Understanding chromosome disorders

Unique

22q11.2 distal deletion syndrome

rarechromo.org

Sources and references

The information in this guide 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 (http://www.ncbi.nlm.nih.gov/pubmed/). If you wish, you can obtain most articles from Unique. In addition, this guide draws on information from a survey of members of Unique conducted in 2012/13, referenced Unique. When this guide was published in February 2013 Unique had 10 members with distal 22q11.2 deletion syndrome ranging in age from a toddler to two adults.

22q11.2 distal deletion syndrome

A 22q11.2 distal deletion is a rare genetic condition caused by a tiny missing part of one of the body's 46 chromosomes – chromosome 22. For healthy development, chromosomes should contain just the right amount of material – not too much and not too little. Even a tiny piece of missing material can disturb development, although it doesn't always do so.

Background on Chromosomes

Chromosomes are structures found in the nucleus of the body's cells. Every chromosome contains thousands of genes which may be thought of as individual instruction booklets (or recipes) that contain all the genetic information telling the body how to develop, grow and function. Chromosomes (and genes) usually come in pairs with one chromosome in each pair being inherited from each parent. Humans have 23 pairs of chromosomes giving a total of 46 individual chromosomes.

Of these 46 chromosomes, two are the sex chromosomes that determine gender. Females have two X chromosomes and males have one X chromosome and one Y chromosome. The remaining 44 chromosomes are grouped in 22 pairs, numbered 1 to 22 approximately from the largest to the smallest. Each chromosome has a short or petit (p) arm (shown at the top in the diagram on page 4) and a long (q) arm (the bottom part of the chromosome).

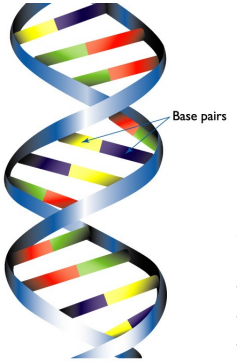
Chromosome Deletions

A sperm cell from the father and an egg cell from the mother each carries just one copy of each chromosome. When they join together they form a single cell that now carries two copies of each chromosome. This cell must make many copies of itself (and all the chromosomes and genetic material) in order to make all of the many cells that form during human growth and development. Sometimes during the formation of the egg or sperm cells or during this complicated copying and replication process, parts of the chromosomes can break off or become arranged differently from usual. People with a distal 22q11.2 deletion have one intact chromosome 22, but a piece from the long arm of the other copy is missing. Although the exact numbers and types of genes that are affected by the deletion are not always known, since some genes are missing there can be effects on a person's learning and physical development. Therefore it is believed that most of the clinical difficulties are probably caused by having only one copy (instead of the usual two) of a number of genes. We are still learning about the specific jobs or functions of the genes in this region. It is important to keep in mind that a child's other genes, environment and unique personality also help to determine future development, needs and achievements.

Looking at 22q11.2

You can't see chromosomes with the naked eye, but if you stain them and magnify them under a microscope, you can see that each one has a distinctive pattern of light and dark bands. You can see these bands in the diagram of the long arm of chromosome 22 on the right. The bands are numbered outwards starting from the point at the top of the diagram where the short and long arms meet (the centromere). A low number such as q11 is close to the centromere. You can see that q11.2 is quite close to the centromere.

Even if you magnify the chromosomes as much as possible, to about 850 times life size, a chromosome 22 with the microdeletion at q11.2 looks normal. People who have missing material on a chromosome are said to have a deletion but when the amount is so small that it can't be seen even under a high-powered microscope (known as karyotyping), it is called a microdeletion. The 22q11.2 distal deletion can only be found using molecular or DNA technology, in particular a technique using microarrays (array-CGH), that shows gains and losses of tiny amounts of DNA throughout the genome and can demonstrate whether particular genes are present or not. It is believed that the effects of the microdeletion are caused by the presence of only one copy of these genes instead of two, as expected.



