Understanding chromosome disorders

Unique

Deletions including 5q22

rarechromo.org

Sources

This booklet draws on information both from Unique's members, of whom 17 have a deletion that includes part or all of 5q22, and on the published medical literature. As the results of molecular tests such as FISH were not universally available for the Unique group and out of 36 cases published in the medical literature, only seven had a molecular study, this leaflet can be read as a general guide only.

References

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 statistical information held by Unique and to information from ten families who completed a detailed questionnaire in 2004 are marked U.

Deletions of chromosome 5 including 5q22

A chromosome deletion that includes band 5q22 is a rare genetic condition, caused by having lost material 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 a deletion including 5q22, the picture varies, depending partly on how much chromosome material and which genes have been lost.

Chromosomes are the microscopically small structures in the nucleus of the body's cells that carry genetic information. They come in different sizes, each with a short (p) and a long (q) arm. Apart from the sex chromosomes (two Xs for a girl and an X and a Y for a boy), they are numbered from largest (1) to smallest (22), approximately according to size.

People with 5q22 deletions have lost a small or larger part of the long arm of one of their two chromosome 5s. The breakpoints are established by examining chromosomes that have been stained so that each has a distinctive pattern of light and dark bands when viewed at about 1000 times life size under a light microscope. However, the part of the long arm of chromosome 5 where most breaks occur that span the 5q21-22 bands can be hard to interpret under a microscope and a special molecular study such as a FISH test is needed to find out more about where the chromosome has broken.

APC gene

Your child's clinical geneticist will tell you whether a particular gene called *APC* (adenomatous polyposis coli) normally found at 5q22.1 has been lost. This is because people who have lost one copy of this gene have a raised risk of developing a type of colon cancer called FAP (familial adenomatous polyposis) as young adults. If so, your child will normally be screened from the age of 10-12 years, or younger if they have any bowel problems including bleeding.

You can find out more about FAP by reading the FAP leaflet produced by University Hospital Southampton (www.uhs.nhs.uk/Media/Controlleddocuments/Patientinformation/Genetics/Familial-Adenomatous-Polyposis-FAP-Childrens-Leaflet.pdf)

Frequent features

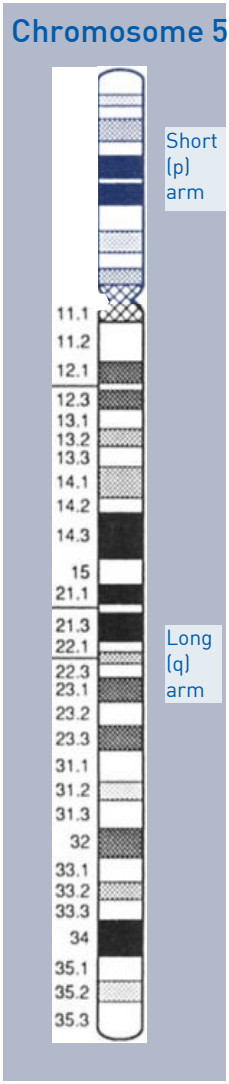
These features have been found in a group of children with a chromosome deletion including 5q22. Most children do appear to experience some degree of developmental delay and learning difficulty but the extent is variable and individual children may or may not be affected by the other features.

- Some degree of developmental delay and learning difficulty. The level varies between individuals
- Hypotonia, seen as floppiness, most obvious in babyhood but improving with maturity
- Difficulties with feeding and putting on weight as a baby, sometimes following growth delay in pregnancy so that the baby is born small for dates. Mild overweight may develop later in childhood
- Oddly positioned or angled feet at birth (such as talipes, club foot)
- Dislocated or easily dislocatable hips at birth
- High or cleft palate (roof of the mouth) or division in the uvula (the piece of soft tissue that hangs down from the palate at the back of the mouth)
- Anomalies of the kidneys, such a horseshoe kidney, where bottom points of the two usually separate kidneys are joined, creating a U (horseshoe) shape
- Heart conditions

(Ohdo 1982; Rodewald 1982; Rivera 1990; Kobayashi 1991; Lindgren 1992; Barber 1994; Pilarski 1999; U).

