



Understanding Chromosome & Gene Disorders

17q12 microdeletions



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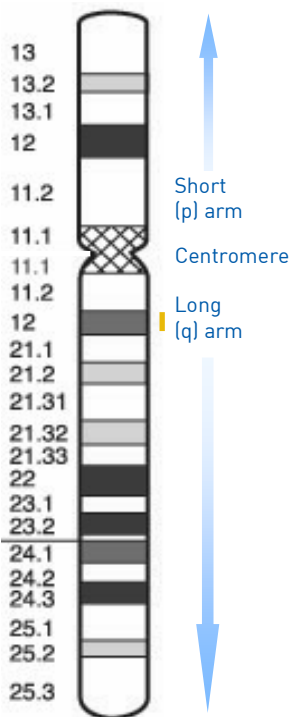
17q12 microdeletions

A chromosome 17q12 microdeletion means that a part of one of the body's chromosomes has been lost or deleted. If the missing chromosome material contains genes with important instructions for the brain or body, developmental delay, some learning and behaviour difficulties, and health problems may occur. How apparent and important these problems are depends on how much of the chromosome has been lost and where the deletion is.

Genes and chromosomes, DNA and base pairs

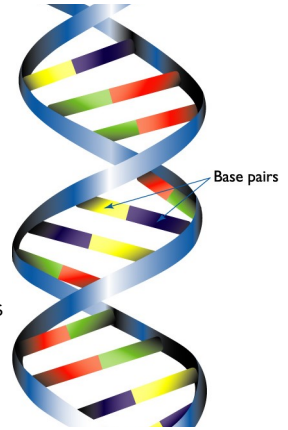
Our bodies are made up of billions of cells. Most of the cells contain a complete set of tens of thousands of genes, made up of DNA. Genes act like a set of instructions, directing our growth and development and how our bodies work. Genes are carried on chromosomes. There are usually 46 chromosomes, 23 inherited from our mother and 23 inherited from our father, so we have two sets of 23 chromosomes in 'pairs'. Apart from two sex chromosomes (two Xs for a girl and an X and a Y for a boy) the chromosomes are numbered 1 to 22, generally from largest to smallest. Each chromosome has a short arm called **p** from *petit*, the French word for small, and a long arm, simply called **q**. In a 17q deletion, material including important genes has been lost from the long arm of one of the two chromosome 17s.

In the diagram below left you can see the chromosome bands are numbered outwards from the point where the short arm meets the long arm (the **centromere**).



Chromosome 17

DNA has a ladder-like structure. The chemicals that form each end of the 'rungs' of this ladder are called bases and since each rung has two ends, bases always come in pairs, known as **base pairs**, or **bp** for short. Base pair numbers are very long, usually in millions, so they are often shortened. For example, 1,800,000 base pairs is usually written 1.8 Mb. **Mb** stands for megabase.



Looking at 17q

Chromosomes can't be seen with the naked eye, but if they are stained and magnified under a microscope, each one has a distinctive pattern of light and dark bands. The missing piece of chromosome can be tiny or much larger. If the missing piece is large enough, it is possible to see where the chromosome has broken and what material is missing under a microscope.

A missing piece that you can see under a microscope is called a deletion.

In people with material missing from 17q12, the missing piece is often so tiny that it can only be identified using new, more sensitive molecular techniques for analysing

chromosomes, such as array comparative genomic hybridisation (array-CGH, also known as microarrays). It is then called a microdeletion. Smaller deletions generally remove fewer genes and molecular techniques can usually show whether particular genes or parts of genes are missing or not.

How common is it to have a 17q12 microdeletion?

No-one really knows how common 17q12 microdeletions are in the general population, but an educated estimate is around 1:20,000. The microdeletion is much more common in groups of people with particular medical conditions: it is among the 10 most common microdeletions found in children with unexplained developmental delay, and has been found in around 1: 875 people with a clinical condition (Moreno de Luca 2010).

Results of the genetic test

Your geneticist or genetic counsellor will be able to tell you about the points where the chromosome has broken. The results are likely to read something like this:

arr[hg19] 17q12(34819670-36203752)x1 dn

arr The analysis was by array CGH
hg19 hg19 specifies which version of the human genome was used. In 2013, hg19 was the latest version. Base pair numbers vary a little between the different versions.