1 base pair = bp
1,000 base pairs = 1kb
1,000,000 base pairs = 1Mb

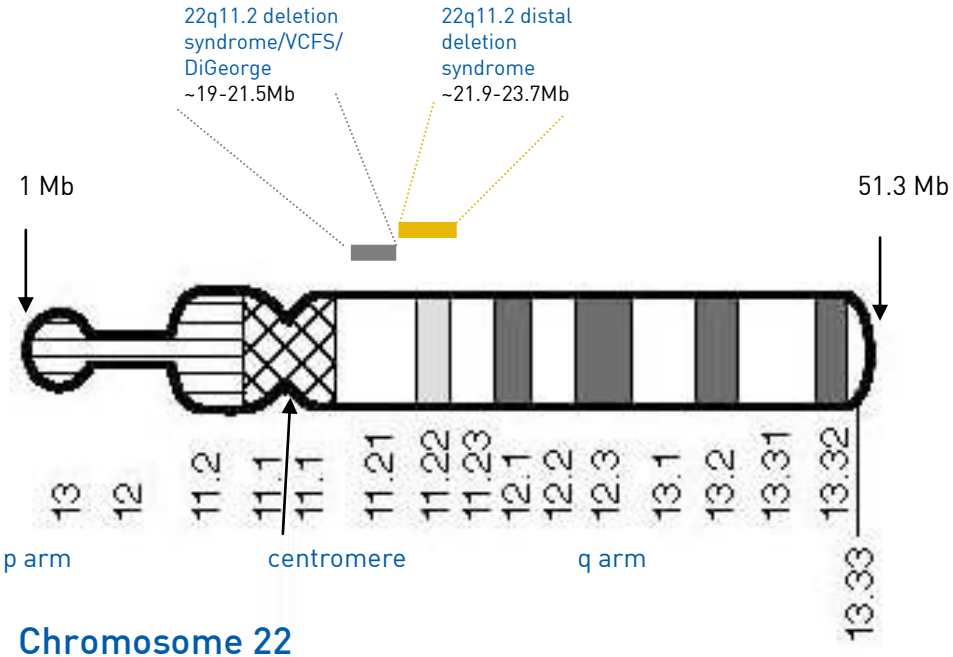
22q11.2 deletion syndrome/VCFS/DiGeorge

Microdeletions of chromosome 22q11.2 are one of the most common microdeletions and affect around 1 in 4,000 babies (Verhoeven 2010). The most common form of a 22q11.2 deletion is a 2.5-3 Mb deletion (see diagram on page 4) which causes 22q11.2 deletion syndrome, DiGeorge syndrome or Velocardiofacial syndrome (VCFS). Unique produces a separate information guide to these deletions [called Velocardiofacial syndrome (22q11.2 deletion syndrome)].

This guide however, focuses on those people who have a rarer deletion which does not overlap with the common 22q11.2 deletion (see diagram). These deletions are located further away from (distal) the centromere and so are called 22q11.2 distal deletions.

22q11.2 distal deletion syndrome

The first published description of a person with a distal 22q11.2 deletion was in 1999. There have since been more than 50 cases reported in the medical literature worldwide. When a particular set of developmental features occurs in a recognisable and consistent pattern in enough people, as a result of a single cause, the condition is called a syndrome. The features of a distal 22q11.2 deletion do occur in this way, so the disorder is often known as 22q11.2 distal deletion syndrome**.** The deletion seems to occur equally often in males and females. There are reports of people who are unaffected by carrying the deletion and only discovered it after their child was diagnosed. It seems that the 22q11.2 distal deletion can be 'silent' and that no-one knows how many people out there have a silent form of this syndrome.



Chromosome 22

Your geneticist or genetic counsellor will be able to tell you about the points where the chromosome has broken in your child. With a 22q11.2 distal deletion, the results are likely to read something like the following example:

arr[hg19] 22q11.2 (21,808,980-23,756,843)x1

arr	The analysis was by array (arr) comparative genomic hybridisation
hg19	Human Genome build 19. This is the reference DNA sequence that the base pair numbers refer to. As more information about the human genome is found, new "builds" of the genome are made and the base pair numbers may be adjusted
22q11.2	The chromosome involved is 22, region q11.2
21,808,980-23,756,843	The base pairs between 21,808,980 (around 21.8Mb)and 23,756,843 (around 23.8Mb) have been shown to be deleted. Take the first long number from the second and you get 1,947,863 (1.9Mb). This is the number of base pairs that are deleted.
x1	This means there is one copy of these base pairs, not two – one on each chromosome 22 – as you would normally expect

How much do we know?

Comparing different children and adults with 22q11.2 distal deletions shows that some effects seem to be very broadly similar. This information guide tells you what is known about those effects. Comparing your child's array results with others, both in 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 an apparently similar array result. It is very important to see your child as an individual and not to make direct comparisons with others with the same genetic test results. After all, each of us is unique.

