

Support and Information



Rare Chromosome Disorder Support Group,
The Stables, Station Road West, Oxted, Surrey RH8 9EE, UK
Tel: +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/donate Please help us to help you!

In the UK, the Childhood Eye Cancer Trust has links to many support services, organisations and email discussion groups
www.chect.org.uk

Unique mentions other organisations' message boards and websites to help families looking for information. This does not imply that we endorse their content or have any responsibility for it.

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.

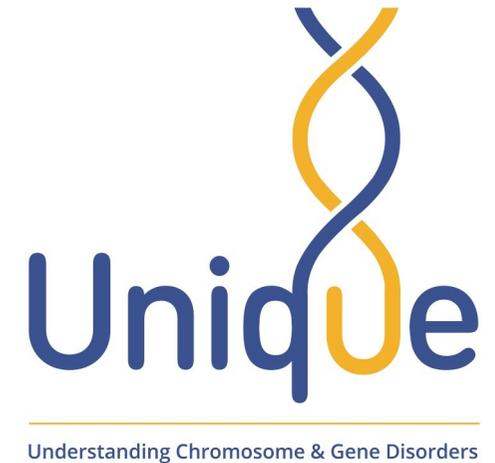
This guide was compiled by Unique and reviewed by Dr Elisabeth Rosser, Institute of Child Health, London, UK 2004, by Professor Dorothy Warburton, Professor of Clinical Genetics and Development, Columbia University, New York, US 2005 and by Professor Maj Hulten, Professor of Medical Genetics, University of Warwick, UK.

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13q deletions including *RB1*



Sources & References

This leaflet draws on information on the thirty to forty people with this chromosome disorder who have been described in the 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*. Some information also comes from the families of eleven affected *Unique* members. References to this information are marked (U).

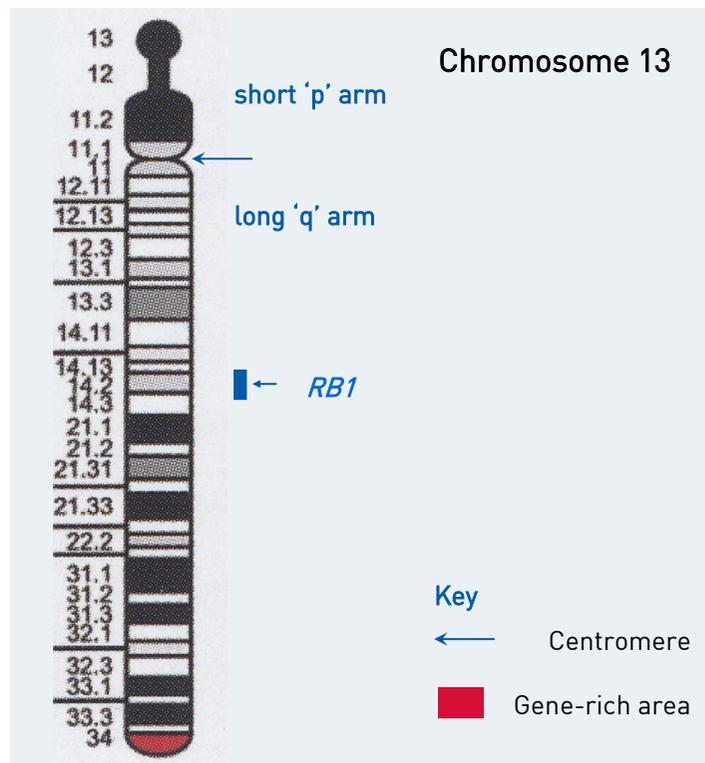
Losing part of the long arm of one copy of chromosome 13 including the *RB1* gene at q14.2 is very rare. Apart from the effects of losing the *RB1* gene (*see pages 6-7*), the effects depend mostly on how much material is missing and as this varies from person to person, individuals experience different effects.