Appearance

Some children are short, especially in early childhood. However, at least one Unique member is tall and thin. As far as facial features are concerned, doctors sometimes notice subtle differences that do not seem remarkable to parents. Features that are believed to be typical of children with this chromosome deletion include ears that are placed low and are sometimes unusually moulded; eyes that are spaced wide apart with a flat bridge to the nose and sometimes with tiny folds of skin across the inner corner of the eye (epicanthic folds); a high and sometimes rounded forehead; a short, thick neck and an unusually small or large and jutting jaw. Other features that have occasionally been noticed include a flat, broad head and abundant, coarse hair. Boys may be born with small genitals. The anus may be placed somewhat far forward.



“She is a learning experience for me every day in patience, love and understanding.

Growth, feeding and gaining weight

Babies may be born underweight or a good size for their gestation. Regardless of birth weight, many babies have great difficulty in gaining weight after birth. Out of 10 Unique families who have given information about feeding and eating, eight experienced specific problems, including six who highlighted their baby's failure to thrive. Some babies find sucking difficult and a number of parents note the absence of a sucking reflex. Babies with a high arched or cleft palate (five families have remarked on this, as well as many in the medical literature) usually find it particularly hard to suck effectively and expert feeding support should be available.

> *I have to chop hard foods up for D. He cannot chew meat so we supplement his diet with alternative protein sources – eggs or cheese - or feed soft meats like sausages that are easily chewed* - D, age 23.

Once on solids, a number of toddlers continued to have difficulties chewing and drinking, and needed thickened drinks and well chopped or mashed food to avoid choking. An unusually large number of families commented on their child's difficulties with chewing and these could be long-lasting. By contrast with these reports, a tendency to overeating and overweight has been mentioned in adults.

The Unique experience suggests that children put on weight faster from middle childhood or later. Some showed catch-up growth, others remained short. One Unique member is tall and thin and this build has been noticed in one child described in a medical journal (Barber 1994; Bennett 1997; Pilarski 1999; U).

Learning

Some level of learning disability is usual but it is Unique's experience that the level is highly variable. Among its membership are children with abilities above their chronological age and others with severe learning difficulties. There is no immediately obvious link between the level of learning disability and which portion of the chromosome is missing. There is little detailed information in the medical literature but an adult with a 5q22q23.2 deletion is described as having highly variable cognitive abilities, scoring 55/100 on comprehension tests and 100 on arithmetic at age 12, with performance IQ scores varying between 60 and 90 (Bennett 1997).

No learning difficulty

One Unique member was reported to be of average or above average ability. However, in her early teens she found the social experience of school difficult.

Mild learning difficulty

Three children had a mild learning difficulty. Typically, they were on a par with their peers in some aspects of learning such as reading but trailed in subjects like mathematics.

❝ *E performs at an average 7 to 8 year level. Her strengths are determination and focus, problem solving and her attention span. Her weaknesses are memory, processing and fine motor (writing) skills. She loves to read and does so every day. Maths is very hard for her because of the memorisation. She understands concepts in science and social studies but again has trouble remembering details* – age 10.

❝ *A loves to learn and her concentration has improved greatly. She has determination when trying to complete a task. She can identify shapes and colours and loves 'reading' story books. She has a natural rhythm and loves musical activities* - age 4.

Moderate learning difficulty

❝ *A reads large print books like a 5 or 6 year old but she doesn't read to enjoy a story as the act of reading is itself a struggle. She has large, untidy writing as she has poor fine motor control but she enjoys copying out text from comics and sports books. She understands topics when they are current at school but doesn't retain maths concepts. She enjoys school and participates in all areas of the curriculum. She has friends at her school who are on her own wave length in maturity and social skills and a few friends in the neighbourhood who are her own age. She attended a mainstream school until she was 11, then moved to a school for students with moderate learning difficulties* - age 12.