Most common features

Every person with a distal 22q11.2 deletion is unique and so each person will have different medical and developmental concerns. Additionally, no one person will have all of the features listed in this information guide. However, a number of common features have emerged:

- Some children are likely to need support with learning. The amount of support needed by each child will vary
- Speech is often delayed and some children have articulation problems
- Growth delay both in the womb and after birth
- Heart problems
- Behavioural difficulties such as difficulties with concentration and anxiety
- Subtly unusual facial features. Families may notice similarities between their own child and others with the deletion

What is the outlook?

We can't be certain yet but there appears to be no reason why people who are healthy should not enjoy a normal lifespan and there are a number of adults both at Unique and in the published medical literature (see Adults with 22q11.2 distal deletion syndrome page 12) (Garcia-Minaur 2002; Beddow 2011; Michaelovsky 2012; Unique).

Pregnancy and birth

Most pregnancies were uncomplicated but some babies are born prematurely

The majority of mothers carrying babies with a 22q11.2 distal deletion syndrome experienced no pregnancy problems, had a normal delivery and only discovered their baby was affected after the birth. However, some babies with 22q11.2 distal deletion syndrome were born prematurely (before 37 weeks). At least nine babies out of 42 were premature and a further three were born in the 37th week (Ben-Shachar 2008; Rodningen 2008; Ogilvie 2009; Garavelli 2011; Verhoeven 2011; Fagerberg 2013; Unique).

Some babies had intrauterine growth retardation (IUGR). This is a term used to describe babies whose growth in the womb has slowed resulting in babies that are smaller than expected for the number of weeks of pregnancy. Two babies showed less fetal movement than expected while in the womb. One baby had bowel problems detected at the 13-week ultrasound scan. Five mothers in the published medical literature had an amniocentesis followed by conventional karyotyping; one for advanced maternal age and three after an anomaly was seen on a prenatal ultrasound scan. In three cases the results were interpreted as normal (due to the small size of the microdeletion) despite the babies later being diagnosed with 22q11.2 distal deletion syndrome. One baby had an arrayCGH after amniocentesis and the 22q11.2 distal deletion was detected. In another case the deletion was diagnosed and the mother chose to terminate the pregnancy at 22 weeks (Rodningen 2008; Ogilvie 2009; Garavelli 2011; Verhagen 2012).

Feeding and growth

Feeding and growth can be affected in children with 22q11.2 distal deletion syndrome

Some babies are born small and light for dates, even taking into account their gestational age (Ben-Shachar 2008; Unique).

One baby had feeding problems initially but was breastfeeding by 2 months of age. Two Unique babies and a further baby in the medical literature had feeding problems. One needed tiny and frequent feeds as a baby and continued to have food puréed until she was 5 years old; at 24 years old she has no interest in food and is still difficult to feed. Another would not breastfeed as a baby and at 5 years has a very limited variety of food (Rodningen 2008; Verhoeven 2010; Unique).

Many people with 22q11 distal deletion have short stature or height in the lower normal range. One child takes a growth hormone supplement (Ben-Shachar 2008; Rodningen 2008; Ogilvie 2009; Fernandez 2011; Verhoeven 2011; Michaelovsky 2012; Unique).

One child who was obese at the age of 11 years had growth delay until the age of 6. One Unique member is tall but considerably shorter than her three siblings and at the age of 24 is overweight. Three further children in the medical literature are obese, two of whom had a strong craving for food (Ben-Shachar 2008; Fagerberg 2013; Unique).

Learning

Some children with 22q11.2 distal deletion syndrome have a learning disability; most often mild.

Some children with 22q11.2 distal deletion syndrome have no learning (intellectual) disabilities. For those who have been observed to have a learning disability, it is generally mild or in one child moderate and two people have a severe level of learning disability. One child in the medical literature had problems with attention and one was diagnosed with dysgraphia (a difficulty in automatically remembering and mastering the sequence of muscle motor movements needed in writing letters or numbers) and dyscalculia (a condition that affects the ability to acquire arithmetical skills) at aged 5. Another girl attended special and structured education because of difficulties with planning, concentration and calculation, as well as visuo-spatial perception (ability to process and interpret visual information about where objects are in space). A number of children benefited from attending a special educational school (Ben-Shachar 2008; Beddow 2011; Garavelli 2011; Verhoeven 2011; Michaelovsky 2012; Verhagen 2012; Fagerberg 2013; Unique).