17q12 A change was found in band 17q12
(34819670-36203752)x1

The first base pair shown to be missing is number 34,819,670, counting from the top of the chromosome. The last base pair shown to be missing is 36,203,752. Take the first long number from the second and you get the number of base pairs that are missing

de novo or **dn** The deletion occurred de novo (or as a 'new event'). The parents have had a blood test, their chromosomes have been checked and no deletion or other chromosome change was found at 17q12. The microdeletion is very unlikely to be inherited and has almost certainly occurred for the first time in this family with this child

Has everyone with a 17q12 microdeletion lost the same genes and DNA?

No. People can lose a larger or smaller bit of the chromosome. Typically, people lose a bit that is 1.8 Mb long and contains 19 genes. And everyone has lost a particular stretch of 17q12 that contains 15 genes and is 1.4 Mb long (Moreno de Luca 2010). Some people have other chromosome changes as well as the 17q12 deletion.

Sources and references

The information in this guide is drawn from what has been published in the medical literature about babies, children and adults with a microdeletion from 17q12.

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

(www.ncbi.nlm.nih.gov/pubmed).

If you wish, you can obtain articles from Unique. This guide also draws on information in the Decipher database (<https://decipher.sanger.ac.uk>)

and in Unique's database. When this guide was published, Unique had four members with a 17q12

deletion (Mefford 2007; Cheroki 2008; Bernardini 2009; Elia 2010; Loirat 2010; Moreno de Luca 2010;

Nagamani 2010; Nik-Zainal 2011; Mitchel 2016; Verbitsky 2019; Decipher; Unique).

What is special about my child?

“ He is very close to me and has made me be a better person who is more sensitive to other children with disabilities. I am grateful for his progress and how well he is now doing. Naturally, I fear what the future brings in terms of medical complications that can arise including polycystic kidney, diabetes, and schizophrenia that have been linked to this deletion in the literature. ”

Are there people with a 17q12 microdeletion who are healthy, have no major medical problems or birth defects, and have developed normally?

So far, virtually everyone whose chromosomes have been checked has been affected. But the effects have been different in different people and sometimes people are only mildly affected. Some people have learning difficulties; others don't. Some people have kidney problems; others don't. Some people have defects in the reproductive tract, while others are unaffected.

Key features

People with a 17q12 deletion share some common features that add up to an emerging syndrome known as the 17q12 deletion syndrome. Much remains to be discovered, but the following points are reasonably clear.

The most common features are:

- Developmental delay
- Language delay
- Variable impact on learning ability, ranging from no impact to mild or moderate. When there are other chromosome changes as well as the 17q12 deletion, the impact on learning can be more significant
- Autism or autistic features
- Kidney and urinary tract problems
- Reproductive tract problems
- Raised risk of developing diabetes
- Problems with coordination and motor skills
- Behaviour concerns, including high levels of anxiety
- Some common facial features

These features do not affect everyone, and in any individual they can be more or less obvious.

■ Developmental delay

Some delay in development is common, although not universal. The degree of delay appears to vary quite widely, and development in some people with a 17q12 microdeletion is indistinguishable from normal, some children operate at the level of a child half their age, while others are more severely affected. Early signs of developmental delay can usually be seen within the first two years of a child's life and are very often the reason for seeking a genetic diagnosis (Bernardini 2009; Loirat 2010; Unique).

“ He was delayed globally but has caught up in most areas. ” *4 years*

“ Developmental delay compared with her peers in fine motor skills and language development, but cognitive tests have her in average ranges. ” *6 years*

“ Delayed motor skills, but otherwise entirely normal development. ” *Adult*

■ Language delay

Researchers have recently identified communication, speech and language as the area of development that is most likely to be affected by a 17q12 microdeletion. In some children, it is the only area of delay. Young babies typically show little interest either in people or in playthings and do not develop a social smile as expected in the first two months of life. Eye contact may be lacking and the expected sequence of reciprocal noises, babbling, jargon and words does not emerge in the first 18 months. Despite this significant delay, many children do learn to talk but parents stress that support and stimulation are vital (Loirat 2010; Moreno de Luca 2010; Nagamani 2010; Unique).