❝ *Z knows as much as most 5 year olds but has poor behaviour and lacks communication and social skills* - age 5.

Severe learning difficulty

❝ *D has a mental age of perhaps 5 years. His strengths are his good memory, his ease at picking up rhythms and keeping rhythm with all sorts of music* - age 23.

Speech and language

There is little information in the medical literature on communication and language skills. The combined experience of eleven Unique families who have given information is of a wide range of ability. All children except two over the age of 5 use some words, and many use long and complex sentences. Two of the three members who are known to have no speech have more complex chromosome rearrangements and two were aged under six when the survey was conducted.

First words typically emerged between the ages of three and five, although one child was speaking at 18 months. In the pre-speech years, children used a variety of ways to communicate including gestures and vocal noises. Most learned to sign successfully and used signing alongside speech. All families believed that understanding was at a higher level than expression. In the early

years of speaking, articulation was often unclear, making it hard for people outside the family to understand. Articulation problems could be persistent even when there was no evidence of a hearing impairment and at the age of 12, one child who used long and complex sentences still had difficulty with the speech sounds *v, w, ch, sh, r*. All children benefited from speech therapy and by the later primary (elementary) school years might be using five to six word sentences, although children might have difficulty in word retrieval.

- *N uses some signing and a little speech as well as screaming, pushing and pulling. She started to use words at 18 months and by 9 months used the signs for more, shoes, eat, all done* – N, age 3.
- *A communicates by signing, pulling, pushing and gestures. She understands everything in context and is rarely frustrated by her inability to express herself but when she is, she stamps her feet and uses loud vocal noises* – A, age 4.
- *Z now uses one-word sentences but understands a lot more than he can express. Speech is still unclear* – Z, age 5.
- *E uses simple 3-6 word sentences but has always understood more. She often has difficulty searching for words to express herself and has multiple articulation problems* – E, age10.
- *A uses long, complex sentences. If she can't get the words out fast enough she waves her arms about and slaps her head* – A, age 12.

These two snapshots give an idea of how people communicate without speech.

- *We interpret J's needs through his different vocalisations. He loves music and through waving his arms he lets us know when he wants to play the piano (he loves the cause and effect). We use short clear 2-3 word sentences and can see that he understands more than he can express* – J, age 5.

Sitting, standing, moving, walking

Typically, almost all babies are late to reach their motor development 'milestones' but with continuing physiotherapy most children do achieve mobility. Hypotonia – a low muscle tone showing as 'floppiness' – is very common but gradually improves with maturity and practice. Specific problems with hip and ankle joints delay walking for some children. Unique children showed a range of effects, from one child who was scarcely affected to another who was only mobile in a wheelchair. On average, babies rolled over between four and fourteen months and sat without support between the latter months of their first year and their second birthday. Many children took their first steps by

the age of two, but those who were late to achieve independent sitting were also much later to walk. With mobility aids like standers and walkers and with support for their ankles and feet, most children became mobile. Children typically had balance problems at first for which they compensated with a wide gait and they tired easily but with practice became more skilled. By the age of 10 some children could ride a two-wheeler and swim, if untidily, and one child was learning to ski.

For a few children unsupported sitting and independent walking have not proved possible and at least two children were not walking at the age of five. However, families tried not to allow this to limit their activities.

> *J will initiate some steps in his walker but needs other people to help him take unsupported steps. But he loves people and we take him everywhere – to concerts, football matches and shopping* – J, age 5.

> *Z sat at 8 months and walked at 16 months. He has no problems at all with gross motor skills* – Z, age 5.

Medical concerns

All babies and children in whom a chromosome disorder is suspected or diagnosed will receive a very thorough clinical examination. In a group of babies or children with a deletion spanning 5q22, these conditions have been noted. This does not mean that your child will necessarily be affected by any of them, but the doctors caring for your child will be especially alert to any concerns you may have.

