

## Families say:

“ Matthew has taught us that every challenge overcome is a huge achievement for him. Nothing is taken for granted. Never underestimate what you can achieve as a parent. You are not alone; there are others out there. Have confidence in your own instinct with your child, this is normally right. ”

“ If your child is late crawling, walking, talking etc express your concerns to your doctors. Don't be afraid to see a specialist because it could definitely be a part of a much bigger picture. Trust your instincts. ”

“ I would like other families to know that despite getting a diagnosis such as this it is still possible to lead an everyday life with your child. ”

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Understanding Chromosome & Gene Disorders

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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 John Rosendahl Østergaard, Center for Rare Diseases, Department of Pediatrics, Aarhus University Hospital, Aarhus, Denmark and Professor Maj Hultén, Professor of Medical Genetics, University of Warwick, UK

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Understanding Chromosome & Gene Disorders

# 17p13.3 microdeletions



[rarechromo.org](http://rarechromo.org)

## Sources

The information in this guide encompasses details on 28 separate individuals with 17p13.3 microdeletions. This information is drawn partly from the published medical literature. There were 21 published cases in the medical literature with the oldest person reported being 50 years old [Bruno 2010]. 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](http://www.ncbi.nlm.nih.gov/pubmed)). If you wish, you can obtain most articles from Unique.

In addition this guide draws on a survey of members of Unique conducted in the summer of 2012, referenced Unique. At the time of writing (May 2013) Unique had seven members with a 17p13.3 microdeletion ranging in age from two years old to 28 years old.

## 17p13.3 microdeletions

A 17p13.3 microdeletion is a rare disorder in which a small part of the genetic material that makes up one of the body's 46 chromosomes is missing. Although the other chromosomes are intact, this small missing piece does increase the possibility of developmental delay and learning difficulties. However the problems can vary and depend very much on what genetic material is missing.

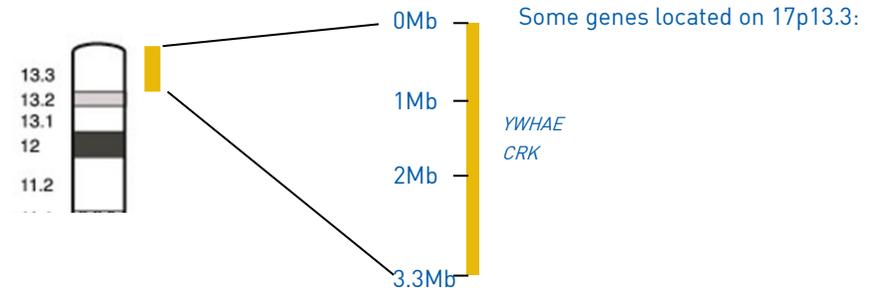
Chromosomes are made up mostly of DNA and are the structures in the nucleus of the body's cells that carry genetic information (known as genes), telling the body how to develop and function. Chromosomes usually come in pairs, one from each parent, and are numbered 1 to 22 approximately from the largest to the smallest. In addition to these 44 chromosomes, each person has another pair of chromosomes, called the sex chromosomes. Girls have two Xs (XX), whereas boys have an X and a Y chromosome (XY). Each chromosome has a short (p) arm (shown at the top in the diagram below) and a long (q) arm (the bottom part of the chromosome).

For healthy development, chromosomes should contain just the right amount of material – not too much and not too little. People with 17p13.3 microdeletions have one intact chromosome 17, but the other is missing a tiny piece from the short arm which can affect their learning and physical development. Most of the clinical difficulties are probably caused by the presence of only one copy (instead of the usual two) of a number of genes. However, a child's other genes and environment also helps to determine future development, needs and achievements.

## Looking at Chromosome 17p13.3

People who have missing material on a chromosome are said to have a deletion. Sometimes the deletion is very small and cannot be seen even under a high powered microscope (known as karyotyping): in these cases it is called a **microdeletion**. The 17p13.3 microdeletion can be found using molecular or DNA technology, in particular a technique such as array comparative genomic hybridisation (array-CGH).

Base pairs are the chemicals in DNA that form the end of the 'rungs' of its ladder-like structure. In different



It is important to remember that while identifying gene(s) responsible for certain features of the 17p13.3 microdeletions is valuable and may 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 the 17p13.3 microdeletion occur?

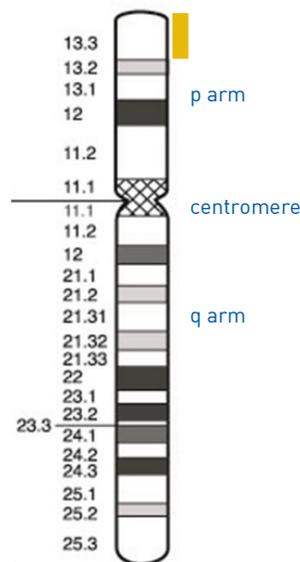
A blood test to check both parents' chromosomes is needed to find out why the 17p13.3 microdeletion occurred. In most cases that we have information on, the microdeletion occurred when both parents have usual chromosomes. The term that geneticists use for this is *de novo* (dn) which means 'new'. *De novo* 17p13.3 microdeletions 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. In some cases, the child inherits the microdeletion from a parent. However symptoms and experiences can still vary greatly between family members. As a parent there is nothing you did to cause the 17p13.3 microdeletion and nothing you could have done would have prevented it from occurring in your baby. No environmental, dietary or lifestyle factors are known to cause these chromosome changes. No one is to blame when this occurs and nobody is at fault.

## Can it happen again?

Where both parents have normal chromosomes, it is unlikely that another child will be born with a 17p13.3 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 17p13.3 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.