"He has just been given an iPad and it is really assisting with his learning. He is very difficult to engage to try and learn anything – 5 years

"She has a good memory although sometimes she remembers things differently from the rest of us! She attended a special school from the age of 6¾ years. The teachers' methods worked well – they were kind but firm and she had fixed boundaries and routine – 24 years

Speech and communication delay

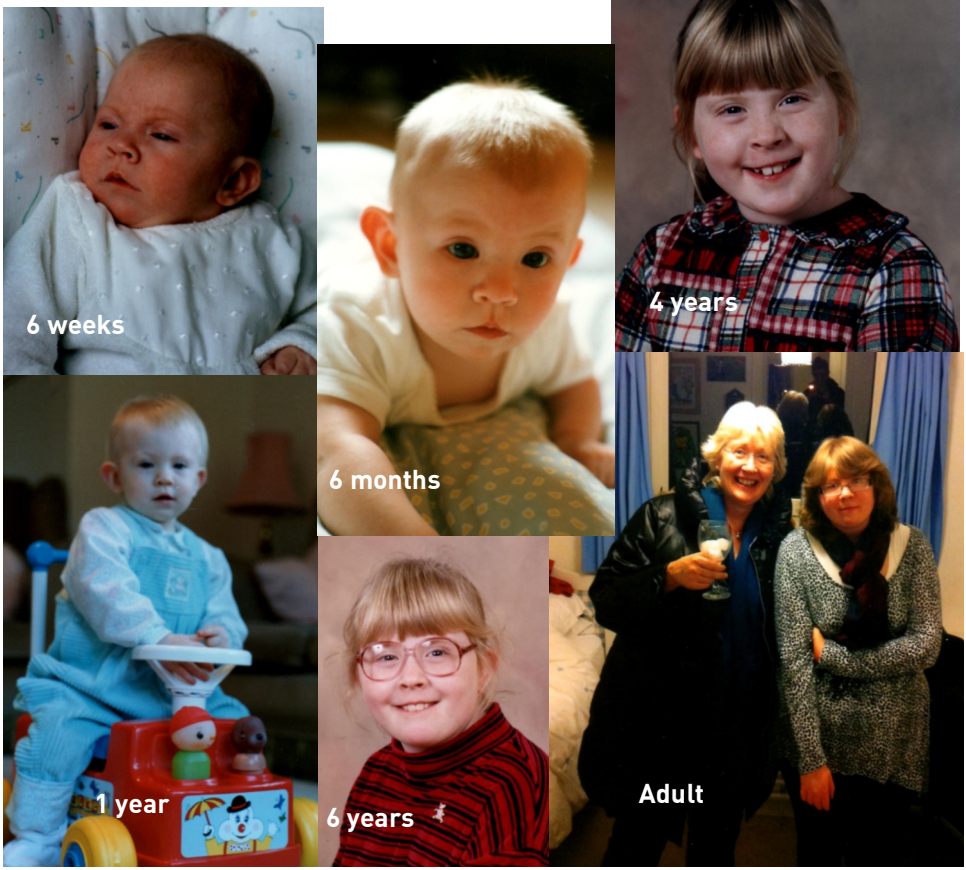
Speech and language delay is common in children with a 22q11.2 distal deletion

Speech and language development was delayed in many, but not all, children but it is not known whether the delay was in line with the child's cognitive abilities. One child had

articulation problems until the age of 5 and speech that was difficult to understand. At 5 years and 10 months her language was assessed to be at the level of a 4-year-old. A 7-year-old developed speech late and although articulation has improved he still has difficulties with some sounds. He has problems understanding instructions and messages as well as understanding long sentences. He also has a high-pitched voice. A 17-year-old and a 20-year-old both have nasal speech. A 24-year-old talks normally but did have delays when younger. Expressive language (speaking) appears to be more delayed than receptive language (understanding): children are able to understand more than they are able to express. Speech therapy has proved extremely beneficial to many children. One child had no speech at aged 6 and another no speech at 18 years (Rodningen 2008; Verhoeven 2010; Garavelli 2011; Michaelovsky 2012; Verhagen 2012; Unique).

