Understanding chromosome disorders

Unique

13q deletions various

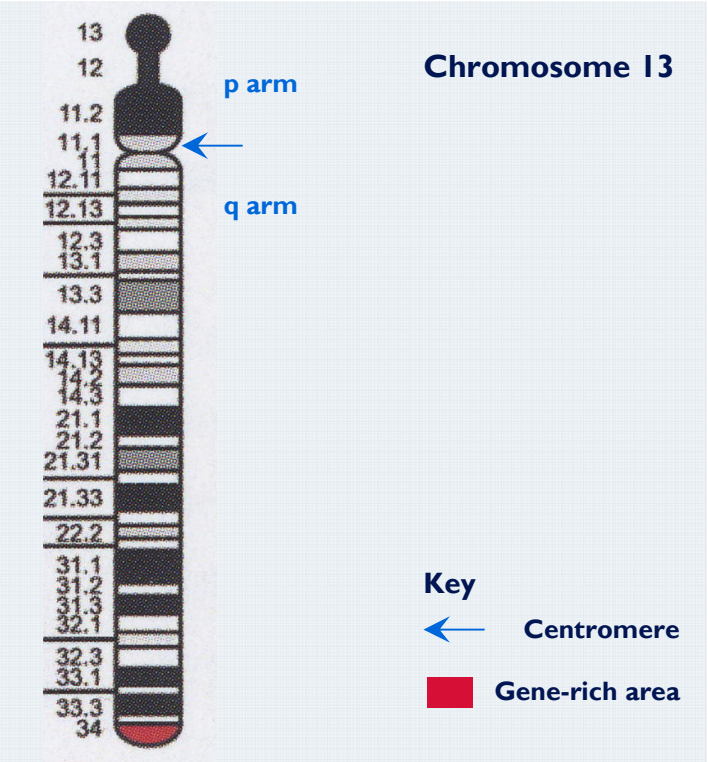
Sources & References

The text contains references to articles 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.

References to information from the Unique database and a questionnaire completed by Unique families are marked U.

A 13q deletion is a rare genetic condition. It means that material has been lost from one of the body's 46 chromosomes. Generally speaking, losing chromosome material increases the risk for problems such as birth defects and growth and developmental delay. With 13q deletions the picture is very variable, depending mostly on how much material has been lost and from which part of the chromosome. The complete DNA sequence and analysis of chromosome 13, published in 2004, revealed a low overall density of genes, especially in two regions corresponding to bands 13q21 and 13q31.

Chromosomes are the microscopically small structures in the nucleus of the body's cells that carry genetic information. They come in different sizes and apart from the sex chromosomes (two Xs for a girl and an X and a Y for a boy), they are numbered 1 to 22 from largest to smallest approximately according to size. Each chromosome has a short (p) and a long (q) arm. In a 13q deletion, material has been lost from the long arm of one of the two chromosome 13s.



Notes on deletions between 13q12 and 13q14.1

Five babies or young children have been described with a small loss of material between the centromere (the point where the short and long arms of the chromosome meet) and band 13q14.2, where the *RB1* gene that protects against the eye cancer retinoblastoma is situated. In these people the *RB1* gene is present and intact, so they are not expected to have an increased risk of developing the eye cancer retinoblastoma or tumours in other parts of the body (osteosarcoma). All the same, if the breakpoint is close to the *RB1* gene, they may be advised to have regular examinations for any early signs of tumour growth.

From the limited information available, it seems that people with this chromosome deletion are not at an increased risk of anomalies affecting the major organs, including the heart, lungs and kidneys. However, one baby with a mosaic deletion between 13q12.1 and q12.3 had hydrocephalus, excessive fluid within the brain; a baby with a 13q12.1-q14.1 deletion had microcephaly, an unusually small head and brain.

Where pregnancy has been described, it was normal and babies' birthweights at term were within the normal range, from 6lb 15oz (3150g) to 8lb 1oz (3656g). Postnatally, two babies were considered to have a facial palsy and one girl with a deletion of 13q12.2 had Moebius syndrome, a lifelong facial paralysis that stops babies from sucking or feeding properly and people from smiling or frowning and is caused by two important nerves, the sixth and seventh cranial nerves, being not fully developed.

