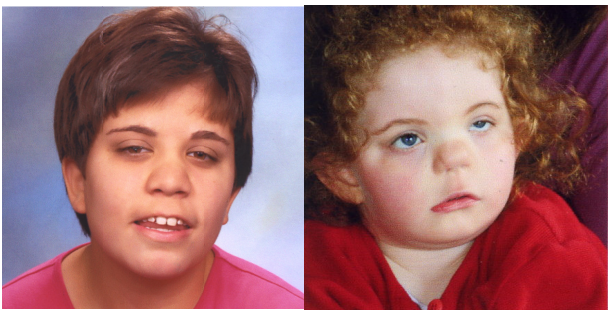
Understanding chromosome disorders

Unique

14q deletions between 14q22 and 14q32

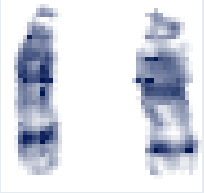


rarechromo.org

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. If you wish, you can obtain abstracts and articles from *Unique*.

The leaflet also draws on *Unique*'s database. When this leaflet was revised in 2011, *Unique* had 100 members with a 14q deletion, of whom 72 had a pure 14q deletion with no other chromosome involved.



Two chromosome 14s, stained and magnified

14q deletions

A chromosome 14 deletion means that part of one of the body's chromosomes has been lost or deleted. If the material that has been deleted contains important instructions for the body, learning disability, developmental delay and health problems may occur. How serious these problems are depends on how much of the chromosome has been deleted and where the deletion is.

Genes and chromosomes

Our bodies are made up of billions of cells. Most cells contain a complete set of genes. We have 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'. The chromosomes and the genes are made up of a chemical substance called DNA.

Chromosomes come in different sizes and apart from two sex chromosomes (two Xs for a girl and an X and a Y for a boy) they are numbered 1 to 22, generally from largest to smallest. Each chromosome has a short (p) and a long (q) arm. In a 14q deletion, material has been lost from the long arm of one of the two chromosome 14s. The short arm of chromosome 14 contains no unique genes, so losing material from the short arm generally has no harmful effect.

You can't see chromosomes with the naked eye, but if you stain them and magnify their image with a computer or under a microscope, you can see that each one has a distinctive pattern of light and dark bands.

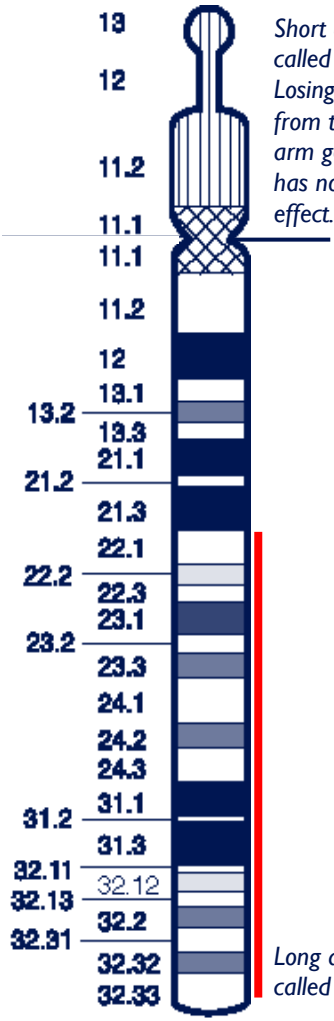
Chromosome deletions

A small or very large piece of the chromosome can be missing. If the piece is visibly missing when the chromosomes are magnified, it is called a **deletion**. The missing piece may be so tiny that the magnified chromosome looks normal and it can only be found using recently developed techniques, including molecular chromosome tests with or without DNA analysis. It is then called a **microdeletion**.

One type of deletion is called **terminal**. There is one breakpoint and the chromosome from the breakpoint to the end of the arm is missing. Another type of deletion is called **interstitial**. There are two breakpoints in the same arm that have rejoined and the part of the chromosome between them is missing.

This leaflet tells you what we know about **interstitial deletions between band 14q22 and band 14q32**.

Your geneticist or genetic counsellor can tell you more about the chromosome material that has been lost. You will almost certainly be given a **karyotype**, a shorthand code for the image of your child's chromosome make-up that will show the points where the chromosome has broken and rejoined. Comparing your child's karyotype with others, both from the medical literature and within *Unique*, can help to build up a general picture of what to expect. But there will still be differences, sometimes quite marked, between your child and others with apparently similar deletions. It is very important to see your child as an individual and not to make direct comparisons with others with the same karyotype. After all, each one of us is unique.