In general, people who have lost larger bits experience more effects. Some people have a mixture of cells with complete chromosome 13s and cells with a bit missing from one chromosome 13. This is called mosaicism and in general, it means that people have fewer effects (Baud 1999).

Main features

The most common effects are:

- Short stature
- Delay in reaching developmental milestones
- Learning difficulties or disability



Screening for retinoblastoma

Your child is likely to be checked regularly until the oncologists, who specialise in children's cancers, are confident that no tumours will develop. Screening isn't painful, but as your child will need to lie completely still for a screening test, a general anaesthetic is usually given. Although the great majority of cancers develop before the age of 5, screening usually continues to the age of 8.

What happens if a child develops retinoblastoma?

So long as retinoblastoma is identified early, it usually responds well to treatment, whether it is associated with a 13q deletion or not. A recent follow-up study of children with a chromosome deletion to 20 years after diagnosis showed that more than nine out of 10 were still alive. The oldest survivor of retinoblastoma with loss of material from chromosome 13 was 64 years old when a research report was written about them (Ward 1984; Baud 1999).

“ As he had quite a lot of treatment and is more likely to get other cancers it was decided the removal of his eye would be the safest so he could have more chemo in the future if needed.

Treatment for retinoblastoma

There is a variety of treatments for retinoblastoma that your child's ophthalmic surgeon will discuss with you. They include cryotherapy (freezing) for small tumours; applying a radioactive plaque containing iodine or ruthenium; drug treatment (chemotherapy) as the first line of treatment and to treat any spread of the tumours; drug treatment together with laser therapy; and external beam radiotherapy for tumours that have not responded well to drug treatment or have recurred. For very large tumours that have permanently damaged eyesight, the safest option may be surgery to remove the eye (called enucleation). Out of four *Unique* children with retinoblastoma, two had an eye removed (U).

People who have developed retinoblastoma have a small chance of developing other tumours in other parts of their body. These usually affect the bones or muscles or appear as moles or lumps in the skin. It is important to wear a high factor sunscreen to protect the skin and to be alert to any changes in moles or worrying symptoms.

Was this my fault?

The reason for the changes in chromosome 13 is not fully understood but usually occurs as a natural process when the parent's sperm or egg cells are forming. The change in the gene on the other chromosome may occur at the same time or later. These types of genetic changes happen to everyone, it's only when an important gene is affected that symptoms and features are noticed. The changes are not caused by anything that parents did or did not do.

Can this happen again?

So long as both parents have unaffected chromosomes, it is extremely unlikely that they would have another child with the same genetic change. In a minority of families – eight out of 39 in the most recent review – one parent has an unusual chromosome arrangement, usually what is known as a balanced translocation of material between two chromosomes. They may be unaware of this because with no chromosome material lost or gained the rearrangement has not had an affect so far. However, their chances of having another child with a 13q deletion are much higher than for someone with unaffected chromosomes. Each family's situation is different and it is important to have a chromosome analysis and to seek advice from a genetics service (Baud 1999; Schinzel 2001).

Three babies experienced reflux – the form of extreme possetting that occurs when babies bring their feeds back repeatedly – and two babies were fed by gastrostomy direct into the stomach (Weigel 1998).

Retinoblastoma

The gene associated with a rare and treatable cancer of the retina (retinoblastoma) is located in band 13q14.2. Babies and children who have lost all or parts of band 14.2 and, usually, 14.3 on the long arm of chromosome 13 will therefore be regularly screened for development of retinoblastoma, which affects around half of the children with this deletion.

“ Try to find out as much information as possible. Stay optimistic and don't stick your head in the sand

“ You need support from family and friends during diagnosis and treatment. It is a very hard time for you, the parents and heart-breaking to know your child has cancer

Families of children who developed retinoblastoma

What is retinoblastoma?