If either parent has a chromosome rearrangement or deletion involving 17p13.3, the possibility of having other affected pregnancies is greatly increased.

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



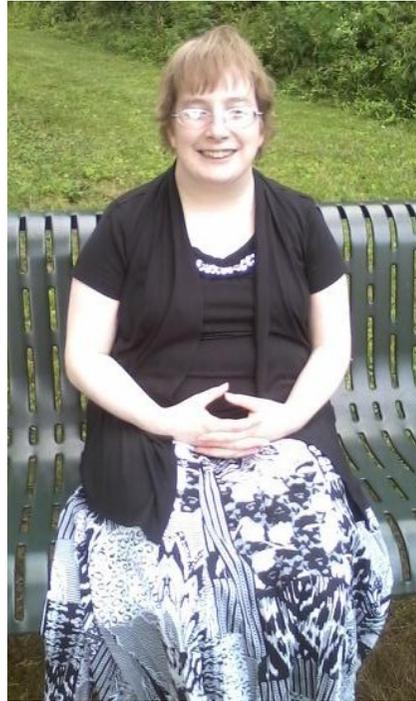
## Adults with 17p13.3 microdeletions

There are two Unique members with 17p13.3 microdeletion over the age of 18. One aged 20 has severe learning disabilities and attended a special educational school. The second woman, now aged 28, has mild to moderate learning disabilities with difficulties with comprehension. She attended mainstream school with extra help. She now works in a school. Her parents are her legal guardians and conservators [Unique].

In the literature there are four reported adults with 17p13.3 microdeletion. They range in age from a man of 21 years old to a woman of 50 years old. One woman has moderate learning disabilities but is able to work in a protected environment [Bruno 2010; Schiff 2010].

There will certainly be more children and adults diagnosed in the future with 17p13.3 microdeletions. As the molecular tests which are required to detect this microdeletion become more commonplace, further people are likely to be diagnosed.

“ She has worked a variety of jobs: retail and fast food (which she hated) and childcare (which she loves). She recently began a job at a local elementary school as a Noon Duty – she helps supervise and assist children in the lunchroom and also helps supervise the playground. Each day before her work shift she volunteers at the school in either the kindergarten class or special needs preschool class.” 28 years



## Ongoing research

The features of 17p13.3 microdeletions are likely to be the result of the loss of one or a number of genes found in this region (see diagram on page 19).

Some genes have been identified in the literature as being likely to play a part in a particular symptom or problem and are described below.

A deletion of one copy of the *YWHAE* gene, which codes for the protein 14-3-3epsilon, is thought to cause developmental delay and specific craniofacial features [Nagamani 2009; Schiff 2010; Ostergaard 2012]. It has been suggested that deletion of this gene could increase the risk of seizures [Tenney 2010]. It has also been suggested that affected individuals undergo magnetic resonance imaging of the brain [Nagamani 2009].

A deletion of the *CRK* gene is thought to be responsible for growth delay [Nagamani 2009; Bruno 2010; Schiff 2010; Ostergaard 2012]. It has also been suggested that its deletion could result in specific craniofacial (head and facial) features and limb anomalies [Ostergaard 2012] as well as increased risk of seizures [Tenney 2010].

people, the base pairs where the chromosome has broken (the ‘breakpoints’) are different and so the size of the microdeletion is variable. The 17p13.3 region is denoted by the red bar on the diagram on the right. Band 17p13.3 contains about three million base pairs or 3 Mb which is approximately 3.75 per cent of the DNA in chromosome 17.

Chromosome 17 spans about 80 Mb and represents between two and a half percent and three percent of the total DNA in cells.

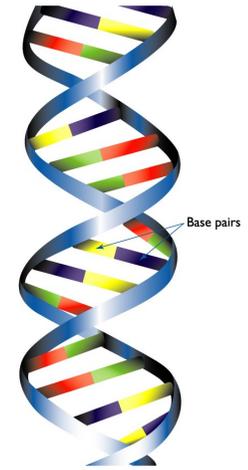
## Genetic testing

Techniques that are commonly used include FISH and microarrays:

- Fluorescence *in situ* hybridisation (FISH) uses fluorescent dyes to visualise under a microscope the number of copies of small sections of chromosomes. Unique publishes a separate guide to FISH

However, rare chromosome disorders may be caused by subtle changes in the chromosomes that are too small to see using a microscope.

- Microarray comparative genomic hybridisation (array CGH) is a sensitive technique which shows gains (and losses) of tiny amounts of DNA throughout the chromosomes. Array CGH identifies duplicated or absent DNA. Unique publishes a separate guide to array CGH.



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

## Is there a 17p13.3 microdeletion syndrome?

When a particular set of developmental features occurs in a recognisable and consistent pattern in enough people with the condition as a result of a single cause, it is called a syndrome. 17p13.3 microdeletions have not been commonly described as a syndrome. However two medical reports have used the term syndrome to refer to deletions involving 17p13.3 [Tenney 2010; Ostergaard 2012].

## Miller-Dieker Syndrome

A deletion of part of 17p13.3, including both the *LIS1* (also known as *PAFAH1B1*) gene and the *YWHAE* gene, is known as Miller-Dieker Syndrome. This syndrome is characterised by lissencephaly (‘smooth brain’) as well as unusual facial features, learning difficulties, and various other symptoms such as seizures. This information guide will not specifically cover Miller-Dieker Syndrome. However, if you would like more information on the syndrome, please contact your genetics team.

This 17p13.3 microdeletion information guide includes information on 17p13.3 microdeletions that include the *YWHAE* gene but not the *LIS1/PAFAH1B1* gene (please see ‘Ongoing Research’ on page 18 for more information on individual genes).