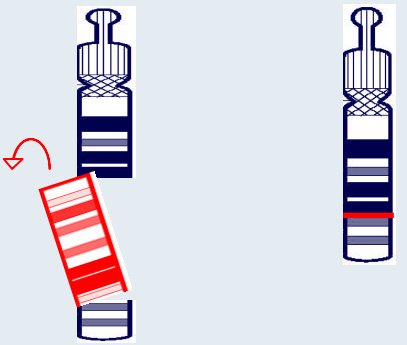


Some fifteen cases with a pure deletion in this area are described, at least seven in the medical literature and eight members of *Unique*. The oldest member of *Unique* with an interstitial 14q deletion was 19 years old when this leaflet was written. This is not to imply that there are not older people with an interstitial 14q deletion, but they have not necessarily been diagnosed or reported.

(Le Meur 2005; Ochi 1998; Karnitis 1992; Rivera 1992; Yamamoto 1986; Turlau 1984; *Unique*)

There is specific information on **deletions from bands 14q22-23** on pages 13-15.

An interstitial deletion



Chromosome 14 showing part between 14q22.1 and 14q32.13 being lost

Chromosome 14, broken and re-joined with interstitial deletion

Of seven cases where the **pregnancy** was described, it was normal in five. However, one mother experienced progressive swelling in the legs and feet during pregnancy and a raised blood pressure. The baby was delivered by Caesarean section at 30 weeks, after an ultrasound scan showed low blood flow to the placenta, a single umbilical artery and decreased fetal movements. In another case growth delay was identified on ultrasound at 33 weeks. Two babies are known to have been delivered prematurely.

" Great pregnancy – no problems " - *14q24.1q32.1 deletion*

At birth

What was unusual?	How many babies affected?
■ Reluctant or unable to feed	Most
■ Low muscle tone (floppiness)	Most
■ Structural heart problem (see page 7)	8/14
■ Unusual hand features (various)	6/14
■ Unusual features affecting feet	4/14
■ Anomaly of bones in forearm and hands	2/14
■ Premature birth	2/14

Range of birth weights at or near term: 5lb 1oz/2.3 kg to 8lb 9oz/3.88 kg.

Most babies had a generally trouble-free newborn period, apart from feeding issues. But one baby with a 14q24.1q32.1 deletion was born with a heart defect (treated with diuretic medication, resolved) and a punctured lung.

■ Feeding

Feeding difficulty was common at birth, with babies finding it hard to latch on, suck and coordinate sucking with swallowing. The mother of one baby with a deletion from 14q24.3 to q32.1 succeeded with difficulty in breastfeeding and two mothers achieved partial breastfeeding. The evidence suggests that most babies will need careful feeding to ensure steady growth and weight gain. Weak sucking and uncoordinated swallowing, persisting in some cases into childhood, mean that babies may not meet their own nutritional needs. All the same, only one baby is described as being fed (with expressed breast milk) by nasogastric tube and from eight months to 3 years by gastrostomy tube direct into the stomach, supplemented by oral feeding.

In most children low muscle tone (floppiness, hypotonia) contributed significantly to the feeding difficulties with no underlying anatomical problem, but one boy with a 14q24.1q32.1 deletion needed surgery and a tonsillectomy to enlarge his throat.

Gastro oesophageal reflux (GERD, GORD, where the stomach contents flush readily back up the food passage) may also occur and cause two secondary problems, an inflammation of the food passage (oesophagitis) and aspiration, where

the returned feed is inhaled into the lungs, with the risk of causing an infection. Reflux can be eased by careful semi-upright positioning during and after feeds, raising the head end of the baby's cot, giving thickened feeds and if necessary by prescribed medication that helps to keep the feed within the stomach. 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 passage and stomach. Continuing problems with food may occur, leading to late weaning and issues with lumpy food and handling different flavours and textures, but eventually all children known to *Unique* have progressed to a varied, healthy diet of solid and liquid foods.

Many children with a chromosome disorder are prone to constipation, due in part to their relative lack of mobility and activity, their necessarily high-energy, low-fibre diet and to a relatively low fluid intake. If it is not possible to adapt the diet, early treatment with laxatives can prevent the problem from becoming severe.