Hips and feet

There are many reports in the medical literature of children born with dislocated or easily dislocatable hips and talipes (club feet) or other unusual foot positions. Seven Unique babies out of 15 were found to have abnormally developed hip joints and nine had talipes or another type of club foot. Four children were treated with splinting or surgery and two others needed shoe inserts or orthoses (supports) to improve their walking. One child had two extra toes removed from one foot. A child who developed juvenile arthritis at the age of 5 was successfully treated with steroid and anti-inflammatory treatment (Felding 1980; Rodewald 1982; Lindgren 1992; Barber 1994; Courtens 1998; U).

Spine

Two Unique children and some described in medical journals developed a curved spine. One child developed both a sideways and a forwards spinal curve, corrected with a brace and surgery to fuse his spine (Barber 1994; Pilarski 1999; U).

Seizures

Seizures have been observed. Seven out of 17 Unique children have experienced seizures, although two have outgrown them and in the others they have been well controlled with medication (Lindgren 1992; U).

Heart conditions

Any heart conditions appear to be usually relatively minor. Four Unique babies were found to have a heart murmur at birth. In all babies the problem resolved naturally without treatment and none required surgery. One child had multiple tiny holes between the chambers of the heart and another had a bicuspid aortic valve which currently needs no more than annual monitoring. (The aortic valve regulates blood flow from the heart into the aorta, the vessel that takes blood around the body. The valve normally has three flaps or valves, but a bicuspid valve has only two).

Heart conditions described in the medical literature were usually minor with one child with a slight narrowing of the aorta and another requiring surgery to close a persistent ductus arteriosus. The ductus arteriosus is a channel between the blood vessels leading from the heart to the body and to the lungs that is open during fetal life but usually closes soon after birth. When it stays open, the lungs receive more blood than they should and the heart has to work too hard (Felding 1980; Harprecht-Beato 1983; Pilarski 1999; U).

Infections

Children with chromosome disorders may be prone to respiratory infections and four families mentioned this. Recurrent pneumonia and asthma have also been described in the medical literature (Pilarski 1999; U).

Kidneys and urinary tract

Anomalies in the structure of the kidneys or the urinary tract may be found. In the medical literature two children are described as having a stricture in part of the urinary tract, one had a ureter leading from the kidney that did not connect with the bladder, one had repeated urinary infections and two had horseshoe kidneys, where the bottom points of the two usually separate kidneys are joined, creating a U (horseshoe) shape. In itself this is not harmful but horseshoe kidneys may be associated with impaired drainage of the urine to the bladder.

Two Unique girls were prone to urinary infections and reflux of the urine from the bladder to the kidneys. One had a misshapen bladder that is not growing adequately and was catheterised. The other girl had a kidney removed at the age of 6 (Felding 1980; Lindgren 1992; Pilarski 1999; U).

Hearing

Children will usually be carefully screened for any hearing impairment. Some hearing loss was found in five out 17 Unique children, although the level varied from mild to a 60 per cent loss.

Vision

Your child's vision will also be carefully checked. The most common problem found in Unique children was a squint (strabismus), found in seven out of 17 children. This can be usually corrected with exercises, patching or in some cases surgery to realign the muscles controlling the movements of the eyeball. Two children were severely short-sighted and a 12-year-old was registered as partially sighted (Kobayashi 1991; Lindgren 1992; U).

Other features

Hands Five Unique members have unusual hands: two have long, slender fingers, in one case partly bridged with skin; two have clenched fingers or fingers of an unusual shape and two others have unusual hand creases (Ohdo 1982; Lindgren 1992; U).

Teeth A wide variety of dental problems has been seen including overcrowding of the teeth, extra or missing teeth and enamel deficiencies (Kobayashi 1991; U).

