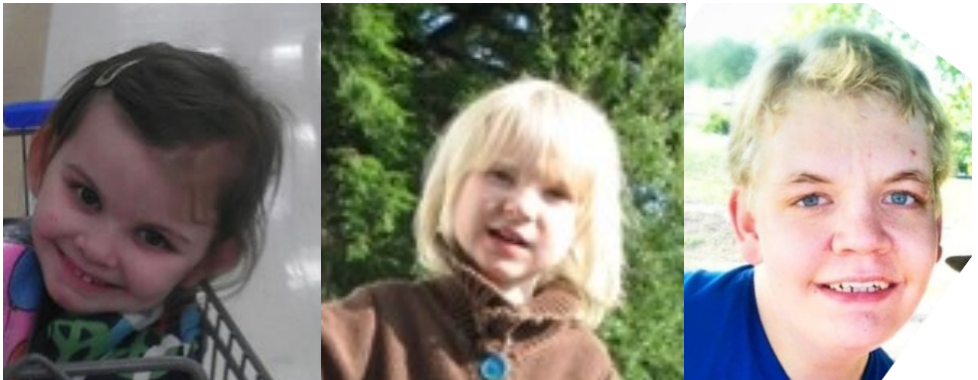




Understanding Chromosome & Gene Disorders

# 19p13.2 microdeletions



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

## Sources

The information in this guide is drawn from four sources: the medical literature, the chromosome database Decipher ([decipher.sanger.ac.uk](http://decipher.sanger.ac.uk)), the Unique members' database and a survey of Unique members. For 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 ([www.ncbi.nlm.nih.gov/pubmed/](http://www.ncbi.nlm.nih.gov/pubmed/)). If you wish, you can obtain most articles from Unique.

This guide mainly draws on detailed information from a survey of seven members of Unique conducted in mid 2012, referenced Unique. When this guide was written (Spring 2013), Unique had nine members (five female, four male) with a 19p13.2 microdeletion. This includes one surveyed member who has a deletion that extends into a small part of the neighbouring region, 19p13.13 (see also Lysy 2009). The nine Unique members range in age from 1 – 16 years old; the average age is 8 years old.

There are three people described in the medical literature (Lysy 2009; Haberlandt 2012; Wangenstein 2013). The Decipher database (July 2013) also lists 22 people with a 19p13.2 microdeletion. Sixteen of these do not have any other chromosome abnormality; of these sixteen, three have a 19p13.2 microdeletion that extends into the neighbouring regions of chromosome 19 (19p13.13/13.12). Medical information provided by Decipher and the published literature does not go into as much depth as the Unique member surveys.

## 19p13.2 microdeletions

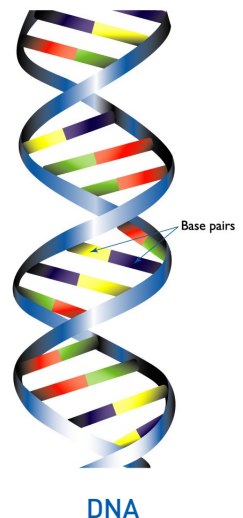
A 19p13.2 microdeletion is a very rare genetic condition in which there is a tiny piece of one of the 46 chromosomes missing. In this case, it is from the region known as p13.2, on chromosome 19 (see diagram on page 3). The absent piece of chromosome is very small and therefore is called a microdeletion.

Much of what is known about 19p13.2 microdeletions comes from studying people who have been referred for genetic testing. This may have been due to developmental delay, unusual behaviour or a health problem; occasionally the 19p13.2 microdeletion has been identified in someone else in the family. This gives us a biased sample. If we looked for the 19p13.2 microdeletion in the general population, we would have an unbiased sample but it is very difficult to do so. This means that we can't be certain about the cause and effects of 19p13.2 microdeletions. There is still a lot to learn but this guide contains the best information available to date.

## Genes and chromosomes

The human body is made up of trillions of cells. Most of the cells contain a set of around 20,000 different genes; this genetic information tells the body how to develop, grow and function. Genes are carried on structures called chromosomes, which carry the genetic material, or DNA, that makes up our genes.

Chromosomes usually come in pairs: one chromosome from each parent. Of the 46 chromosomes, two are a pair of sex chromosomes: XX (a pair of X chromosomes) in females and XY (one X chromosome and one Y chromosome) in males. The remaining 44 chromosomes are grouped into 22 pairs and are numbered 1 to 22



approximately from the largest to the smallest. Each chromosome has a short (p) arm, (from the French for small, petit) and a long (q) arm (see diagram on page 3).