Growth was affected in a girl with a 13q12.1-14.1 deletion, who was short. A girl with a 13q12.1-12.3 deletion had normal stature. Feeding problems were described in two babies, with a poor suck at the breast aggravated in one baby by a small jaw, tongue and high palate. In one baby feeding difficulties were resolved with the insertion of a gastrostomy tube for direct feeding into the stomach.

Information on development is limited but two *Unique* children showed a degree of developmental delay. In terms of mobility, rolling over was achieved at 5-6 months, sitting at 7-10 months and one child was walking by 20 months. One child was diagnosed with hypotonia, muscular floppiness. In terms of communication, one child with a deletion between 13q12.3 and q14.1 said his first words at 18 months and by the age of four had a vocabulary of a few hundred words. A one-year-old baby with a deletion between 13q12 and q14.11 was described as having 'wonderful social skills'.

(Palmer 1987; Slee 1991; Drummond-Borg 2002; U)

How common are 13q deletions?

More than 140 people have been described in the medical literature and in 2006, when this information was compiled, *Unique* had more than 110 members with a 13q deletion. *Unique* can put families who wish to make contact in touch with each other.

This leaflet describes the experience of people who have lost part of 13q near the point where the long and short arms of the chromosome meet (the centromere) or who have lost a part of the chromosome not described in *Unique*'s other leaflets (*see back page*).

A note on 13q deletions q14.3 to q21

People with this deletion are often relatively mildly affected with only mild to moderate learning problems, minor birth defects and growth delay. There is a recent report of a child with this deletion who is essentially normal: as a baby he showed failure to thrive, low muscle tone and some feeding difficulties. His 'baby milestones' were somewhat delayed but he achieved rolling over at 4 months, sitting alone at 8 months and walking at 22 months. Apart from revealing a small left kidney, other investigations were normal. His mental development and language acquisition were also normal and by the age of 4 his IQ was measured at 120. The reason for this child's normal development is that his chromosome deletion turned out on analysis using a new 'ultra high resolution' microarray method called ROMA (representational oligonucleotide microarray analysis) not to be continuous but to consist of two separate deletions within a 'gene desert' on 13q. He is only known to have lost six identified genes, and none of them have any known clinical importance.

" Isaac is very witty and creative. He can ride a bike, run and play soccer and his motor skills are normal but he is a little less co-ordinated than other children his age. His fine motor skills are normal and he can spell and write his name. He can add small numbers and reason. For example, if he can't pronounce a word well in speech, he will say "I didn't get enough sleep last night" – *age 4*

(Nielsen 1977; Brown 1993; Dunham 2004; Jobanputra 2005; U)

Notes on 13q deletions q21to q22

There has not been any formal survey of deletions in bands 13q21q22, but there are nine reports in the medical literature and *Unique* has eight members with a deletion of part or all of these bands, making seventeen descriptions in all.

There is quite a lot of variability and some children seem to be only mildly affected and are strong and healthy. This is true even among children described in the medical literature where there is a natural skew towards children with more severe symptoms. The variability, together with the knowledge from the publication of the full sequence of chromosome 13 showing that 13q21 is a region with very few genes, has led to the suggestion that the deletion from 13q22 causes the more severe effects.

Two adults are known to have a 13q21 deletion with no effect other than on the miscarriage rate when trying to have children. In one adult with a 13q21.2q22 deletion in mosaic form (normal cells co-exist in the body with cells with the 13q deletion) the only anomaly was duplex kidneys, where the drainage system from the kidneys occurs in duplicate.

Among the remaining children, birth weights were typically low, with apart from one case weights in the normal range occurring only where the chromosome make-up was mosaic (cells with normal chromosomes co-existed with cells with the 13q deletion). Babies then typically grew and put on weight slowly so that eventual stature was short, most often in the lowest three per cent of the population for height.