## Results of the genetic test

You are likely to be given the results of molecular analysis such as FISH or array-CGH for your child. In this case the results are likely to read something like the following example:

### arr [hg19] 17p13.3 (1188272-2256085)x1

arr hg 19 The analysis was by array-CGH 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 pairs numbers may be adjusted

17p13.3 (1188272-2256085)x1 The chromosome involved in chromosomes 17 in the region p13.3

The base pairs between 1188272 (around 12 Mb) and 2256085 (around 22 Mb) have been shown to be deleted. Take the first long number from the second and you get 1067813 (around 1Mb). This is the number of base pairs that are deleted. x1 means there is one copy of these base pairs, not two - one on each chromosome 17 - as you would normally expect.

## Age at diagnosis and first signs

The age at which 17p13.3 microdeletion has been diagnosed in individuals, ranges from approximately six months of age to 22 years old [Schiff 2010; Tenney 2010]. Reasons that children or adults were tested include developmental delay, birth parents with learning difficulties, 'failure to thrive' (when a child's current weight or rate of weight gain is significantly lower than that of other children of similar age and gender), growth restriction/short stature, unusual facial features, low muscle tone (hypotonia) or physical problems such as eye problems [Nagamani 2009; Schiff 2010; Tenney 2010; Unique].



loud noises. He has difficulty concentrating at school when there are lots of children making a noise in the classroom. Anxiety is a problem for him. He loves computers, music, playing with cars and going for walks in the countryside." 7 years

" Her behaviour issues subsided somewhat after she moved into an Assisted Living Home (with a licensed caregiver). She feels more independent and she enjoys her family more. We (her parents) are her legal guardians and conservators as she is somewhat impulsive and somewhat unable to make wise decisions. She is more accepting of this now that her Caregiver monitors the in-home daily living routine. She likes to watch TV and talk on the phone. She enjoys doing craft from time to time. She is also active in her church, gets out and enjoys recreation, movies and community events with a life coach or with friends." 28 years

## Sleep.

Children with 17p13.3 micro deletions seem to have variation in their sleep patterns and behaviour (please see quotes).

" Brooke was a terrible sleeper as an infant. She would nap all through the day but only for an hour or so at a time. She woke every few hours through the first year. She would never fall asleep at night without several aids - pacifier, white noise machine, vibrating toy, music etc - all at the same time. She was swaddled for the first six months or so. She has continued to be a slightly difficult sleeper but has gotten better overall. She does really well with a night time routine - dark lights, no TV, calm environment, warm bath, lavender lotion, snack and milk. It's her 'wind down' time. She still naps from about 1-3pm and sleeps at night from 8pm to 7am usually. She does not really wake any more at night, only occasionally." 2.5 years

" She is a good sleeper though there have been a few instances of her waking and not settling for up to five hours. She is a deep sleeper but if woken up fully she then is happy, but doesn't want to go back to sleep whatever time of night or early morning." 4 years

" He is a great sleeper!" 5 years

" When he was younger he always had a bad time sleeping and would wake up to eight times a night. He slept through the night from the age of five. Once he started school things improved. When anxious, he wakes at night a lot which makes life difficult." 7 years

## Puberty and fertility

There is little information on the experience of puberty in those with a 17p13.3 microdeletion. However one woman aged 28 has experienced an irregular menstrual cycle and was put on contraceptive medication to regulate this [Unique]. Another child went spontaneously into puberty after starting growth hormone treatment for growth restriction. He also had growth catch up [Ostergaard 2012].

There have been reports of adults with the microdeletion having children. One 38-year-old woman reported in the literature gave birth to two children who have both inherited her 17p13.3 microdeletion. However the three family members have differences in their symptoms and experiences, with the mother less affected than her two children. The microdeletion arose as a new event in the mother, and was not inherited from her parents [Bruno 2010].

An adult woman has had some psychiatric problems including depression and obsessive compulsive disorder (OCD) which is an anxiety disorder. She also has oppositional defiant behaviour (ODD) which is a disorder where children have disruptive behaviour particularly directed towards authority figures. She is currently on minimal doses of medication and sees a counsellor [Unique].

“ She is very happy and loving. She is very pleasant to be around. She does very well at playing by herself or with others. She has the occasional tantrum but nothing out of the ordinary. The only time she gets very upset is when you bring her inside from playing outside before she is ready. She enjoys books, puzzles, play dough, kicking and rolling balls, cars, drawing and anything with sounds/music/flashing lights. She’s very loving towards out dog and pets/hugs him often. She is very social and doesn’t seem to have any separation anxiety ” 2.5 years



“ At four years old, she is not very aware of danger. Strengths include music, social and friendliness (though no fear of strangers and will drag people to playroom). In play, tends to ‘flit’. She is very caring, loving, gentle and empathetic. She senses when people are sad and cuddles them. She is a very determined child and will hit and kick if she doesn’t want to do something. You usually have to

make something funny or get her toys doing it with her. She likes routine. She is quite emotional and can be tearful very easily (often with small issues e.g. doll falling out of buggy). She still uses crying as communication like when she wakes up in the morning and to get out of cotbed. She is sensitive to loud noises and gets distressed. She is very sensory minded - she finds out things by touching, pouring, digging etc e.g. feeling soil, pouring drink over tray to play with juice. ” 4 yrs

