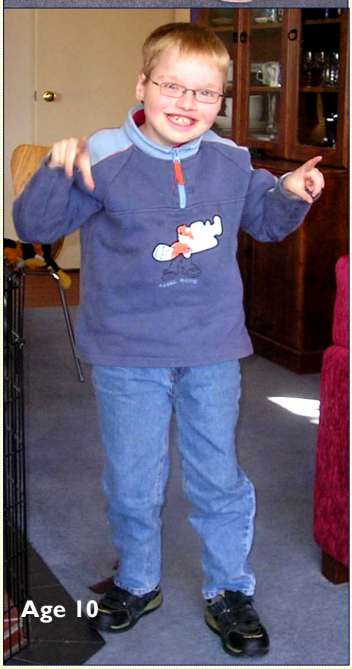

Age 3-4

At birth, Andrew was somewhat underweight – 2.4kg (5lb 5oz) – and had unusually low muscle tone. He was breastfed but was a slow feeder and his growth rate tracked the lowest curve on the growth charts for the first nine months of his life until he went onto solid foods and started to catch up. At the age of 10, he was rather shorter than his school friends but weighed 27 kilos, a little over four stone.

Andrew has been generally healthy, catching the normal range of colds and coughs that affect young children. Occasional infections of his tear ducts are treated with antibiotics. He wears glasses; when he was five years old, he had surgery to bring down his testes which had not descended into the scrotum. He was born with small teeth at the front of the mouth; these eventually detached and his adult teeth came in at the normal time.

Andrew's general development is delayed but he has made considerable strides since the age of nine. At 10, he still needed adult help with personal care but could eat with a fork and drink from a sealed cup with an integral straw. He had also mastered a computer mouse and the TV remote control.

Andrew's main means of getting around is walking; he likes to hold an adult's hand when walking on uneven surfaces or for longer distances and his family uses a stroller outdoors. Andrew can also climb stairs with an adult but is unable to get up from the floor alone. Andrew's feet are small and have little arch.



To stimulate the feeling in Andrew's feet and his other muscles, his family used an innovative therapy known as point percussion therapy. This is a particular physical therapy that has not yet been objectively evaluated long-term but it is known that physical therapies when intensively applied are likely to have short-term benefits. A report of an attempt to investigate the therapy is available from *Unique*. Meanwhile, *Unique* does not endorse any particular innovative therapy but recommends families to seek individual treatment for their child from their physiotherapist or physical therapist.

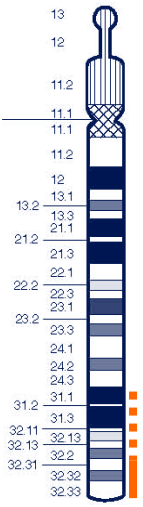
Andrew is sociable; he is proud of himself and has a good self-esteem. If people invade his personal space, he can be assertive to the point of aggression, but his family manage this by praising good behaviour and asking others to understand that Andrew is uncomfortable with them being too close.

Andrew's first language was signing and by the age of five, he had a vocabulary of over 400 words. At 10, signing remained his language of choice with unfamiliar people. Since the age of nine he has increasingly begun to vocalise and has occasionally used long, complex sentences although his diction was still immature with many consonant sounds yet to fully develop. Andrew's understanding is very much greater than his ability to express himself but he can ask, for example, 'May I please leave the table now?'

Andrew is a keen and successful learner. He uses a computer with an IntelliKeys keyboard and learns well when tasks are broken down and he is encouraged. He has a good memory for names and faces. So long as he works with hand-over-hand guidance, Andrew is able to write sentences and do mathematics. Alone, he cannot tell you what one plus one equals. But with this guidance, he can do addition, subtraction, multiplication to the twelve times table and division.

He is highly literate. At 8, his spelling age was well above his actual age. At 10, he could read children's books, newspaper headlines, the TV guide, children's prayer and Bible books. His family says that it is difficult to assess when he started to read alone, but by the age of 11 he was telling them to go away when he was reading in bed.

Smaller duplications of the end of the long arm: starting from 14q31 or 14q32



Three adults, the oldest 29 years old, and three children have been described in the medical literature with a pure duplication of the end of the long arm starting from band 14q31. Among *Unique*'s membership, one child has a pure duplication from 14q32 and many more children have a distal 14q duplication as well as a deletion or duplication of another chromosome (2, 4, 5, 6, 9, 15, 18 or 22) (Palmer 2006; Sutton 2002; Mignon-Ravix 2001; Magnani 1993; Masada 1989; Carr 1986; Trunca 1977; Weinstein 1977; *Unique*).