Among the medical conditions that have been described, recurrent respiratory infections appear most commonly. Many young babies have difficulties with sucking and swallowing and are vulnerable to aspiration pneumonia. In some babies respiratory conditions are aggravated by the voicebox and/or the windpipe being abnormally soft and liable to collapse (laryngomalacia, tracheomalacia). One *Unique* child had a laryngeal web, a bridge of tissue joining the vocal cords in the voice box. Two *Unique* babies needed a temporary tracheostomy (a tube inserted into the windpipe) to allow air and oxygen to reach the lungs. In one child the trachea (wind pipe) was very small but she was breathing normally without the tracheostomy tube by age four, although she has asthma. Another child who needed a tracheostomy has had a collapsed lung.

Duodenal atresia (the first part of the small intestine has not developed properly so stomach contents cannot pass through) has been found in some babies with this 13q deletion, and Hirschsprung's disease has also been found in babies with duodenal atresia. In Hirschsprung's disease, the nerve cells that normally control the movement of matter through the bowel are missing from certain sections. Out of seventeen individuals with a 13q21q22 deletion observed, three had duodenal atresia.

Vision defects may occur in children with 13q deletions. In this group of individuals, incorrect alignment of the eyes (strabismus, squint) was seen most commonly. One child with a 13q21.2q22 deletion had underdeveloped optic nerves; when this occurs, visual function ranges from normal to an inability to perceive light. Two children had a hearing loss significant enough to need a hearing aid.

Conditions that affected individual children include seizures and mild talipes (club foot). Teeth were also often misaligned, and both extra teeth and missing teeth have been observed.

In terms of behaviour, hyperactivity is the most common complaint.
The *Unique* series shows that as babies, children can have considerable difficulties with feeding, may have a very weak sucking action or no suck and significant gastro oesophageal reflux and may need a nasogastric (NG) or gastrostomy tube (a tube to allow feeding direct into the stomach) in babyhood. One girl with a deletion between 13q21.1 and 13q22 who needed an NG tube was feeding normally by the age of seven.

In terms of development and learning, a young man and his mother described in the medical literature with a small deletion in band 13q21 had normal development and two children with a 13q21q22 deletion showed only a mild delay in learning. *Unique*'s experience reflects this, with families typically reporting a delay of one to two years in learning and reading and writing skills emerging in the early school years between the ages of 6 and 8. In older medical descriptions, when it was conventional to report IQ, ranges quoted were from 61 to 74.

It has been suggested repeatedly that speech is specifically affected in children with a 13q21q22 deletion and that expressive language lags behind understanding or cognitive ability. *Unique*'s experience is of considerable individual variation with first words emerging between 12 and 41 months. In one child with a 13q21q22 deletion, the use of signing and a talking computer has supported the development of phrased speech, an extensive vocabulary and social skills.

In terms of mobility, *Unique* records show that children have a moderate delay in

reaching their developmental 'milestones', rolling over between 8 and 18 months, sitting between 9 and 20 months, crawling between seven and thirty months and walking between 16 and 36 months. Most children are hypotonic (their muscle tone is low, making them feel floppy) and two children also had ataxia, leading to an unsteady gait.
(Noel 1976; Toomey 1978; Couturier 1985; Onufer 1987; Tranebjaerg 1988; Dean 1991; Kotzot 1991; Khong 1994; Jobanputra 2005; U)

Notes on 13q deletions between 13q31 and 13q34

There has been no formal survey of people with a relatively small deletion of chromosome material from near the end of the long arm of one chromosome 13. However, there are seven reports in the medical literature and at the time of writing, *Unique* had seven affected members, the oldest a child of 10 years. In all, five people had a deletion between bands 13q32 and q34, two had breakpoints at 13q33 and q34; the others had individually different breakpoints.

Within this group of fourteen people there is quite a degree of variation, particularly in terms of organ involvement. Babies were born with healthy hearts, although in one baby with a 13q32-34 deletion the foramen ovale between the upper chambers of the heart was still open at birth, but closed naturally. Lungs were also healthy, and the high rates of respiratory infections typical of children with many other chromosome disorders were not seen. The kidneys and urinary system were also healthy, although one baby with a 13q33-34 deletion had reflux (the urine flushes back from the bladder towards the kidneys) and repeated urinary infections.