One child is reported with pica, eating non-food items such as hair and sand, so that she needs constant supervision.

■ Hypotonia (floppiness)

An unusually low muscle tone, so that the baby or child feels floppy to handle. Babies with hypotonia tend to lie with their arms and legs loosely outstretched instead of bent at the knee or elbow. When held under the arms, their bodies easily slip through the hands. Babies and children with hypotonia benefit from early physiotherapy.

■ Unusual hand features (various)

Minor, non-functional anomalies of the hands and feet are relatively common in children with chromosome disorders. In this group, one child is described as having small hands with short fingers and four children have a single palm crease. One child is described as having 'sensitive' palms and soles.

" Soft, child-like hands **"**

■ Unusual features affecting feet

One child has flat feet with slightly webbed toes (partial syndactyly) and a fifth toe that rolls over to face the floor. Another child has overriding toes, for which she wears 'good' shoes, with orthopaedic soles.

■ Developmental anomaly of bones in forearm and hands

Two children in the medical literature but none in the *Unique* series with a deletion overlap at 14q23.3 to q24.2 had a more serious limb defect: in one child, the left outer bone in the forearm (radius) was missing and the right shortened, with bowing of the inner bone (ulna). This baby was also missing the 5th sacral vertebra and had a delayed bone age. In the other child both forearm bones were underdeveloped and curved and one thumb was abnormally placed (Le Meur 2005; Turleau 1984).

■ Premature birth

Two babies born prematurely with a very low birth weight (998g/2lb 3oz at 30 weeks; 1540g/3lb 6oz at 36 weeks) faced extra difficulties caused by their prematurity, with the less mature ventilated for six weeks but without long-term respiratory problems.

Appearance

You and the doctors may notice that your baby has a slightly unusual head or face. He or she may have features that make him look more like other children in this leaflet than like his own family.

Typical features can include: a round or oval face sometimes with some facial hair, usually around the forehead, thick eyebrows, wide-set eyes (hypertelorism) that may be small or narrow and sometimes have a tiny skinfold across the inner corner of the eye (epicanthic fold), hooded upper eyelids (ptosis), a small, upturned or bulbous nose, low set and sometimes large ears that may be cupped or prominent and may not be symmetrical, a small mouth, a small chin and receding jaw (microretrognathia), a short neck with loose skin at the back. The shape of the head may be unexpectedly long or square. One baby was born with skin tags in front of the ears. The palate (roof of the mouth) may be high and one baby had a cleft in the front hard part.

“ Beautiful ringlet curls of dark hair ” – *14q22q32 deletion*

Medical concerns

	How many affected?
Difficulties with growth or weight gain	Most
Head and brain growth	Most
Structural heart problem	8/14
Frequent respiratory infections	7/12
Kidney problems	6/14
Seizures	3/11
Liver disorder	3/12

For information on deletions from 14q22q23 and specifically on eye development, see pages 13-15.

Growth

Regardless of birth weight or length, most children with an interstitial 14q deletion grow slowly after birth, with their growth curve typically at or below the lowest line on a growth chart. The evidence suggests that stature is proportionately small, affecting height, weight and head circumference. In this situation, additional feeding may boost weight without any effect on height. This pattern of short stature and slow growth may not be universal; growth in one child with a deletion of 14q24.3q32.1 was normal at 3.5 years. The evidence on eventual adult height is slim, but the adult height of one *Unique* member is 1.47m (4' 10"), with a body weight of 54 kilos (120lb).

Head and brain

Measurement of the head circumference shows that most babies have a proportionately small head; this appears to grow in line with body length after birth. Imaging of children's brains by CT scan and MRI has revealed a variety of conditions including enlarged fluid-filled ventricles, a generalised decrease in the solid matter of the brain, increased white matter around the ventricles and a thinned corpus callosum (the band of nerve fibres that links the two hemispheres of the brain) and wasting of the vermis, the central structure within the cerebellum. Delayed myelination (insulation of nerve fibres, a process that continues long after birth) has also been noted.