“ The area he continues to struggle in is speech and socialisation. He communicates with words in full sentences but does have difficulties with some sounds, such as *r*, *th* and *l*. We did use sign language and a communication board but he does not use these any more. We also do listening/music therapy. His language comprehension is better than his expression, but both are good now. Early intervention is key, and you must do work at home as well. The therapists are only with the children for a limited amount of time. ” *4 years*

“ There is a strong suspicion that she may have speech apraxia, but she is still being evaluated to determine if this is the official diagnosis. She first smiled at two months, babbled at six months, and said her first words at almost two years of age but they were very limited. She speaks in full sentences, but is still delayed and is difficult to understand. For example, she uses *ellow* for *yellow* and *new-new* for *noodle* and has difficulties with the *s* blend and *l* sound. She understands much more than she can effectively communicate and gets frustrated because she cannot communicate as well as her peers, and other children and adults have a hard time understanding her. Speech therapy in school and privately seems to be helping her with some tools and having her slow down helps as well. ” *6 years*

“ No language or communication delay. ” *Adult*

■ Variable impact on learning ability, ranging from no impact to mild or moderate difficulties

17q12 microdeletions are a rare example of a chromosomal deletion that was initially thought not to affect cognitive ability. One researcher examined eight people with the typical 1.8 Mb deletion, among whom learning difficulties were not evident based on a general impression (Mefford 2007). However, since that study was published, other researchers have found a broader spectrum of need for special support with learning,

with ability ranging from a mild to moderate delay. Tested IQs have been in the 50-85 range, but can vary widely.

Some children attend mainstream (regular) school, others attend a speech and language unit, others attend a school for children with special needs, yet others a unit for children with an autism spectrum disorder. Unique has a member who is a high-grade university graduate, has worked as a stock trader and has run his own company (Mefford 2007; Moreno De Luca 2010; Unique).

“ His IQ testing was normal. He is very shy, slow to warm up, and uses diversion when challenged. His memory is OK but he is only good at things he enjoys. He has a strong preference for females and ‘girl’ activities. He likes playing dress up and the colors pink and purple. ” *4 years*

“ She has not been diagnosed with any official learning disabilities other than speech delay, and is more advanced in math than some of her peers although her writing ability seems to be delayed. She also has a very good memory - remembers everything and all the details too - so overall she is better at math and memory-based activities. She is very determined and enjoys praise and doing things right. This is often combined with frustration and a lot of patience to get the work done, but she feels really good about finishing something or doing well, probably similarly to most people. She sometimes does lose attention quickly, so it is important to keep the ‘eye on the prize’, so to speak. She attends a regular public school in the first grade, at the normal age and with no delays in starting school. ” *6 years*

■ Autism or autistic features

Recent research has shown a high rate of autism or autistic behaviour, particularly in boys with a 17q12 microdeletion. Two researchers have found a 100 per cent rate of autistic behaviours among boys with the deletion. In one study, 4/6 boys met the full diagnostic criteria for autism, while two others showed autistic traits. In this study, girls with the deletion were not as affected. In the second study, three boys had no interest in people or objects between the ages of 2 - 6 months and didn’t smile responsively; later on, they didn’t make eye contact or talk, and were restless, with repetitive types of behaviour. However, the number of persons with the deletion these studies looked at is not large enough to see if there are any conclusive differences regarding the autism diagnosis depending on gender. The evidence from Unique only partly echoes these findings; one adult, a man, has no autistic features or behaviours at all (Loirat 2010; Moreno de Luca 2010; Unique).

“ He can’t look people in the eye and has difficulty answering questions if people are new to him. Even with those who know him well, he will have a warm-up period every time he sees them. He has a hard time meeting new children and playing with others. He does better with adults than children. He never kissed us until after he was 2 and today still has poor eye contact, difficulty recognizing non-verbal cues and difficulty empathising with others. He was diagnosed with autism at the age of one. Today he likes routine and to know what is going to happen. With age he has more empathy toward others and has become more caring. ” *Boy, 4 years*

“ No diagnosis of autism. ” *Girl, 6 years*

■ Kidney or urinary tract problems

A high proportion of babies, children and adults with a 17q12 microdeletion are known to have some anomaly of their kidneys or urinary tract (Mitchel 2016; Verbitsky 2019).