“ He is getting cheekier and funnier by the day. He is quite sensitive and emotional, and perceptive of others emotions. He is a good listener. Her enjoys riding his bike, playing outdoors, watching TV, computers, Lego, drawing and writing. He plays well on his own but is starting to play more with others as he develops. He has a great sense of humour. He is shy and doesn’t like the unknown, but is capable of working things out and getting comfortable with them. He is generally calm, polite and doesn’t have large emotional swings. He likes limited interaction with others, as shyness overrides. But with time he interacts well. He has possible sensory issues (possibly to noise?) but this is just something parents have noticed and it has not been explored by doctors. ” 4 years

“ He has challenging behaviour. Due to his sensory problems he can’t stand touch and can spit at people, punch and kick. He also can get sensory overload from hearing

## Emerging phenotype: what to expect

When only very small numbers of affected people have been identified, it is not yet possible to be certain what the full range of effects of the 17p13.3 microdeletion will be. The features that are most striking and most common at present are:

- Learning (intellectual) disabilities requiring extra support in school
- Speech and language delay
- Feeding problems as a baby
- Poor growth in the womb and/or as a child
- Short stature and slim build

Less common features are:

- Hypotonia
- Heart problems
- Genital anomalies
- Ear problems
- Eye problems
- Seizures

## Pregnancy

Many mothers carrying babies with a 17p13.3 microdeletion experienced no major problems in pregnancy, had an uncomplicated delivery and only discovered their baby was affected with the microdeletion after the birth

There were no problems reported in four out of 17 pregnancies and/or births of children with a 17p13.3 microdeletion. Intrauterine growth restriction or IUGR (babies whose growth in the womb has slowed resulting in babies that are smaller than expected for the number of weeks of pregnancy) was described in five pregnancies. One of these babies was found to have anomalies in the structure of the brain before birth [Schiff 2010].

Nine pregnancies were carried full term (between 37-42 weeks). Three births were slightly early (between 35-37 weeks), one baby was induced at 33 weeks because of IUGR [Tenney 2010] and one birth is described simply as ‘premature’ [Bruno, 2010]. One baby was born by Caesarean section for polyhydramnios (increase in amniotic fluid). One mother went into premature labour at 29 weeks and had medical treatment which halted the labour. She later went on to give birth at full term. One baby had a temporary irregular heart beat when he was still in the womb at 36 weeks of gestation, this fully resolved by the time the baby was born [Bruno 2010; Schiff 2010; Tenney 2010; Ostergaard 2012; Unique].

## Newborn

There is very limited information available on newborn babies with 17p13.3 microdeletions. Three babies were born with no problems [Unique]. One of these babies however became ill when he was about four hours old and was subsequently diagnosed with a complex heart condition (Tetralogy of Fallot, see ‘Heart Problems’ page 13). He required two operations within the first year of life to correct this [Unique]. One baby was born with a high palate and submucous cleft. Two other babies were born with submucous cleft palates [Nagamani 2009; Bruno 2010; Unique].

## Feeding and growth

Many babies with 17p13.3 microdeletions were born at or near term, and had a birth weight within normal range. Feeding difficulties appear to be common and often feeding problems commence at birth

Out of seventeen babies where the birth weight and gestation are both known, twelve had a birth weight within normal range. Five babies had low birth weight (less than 2.5kg or 5lb 8 oz at term) [Bruno 2010; Schiff 2010; Tenney 2010; Unique].

Newborn feeding difficulties have been reported in a third of the cases in the medical literature [7/21] [Bruno 2010; Schiff 2010; Tenney 2010; Ostergaard 2012] and in four cases out of seven in Unique members. One baby was born with a floppy larynx and required being nursed in a more upright position [Unique]. The hypotonia (low muscle tone) that affects some babies with 17p13.3 microdeletions can lead to difficulties with sucking and swallowing, and/or latching onto the breast.

“ She latched on well initially but wouldn't feed for long. It seemed like she would just get tired of sucking and give up. We had to 'force-feed' her every two hours – approx 2 ounces at a time- to get her to gain weight. She got better with the eating but never overindulged at all. She is now a very particular eater...she will not eat pasta or bread; also she will eat a whole lot of something for days and days and then never want it again (peanut butter and jelly, scrambled eggs etc). ” 2.5 years

“ She had a floppy larynx diagnosed at one month and was nursed in a more upright position.” 4 years

“ He was breast fed for thirteen months – he was very difficult and slow to feed. In the first few months he had quite concentrated top ups of formula from a small syringe just to give him a few extra calories. ” 5 years

“ He didn't feed very well by breast or bottle due to low muscle tone in his mouth. He had a naso-gastric feed tube fitted at 6 months (when he got pneumonia) and this was used on and off until he was 18 months old. Once he was able to eat, things got better but it was very messy and he needed distraction to help him eat because using his mouth muscles was very difficult. Now at 7 years he eats very well. ” 7 years

## Stature

Children with 17p13.3 microdeletions are often small and slight for their age

Most individuals in the medical literature (15/21) and four out of seven Unique members are described as having growth delay after birth. Some children were seen by a growth specialist and diagnosed with growth hormone deficiency. Six individuals were given growth hormone injections during childhood [Bruno 2010; Schiff 2010; Tenney 2010; Unique]. Two children in the literature were reported to have a good catch up rate with this treatment [Bruno 2010]. One 11-year-old boy had a bone age of eight years. After growth hormone treatment, he had growth catch up and went spontaneously into puberty [Ostergaard 2012]. Another individual had growth hormone treatment during childhood, but at age 22 is still small with a small head [Schiff 2010].

Some children with 17p13.3 microdeletion have a head size within normal range. However, four children in the literature are described as having macrocephaly (a large head) [Schiff 2010; Tenney 2010]. Two other children in the literature were described as having microcephaly (a small head) although these were also children who had growth delay, so the size of the head is in proportion to the body. One Unique child is small for his

implants to replace two missing permanent teeth [Unique].