Heart

More than half of the children in this series (8/14) were born with a heart condition; there was no obvious relationship between the size or site of the deletion and the presence of a heart defect. In three babies the heart condition resolved at least partly in time; in one case a pulmonary stenosis (narrowing in the valve in the artery that takes blood from the heart to the lungs); in another case a hole between the lower chambers of the heart (ventricular septal defect, VSD) that resolved after medication; in a third case both a VSD and a large hole between the upper chambers of the heart (atrial

septal defect, ASD) resolved naturally. Five babies had a significant heart defect, each with an ASD and further anomalies including valve defects, narrowing of a blood vessel or an additional VSD. In one child, the complex of anomalies resembled Tetralogy of Fallot, combining pulmonary stenosis and a VSD. Most of these children required open heart surgery to correct the anomalies, but one child had a medical procedure (an angioplasty) to enlarge the aorta. *Unique*'s experience is that children thrived after surgery, but one child with a pulmonary stenosis and ASD treated with diuretics died at six months.

Chest infections

Seven of 12 children are known to have had repeated chest infections, in most cases leading to pneumonia and in two cases causing a pneumothorax, an escape of air from the lung, causing it to collapse. Swallowing difficulties will have caused some cases of pneumonia (by aspiration), and many children have long-term respiratory problems and require ongoing bronchodilator and steroid inhaler therapy.

Kidneys

Six of 14 children are known to have had kidney problems or problems with the flow of urine. One unborn baby experienced an obstruction in the outflow from the bladder (urethra), causing bladder enlargement and mild enlargement of the kidneys; two children have horseshoe kidneys (the lower tips of the kidneys are joined, in itself a harmless anomaly unless the drainage outlets are implicated); two have recurrent urinary infections and take low-dose antibiotics to protect their kidneys; one child has a normally functioning left kidney but her right, multicystic kidney was removed.

Seizures

Four of 11 children are known to have experienced seizures. In one child absence seizures occurred in babyhood but resolved. Another child had a single seizure at two years but was not diagnosed with epilepsy. A 5-year-old had seizures controlled with the anti-epileptic medication sodium valproate.

Liver

Three children are known to have liver problems: unspecified in one, cysts in another and an atypical inflammatory reaction to antibiotic treatment in a third.

Hernias and genital area

Four children are known to have had an inguinal hernia (in the groin), needing surgical correction. In boys, the surgery was typically performed at the same time as undescended testes were brought down and fixed in the scrotum. In three boys, the undescended testes were the only genital anomaly, but one boy also had an unusually small penis.

Other

One boy with a 14q24.1q32.1 deletion experienced transient (7 weeks) idiopathic thrombocytopaenia as a baby, with poor platelet function; a girl with a 14q22q32 deletion responded as a baby to periods of fasting with ketotic hypoglycaemia, where her blood sugar dropped and she started to metabolise fat for energy. One child showed raised thyroid activity.

Temperature control

Two children in the *Unique* series showed abnormal regulation of body heat, with frequent high or low body temperatures.

“ No treatment, but we refresh her with a bath, water… ”

Eyesight

One child with a 14q24.1q31.2 deletion had markedly delayed visual maturity and has required visual re-education therapy. As a baby she showed the roving eye movements known as nystagmus but as her visual pathways matured, this lessened and by the age of 2, she was able to see objects at 20-25 cm (8-10”). A boy with a 14q24.3q31.3 deletion had cataracts. Three children have strabismus (squint), which may be amenable to patching or correction with the use of glasses but is more likely to need surgical correction.

For more information on eye development when 14q22q23 is deleted, see pages 13-15.

Hearing

In early childhood a number of children experience the transient hearing loss caused by glue ear and relieved by placing tubes in the eardrum. A single case of permanent hearing loss was observed in a child with a 14q24.1q31.2 deletion who has a cochlear (inner ear) malformation and requires hearing aids. Another child has auditory neuropathy, in which sounds enter the ear normally but the transmission of signals from the inner ear to the brain is impaired. Four children have a marked over-reaction to environmental nose and need careful handling when sudden or loud noises are expected.

“ She can’t stand sudden or loud noises. She immediately cries with fear. It is difficult for example at school, concerts, sports matches ” – *4 years*

Teeth

In two children whose deletion overlap was 14q24.3q32.1, one or more lateral incisor teeth was missing. One other child has needed surgery for breaking and broken teeth.

Outlook

The medical outlook for an individual child is best described by the specialists looking after them. We know from this series that none of the *Unique* children has died and some thrived after complex heart surgery. One baby described in the medical literature died at 2 years, but almost a generation ago when medical care was almost certainly less advanced. Another baby died more recently at 6 months of cardiac failure.