Brain anomalies were seen more commonly, affecting seven babies or children (one in two), regardless of specific breakpoint in the chromosome. In two babies the corpus callosum that links the two hemispheres of the brain was missing; two babies had semilobar holoprosencephaly, a developmental defect that leaves the two hemispheres incompletely separated. Two babies had hydrocephalus, a build up of cerebrospinal fluid within the brain, requiring drainage through a shunt; one baby had a shrinkage of the frontal lobes of the brain and another had a defect in the blood supply to the brain. One baby had an encephalocele, where brain tissue protrudes through a gap in the skull. A very small head and brain (microcephaly) is believed to be typical of babies born with deletions near the end of 13q and was reported in four children; however, two babies (without hydrocephalus) had a head size at the upper limit of normal.

Anomalies of the genitals are sometimes seen in boys with a deletion of the end of 13q and were described in three out of five boys in the medical literature. The range was broad, from undescended testicles at birth to ambiguous genitalia. However, none of the four boys in the *Unique* series was reported to have a genital anomaly and it may be that reports in the medical literature are subject to bias.

A narrowed or covered anus is sometimes reported in babies with a loss of the end of 13q and was seen in one baby with a 13q32-34 deletion. Two other babies had the opening of the anus positioned unusually far forward. Again, none of the *Unique* babies was affected in this way.

Small or missing thumbs are often described in babies with a 13q deletion, but occurred only in babies described in the medical literature, one with a 13q31-32 deletion, the other with a 13q31.2-34 deletion. No *Unique* children were reported to be affected.

Development

The most consistent effect of the chromosome loss was on development. All children were described as experiencing some level of delayed development, although in one *Unique* child with a 13q33.2-34 deletion who was walking by the age of 16 months, the delay in mobility was marginal. Other children were usually sitting by their first birthday and walking by the pre-school years, although this was not possible for all. There was no clear link between the amount of chromosome material lost and development of mobility, with two children with very similar breakpoints at either end of the spectrum of mobility. Five children were described with altered muscle tone, four of them with floppiness (hypotonia).

Children also experienced delay in learning and while the extent is hard to describe accurately, in most it seemed to be quite marked. Speech was also slow to develop, with single words typically emerging in the early learning years. At least one child with a severe speech delay was proficient at signing his needs.

Hearing is not typically affected in children with a 13q deletion, but one child with a 13q31-33 loss had a severe hearing impairment with malformation of the cochlea in both ears and another child had the conductive hearing loss that frequently follows repeated ear infections in children, with or without chromosome disorders.

Most children had normal vision, but three children had a marked visual disturbance. In one, the retina in both eyes was deformed, leaving him blind; in another child with structurally normal eyes the brain did not apparently register visual information. A third child was born with small eyes and a developmental defect in the iris (the coloured part of the eye). Each of these children had a deletion that started in band 13q31.

Eating and digestion

Although some babies were born small for dates, this was not universal. Feeding is a concern for most babies with a chromosome disorder and most *Unique* families reported difficulties: poor suck as a baby, a small appetite; and reflux, so that food is propelled back from the stomach up the food pipe. The small food intake did not lead to short stature and there was marked variation in children's heights.

One boy with a 13q32.3-33.2 deletion experienced severe constipation from birth, which worsened at weaning. Investigation showed that he had Hirschsprung's disease, in which parts of the colon lack the nerves that propel waste matter through.

Behaviour

Information on behaviour is too scant for general conclusions to be drawn, but one boy was diagnosed with autism and three children were prone to temper outbursts. (Carakushansky 1979; Emanuel 1979; Juberg 1984; Bottani 1991; Brown 1993; Bartsch 1996; U)

Support and Information

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Chromosome 13 Facebook groups
www.facebook.com/chromosome13
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also
www.chromosome13deletion.com

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.

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