-One child has hypothyroidism and is on medication at the age of four years [Unique].

-Regarding breathing issues in individuals with 17p13.3 micro deletions, one girl, aged four, needs an inhaler occasionally when the pollen count is high. Another girl aged eight has asthma. A four year old and a two year old have had had no breathing problems to date [Unique].

-Regarding the immune system, one adult with 17p13.3 microdeletions had low antibody levels and gammaglobulin injections as a child and required gammaglobulin injections between the ages of two years and four years old [Unique]. Two individuals reported in the medical literature have experienced recurrent infections [Bruno 2010].

-Occasionally, children with 17p13.3 micro deletions have had unusual body features. One Unique member, now aged 20, has a hairy spinal dimple. She was found to have spina bifida occulta. Spina bifida is a condition which may cause damage of the central nervous system. However spina bifida occulta is a mild form and rarely causes disability. Another boy also had a sacral dimple but had no problems associated with it. One eight year old boy in the medical literature had pectus excavatum (sunken chest) [Nagamani 2009; Unique].

-Two individuals have eczema [Unique].

## Behaviour

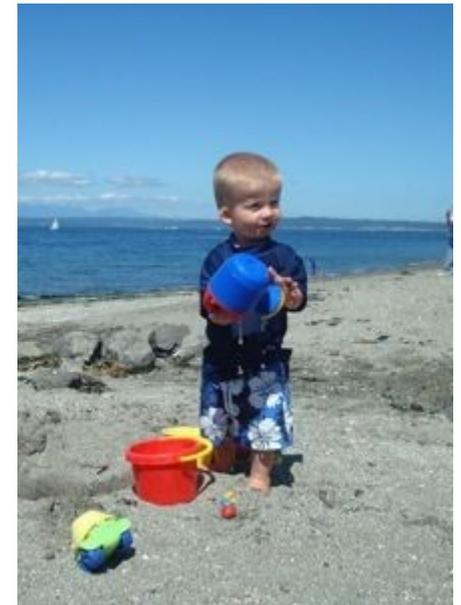
Children with 17p13.3 microdeletions can be caring and loving and have a very good sense of humour but they may also have behavioural problems

Children with a 17p13.3 microdeletion can be very sensitive towards others and extremely empathetic. However, they are as vulnerable to frustration as other children with a communication difficulty and some children can succumb to temper tantrums and aggressive behaviour. Behaviour can vary greatly; some children have no behavioural problems and others have severe problems.

In the medical literature, a third of individuals are reported as having no behavioural problems [7/21]. However one individual is described as having echolalia (a disorder where an individual repeats or 'echoes' what another person has just said). Another child has problems with concentration [Bruno 2010].

Among the Unique children, one child has been diagnosed with autism spectrum disorder (ASD) and severe behavioural problems [Unique]. ASD is a developmental disorder that is usually diagnosed in childhood. Autistic traits can include difficulty adjusting to a new routine or environment; poor social awareness and a lack of eye contact.

A seven year old boy has some challenging behavioural issues and autistic traits. He also



one of the children [Tenney 2010]. These can also be called atonic seizures. In a drop attack, the sufferer can fall to the ground. These children both had abnormal electroencephalograms (EEGs). This is a test which measures electrical patterns in the brain, and can sometimes help diagnose seizures.

### ■ Brain

Children with 17p13.3 microdeletions often have a brain magnetic resonance imaging or MRI scan. This is a non-invasive medical imaging technique which uses radio and magnetic waves to provide a very detailed image of organs, bones and tissues inside the body. Twenty individuals are known to have had an MRI scan of the brain. Of these, three children had a normal MRI and 17 children had an MRI which showed changes. The MRI in four children revealed a Chiari Type I malformation. Chiari malformations (CMs) are structural defects in the cerebellum, or the part of the brain that controls balance. Type I malformations often produce no symptoms, but if problems occur, then surgery can be required. One child described in the medical literature needed corrective surgery at the age of six years and eight months [Nagamani 2009; Bruno 2010; Schiff 2010; Tenney 2010; Ostergaard 2012; Unique].

### ■ Digestion

Two-thirds [4/6] of Unique children had experienced constipation. Family members have tried dietary changes and medication to help with this. One Unique child had reflux as a baby (gastro – oesophageal reflux where food and acid can come back up into the oesophagus or food pipe from the stomach and cause discomfort). She was given anti-reflux medication for several months but soon did not require it. There is no information in the medical literature on digestion problems.

“ She has constipation - we have tried increasing fluid and more fruit. ” 4 years 3 months

“ We used to give him a laxative to keep things freely flowing in the first couple of years. He doesn't have anything now and does not suffer from constipation. ” 5 years

“ We use a laxative regularly to help keep the bowels loose. He will only have a bowel movement once a week if he doesn't have some help. ” 7 years.

### ■ Limbs and Joints

Most Unique members [5/7] had no problems with limbs and joints. There are two Unique members with joint laxity (hypermobility). One of these individuals has a delayed bone age and low bone mineral density and takes calcium supplements [Unique].

In the medical literature, there is little information about limbs and joints. However there is a report of one individual with arthrogryposis of upper limbs (a neuro-musculo-skeletal disorder that affects various joints in the body causing stiffness, poor mobility or immobility and muscle fatigue) [Nagamani 2010; Ostergaard 2012].

“ She has hyperextensive knees and elbows and has dislocated her left elbow four times (from 12 to 18 years). The dislocated elbow was immobilised for weeks each time. ” 27 years

### ■ Other medical problems

It is important to remember that when only one person or very few people have been described with a medical concern, it may be coincidental, and not related to the microdeletion.