From the reports in the medical literature, growth delay is common both before and after birth and may be very marked; one 24-year-old was the average height of an eight-year-old. Growth delay is not consistent, however: three babies had a normal birth weight and a five-year-old with a duplication from 14q32.1 was a normal weight and height.

A degree of developmental delay is also to be expected. Marked delay in reaching developmental milestones of rolling over and sitting has been observed and at least two individuals had tightly contracted joints; one adult was not able to walk. Little information is available on the ability to learn, but one child was able to say some words by three years and one adult was functioning at the level of an 11-year-old child, although another adult was not able to speak.

Most individuals were generally healthy, but one child had complex anomalies of the heart and great vessels, as well as a neural tube defect exposing the spinal cord (lumbosacral myelomeningocele) and a cerebral anomaly with a partly missing corpus callosum, the broad band of nerve fibres that usually connects the two hemispheres of the brain. A 19-year-old with a mosaic duplication of 14q32.1 - that is, she had cells in her body with the duplication and others with a normal chromosome make-up - had frequent respiratory tract infections and a seizure disorder.

Generally speaking, *Unique*'s experience is that its members fare better than the depictions in the medical literature would suggest.

Becky

Becky has lost the tip of the long arm of chromosome 15 with a break point at 15q26.3 and has a duplication of the end of chromosome 14 from 14q31.3. The chief effects of her chromosome disorder have been on her development, and she has also had some health problems to contend with. By the age of 16 Becky had grown into a young lady with a cheerful disposition and a happy manner albeit very considerable developmental problems.

Becky was born one month early, weighing 2.69kg (5lb 15oz), and, although breathing, did not cry at birth. Her fontanelle

(soft spot) was very large, raising concern among the doctors. She had a small hole in her heart, which eventually resolved naturally, but otherwise was healthy.
Becky was to later develop some health problems, including seizures from the age of 3 to11 years as well as frequent ear infections in early childhood, but by the age of 16 was generally healthy and puberty had proceeded normally.

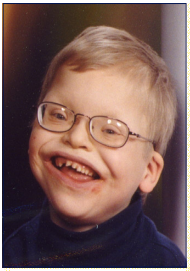
> " She has the most wonderful smile and friendly, sociable personality and is just a joy to be around, although very tiring. "

As a baby and child, feeding was an ongoing challenge but she made steady progress. Unable to breastfeed, she was fed by nasogastric tube for four months, then bottle fed. By the age of two, she could take mashed or liquidised food and small pieces of cake and by three could take a loaded spoon to her mouth. By five, she could feed herself with a spoon and drink from a feeder cup. By ten she could eat independently if her food was cut into bite-sized pieces. As a teenager, she had a good appetite, although she sometimes overfilled her mouth and choked, but was growing and putting on weight acceptably. However, Becky was small for her age, 144cm (4' 9") tall at 16 years.

Becky's mobility has been considerably delayed and while in early childhood many of her joints were loose and in some cases unstable due to her underlying low muscle tone, excessive tone and muscle contractures became an increasing problem over time.
She was creeping on her stomach by the age of two and walking by five, with a gradual improvement in balance over the following years. She needed regular physiotherapy, passive stretching, splinting and gaiters to counteract her joint contractures but by 10 years was a confident swimmer and by the teen years was able to run, if unsteadily.
Becky's fine motor skills were also delayed, but by five years she was able to point and to manipulate objects, by eight she could draw a straight line, by ten she could take off her coat and try to hang it on a peg and attempt to use large-handled cutlery.

Becky is sociable and popular and although her speech is very limited, she communicates well through direct experience and to some extent signing, gestures and a Dynamite communication aid. Her understanding is greater than her ability to express herself. Becky's level of communication reflects her learning ability. Her difficulties with concentration improved during the primary school years but remained prominent. As a teenager she was able to use a basic keyboard. Becky has worked with a behaviour therapist to address her challenging behaviour and responds well to familiar people and consistent boundaries.

Davis



Age 11

Davis has a deletion from the end of the long arm of chromosome 18 with a breakpoint at 18q23 and a duplication of the end of the long arm of chromosome 14 with a breakpoint at 14q31.3. His striking facial features, which include sparse eyebrows, low ears, eyes far apart and a large smile, were noticed at birth, six weeks early. Davis had considerable difficulties as a newborn baby: difficulty feeding that resulted in a gastrostomy tube placement at five weeks of age, difficulty breathing that resulted in a tracheostomy placement at six weeks (removed when he turned three years of age) and chronic RSV (respiratory syncytial virus, causing respiratory