Development

Sitting, moving: gross motor skills

Babies and children with an interstitial 14q deletion do face delay in reaching their mobility milestones, but they eventually walk, run and climb stairs. Most have a low or variable muscletone (hypotonia) which makes purposeful movement tiring and need to be encouraged and taught to make the movements that come naturally to others. Their joints are typically hypermobile (they may appear to be double-jointed) and may need supporting with splints. Children benefit from early physiotherapy and may need a walker in the early stages of walking and a wheelchair for outdoor use. In some children the feet
are flat and barefoot walking indoors may help to strengthen the arches.

In this series, rolling was achieved between 5 and 11 months; sitting between 7 and 25 months; crawling between 12 and 30 months and walking between 18 and 42 months. This broad range shows how varied development can be; in general, early rolling was a good predictor of early walking. The underlying flexibility caused by hypotonia remains, although increasing strength helps, but it is likely to show in children's style of walking which can appear clumsy.

Using their hands: fine motor and coordination skills

Babies are typically late to reach out and grasp for toys, to hold a bottle or a marker and to transfer toys from one hand to the other. They spend longer than other babies feeling and handling clothes, faces and hands and benefit from stimulation and early access to occupational therapy. In addition, there is some evidence that some children have sensory disorders and at least one child has a tremor when attempting fine motor tasks.

Pace of development is individual, but as a guideline, one child with a 14q24.1q31.2 deletion was able to bring her spoon to her mouth with help by age 5. Hand-eye coordination emerged around 3.5 years; she showed an interest in books around 2.5 years; and in toys around 4 years.

" She likes motion, deep pressure and has definite preferences and dislikes. This has been helped greatly with OT "

Learning

A degree of learning disability is typical, but the extent is variable. From the very slight evidence available, it seems that a moderate to severe learning disability can be expected. A girl with a 14q24.3q32.1 deletion learned to read at 6 years, to write at 7 years and to use a computer and mouse at 10 years. At 19 years, she has a good memory, can read the TV guide and short books; her writing is large. She has an individual education plan and attends a special school. At the age of 7, a boy with a 14q24.1q32.1 deletion has a patchy memory, acquires computer skills but needs frequent reinforcement and is not yet reading or writing. At almost 5 years, a girl with a 14q24.1q31.2 deletion has been using a keyboard from 4 years old as a game, recognizes music and songs and enjoys looking at baby books.

Speech and communication

Children typically experience some speech delay and language development appears to reflect the level of learning disability. Alongside vocal noises, gestures, signing and other communication systems, most children appear to develop some speech, with first words emerging between two and seven years (although it may be later), but words are limited and articulation may not be distinct. Regular speech therapy should be available; music therapy may also help. Many children sign and some need a communication aid.

“ She spoke her first words at 4 years and can now talk using full, simple sentences but is sometimes hard to understand; she understands better than she can express. She seems to be an obligate mouth breather ” - *14q24.3q32.1 deletion, at 19 years*

“ He signs and uses a communication aid and seems to understand. He can say mama and dada but does not repeat these words ” - *14q24.1q32.1 deletion, at 6 years*

“ She understands sentences like ‘Look at me’ or ‘Shall we go into the garden?’ but often answers with her body (shaking her hands or legs for example, when she agrees). She can say ‘No’ very clearly when disagreeing ” - *14q24.1q31.2 deletion, 5 years*

Behaviour

At 4 years: Sociable; affectionate; difficult behaviour is rare. Sometimes cries with pain or anger, mostly due to digestive problems or tiredness. Enjoys listening to music, looking at books and listening to stories, playing with train or electronic games. No interest in TV, little in drawing or painting.

At 5 years: no sense of danger or inappropriateness. She enjoys TV, music, sensory activities and water play.

At 6 years: Enjoys TV, music, football, banging things together, relaxing on his bed, his bike, car rides, shopping. Self harms for body awareness, showing no sense of pain or ability to stop. Playing games helps and a large dolly goes everywhere.

At 19 years: Since 15, behaviour has been the hardest aspect. Has pervasive developmental disorder, treated with ziprasidone (Geodon) and slight autistic tendencies, is often obsessed with dates and repetitive. Can act defiantly and be stubborn. Enjoys music, dance, DVDs, videos, word searches, cutting pictures, cards, movies and swimming.