-One adult has experienced many dental problems. She has also required orthodontic

age at 7 years old and has a small head circumference [Ostergaard 2012; Schiff 2010; Unique].

“ It was at around 6 months old that her growth took a slight dive. We increased food, formula and vitamins which helped get her back on track. Brooke is slightly on the smaller side (around the 10<sup>th</sup> percentile) but not in any way that's out of the ordinary given my husband's and my weight and height. ” 2.5 years

“ She has a long torso and shorter arms and legs. ” 4 years

“ He is short and skinny. With the aid of growth hormone injections he has finally got back on to the lowest percentile of the height/weight charts. ” 5 years

“ Matthew is short with a slim build. ” 7 years

“ She is short for her age and saw a growth specialist for many years. ” 20 years

“ She had poor weight gain and growth hormone deficiency. She had Protropin (growth hormone) injections from three years to sixteen years. ” 28 years

## Appearance

Most children only have very subtly different facial features, if any at all. However there are some features described which can appear more commonly in these children. These can include laterally extended eyebrows (eyebrows that do not curve down), hypertelorism (wide space between the eyes) broad nose, slightly wider mouth, retrognathia (receding jaw), infraorbital folds (fold in skin below lower eyelid), low set ears, prominent forehead and eye ptosis (drooping eyelid) [Nagamani 2009; Bruno 2010; Schiff 2010; Tenney 2010; Ostergaard 2012; Unique].

## Development : sitting, moving, walking (gross motor skills)

Some children with a 17p13.3 microdeletion are delayed in learning to sit and walk. Many of those for whom milestones have been reported have had delays which means it may take a little longer for them to roll over, sit, crawl and walk. From the information that is available, babies rolled over between two months and 12 months (average 6.5 months); sat unaided between five months and 13 months (average 13 months); crawled between 10 months and 14 months (average 12 months) and walked between 12 and 36 months (average 20 months) [Schiff 2010; Unique].

Of 28 individuals with a 17p13.3 microdeletion, eight were reported as having hypotonia [Nagamani 2009; Bruno 2010; Tenney 2010; Unique]. Children with hypotonia generally find it harder to perform gross motor skills and so are more



likely to have delays in reaching developmental milestones.

“ She was late crawling and later walking. She has hypotonia which may have contributed. She now moves around really well but not quite as well as other 2½-year-olds. She climbs up into a chair or onto the couch with some effort. She continues to struggle with jumping, kicking and running. We do not have stairs but in other places she loves to go up and down the stairs. She still steps onto each step with both feet before going onto the next one. But if you hold her hand and help her, she will go up or down with one foot after another. She moves around outside well. She goes up the ladder of her play set with little effort, and even attempts to climb the mini rockwall. ” 2½ years

“ She moves around quite quickly! She is very slow with stairs. She is described as about one to two years behind depending on the area of development. She uses specialist equipment to help her, including a specialist high chair with hip pads, wide steps for using the sink and stools to get in and out of the bath. ” 4 years

“ He loves riding his bike and being generally active outside. His gross motor skills are good although his physical size and strength are below those of his age – but consistent with his size. ” 5 years

“ Matthew has low musculature in his mouth and body. He slumps at a table so needs support for feet such as a stool and cushions for his back. He walks with a forward gait. The K frame (walking frame) was fantastic to help him walk, especially outdoors. ” 7 years

“ Had previous developmental delay. Walked with help from 15 months and unassisted from 24 months. ” 19 years

“ She participates in Special Olympics bowling and swimming. She does not drive but is proficient in navigating the local public transportation system. ” 28 years



## Development: hand-eye co-ordination and dexterity (fine motor skills) and self care

From the limited information available, it seems that children with 17p13.3 microdeletions can sometimes have delays in fine motor skills

## ■ Genitourinary and Kidney

Minor anomalies of the genitals are common in babies with chromosome disorders, most often affecting boys. Out of seven Unique children, four have no genital anomalies. Two Unique children with 17p13.3 microdeletions have features which do not require treatment; one boy has a shawl scrotum (where the scrotum surrounds the penis, resembling a shawl) and a four year old girl has some ‘scarring’ above the tailbone and a longer than normal crease between the buttocks. There are three reports of baby boys who had undescended testicles at birth (cryptorchidism); one of these children underwent a corrective procedure when he was about one year old.

In the medical literature, several different genitourinary and kidney issues were noted. One baby boy had hypospadias (when the opening hole of the penis is not at the tip). Hypospadias can be surgically corrected if necessary. A 13-year-old boy was described as having an anteriorly placed anus (where the anal opening is in a slightly more forward position). He also had hydronephrosis (swelling of a kidney due to a back up of urine) and vesico-ureteric reflux (where the urine flows upwards from the bladder back up towards the kidneys, potentially damaging the kidneys). One girl had multiple bilateral urolithiasis (kidney stones) as well as an ectopic ureter (where the tube that carries urine from the kidneys to the bladder is incorrectly placed). She underwent corrective surgery for this [Nagamani 2009; Bruno 2010; Schiff 2010; Unique].