"He can talk a little and is getting clearer, but when he starts a conversation it is babble. He can speak in 2-3 word phrases. He also uses pictures and Makaton to communicate – 5 years

"She talks normally now but was a couple of years late with speech development – 24 years



Behaviour

Some children with 22q11.2 distal deletion syndrome have behavioural difficulties

Several people with 22q11.2 distal deletion syndrome have been reported to have behavioural problems. Four children have been reported with attention deficit hyperactivity disorder (ADHD), hyperactivity or attention problems. One child, with normal development, had severe behavioural issues including uncontrolled aggression. One person was reported to have obsessive compulsive disorder [OCD: an anxiety disorder characterised by intrusive thoughts that produce anxiety, by repetitive behaviours aimed at reducing anxiety or by a combination of such thoughts (obsessions) and behaviours (compulsions)]. (Mikhail 2007; Ben-Shachar 2008; Rodningen 2008; Michaelovsky 2012; Verhagen 2012; Fagerberg 2013).

A 6-year-old girl had increased anxiety and two adolescent girls had severe anxiety. One had normal intelligence but had anxiety, mood instability and irritability, typically related to stressful events. The other was diagnosed with a psychotic disorder (Verhoeven 2011; Michaelovsky 2012).

One child is described as being a quiet, positive and co-operative person. However, at home he challenges limits set by his parents and in stressful situations he is somewhat rigid and prefers familiar rules and routines (Rodningen 2008).
Two children have had sleep problems; one has difficulty falling asleep (Rodningen 2008; Verhoeven 2011).

"He is very difficult to engage to try and get him to learn anything, he thinks everything is funny. He is very friendly with other children and loves movies, his dog, trains, books and his iPad – 5 years

"She is very loving, accepting, gentle, kind and can often make people laugh. She is very set in her ways and likes her day to run according to familiar routines. She likes to know what she is going to eat and when and who (in the family) is where and when they'll be around. Given that, she is a lovely, gentle soul to be around. Change can throw her though and bring out a stubborn side! She is sociable and thoughtful towards other people – 24 years

6 years old with her two younger siblings

Motor skills (sitting, moving, walking)

Children with 22q11.2 distal deletion syndrome are often slightly delayed in learning to sit and walk.

One of the causes of the delay in mobility in children with a 22q11.2 distal deletion is low muscle tone (hypotonia), reported in a number of individuals. This makes a child or baby feel floppy to handle and generally improves and may disappear with physiotherapy and exercises. However, this means it may take a little longer for them to roll over, sit, crawl and walk. From the information that is available, sitting unaided is mastered between 6 months and 20 months (at an average of 11 months) and walking is mastered between 14 months and 5 years (an average of 27 months) (Rodningen 2008; Fernandez 2011; Verhoeven 2011; Verhagen 2012; Fagerberg 2013; Unique).

One child has a stiff gait with reduced hip rotation and one child is described as having clumsy motor functioning and had physiotherapy (Rodningen 2008; Verhoeven 2011).

"He is fine moving around. He loves going to play gyms but has only just this week begun riding a trike and still finds it very difficult – 5 years

"She moves around normally but is now very sedentary and dislikes physical activity – 24 years

Fine motor skills and self care

Fine motor skills may be affected in children with 2211.2 distal deletion syndrome

Very little is known about the fine motor skills of children with 22q11.2 distal deletion syndrome. A 7-year-old has difficulties with some but not all fine motor tasks. Another 7-year-old has difficulty with activities involving complex co-ordination as well as fine motor skills (Rodningen 2008; Verhoeven 2010; Unique).

Toilet training is only known for three children who achieved bladder and bowel control between 4 and 5 years. One of these children had soiling several times a day until the age of 7 years when a behavioural routine with substantial parental effort resulted in significant improvement. Another child achieved bladder and bowel control during the daytime at age 5 but was in nappies at night-time until 7 years (Rodningen 2008; Unique).

"He needs a lot of help in all areas although he is mainly toilet trained during the day and he has only just begun feeding himself in the last month – 5 years

"She was late in all areas of fine motor skills – 24 years

Facial appearance

Children with 22q11.2 distal deletion syndrome may have a subtle characteristic facial appearance.

Babies and children with this microdeletion may have subtly different facial features that would not, however, necessarily make them stand out from a crowd of other children. Geneticists trained to note unusual features may find features such as deep-set, upslanting eyes, a smooth philtrum (no vertical groove in the skin between the upper lip and the nose, a thin upper lip, a small, pointed chin and unusual shaped ears which often have ear tags. Some children have an unusually small head (microcephaly) (Ben-Shachar 2008; Garavelli 2011; Verhagen 2012; Fagerberg 2013; Unique).