Retinoblastoma is an eye cancer that develops in children in the cells of the retina, the light sensitive lining of the eye. It is usually diagnosed in the first six months of life, but may sometimes develop later. In the largest series of children considered to date, the age range at diagnosis was three months to three years. A single tumour may develop (unifocal) or more than one (multifocal). Usually one eye is affected but in a substantial minority of children both eyes are involved (Baud 1999).

How is retinoblastoma caused by a deletion or change in band 13q14?

In a child with a chromosome disorder, retinoblastoma is caused by the absence of the *RB1* gene from one chromosome 13 and by changes in the *RB1* gene on the other. *RB1*, the gene that protects against retinoblastoma, is located on the long arm of chromosome 13 at band 14.2. People normally have two chromosome 13s and therefore two copies of the gene. Losing the *RB1* gene at 13q14.2 raises the risk of retinoblastoma substantially but does not mean that a child will inevitably develop it. For retinoblastoma to develop, both copies of the gene must be damaged or missing. Children with a chromosome disorder where 13q14.2 is missing only have one copy of the gene. If that copy is damaged, as can happen when genes are copying themselves when cells divide, they will develop retinoblastoma.

Signs of retinoblastoma

The pupil reflects light as a white reflex. This may be seen instead of a red reflex in photographs. The eye itself may become red and inflamed.

Out of seven *Unique* families who have given relevant information, three children have stayed free from retinoblastoma – two to the age of nine, the other to 2½ years. Of the four children who have developed retinoblastoma, two have a tumour in one eye and in the others both eyes are affected (U).

Appearance

Children with this chromosome disorder are believed by doctors to have a distinctive appearance. However, from a parent's point of view, this may be subtle. The features that doctors may point to include thick, forward-slanting ear lobes, a high, broad forehead and a prominent philtrum (the groove between the nose and mouth). *Unique* parents have noted most often their child's wide nasal bridge and one parent also noted small lips and low set ears. One child was born with a lipoma (a benign tumour composed of fat cells) in the middle of the forehead (Baud 1999; U).

Growth

Research reports show that a minority of children (6/22) are very small for dates at birth. The *Unique* experience supports this. Out of seven *Unique* families who have given information on size, five babies were small at birth and put on weight slowly afterwards. One baby weighed 1350 grams (2lb 15 oz) when born at 38 weeks. By contrast, two others had an average birth weight of 3300 to 3500 grams (7lb 6/10 oz) (Baud 1999; U).

Learning

The amount of lost chromosome material is believed to have an impact on children's ability to learn, and children who have only lost chromosome material from within band 13q14 may be very mildly affected. *Unique* has no members with such a small chromosome change, but the evidence from its other members with larger changes suggests that learning ability may be moderately affected.

Of *Unique's* four school age members, none has more than a moderate learning difficulty. One nine-year-old knew the alphabet before he was 2 and started to write when he started school at the age of 5. He is now 'excellent' at spelling and reading, is reading age-appropriate books and can write short sentences. Another nine-year-old is reading well and printing whole sentences and using a computer and a play station. This evidence suggests that the research reports showing that most children (11 out of 16, or 69 per cent) have a severe learning disability should be treated with caution (Motege 1987; Baud 1999; U).

Speech and language

There is no specific information in the medical literature on children's ability to communicate, so this section relies on the experience of *Unique* members. Out of seven families who have given information on speech and communication, all have noted a moderate to severe speech delay. First words generally arrived late at around three or four years and before that children used vocal noises, gestures and eye pointing to indicate their needs and wishes. Parents' perceptions of their child's level of understanding varied – in some children understanding outstripped speech, in others the reverse was true.

“ She is better at reading and writing than number work. She still needs a visual aid such as bricks or a number line to add and subtract – age 9

Four *Unique* members noted concerns with articulation: in two the concerns centred around specific speech sounds, in particular 'th'. A third child had a diagnosis of articulatory dyspraxia; the fourth had 'good understanding but problems with pronunciation'.