## ■ Heart

Heart problems have been rarely reported. Most people with 17p13.3 micro deletions that there is information on had had no heart problems [17/27]. Four children had had a patent ductus arteriosus (PDA). This occurs when one of the foetal blood vessels, the ductus arteriosus, does not close at birth. Occasionally a PDA requires no treatment but sometimes it can require medical or surgical treatment. One child required surgery for this at three years of age and, as an adult, has unexplained chronic pulmonary arterial hypertension (an increase in blood pressure in the vessels supplying the lungs) [Schiff 2010]. Two children had a patent foramen ovale (PFO). This is a hole between the left and right upper chambers of the heart that fails to close naturally soon after a baby is born. Most PFOs close spontaneously, but others may require medical or surgical treatment. One Unique child was found to have ‘holes in the heart’ (no other information available) and another child has a tiny VSD (ventricular septal defect – hole in the wall dividing the two larger chambers of the heart). She needs no treatment for this at present. Another little boy had Tetralogy of Fallot. This is a heart condition which requires surgery. This child had a temporary operation for this aged three weeks, then a successful full surgical repair at ten months of age. A third child has yearly heart check-ups. She has had a leaky heart valve and scar tissue, possibly from a healed hole in the heart [Bruno 2010; Nagamani 2010; Schiff 2010; Ostergaard 2012; Unique].

“ She has a leaky heart valve. She has to be more careful with infection as she is slightly more at risk of endocarditis (a infection of the heart). Her heart is misshapen but works normally. She has normal energy levels. ” 4 yrs 3 m

## ■ Seizures

Most Unique members with 17p13.3 microdeletions do not have seizures [5/6]. However one child has epilepsy. This seven year old child had a seizure at the age of three but he has not had any since [Unique]. In the medical literature, there are reports of epilepsy in two children, which takes the form of the head dropping down, as well as drop attacks in

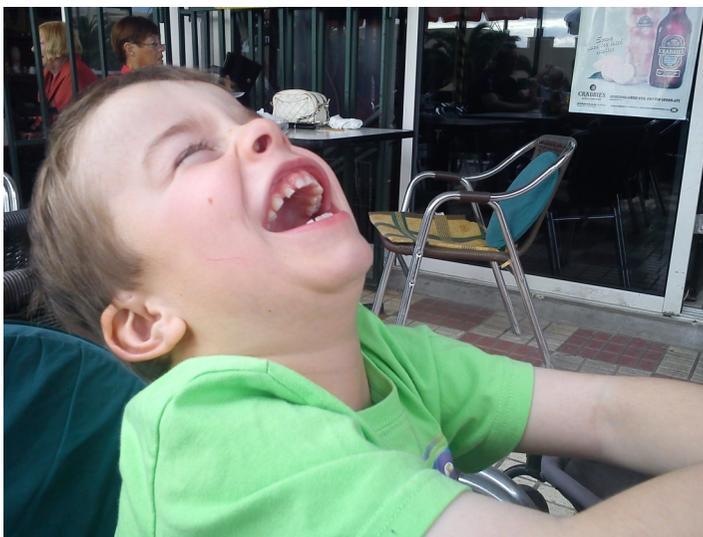
the curvature of the front surface, or cornea, of the eye which can cause blurred vision). One woman, aged 20, has strabismus (a squint) where one or both eyes can turn inwards, outwards or upwards. She has had three surgical procedures to try and treat the squint. She also has poor sight in that eye and wears glasses. A seven year old boy has nystagmus (involuntary eye movement) and a squint [Unique].

In the medical literature, eye findings which have been reported include coloboma (a developmental defect in the structure of the eye) [3/19], ptosis (drooping of the eyelid) [2/19] and epicanthus inversus (where the skin fold of the lower eyelid near the inner corner of the eye folds upwards) [1/19]. One affected individual has several eye findings including a coloboma, malformation of the eye, ptosis and microcornea (a small cornea, or transparent front part of the eye) [Nagamani 2009; Bruno 2010; Schiff 2010].

## ■ Hands and Feet

Individuals with 17p13.3 microdeletions may, in some cases, have hands or feet that look slightly different

The most common hand feature noted is clinodactyly (curved finger) of the fifth finger [7/28]. Other features noted in the literature include brachydactyly (short digits) [3/21] and narrow fingernails with broad digits [1/21]. One boy was found to have partial cutaneous syndactyly (a condition where there is partial joining together of the digits, but involving only the skin, not the bones) between the third and fourth finger on his right hand. Some individuals had more than one hand finding [4/21]. Overall, the pattern is of variable minor hand anomalies [Bruno 2010; Nagamani 2010; Ostergaard 2012; Unique]. There were fewer foot features noted. In the medical literature, there were two cases of medially deviating great toes (big toes that deviate towards the middle of the body); one of these individuals also had partial cutaneous syndactyly (partial fusion involving the skin only) of their third and fourth toe on his right foot. One person had had a club foot which had required orthopaedic care. Club foot or congenital equinovarus is a condition present from birth. The affected foot, or feet, usually points downwards and inwards but can point in other directions. Treatment includes physiotherapy and/or orthopaedic input, including surgery in severe cases [Bruno 2010; Schiff 2010; Ostergaard 2012].



Hypotonia can also affect fine motor skills in children with 17p13.3 microdeletions and they may take longer to reach for and grab toys and hold a bottle or cup. This can lead to delays in children being able to self-feed, dress themselves (zips and buttons can be especially problematic) and hold a pen to write or draw. Special chunky cutlery, cups with handles and cutting up food have helped some children. For those children who have problems holding and controlling a writing implement, mastering a keyboard or touch screen computer can often be easier.