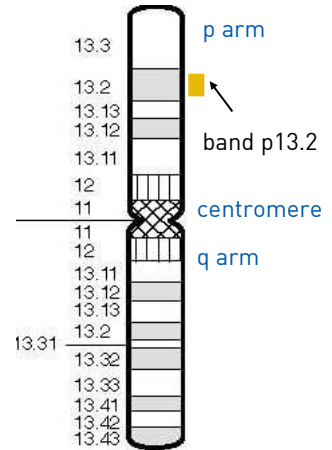
In general, the right amount of genetic material is needed for correct development – not too little and not too much. How an individual develops, his/her personality, needs and achievements, is influenced by both the genetic material he or she has and the environment in which he or she lives.

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

## Looking at chromosome 19p13.2

Each band of DNA (see diagram) contains millions of base pairs (Mb) that make up the genes.

The bands of chromosome 19 are numbered outwards from the point where the long arm meets the short arm. A microdeletion occurs when a small segment of a chromosome is missing. In individuals with a 19p13.2 microdeletion, a small amount of the short arm of chromosome 19 is absent. People with a microdeletion of band 19p13.2 have between 0.18Mb to 3.42Mb deleted. The average is 1.2Mb which accounts for less than 2 percent of the DNA on chromosome 19.



Chromosome 19

## Genetic testing

Microdeletions of chromosome 19p are too small to be seen using microscope-based techniques and are commonly less than 5Mb in size. Molecular DNA technology gives a more precise understanding of the size and position of the deletion. This is important as scientists identify genes and pinpoint their location on chromosomes.

### 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, disrupted or absent DNA. Unique publishes a separate guide to array CGH.

Modern genetic testing can reveal the precise nature of the deleted genetic material. A microarray genetic report will tell you the size of the deletion:

## arr[hg19] 19p13.2 (10275105 – 10871044) x1 dn

- arr** The analysis was by array (arr) comparative genomic hybridisation (cgh)
- hg 19** 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
- 19p13.2** The chromosome involved is 19, band 13.2 of the short p arm
- 10275105 – 10871044** The region from base pair 10275105 – 10871044 of the short arm (p) has been deleted. By deducting the first number for the second, you get 595,939. This is the number of base pairs that have been deleted (approximately 0.60Mb).
- x1** One copy of this segment of band 19p13.2, not two – one on each chromosome 19 – as you would normally expect.
- dn** de novo – Latin for new, meaning that the microdeletion has arisen for the first time in that individual and is not inherited from either parent. Some genetic reports will say ‘pat’ or ‘mat’ at the end, showing that the microdeletion is inherited from the father (paternal) or mother (maternal).

## Emerging phenotype: what to expect

Chromosome changes involving chromosome 19 are uncommon in live births and microdeletions have rarely been reported. No microdeletion or duplication syndrome is currently mapped to this chromosome. Only nine Unique members (from a database of nearly 10,000) have a 19p13.2 microdeletion.

Recently, several individuals with deletions on 19p were published in the medical literature; most of these were found on 19p13.3, 19p13.13 and/or 19p13.12. Two reports describe children with microdeletions that just include the 19p13.2 region (Haberlandt 2012; Wangenstein 2013) with one example which is mainly the 19p13.2 region but crosses over into part of the neighbouring 19p13.13 region (Lysy 2009).

As the number of affected individuals is so small, it is not certain what the full range of possible effects of the microdeletion is. The most consistent features are:

- **Feeding and growth** – infant feeding problems and/or failure to thrive. Often of short stature and underweight. Thin stature persists.
- **Delayed development** – occupational therapy can help with difficulties with motor skills; most children are affected, although fine motor skills (handling objects etc) may be more impaired than gross motor skills (walking etc)
- **Communication problems with speech delay in some children** - speech and occupational therapy are beneficial.
- **Behavioural/emotional disorders** – one or more of the following disorders is prevalent and often quite severe: autism, attention deficit hyperactivity disorder (ADHD), aggressive behaviour, obsessive compulsive disorder (OCD), anxiety and/or sensory processing disorder. These require significant extra support at home and school and medication.
- **Learning (intellectual) disabilities** – Learning disabilities are common in children with a 19p13.2 microdeletion. Although the level of impairment may vary, most have a moderate to severe learning disability. Behavioural disorders affect

children's ability to learn. Learning support is necessary, with a range of support needed depending on the level of learning disability and behavioural issues.

- **Sleep** – insomnia is common and often requires medication and/or sleep training.
- **Eyesight** - many children with a 19p13.2 microdeletion have eye problems and it is common to have a prescription that requires glasses.

These features are discussed in more detail below. The number of children with any particular feature may be given as, for example, six out of nine Unique members (6/9) or four out of nine people detailed on the Decipher database (4/9). Detailed information is not always available on all the known cases.