By the age of nine, two *Unique* members were speaking well but not fluently:

“ Her comprehension of the spoken word is probably the thing that holds her back the most. She needs time to process what is being said to her and understand it. Then she needs more time to respond and can't always find the words to express what she wants to say.

“ He speaks as if he is reading out loud, quite stilted, still makes vocal noises when he gets frustrated and can't say the words he wants.

“ She has difficulty with prepositions and pronouns and understanding abstract ideas.

Sitting, standing, moving

The experience of *Unique* members shows that babies and children were late in reaching their developmental milestones of sitting and walking – but with extra practice and physiotherapy they reached them. As babies, many felt floppy to handle and had difficulty in holding their heads steady. Six out of eleven families positively noted their child's hypotonia (low muscle tone) and only one said their baby was not floppy. Sitting was achieved between 11 and 15 months and walking between 20 and 27 months.

At nine years of age, *Unique*'s two oldest members each had co-ordination problems. One could ride a bicycle without stabilisers but could not kick or catch a ball very well, while the other could swim a few yards, dance and cycle and had recently started gymnastics (U).

She has lots of personality and a good sense of humour. She is completely innocent and unselfconscious. She loves to sing and dance and to be going places. We get so much joy from her small achievements and seeing her enjoy things like camping trips and riding her new 'bike'. She makes us laugh and gives many people pleasure. We think we were chosen to have her.



Medical concerns apart from retinoblastoma

There are few typical medical concerns and as a rule, the *Unique* experience was that children are healthy. This was confirmed by a survey of 22 children, where none was found to have a heart condition, any kidney problems or disorders affecting their bones. The only structural problem revealed was partial agenesis of the corpus callosum (the broad band of nervous tissue that connects the two hemispheres of the brain) in two children and enlarged ventricles within the brain in another (Baud 1999; U).

Occasional health concerns affected one child in six (Schinzel 2001). These included: microphthalmia (small eyes); coloboma (a developmental defect in the structures of the eye); cataracts (clouding of the lens); cloudy corneas (clouding of the usually invisible and transparent front part of the eye); optic hypoplasia or atrophy (underdevelopment of the nerve connecting the eye and the brain); cleft palate; hernias, including an omphalocele (part of the bowel protrudes into a sac through a hole in the abdomen near the base of the umbilical cord); and defects of the gastrointestinal system (intestinal atresia – a section of the intestines has not formed completely, stopping food from passing through; Hirschsprung's disease – areas of nerve cells are missing that normally control the rhythmic contractions that lead to matter being pushed through the intestines) or the hands and feet (extra fingers or toes, joined fingers or toes, clubfoot).

Individual *Unique* families noted these concerns: unusually severe upper respiratory tract infections to age 7; severe stridor (noisy breathing caused by obstruction in the airways or voice box); in a boy, small genitalia; partial duplex kidney – a duplication of part of the kidney's drainage system; constipation. Three children have experienced confirmed or possible seizures: a 2-year-old experienced neonatal seizures that have not recurred; two older children were diagnosed with seizures at the age of nine, one after 'absences' were confirmed by an EEG tracing.

Behaviour

The *Unique* series shows no consistent pattern of behaviour.

“ A cheerful child, very affectionate with adults and likes to be close to adults - age 6

“ She is generally well behaved, happy natured and very affectionate. She is becoming aware of what is appropriate – like not kissing a visiting male teacher! - age 9

“ He lives in his own little world and comes into ours when he wants to - age 9

Food and eating

Feeding problems may arise but the *Unique* experience shows that most babies learn to suck strongly enough to meet their own needs for nutrition and to eat solid foods, albeit later than you might expect. Newborn babies were typically too weak to suck strongly at the breast and only one of the ten *Unique* families succeeded in breastfeeding. Three babies were tube fed, one for 10 months.

“ The deletion appears to affect her tolerance to medication. She has difficulty awakening after anaesthesia