Anomalies reported include:

- absent kidney/s (renal agenesis),
- small kidneys (renal hypoplasia), which can also have abnormal tissue (renal hypodysplasia), such as cysts (cystic dysplasia),
- horseshoe kidney, where the two, usually separate kidneys are joined together at the bottom,
- posterior urethral valves, extra flaps of tissue in the urethra (the tube that drains urine from the bladder), which can block urine from flowing out (from the urethra into the bladder),
- duplicated collecting system, where instead of having the (usual) one ureter (the tube that carries urine from the kidney to the bladder), a kidney has two ureters,
- vesicoureteral reflux, where urine flows backwards, from the bladder towards the kidneys.

Apart from structural anomalies of the kidneys or urinary tract, individuals may have tubulointerstitial kidney disease: here, the tubules of the kidney, which are involved in filtering minerals and waste products from the blood to make urine, are damaged, leading to abnormal levels of these minerals and wastes in the blood.

Structural anomalies of the kidneys or urinary tract may be found prenatally during pregnancy, when an ultrasound scan shows abnormal kidneys. In terms of the eventual impact, most children have normal kidney function but there is a huge range of severity, from no functional impact at all to early-onset end-stage renal disease requiring dialysis and kidney transplant.

Underlying the kidney and urinary tract problems seen in many people with a 17q12 microdeletion is the loss or mutation of a gene known as HNF1B (see page 15). The high rate of kidney and urinary tract abnormalities means that everyone with a 17q12 microdeletion can expect to have a scan of their renal system and to be monitored regularly throughout childhood and adulthood.

“In utero, the ultrasound revealed enlarged kidneys. The ultrasound was repeated after birth and the kidneys looked better, but were still on the large side. Due to the deletion, he has had subsequent ultrasound scans of his kidneys that were all normal.” 4 years

“She has regular blood tests, blood pressure checks and periodic ultrasound. Apart from that, it is just ‘watchful waiting’.” 6 years

“Started to exhibit signs of cystic kidneys at 35½ years after a dehydration episode, when kidney function tests, ultrasound and CT (computerised tomography) scan were performed. Initially he had a very high creatinine clearance (a kidney function test), but the cysts only showed up on follow-up CT scans.” Adult

■ Reproductive tract problems

A high proportion of people with a 17q12 microdeletion have some anomaly of the genital or reproductive system. Both females and males can be affected, but it's important to stress that the reproductive tract may also be entirely normal.

The anomalies found so far include a number of women with a condition known as Müllerian aplasia. This is a developmental defect in which the uterus, cervix and upper vagina is rudimentary or missing. In one study of Müllerian aplasia, 4/63 cases (6 per cent) were linked to a 17q12 microdeletion. In another similar study, 1/14 patients had a

17q12 microdeletion. Despite the absence of a uterus and upper vagina, females may show no outward sign, as the ovaries may be preserved and secondary sexual characteristics develop normally. Reconstructive surgery is likely to be needed in these cases.

The uterus abnormalities may take other forms. One teenager was missing the top and middle sections of the vagina and her uterus had an unusual shape. Another woman had a double uterus, with dual cervixes, known as a uterus didelphys (Cheroki 2008; Bernardini 2009; Moreno de Luca 2010; Nik-Zainal 2011).

Among the males, two have a shawl scrotum, where the scrotum surrounds the penis like a shawl. Another has hypospadias, where the hole normally at the end of the penis is situated on the underside instead, as well as an undescended testicle and overall small genitals. He also had a hernia in the groin and a hydrocele: fluid round the testis in the scrotum. An internal scan came back normal and, following corrective surgery for the hypospadias and undescended testicle, these unusual features cause the teenager involved no problems (Nagamani 2010; Unique).

■ Raised risk of developing diabetes

People with changes in the *HNFB* gene or loss of the gene (*see page 15*), which is always lost in patients with the typical 17q12 deletion, have a raised risk of developing a particular type of diabetes. It is called MODY5 (maturity onset diabetes of the young type 5), and usually develops before the age of 30 but can emerge at any age from babyhood onwards. The degree of insulin shortage varies and the pancreas, which houses the cells which produce insulin, is typically wasted. Because of this well-known risk, tests for diabetes should form part of the regular screening of people with a 17q12 microdeletion (Mefford 2007; Moreno de Luca 2010; Nagamani 2010).