infection). At one week of age, Davis had an MRI and CT scan of the head and brain that showed he has complete agenesis of the corpus callosum, the band of nerve fibres that connects the two hemispheres of the brain. Although Davis was a good weight at birth for a premature baby, his size slipped down the growth curves and currently he is the size of a 4-year-old instead of a 12-year-old. From age 3 to 10, Davis took growth hormone shots but these proved to be ineffective and were stopped. Davis' chronic RSV resulted in multiple hospitalisations from birth until age 7. On average he spent about 2½ months a year in hospital recovering from RSV and the complications. At age 12, Davis has now gone 4½ years without a hospitalisation and seems to have outgrown RSV. He even got an award last year for perfect school attendance. Davis is extremely nearsighted and has a mild hearing loss that does not require hearing aids, yet. His ear canals are very narrow and he had surgery to correct this in his right ear when he was four years old. Davis has global developmental delays but is not labelled as having mental retardation or an intellectual disability. The consensus among his medical team is that Davis has the cognition but we just do not know how to get at what he knows. Davis did not start walking until he was six and at 12 still uses a walker and wheelchair. He can sit himself in a chair, use stairs (with assistance) and even run using his walker. Davis is a very social and happy child and loves playing with his 'typically developing peers' especially during breaks between classes. Davis' speech is limited but it is believed that he understands 90 per cent of what he is told. He can generate complete sentences on his computer, his best educational tool that he has worked on since the age of 2½. His communication with his peers has increased with the help of his assistive technology device, Springboard. Davis is currently experiencing his fourth year in full inclusion (educated in a regular education classroom). As a 3rd grader, Davis has grown up with his classmates since they have all been together since kindergarten. Davis does benefit from a 1:1 instructional assistant who helps facilitate his education within the regular education classroom.

Boo

Age 13

Boo has an additional chromosome made up from the short arm of chromosome 9, a small piece of the long arm and the end of chromosome 14 from 14q32.1. He was born after a problem-free pregnancy, a good weight and in good condition. He breastfed for six weeks without problems, except for a split gum. Boo grew well, and by the age of 13 was an average height for his age. Boo had some health concerns including an umbilical hernia (the abdominal lining and sometimes part of the abdomen bulges through an area round the navel) that was surgically corrected and a hernia in the groin, glue ear treated with tubes and pneumonia as a baby followed by asthma as a child, although he outgrew this. Boo is also short sighted and has a convergent squint (the eyes look inwards) that was corrected with laser surgery. As a baby, Boo developed hydrocephalus (excess fluid within the brain), treated with a shunt.

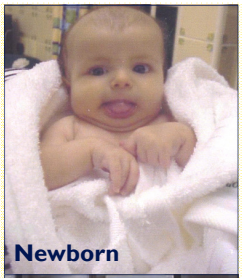
As regards appearance, Boo has some unusual features: some of his toes overlap each other, he has unusual ears and the back of his

head is flat. The soft spots (fontanelles) on the top of his head were large when he was a baby.

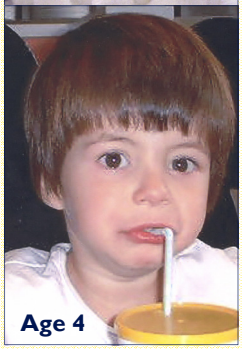
Boo's development has been supported by speech, occupational and physiotherapy as well as special education. He has low muscle tone and his mobility was somewhat delayed: he could sit by nine months, walk and climb stairs by three years and run by seven years. By 13, he could manage cutlery and hold a pencil but not apply enough pressure, although he could write his first name and the letters of the alphabet. At school he enjoyed using a whole word keyboard. He has a good memory, particularly for directions and rap music and enjoys playing drums with his hands. His speech has progressed well although he still has difficulty with word order and tenses and uses a fluency device (SpeechEasy) to improve a stammer.

At 13, Boo was experiencing puberty. Within his family, Boo is endearing, affectionate and loves adult attention. With strangers, he can on occasion be overfriendly.

Emel



Newborn



Age 4

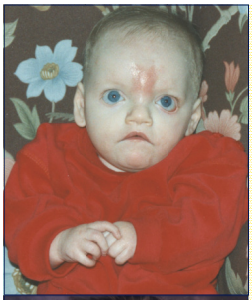
Emel has lost the end of the long arm of chromosome 22 from 22q13.31 (Phelan-McDermid syndrome), and has a duplication of the end chromosome 14 from 14q32.1. Her major issues are eating, sleeping, anxiety, toileting and communication.