Sleep

Two families have described marked sleep problems. One family started melatonin treatment at 3 years, continuing until almost 5 years and found this helpful. Once melatonin was stopped, the child continued to sleep well.
In another family, the sleep problems have continued to age 6 years. The child sleeps on average for 3 to 4 hours, then wakes in pain or is thirsty and gets into his parents' bed. Then he is tired in the mornings. Music playing in the room, darkened blinds, a bottle of milk and a weighted blanket have all helped.

Personal care and independence

Self care skills are late to develop and children are typically late to be toilet trained. One child was dry and clean by 3 years, another was starting the process at 5 years and another had not started at 6 years. Fine motor delay means that children are late to learn to dress themselves and may be dependent on parents for this at mid-childhood. They also need considerable help with feeding. The 19-year-old adult was able to carry out personal care but needed help with such activities as tying shoes and brushing hair.

This adds up to a picture of children who are likely to need support throughout childhood and into adulthood and are may achieve a limited measure of independence.

Why did the deletion occur?

Most 14q interstitial deletions occur when both parents have normal chromosomes. The term that geneticists use for this is de novo (dn). A blood test to check the parents' chromosomes will show if this is the case.

De novo 14q deletions 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. This only occasionally leads to problems.

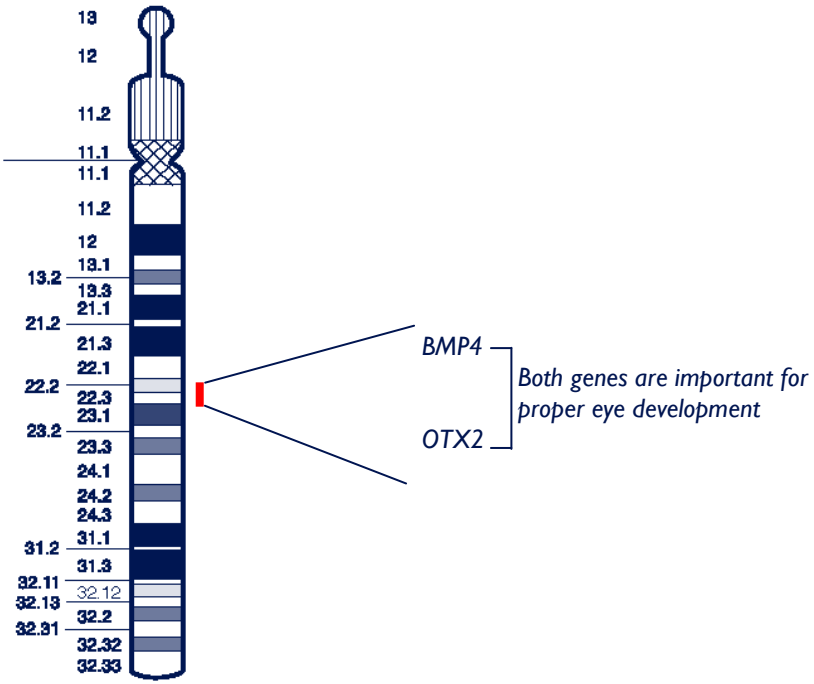
The breaking and rejoining is part of a natural process and as a parent you cannot change or control it. Children from all parts of the world and from all types of background have 14q deletions. No environmental, dietary or lifestyle factors are known to cause them. There is nothing that either parent did before or during pregnancy that can be shown to have caused the deletion 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 deletion depends on the parents' chromosomes. If both parents have normal chromosomes, the 14q deletion 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 a family chromosome change is known, a test in any future pregnancy can find out whether the baby's chromosomes are affected.

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

Eyesight and deletion from 14q22q23

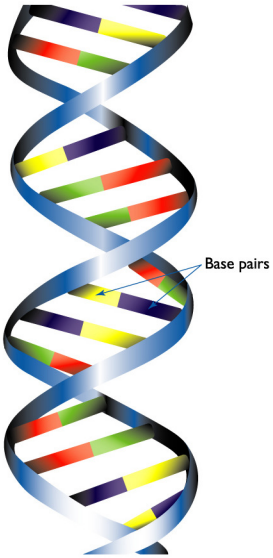


It has been known for 20 years that deletions from bands 14q22 and 14q23 are associated with severe eye defects as well as pituitary, growth, developmental and brain anomalies, some distinctive facial features and generally minor abnormalities of the toes and fingers, as well in some cases as a hearing impairment.