■ Problems with coordination and motor skills

Babies and toddlers may be late to sit, move around and walk, and also to handle toys. Having said that, children continue to make progress and any delay in mobility seems to be usually fairly mild, with babies learning to sit between 5 and 12 months and to walk between 15 months and 2 years. Once on their feet, some children have a poor sense of balance and walk with their feet wide apart, falling quite frequently. Fine motor skills – hand use and hand-eye coordination – also seem to be affected, creating difficulties in play skills, personal care and, later, at school. As with all other features of a 17q12 microdeletion, some people have no motor skill problems at all (Moreno De Luca 2010; Unique).

“ He doesn’t need any supports or aids when he is walking but tires easily and is very cautious. He has a hard time with balance and falls often. He enjoys playing in sand and at the park and is learning to pedal a bike. He was delayed with using utensils and holding crayons but is doing better now. ” 4 years

“ She has experienced no motor delays: she rolled at two months, sat at four months and walked at 14 months. She is not able to ride a bike without training wheels yet, but not much practice has been given to this. Her fine motor skills are a bit delayed in terms of cutting and colouring or drawing. She is able to hold objects and grasp normally, but her detailed colouring is just improving now and is delayed compared with her peers. Having said that, she is able to manipulate and work with Lego and to follow directions to build a kit, etc. The testing for fine motor delay given by the schools has not produced any action on their part and she tests in the average to normal range overall. As far as personal care is concerned, she can dress, wash and use the toilet independently but often needs reminders or motivation to get the job done. She is toilet trained during the day, but not

yet at night; her nephrologist says that a lot is due to her underlying cystic kidneys and overproduction of urine.” *6 years*

■ Problem behaviours, including high levels of anxiety

Researchers have identified some problem behaviours with high levels of anxiety as a key feature for children and adults with a 17q12 microdeletion. In one study, anxiety was found in 5/9 people; aggression, frequent mood changes and a short attention span in 2/9; and unusual phobias, hyperactivity, obsessive-compulsive behaviour, self-harm and irritability in 1/9 (Moreno de Luca 2010). Another researcher found attention deficit hyperactivity disorder in one child (Elia 2010). Unique's experience is a little different, as you can read below, and some people have no difficult behaviour at all.

“He has severe anxiety, is whiny and clingy. Early intervention is key! Just treat the child, the symptoms and his areas of difficulty. He is scared of pets but loves stuffed animals and anything feminine. He likes music, dressing up, playing make believe and reading.” *4 years*

“She is a happy little girl but gets easily frustrated, due to her communication and speech delays. She seems to exhibit some attention deficit but nothing has been diagnosed officially to date and no medication is being prescribed. She can be fixed on an activity and can get upset if she cannot find something or do a certain task, but often how you respond to her makes a difference. She has no unusual fears and is quite open to trying new things, food and experiences. She is usually very well mannered and tempered, but can be easily agitated or bothered when she gets frustrated. She can also be an absolute joy to share experiences with and remembers the details so well. It is also heart-breaking at times because she struggles to communicate with friends and schoolmates, and other kids can be cruel about her differences, but they don't seem to get her down or bother her as much as they do her mother. As she gets older, she tends to exhibit more frustration at expressing herself. She is very social and wants a lot of friends. She is eager to please but also wants to be heard and is often overshadowed by her peers due to speech issues.” *6 years*

■ Some common facial features

Children and adults with a 17q12 microdeletion may have certain facial features in common, giving them a subtle but characteristic look. In other ways, they are likely to look like the rest of their family. Researchers have identified common facial features which include a high, rounded forehead, arched eyebrows and a relatively large or long head. Out of 15 people, nine have a high, rounded forehead and eight have arched eyebrows. Out of 14 people, eight have a relatively large head (the top 10 per cent of population for head size). Some people may have eyes that slant downwards and some may have a small chin or a lower jaw that is set back (Moreno de Luca 2010; *Unique*).

“He had a rapid increase in head circumference at about four months of age. His head went from about the 25th percentile to around the 90th percentile, and has since remained in the 90s.” *4 years*

“Her head was large as a baby, but is now average. She has none of the other ‘typical’ facial features of people with a 17q12 deletion.” *6 years*



Less common features

- Growth restriction, leading to short stature
 - Seizures
 - Spinal curve
-
- Growth restriction, leading to short stature with heights in the lowest three per cent of the population

Restricted growth has been found in 7/18 children and adults. The range is very wide, with some children being short and occasionally very markedly so, while others grow normally and have a normal body build. Few adult heights are known: a woman of 20 reached 150cm (4' 11"); a man 178cm (5' 10"). The evidence from Unique is that body build may be typically stocky, but can also be normal (Moreno de Luca 2010; Nagamani 2010; Unique).