Hands and feet

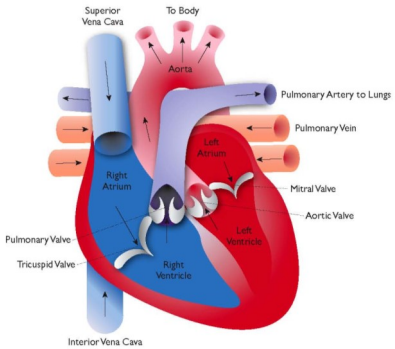
Hand and foot problems appear not to be common in 22q11.2 distal deletion syndrome, although three children have incurving little fingers (5th finger clinodactyly), a feature that is very common in people with a chromosome disorder and quite common in the general population. Two of these children have some fingers which are able to hyperextend (bend backwards). One child has long fingers; one has nails that are short and broad and one has brachydactyly (short fingers). A 24-year-old has very small hands with tapering fingers and slightly unusual joints; she also has small tapering feet. Three children are flat-footed; one of whom also has a 'sandal gap' (an increased gap between the first and second toe) and partial syndactyly (fusion) of the 2nd and 3rd toes. Overall, the pattern is of variable minor hand and feet anomalies (Ben-Shachar 2008; Rodningen 2008; Ogilvie 2009; Garavelli 2011; Unique).

Health matters

Heart problems

Cardiac problems appear to be quite common in people with 22q11.2 distal deletion syndrome

Heart problems range from minor to complex anomalies. Several children were born with holes in the wall of the heart, some of which closed naturally, whereas some required surgery. Some people had truncus arteriosus. Instead of having separate blood vessels leading out of each side of the heart, a baby with a truncus arteriosus has a single blood vessel leaving the heart that then branches into vessels that go to the lungs and the body. This great vessel usually sits over both the ventricles and the upper part of the wall between the two chambers is missing, resulting in a hole in the heart. Early surgical repair is usually needed. Another child had a bicuspid aortic valve [the aortic valve has only two cusps (flaps) rather than the usual three. The aortic valve ensures that the blood flows only in one direction. When the valve is bicuspid there can be a tendency for the valve to leak. Such shape of valve is quite common among the general population as well and usually considered as a minor problem. Three children had



A normal heart

tetralogy of Fallot [a complex cardiac condition where the artery that takes the blood to the lungs has an unusually narrow entrance (pulmonary stenosis) coupled with a hole in the heart]. A minority of children had more complex congenital heart defects (Saitta 1999; Garcia-Minaur 2002; Rauch 2005; Ben-Shachar 2008; Fernandez 2009; Garavelli 2011; Verhoeven 2011; Breckpot 2012; Michaelovsky 2012; Verhagen 2012; Fagerberg 2013; Unique). Children with heart problems need in addition to cardiac follow up to tale prevental antbiotic treatment prior to some medical procedures such as dental treatment and surgeries. This treatment prevent infection of the heart leafs called endocarditis.

Palate

Some children had a cleft palate and one had high-arched palate. A cleft palate is when the palate does not form correctly during development. This results in an opening in the roof of the mouth. A cleft lip occurs when the tissue that forms the upper lip does not fuse during prenatal development. Both cleft and high palates can contribute to the early feeding difficulties seen in children. Palate anomalies may also make speech and making the sounds of speech more difficult (Ben-Shachar 2008; Michaelovsky 2012).

Eyesight

Eyesight problems rarely have been reported. Three people are short-sighted, two of whom wearglasses (Rodningen 2009; Verhagen 2012; Unique).

Hearing

Most children have had normal hearing but there seems to be an increased risk for hearing impairment. One child had a hearing loss in one ear and wore a hearing aid. One child had the fluctuating temporary hearing loss caused by a build-up of fluid behind the eardrum (glue ear) that most children outgrow naturally. If it is severe or persistent tubes (grommets) may be inserted into the eardrum to aerate the space (the middle ear) behind it and improve hearing. Another child had lots of ear infections as a child (Rodningen 2008; Verhagen 2012; Unique).