Twelve reports in medical journals, supplemented by 5 *Unique* families and three reports from the Decipher database [http://decipher.sanger.ac.uk] show a range of eye defects that depends in part on what DNA is missing. Separately and together, two genes - *BMP4* in band 14q22.2 and *OTX2* in band 14q22.3 - are important for proper eye development.

When chromosomes are examined using microarrays [array CGH], it can be possible to tell what genes are missing. A report of an array CGH analysis will frequently specify the extent of a deletion [or duplication] in base pairs. Base pairs are the chemicals in DNA that form the ends of the 'rungs' of its ladder-like structure - see next page. Chromosomes contain many millions of base pairs, so the numbers are very long. The *BMP4* gene is found between base pair 54,416,454 and base pair 54,423,529 within the 14q22.2 band. The *OTX2* gene is found between base pair 57,267,426 and base pair 57,277,187 within the 14q22.3 band.

What are base pairs?



Two strands of DNA are held together in the shape of a double helix by the bonds between base pairs.

When *OTX2* alone is missing, eye defects range from a developmental defect of the iris, called a coloboma, [not causing blindness] through a condition where the eyes are smaller than normal [microphthalmia, with some visual loss] to a complete failure of the eyes and the visual pathways in the brain to develop [anophthalmia, causing blindness]. The *BMP4* gene is adjacent to *OTX2* and other genes: when it is missing, eye problems range from a partly opaque front window of the eye [sclerocornea], a developmental defect of the iris [coloboma], small eye [microphthalmia] to anophthalmia. When babies are born with anophthalmia, the socket is very underdeveloped and the eyelids may be very small.

Babies born with anophthalmia and microphthalmia treated in specialist centres can gain excellent results from a combination of socket expanders and prosthetic eyes for cosmetic improvement. The remaining vision in children with microphthalmia can be maximised through specialist treatment.

In at least half of the people known about with a 14q22q23 deletion, the pituitary gland is not fully developed. Depending on how well any remaining part of the gland is able to function, hormone levels are likely to be disturbed and your child will very likely be under the care of an endocrinologist. Growth hormone levels may be low [in 4 cases, children were very small for their age]; children may also have too little thyroid hormone.

In almost half the people we know about with a 14q22q23 deletion, an MRI scan has shown some anomaly within the structure of the brain. In 11/13 cases, development has been delayed. Babies are likely to sit and stand late and frequently have altered muscle tone – either low tone, making them feel floppy [hypotonia]; or raised tone, so their

muscles feel taut [hypertonia]. Language development is typically delayed and most children will need extra support with their learning.

The ear canals are sometimes affected – one or both may be very narrow or missing. Hearing problems are quite common, affecting 8 children, and may be temporary [conductive loss due to glue ear] or a permanent impairment.

Some children have distinctive facial features that mean they resemble each other as well as being like other members of their family. A high, prominent forehead is typical, as are low set, unusually formed ears and a small lower jaw and chin. Some children have a high palate [roof of the mouth] and in some the soft spot on top of the head [fontanelle] closes unusually late.

A range of minor or more obvious anomalies of the fingers and toes has been found: these include webbing between toes; incurving fifth fingers; short fingers; and additional fingers or thumbs.

A range of further anomalies has been reported in people with a 14q22q23 deletion. These include underdevelopment of the external and internal reproductive system; small kidneys; delayed emergence of teeth; abnormalities of vertebrae in the spine; seizures; heart problems; a dimple at the base of the spine.

[Bennett 1991; Elliott 1993; Phadke 1994; Lemyre 1998; Ahmad 2003; Nolen 2006; Ragge 2007; Bakrania 2008; Wyatt 2008; Decipher; *Unique*]

Support and Information

Rare Chromosome Disorder Support Group,
G1, The Stables, Station Road West, Oxted, Surrey RH8 9EE, United Kingdom
Tel/Fax: +44(0)1883 723356
info@rarechromo.org | www.rarechromo.org

Join Unique for family links, information and support.

Unique is a charity without government funding, existing entirely on donations and grants. If you can, please make a donation via our website at www.rarechromo.org Please help us to help you!