“ His height is now about the 3rd to 5th percentile. He used to be below the growth curve and at one point they thought he had *IGF1* (insulin like growth factor 1) deficiency. He saw several endocrinologists and his *IGF1* levels were low, but now appear to have come up to the low normal range. Unlike my other two children, he is heavier and has a larger belly. ” *4 years*

● Seizures

Around one in three children and adults with a 17q12 microdeletion has a diagnosis of epilepsy. In one adult, now 45 years old, seizures started at one year; two babies developed complex partial seizures in their first year. Unique evidence suggests that anti epilepsy drugs control seizures well.

In three people with seizures, some structural anomaly of the brain was found on imaging. Anomalies include: bright signals known as hyperintensities in the hippocampus, a part of the brain involved in storing memory and spatial navigation; a slight shrinking of the brain, with more substantial shrinkage of the hippocampus; and damage to the insulating sheath around nerve fibres known as demyelination. In a further child, a condition known as benign external hydrocephalus was found: this is a self-limiting problem of fluid accumulation around the brain that usually resolves within a year.

In two further people, the ventricles within the brain were somewhat enlarged, but neither had experienced any seizures (Mefford 2007; Cheroki 2008; Loirat 2010; Nagamani 2010; Unique).

● Spinal curve

In one study, 3/9 people were found to have an abnormal spinal curvature. This has not been seen in others with a 17q12 microdeletion. A hump (kyphosis) was found in one, and an abnormal lateral curvature (scoliosis) was found in two (Moreno de Luca 2010).

Other features

■ Possible susceptibility to infections

Frequent ear, chest and urinary tract infections have been seen in a few children, with respiratory infections having a particular impact on young children under the age of eight. In general, chest infections seem to be somewhat more common in children with any chromosome disorder and it is not known whether they are any more common in those with a 17q12 microdeletion. The good news is that children do seem to outgrow this tendency (Moreno De Luca 2010; Unique).

“ His only problems medically have been respiratory. He has asthma, and minor illnesses cause wheezing. ” *4 years*

■ Eyesight

Long sight has been noted in 2/11 children and adults. Other vision problems noted include: horizontal nystagmus (a jerky movement of the eyes that usually affects vision); punctuate cataracts, where there are opaque spots over the lens; and one very small eye (microphthalmia) (Cheroki 2008; Moreno de Luca 2010; Nagamani 2010; Unique).

“ She needs glasses for her right eye and patching of her left eye to strengthen the right eye. ” *6 years, with right eye microphthalmia*

■ Teeth

Some unusual dental development has been seen in 7/14 children and adults. One child's deciduous teeth were very late to come in and his mouth is very small and crowded. Another child needed protective sealant on eight baby teeth and the first two upper adult teeth appeared to be coming in at an angle, possibly requiring later bracing (Moreno De Luca 2010; Unique).

■ Hands and feet

Hands and feet are frequently somewhat unusual, although there is no clear pattern to the unusual features. Most frequently, hands and feet (or toes and fingers) are long and thin, but Unique has one member with large hands and short fingers; and another with an apparently shorter third than fourth toe on the right foot until the toes are extended. The joints can also be very mobile, although in some children and adults with the deletion they can be a little stiff (Moreno De Luca 2010). Nails can also be unusual: either underdeveloped, or thick, or excessively curved, or prone to infections (Cheroki 2008; Moreno De Luca 2010; Unique).

“ Her left toes are curled oddly and seem to be almost ingrown. The right toes also exhibit the same type of curl, but much less so than on the left side. ” 6 years

■ Possible vulnerability to mental health difficulties

A number of adults with a 17q12 deletion have some kind of mental health problem. This does not mean that everyone with the 17q12 microdeletion will have a mental health problem. The problems vary, but include: autism, schizophrenia, depression and bipolar disorder (Moreno De Luca 2010).