Other

Other health concerns which have been described in only one or two people and may or may not be linked with the microdeletion include: two children who had an abnormal electroencephalogram (EEG, a test that records brain activity), one of whom took anticonvulsants; two children had recurrent infections, one outgrew them around the age of 12-15 years; two people had an inguinal hernia (a bulge of tissue from the intestines located in the lower abdomen); one person had coeliac disease (a common digestive condition where a person has an adverse reaction to gluten); one child had recurrent upper airway and urinary tract infections; one had bilateral hip dysplasia (underdevelopment or misalignment of the hip) and one had an imperforate anus (opening to the anus is missing or blocked) which required surgical correction (Ben-Shachar 2008; Rodningen 2008; Ogilvie 2009; Verhoeven 2011; Verhagen 2012; Fagerberg 2013; Unique).

Puberty

There is limited information available on puberty in both males and females with 22q11.2 distal deletion syndrome. It seems that puberty is generally at the normal age and proceeds as expected. However, one woman had breasts that have not developed fully and has excessive facial hair (Unique).

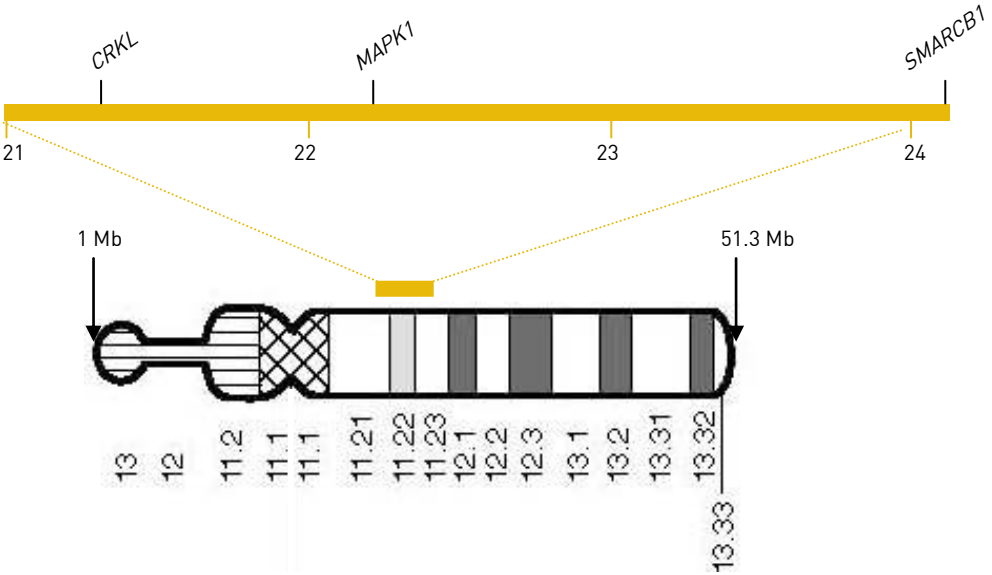
Adults with 22q11.2 distal deletion syndrome

Several adults have been described in the literature and Unique has two adult members. One father and two mothers only discovered that they carried the 22q11.2 distal deletion after it was picked up in their child. The father discovered he had the deletion at the age of 35 and apart from recurrent ear infections as a child and an inguinal hernia he had no health or developmental problems. A 33-year-old woman had mild learning difficulties and short stature. A 37-year-old mother had hyper-reflexia (over responsive reflexes) but otherwise no problems. An 18-year-old has no speech but has a cheerful personality. A 24-year-old woman has a moderate learning disability and is described by her parents as a 'lovely girl' (Verhagen 2012; Unique).

There will certainly be more people, including adults, with 22q11.2 distal deletions. As the molecular techniques which are needed to detect this microdeletion become more commonplace, further people are likely to be diagnosed.

Research involving distal 22q11.2

The features of 22q11.2 distal deletion syndrome are likely to be the result of the loss of a number of different genes found in this region. Most people have an approximately 0.4 to 2.1 Mb deletion (400'000- 2. Millions bases).



Although the gene(s) responsible for the clinical features associated with 22q11.2 distal deletion syndrome have not been clearly defined, several potential candidate genes have been suggested.

CRKL and *MAPK1* genes have been suggested to have a role in the heart anomalies that are common in 22q11.2 distal deletion syndrome (Breckpot 2012; Fagerberg 2013).

MAPK1 has also been suggested to be associated with placental development and therefore having one copy of this gene missing in 22q11.2 distal deletion syndrome may be linked to the tendency for premature birth and IUGR (Fagerberg 2013).