“ Brooke receives occupational therapy but does rather well. She had a hard time holding her bottle by herself as an infant. She is currently working on using both hands during play – one to hold and one to manipulate the object. She eats pretty well with a spoon and fork, but there is some room for improvement. She cannot use scissors yet. She loves to play with PlayDoh™ and to colour, but holds the crayon in a fist, and only tends to draw lines or dots. She wears diapers all day and night and we are currently trying to introduce the ‘potty’. She does not dress herself independently but can help e.g. to put on her socks. ” 2.5 years

“ She can wash and brush her teeth at basic level. She can do some of her own dressing - tops if simple, trousers if loose and easy. She can't pull her socks on fully. If it takes too long, she will give up. She wears nappies full-time. ” 4 years

“ He is a little behind for his age with things like writing in terms of his control, but he is constantly improving...no help required with personal tasks like dressing or toileting. ” 5 years

“ Matthew is not in nappies but going to the toilet he often takes all his clothes off to get comfortable. He finds it difficult to wash his hands. We brush his teeth, he can't arrange his hand to direct the toothbrush correctly. He finds dressing difficult, we motivate him constantly to get this job done. All clothes need to be set out the correct way up for him to put them on. Two handed activities are difficult because he usually uses one hand for balance. He still cannot cut his food, so uses a fork to stab and spoon for scooping. He still needs help tilting yoghurt pots and getting the whole amount out of containers. ” 7 years

“ She is in charge of keeping her room tidy, which can be a challenge as organisation is difficult for her. She is able to do her own laundry with minimal assistance. She can cook a few simple things but does not like to use sharp knives or an oven. ” 28 years



## Speech and communication

Some children with 17p13.3 microdeletions have speech and language delay. Nine out of 28 of known children with 17p13.3 microdeletions have been reported as having a delay in language skills [Bruno 2010; Schiff 2010; Unique]. One child is described

in the literature as having mild speech delay, whilst another has speech delay and a speech defect. A third child spoke their first word at 40 months [Schiff 2010].

There are many reasons for speech delay, including hypotonia as well as the link between the ability to learn and the ability to speak.

“ She does not use words but started signing at about 2 years old. She can make many vocal noises, especially vowel sounds. She will often grab my hand and push/pull me in the direction of what she wants. She can sign words like ‘more’, ‘all done’, ‘help’, ‘open’. Signing has made the biggest difference in our lives. ” 2.5 years

“ She speaks but has a language disorder. Her speech is delayed by 18-24 months. She mixes words up, generalises using one word for lots of things, and is sometimes not intelligible...She sometimes still babbles especially if she wants to join in conversation, and puts random words together. ” 4 years

“ He started to talk at approximately two years. He was a little slow to start talking but again probably no more than a spread of kids his age...he now has full speech consistent with his age. ” 5 years.

“ Makaton [sign language] at an early age helped a lot. Picture communication, especially smiley faces and sad faces to express feelings, helps him a lot. Pictures of tasks such as hand washing, getting changed, going to the toilet, have really helped. At 7 years old, he needs help with making a conversation but can talk and read sufficiently. ” 7 years

## Learning

Learning (intellectual) disabilities are common in children with 17p13.3 microdeletions. Four children in the medical literature were described as having mild learning disabilities, three had mild to moderate learning disabilities and two had moderate learning disabilities (meaning an IQ between 50 and 70). One adult with moderate learning difficulties was working in a supervised environment [Nagamani 2009; Bruno 2010; Schiff 2010; Ostergaard 2012].

Of the Unique members, two individuals are described as having a severe learning disability (IQ below 50). A third member has mild to moderate learning disabilities and problems with comprehension. Another child, aged four, is estimated at being one to two years behind in learning ability. A child with a learning disability is likely to need some learning support and some children benefit from attending a special educational school. She has a full Statement of Special Educational Needs (SEN). A seven year old boy has learning disabilities with a learning age of four years. He has a SEN and a teaching assistant to help him. However one four year old boy does not have a learning disability and is at mainstream school with no learning support needed [Unique].

“ She has a good memory and will remember where she puts things, familiar people and places etc. She learns better when things are presented in a sing-song type way as opposed to just saying a word or pointing out an object. ” 2.5 years

“ She doesn't concentrate very well especially with conceptual problems or table top work/puzzles and she is not very aware of danger. ” 4 years

“ He is at the end of his first year of school. Recognising that he is a June baby and so is young for his class, his teachers rank him mid to lower half of the bottom half of the class. He is however able to access all of the curriculum and is at least keeping up with his peers and possibly catching them up. ” 5 years

“ He is at mainstream school and is doing well with a teaching assistant to help him at all times. He has learning difficulties and has to be shown things many times until he learns. He loves reading and computers. He reads lots of books with pictures. His drawing is at the age of a three to four year old (at seven years old). ” 7 years.



## Medical Concerns

### ■ Hearing

Some children with 17p13.3 microdeletions have ear problems

Generally speaking children have had normal hearing although young children sometimes have glue ear (a fluctuating temporary hearing loss caused by a build-up of fluid behind the eardrum). They usually outgrow this naturally. If the glue ear is persistent, tubes called grommets may be inserted into the eardrum to ventilate the space (middle ear) behind it and improve hearing.

Of seven Unique members with a 17p13.3 microdeletion, three children have currently experienced no problems with their hearing. A 20-year-old is described as having poor hearing. One eight year old is profoundly deaf and she has constant ear infections. She wears a hearing aid and has had grommets. A 28-year-old had been prone to moderate to severe chronic ear infections as a child and had had five sets of grommets between the ages of five to eight, but her symptoms improved after this age. A seven year old previously had recurrent ear infections and a perforated ear drum twice (a perforated ear drum usually heals with no problems). He has now grown out of having ear problems [Unique].

### ■ Vision

Two children have had no visual problems at the ages of 2.5 years and four years. However various symptoms have been reported in other Unique members. These include long sight (hypermetropia) in two children, one of whom needs glasses, whilst the other is being monitored to see if she needs them in the future. Another woman aged 27 has myopia (short sight) and requires glasses. She also has astigmatism (an irregularity in