■ Pregnancy, birth and newborn

We have some information on pregnancy and the newborn period for 17 babies. The most common concern during pregnancy was an ultrasound scan showing a kidney problem (*see pages 7 - 8*). Otherwise, most pregnancies were uneventful. However, six babies were born prematurely and another threatened preterm delivery. The reasons for prematurity include maternal factors such as seizures. One baby was a twin.

Birthweights for babies born around term range from 2.154 kg (4lb 12oz) - 3.530kg (7lb 13oz). Naturally, birthweights for premature babies were lower, starting from 1.5 kg (3lb 5oz) for a baby born at 36 weeks.

Apgar scores (a measure of a newborn baby's wellbeing on a scale of 0 - 10) were generally impressive, with even preterm babies scoring 9 or 10. Babies did not generally need special care but if they did, most thrived well (Bernardini 2009; Moreno De Luca 2010; Unique).

■ Feeding

One researcher has drawn attention to unusual eating patterns among children with a 17q12 microdeletion. He found that one child had pica (eating non-foods) and two had a very selective diet. Unique has found this in only one child, who at four years prefers to drink than to eat and is highly selective about foods. His family believes that the root cause is low muscle tone (making some foods harder to chew and swallow) as well as sensory issues. An adult has a small appetite but drinks large quantities of milk.

Gastro-oesophageal reflux (bringing feeds back due to abnormal action of the valve between the food passage and the stomach) was also found in two adults and one Unique

child. If careful positioning while feeding and lying with the head of the cot raised is not enough to control reflux, specially thickened anti-reflux milks can be prescribed for babies and young children and, where necessary, anti-reflux medication to help keep the stomach contents down and protect the inner walls of the food passage from stomach acid.

Constipation was found in two children. This is not uncommon in children and adults with chromosome disorders and usually responds well to an increase in fluids and high-fibre foods, if possible, or to prescribed stool-softening, and if necessary, laxative medication (Moreno De Luca 2010; Unique).

“ No significant feeding issues. She was unable to breastfeed due to poor milk production and the need to ensure that she was getting the proper amount of nutrition to grow and gain weight. She now has a very good appetite and broad and varied tastes for food. She eats a normal, healthy and varied diet but we watch her salt intake and have been increasing red meat consumption due to her borderline anaemia (low iron stores). ”

6 years

Management recommendations

It's recommended that anyone with a diagnosis of 17q12 microdeletion should have a clinical examination that pays particular attention to the kidneys, urinary tract and reproductive systems; a general review of all their organ systems; and a developmental assessment. They should be regularly monitored for diabetes and kidney function. Therapies introduced early will usually improve outcomes. Speech therapy in particular should be introduced early and assisted or augmentative communication started where needed. Routine developmental assessment and screening should follow.

Why did the 17q12 microdeletion occur?

Many 17q12 microdeletions occur out of the blue for no obvious reason. The genetic term for this is *de novo* (dn), meaning 'new', and when analysed, a blood test from both parents shows normal chromosomes. *De novo* 17q12 deletions are caused by a change that occurred when the parents' sperm or egg cells formed, or possibly during the formation and copying of the early cells after the egg and sperm joined.

Less often, 17q12 microdeletions are inherited from a parent with the same microdeletion. Generally the parents appear to be affected by the microdeletion, although the degree can be very variable; in some cases these parents are just mildly affected and would go undiagnosed until they are tested to follow up the genetic findings in their children (Moreno De Luca 2010; Unique).

The only way to know whether your child's microdeletion is inherited or a new deletion is for both parents' chromosomes to be analysed.

Whether the deletion is inherited or *de novo*, as a parent there is nothing you did to cause it and nothing you could have done would have prevented it from occurring in your baby. No environmental, dietary, workplace or lifestyle factors are known to cause 17q12 microdeletions. There is nothing that either parent did before or during pregnancy that caused the duplication, so no-one is to blame and there is no reason for anyone to feel guilty.

Can this happen again?

Where both parents have normal chromosomes, it is unlikely that another child will be born with a 17q12 microdeletion or any other chromosome disorder. Very rarely (less than 1%), both parents have normal chromosomes by a blood test, but a few of their egg or sperm cells carry the 17q12 microdeletion. This is called **germline mosaicism** and it means that parents whose chromosomes appear normal when their blood is tested can have more than one child with the deletion.