The *MAPKI* gene in mice has been shown to contribute to social behaviour and therefore may play a role in the behavioural problems found in some people with 22q11.2 distal deletion syndrome (Fagerberg 2013).

Very distal deletions including the *SMARCB1* gene are associated with an increased risk of malignant rhabdoid tumours. Very little is known about the magnitude of the risk for malignancy associated with distal 22q11.2 deletion syndrome but it is advised that people with a deletion that includes the *SMARCB1* gene undergo careful, prolonged monitoring for this type of tumour. Most persons with 22q11 distal deletions do not have deletion of the *SMARCB1* gene (Beddow 2011; Chakrapani 2012; Fagerberg 2013).

It is important to remember that while identifying the gene(s) responsible for certain features of the distal 22q11.2 deletion syndrome is valuable and may help guide future studies, it does not lead directly to immediate improved treatment. Additionally, even if the supposedly responsible gene is missing it does not always mean that the associated feature(s) will be present. Other genetic and environmental factors often have a role in determining the presence or absence of a particular feature.

How did this happen?

In the majority of the cases the 22q11.2 deletion occurs out of the blue for no obvious reason. The genetic term for this is *de novo* (dn) and at first sight, both parents have normal chromosomes. *De novo* 22q11.2 distal deletions are caused by a mistake that is thought to occur when the parents' sperm or egg cells are formed. At one point in the formation, all the chromosomes including the two chromosome 22s pair up and swap segments. To pair up precisely, each chromosome 'recognises' matching or near-matching DNA sequences on its partner chromosome. However, throughout the chromosomes there are many DNA sequences that are so similar that it is thought that mispairing can occur. Although no-one has ever seen this happen, it is believed that when the exchange of genetic material - known as 'crossing over' - occurs after mismatching, it is unequal, looping out and excising a length of the chromosome.

One father and three mothers have passed the deletion on directly to their children (Verhagen 2012; Unique). Whether the deletion is *de novo* or inherited, what is certain is that as a parent there is nothing you could have done to prevent this from happening. No environmental, dietary or lifestyle factors are known to cause distal 22q11.2 deletions. There is nothing that either parent did before or during pregnancy that caused the microdeletion.

Can it happen again?

Where both parents have normal chromosomes, it is unlikely that another child will be born with a distal 22q11.2 deletion or any other chromosome disorder. However, there is a very small possibility that the deletion occurred during the formation of the egg or sperm cells in a parent. When this occurs there is a tiny chance that parents with apparently normal chromosomes could have another affected pregnancy.

Where one parent has the same deletion as the child, the possibility of having another child with the deletion can be as high as 50 per cent in each pregnancy. In families where the parent appears to be unaffected but the child is affected, we cannot yet predict whether another child with the deletion would be affected by it or not.
If they wish, parents should have the opportunity to meet a genetic specialist to discuss the specific recurrence risks and options for prenatal and preimplantation genetic diagnosis (PGD). PGD requires the use of in vitro fertilisation and embryo biopsy, and only healthy embryos are transferred to the mother's uterus. If the parents choose to conceive naturally, prenatal diagnosis options include chorionic villus sampling (CVS) and amniocentesis to test the baby's chromosomes. Testing is generally very accurate, although not all of these tests are available in all parts of the world.

Could my child with 22q11.2 distal deletion syndrome also have children with the microdeletion?

Yes, this is possible. The medical literature reports one father and two mothers who have passed the deletion on to their children. Unique has a member who has passed the deletion on to four children. We have not known about the condition for long enough to be certain if it affects fertility but it is likely that fertility will be normal. In each pregnancy, someone with the deletion theoretically has a 50 per cent risk of passing it on and a 50 per cent chance of having a child without the microdeletion. Their ability to look after a child is very likely to be closely related to any learning difficulty they may have themselves (Verhagen 2012; Unique).

Notes

Inform Network Support

Understanding chromosome disorders
Unique

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

There is a Facebook group for families affected by 22q11.2 distal deletion syndrome at www.facebook.com

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!

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 leaflet 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. The information is believed to be the best available at the time of publication. It was compiled by Unique and reviewed by Dr Christina Fagerberg, Odense Universitetshospital, Denmark and Dr Shay Ben Shachar, The Genetic Institute, Tel Aviv, Israel.

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