Behaviour

The experience of Unique is that children generally seem to have a loving, warm temperament and are especially happy in familiar surroundings. There are suggestions from the Unique survey that they may not adapt easily to change. This may show in the early years as a separation anxiety. In some children, a widening gap between their personal maturity level and that of their peers can lead to increasing isolation.

Although most children appear to conform to this general pattern, it is not universal and one child has a diagnosis of autism.

These snapshots illustrate children at different ages.

- A loving, friendly girl – age 4.
- A wonderful, perfect personality and adores his family. Always in fantastic humour except if sick or in pain. He adores his family as we adore him. He only gets upset in unfamiliar surroundings or if familiar people are not with him – age 5.
- Always on the go, has a hard time sitting still – age 5.
- Extremely shy. Lovely and cooperative at school, but sometimes vents her frustration when she gets home. She has difficulty moving between tasks and needs a lot of advance notice. If she is venting frustration from her day, it's best to listen and empathise and to show her tons of love to balance out when other children have been mean to her at school – age 10.

- A friendly, happy, funny, trusting and very likable girl. Socially immature and by now her 'normal' peer group are becoming more estranged. But she is well liked and friendly, if a bit too trusting. She gets nervous in large crowds and unfamiliar places so she doesn't go out of the house or the immediate vicinity alone. She can get overexcited and emotional if for example her football team loses. Some health professionals have suggested methylphenidate (Ritalin) but we are opposed and instead structure around the problems. She likes having a structured routine and it helps to tell her in advance what is going to happen and go over it in the coming days and weeks as she asks for the same information time after time – age 12.
- Bright, extremely happy and loves to interact with people. He is headstrong at times and gets frustrated. He loves to hug and be hugged – age 23.

Will a child ever be able to live independently?

This will be easier to predict as a child grows up. Unique's only adult member lives at home and requires full support, but two adults described in the medical literature were living semi independently. It is likely that most people with this type of chromosome deletion will benefit from supervision and communal living all their lives.

What do they enjoy?

When you have a small baby with a rare chromosome disorder, it can be hard to imagine how they will be when they are older. These snapshots suggest how older people and children with this chromosome disorder enjoy themselves.

- He absolutely lives for classical music! He loves watching videos, especially of car racing. He also enjoys flicking through magazines and identifying company symbols – age 23.
- She likes watching TV, her playstation, watching sport, collecting football stickers, listening to music and sport on the radio, putting things in order and copying text from books – age 12.
- She enjoys playing with dolls, completing worksheets (yes!), computer games and TV – age 10.
- He likes playing with people, singing, rough and tumble, nursery rhymes, face to face contact, and the piano – age 5.

Why did this happen?

Rearrangements occur in chromosomes as part of evolution. They affect children from all parts of the world and from all types of background. They also happen naturally in plants and animals. So there is no reason to suggest that your lifestyle or anything that you did caused the loss of chromosome material.

A chromosome 5q deletion can happen out of the blue, so the child with the chromosome disorder is the only person in the family with rearranged chromosomes, when it is called *de novo.* It can also occur as a result of rearrangements in one parent's own chromosomes. The only way to know if the disorder is inherited or not is for the parents' chromosomes to be checked and the results explained to you.

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

Can it happen again?

Where both parents have normal chromosomes, it is very unlikely that another child will be born with a 5q deletion. In nearly all families the chance of having another similarly affected child is very low.

Where one parent has an atypical chromosome rearrangement, the risk of having another affected pregnancy is much higher. You should be able to talk this over with your genetics service.

There is a very distant possibility that in some people the deletion occurred during the formation of the cells that later give rise to the egg or sperm. This can result in a mixture of normal egg or sperm cells and cells with disordered chromosomes (gonadal mosaicism or germline mosaicism). When this occurs, there is a tiny but real chance that parents with apparently normal chromosomes could have another affected pregnancy.

Inform Network Support

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Version 1.0 (PM)
Version 1.1 (SW)