In families where the 17q12 microdeletion has been inherited from a parent, the possibility of having another child - either a girl or a boy - with the 17q12 microdeletion rises to 50% in each pregnancy. However, the effect of the microdeletion on the child's development, health and behaviour cannot be reliably predicted.

Your genetics centre should be able to offer counselling before you have another pregnancy.



Father and daughter have the same 17q12 microdeletion, but are somewhat differently affected.

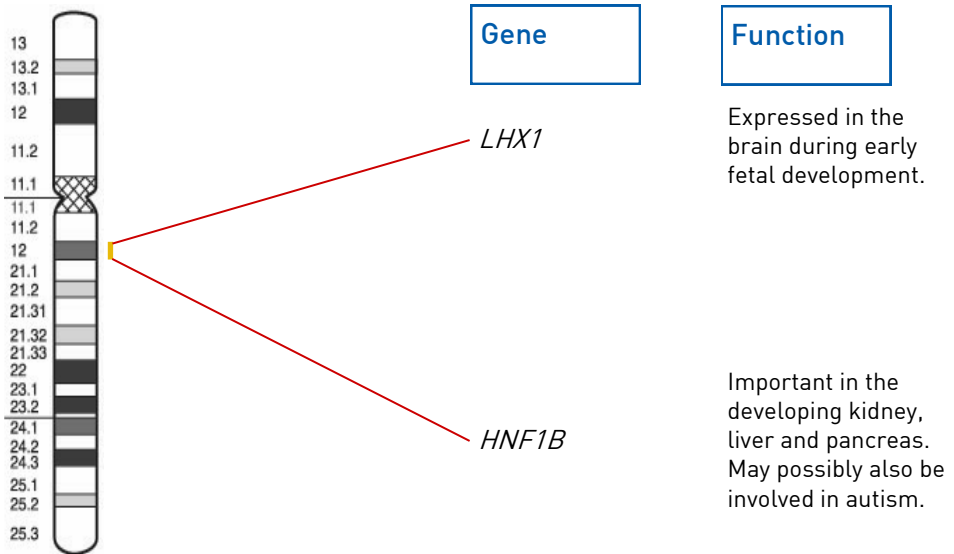
Will my child have similarly affected children?

It is too early to know whether this deletion affects fertility. However, people with the deletion whose reproductive tract is unaffected and are otherwise healthy may well have normal fertility. In each pregnancy, someone with the microdeletion is then likely to have a 50 per cent risk of passing it on and a 50 per cent chance of having a child without it. We haven't known about the syndrome for long enough to be certain of the range of possible effects or how obvious they will be.

Some genes in the deleted area

HNF1B, previously known as *TCF2*, is the gene responsible for a condition known as renal cysts and diabetes syndrome (RCAD) and for the renal structural abnormalities and female reproductive tract malformations. This gene is important in the developing kidney and liver and also regulates the development of the pancreas of the embryo. For this reason, people with a deletion of *HNF1B* can expect to be monitored carefully for liver and pancreatic disease (Moreno de Luca 2010). It has been suggested that this gene may also be implicated in autism (Loirat 2010).

LHX1 is a candidate gene for the neurocognitive phenotype. *LHX1* is expressed in the brain during early development. Mice without the *Lhx1* gene have no uterus or oviducts, so this gene may play a role in the uterine abnormalities seen in some women with a 17q12 microdeletion. But it has not yet been associated with disease in humans (Nagamani 2010; Nik-Zainal 2011).



I wish ...

“I knew how this deletion will affect him and how best to help make him a happy, successful member of society. It is frustrating to know that he has the deletion, but not to know what this means for him medically or in the long term.”

Inform Network Support



Understanding Chromosome & Gene Disorders

Rare Chromosome Disorder Support Group,
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Join Unique for family links, information and support.

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This 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. The information is believed to be the best available at the time of publication. It was compiled by Unique and reviewed by Dr Daniel Moreno De Luca, postdoctoral fellow, Department of Human Genetics, Emory University, Georgia, USA and by Professor Maj Hultén, Professor of Reproductive Genetics, University of Warwick, UK and chief medical advisor to Unique. (PM)

The CAKUT (congenital anomalies of kidney and urinary tract) information in this guide was updated in 2021 by Dr. Emily Groopman, MD/PhD (Broad Institute of MIT and Harvard, Cambridge, MA, USA; Boston Children's Hospital, Boston, MA, USA)

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