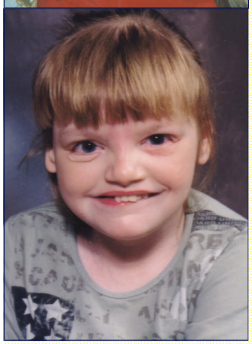
Apart from common childhood illnesses, she has been generally healthy to the age of 7 and tests have shown that her lungs, kidneys and brain are sound. She was a good weight at birth and despite early problems latching on, breastfed with a nipple shield to 15 months. She had problems with solids, tending to inhale food when she was ill, setting up respiratory infections. Until she was 6, Emel's food was pureed and she had calorie and nutritional supplements to ensure she gained weight. At 7, she still has difficulty in chewing.

Emel's muscle tone was low but with input from physiotherapy and the help of a walker she was walking by 3 years and climbing stairs by 5. She has had input from speech and language therapy and uses a rich variety of means to communicate, including signs, symbols, gestures, pictures, body language, facial expression, pointing, a communication book, objects of reference and some spoken words; her longest sentence so far is 'Mummy, help me.' At school aged 7, Emel has started to use a touch screen; she looks at pictures and can draw lines and scribble. So long as lessons are repeated regularly, she has a good memory. Emel is still in nappies being toilet trained and suffers from bladder urgency/ frequency. She does not sleep well and suffers from anxiety.

Hayleigh

Hayleigh has lost the end of the short arm of chromosome 5 from 5p15.31 and has a duplication of the end of chromosome 14 from 14q32.11. She has the same karyotype as Esme (see pages 13-4) but is affected differently. Deletion 5p typically causes a





Age 7

" I would be lost without her. She has me in fits of laughter every day. What else do you need? "

genetic syndrome known as Cri du Chat (named after the cat-like cry of babies with the condition) but where the very tip of chromosome 5p is lost it may cause no features typical of the syndrome.

Hayleigh has an unusual condition seen in some other children with a14q duplication, an underdevelopment of the lower eyelids that makes it impossible to close the eyes. She has had repeated skin grafts and after four surgeries, her eyes close better but remain vulnerable to infection and she still needs to have artificial tears to prevent them from becoming too dry.

By the age of nine, Hayleigh's health was generally very good but she has had numerous hospital stays to deal with her various conditions: surgery to correct her duodenal web (a membrane in the intestines that causes a blockage), ectopic anus (the anus is in front of its normal position) and cleft palate; a Nissen fundoplication to improve the action of the valve between the food passage and the stomach and insertion of a gastrostomy tube and button to allow direct feeding into the stomach; and removal of her tonsils, as well as many chest infections. She had ongoing constipation and asthma but these were controlled with medication.

Hayleigh has very small feet: at 9, her feet were a baby size 7 to 8. In terms of development, she could shuffle on her bottom and stand and walk with support. Three bent fingers on each hand were splinted as a baby, making it easier for her to hold objects. She communicates using gestures and vocal noises and understands more than she can say. At school she is a determined learner and is supported with an SEN statement. She is generally happy and sociable and particularly enjoys rough and tumble games – the rougher the better.

Esme

Esme has lost the end of the short arm of chromosome 5 from 5p15.31 and has a duplication of the end chromosome 14 from 14q32.11. She has the same karyotype as Hayleigh (above) but is affected differently. Esme has lost the region on 5p13.31 that is associated with the typical cat-like cry and plaintive voice of Cri du Chat syndrome. She has no major health concerns but has spent time in hospital with feeding difficulties, pneumonia, urinary infections and reflux, bronchiolitis and gastroenteritis. She had a single seizure at two weeks of age that was probably a febrile convulsion.

Esme was induced at 38 weeks after her growth halted in the womb and she was very small at birth. As a newborn, the main concerns were her inability to latch on and suck and her low muscle tone. High calorie formula ensured that her weight rose to the 50th centile by seven months but her length and head circumference have followed the

Age 14 months

“ She is just so loving and happy, it is infectious! ”

3rd percentile curve. Esme experienced dusky episodes after feeds and was diagnosed with reflux and aspiration, with feeds returning up the food passage and being inhaled into the lungs. Thickened feeds and medication to ensure that feeds stay within the stomach have controlled the reflux. Recently, she has started to have hypoglycaemic episodes (where her blood sugar falls). These often follow a period of minor illness and are being investigated.
Esme has certain features associated with her chromosome disorder: she has very small hands and feet and her facial features include sparse eyebrows, a high forehead, a broad flat bridge of the nose, large fontanelles, a very pronounced groove between the nose and upper lip, a slightly small lower jaw and a slightly prominent upper lip.

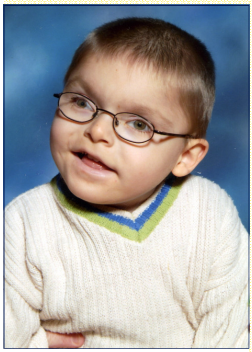
At 14 months, it is too early to be certain how she will develop, but she is extremely sociable and responsive and has a good memory for people. Esme is able to sit independently and although she has shown that she can roll over, she chooses not to. She has had physiotherapy and occupational therapy from birth and from eight months has had conductive education.

Laura

Laura has lost the end of the long arm of chromosome 4 from 4p16.3 and has a duplication of the end chromosome 14 from 14q32.2.

Loss of the terminal band 4p16.3 causes Wolf-Hirschhorn syndrome but Laura does not have classic features of this well-known chromosome disorder. Although she is short for her age and has shown a mild degree of developmental delay, by the age of eight she had learned to walk and ride a bicycle; she first used words at two and by eight was talking in short sentences; she attended a mainstream school where she learned to read and write and was achieving at a level typical of a child perhaps three years her junior; she loved playing with other children and being sociable; she was entirely healthy. Laura showed slightly unusual facial features and an eye movement disorder known as Duane syndrome on the left side but did not need treatment.

Aaron



Age 6
14

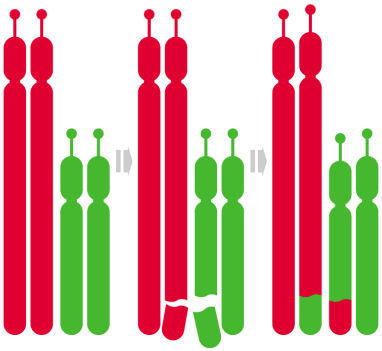
Aaron has lost the end of the short arm of chromosome 18 from 18p11.31 and has a duplication of the end chromosome 14 from 14q32.3. He was born after a normal pregnancy but had an unexpectedly low birth weight and one or two anomalies such as a small head and undescended testicles. After suction and oxygen at birth, Aaron coped, but feeding and swallowing were difficult. Aaron proved to have no major birth defects, but succumbed frequently to viral infections and by 6 had had repeated chest infections and was taking anti-asthma medication. He has also had two or three febrile convulsions but has not been diagnosed with epilepsy. Aaron has also had stomach problems and has severe constipation.

“ He has contributed loads to our lives as he is so happy and loves being around family and is making good progress at school which makes us really proud of him. ”

Aaron needs a lot of help to keep mobile as he cannot yet sit or walk, although he can roll from side to side. At 6, he cannot yet grab or hold, but he swipes at toys and can operate a switch device from his head. He has an unusually high muscle tone, for which he takes the muscle relaxant baclofen. Aaron communicates with vocal noises and eye pointing and at his special school has proved to be a determined learner with a good memory.

How did the duplication arise?

Some 14q duplications are the result of a rearrangement in one parent's chromosomes. This is usually a balanced translocation in which material has swapped places between chromosomes but as no material has been lost or gained the parent usually has no difficulties with health or development. Occasionally one parent is found to have the same duplication as the child.



A balanced translocation

Other 14q duplications occur when both parents have normal chromosomes. The term that geneticists use for this is de novo (dn). De novo 14q duplications are caused by a change that has usually occurred when the parents' sperm or egg cells were formed. We know that chromosomes must break and rejoin when egg and sperm cells are formed but this only sometimes leads to problems.

The breaking and rejoining is part of a natural process and as a parent you cannot change or control it. Children from all parts of the world and from all types of background have 14q duplications. No environmental, dietary or lifestyle factors are known to cause them. There is nothing that either parent did before or during pregnancy that can be shown to have caused the duplication to occur and equally nothing could have been done to prevent it.

Can it happen again?

The possibility of having another pregnancy with a 14q duplication depends on the parents' chromosomes. If both parents have normal chromosomes, the 14q duplication is very unlikely to happen again.

If a blood test shows that either parent has a chromosome change involving 14q, the possibility is increased of having other pregnancies with chromosome changes. Once the family chromosome change is known, a test can be done in any future pregnancy to find out whether the baby's chromosomes are affected.

Discussing the chromosome change with other family members gives them the opportunity to have a blood test to see if they too carry it.

A genetic specialist can give you more guidance for your family.

Support and Information

Rare Chromosome Disorder Support Group,
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info@rarechromo.org | www.rarechromo.org

Join Unique for family links, information and support.

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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. The guide was compiled by Unique and reviewed by Dr Edmond Lemire, Head, Division of Medical Genetics, Royal University Hospital, Saskatoon, Canada and by Professor Maj Hultén BSc PhD MD FRCPath, Professor of Reproductive Genetics, University of Warwick, UK 2007.

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