## Pregnancy and birth

The majority of children with a 19p13.2 microdeletion were born at term after uneventful pregnancies. Birth weights were frequently below average.

Unique members do not report any problems in pregnancy. Two Unique children were born early, one at 36 weeks and another at 36+2 weeks gestation; the latter was subsequently in the special care baby unit for several weeks. One Unique member had a difficult delivery at 38 weeks, as the baby's cord was wrapped around his neck twice. Despite this, his newborn wellbeing scores (the Apgar score – see below) were good. Babies with a 19p13.2 deletion were born with weights in the range of 1.67kg (3lb 10oz) – 3.65kg (8lb 1oz). The average birth weight of nine babies was 2.69kg (5lb 10oz) (Haberlandt 2012; Unique). Two Unique members noted that their child's birth weight was significantly lower than an unaffected sibling. Small babies were sometimes detected *in utero*:

“ At around 22 weeks of pregnancy, during a detailed routine scan, it was commented upon that he looked small. His birth weight was much smaller than his brother, 3.03kg (6lb 10oz) versus 3.71 kg (8lb 3oz) ”

In the medical literature, one child had a normal birth weight (Wangensteen 2013), whilst two others had intrauterine growth restriction and were born with low birth weights of 1.8kg (4lbs) and 2.79kg (6lbs) respectively (Lysy 2009; Haberlandt 2012).

## Newborn

Children with a 19p13.2 microdeletion do not always have detectable signs at birth.

A newborn's physical condition is evaluated using the Apgar scoring system which monitors heart rate, breathing, muscle tone, response to stimuli, and skin colour. Measurements are made at one and five minutes after birth; ten is the ideal maximum score. Apgar scores were generally reported as being high, nine or ten, although one newborn's first score was two at one minute, followed by a score of nine at five minutes. One baby was jaundiced at birth; another newborn was slightly jaundiced looking but testing was negative. In early infancy, this baby was also floppy.

Four Unique members commented on their baby's difficulty feeding. In one case, this resulted in weight loss and difficulty gaining weight.

“ She had trouble nursing – she choked and spit up through her nose a lot ”

One baby had a suspected high palate which did not affect feeding. Another had a submucous cleft palate (which was repaired at 5 years old). This is a type of cleft palate (split in the roof of the mouth) where the cleft is covered over by the lining (mucous membrane) of the roof of the mouth. This covering of the mucosa makes the cleft difficult to see when looking in the mouth.

One newborn was sleepy for a few days after birth. His eyes were puffy and he didn't really open them for a few days. At night he was snuffly and slept propped up. Sleeping problems were particularly highlighted in one newborn (see under 'Sleep', p 18).

Another baby had a visual developmental delay and gained sight at three months (Unique).

## Feeding/digestion

Children with a 19p13.2 microdeletion sometimes have swallowing/feeding difficulties in the early months and years, with slow weight gain as infants. A diagnosis of sensory processing disorder may influence attitudes to food.

Seven out of nine Unique members describe problems with feeding. Of the remaining two, one child eats well at 30 months and another, at eight years, is almost exclusively vegetarian. Breastfeeding was not always possible, with four members describing difficulties, particularly in the two Unique babies who had a cleft palate and a tongue tie (a congenital anomaly in which the mucous membrane under the tongue is too short, limiting the mobility of the tongue) respectively.

Two children had difficulty swallowing. One child had problems swallowing when breastfeeding and then later found swallowing from a 'sippy' cup or a regular cup difficult. At 3 years, 4 months another child was described as having dysphagia (difficulty swallowing) and also found it difficult to chew. Swallowing difficulties can increase the chance of aspiration (inhalation of food).

People who have difficulties feeding can benefit from a gastrostomy. One child was hospitalised twice for malnourishment before four years of age and was fed entirely by gastrostomy tube (Unique). This is a thin, flexible tube that passes through the skin of the abdomen into the stomach, allowing direct feeding into the stomach with specially made liquid food and water. At six years old, she is fed thickened liquids by mouth (Unique). Severe gastro-oesophageal reflux disease (GERD) was also diagnosed at birth in this child. This is a condition in which the stomach contents (food or liquid) leak backwards from the stomach into the oesophagus (the feeding tube from the mouth to the stomach). The reflux was treated by a surgical procedure called Nissen Fundoplication which tightens the poorly functioning valve (sphincter) at the join between the oesophagus and stomach. Three other Unique members report reflux, two of milk but not food. One had severe projectile vomiting up to 2½ years old but gradually grew out of it.

Swallowing difficulties as an infant/toddler may extend to strong food dislikes as an older child. At seven years, one child is a very picky eater and doesn't like consuming foods with an extreme texture – nothing mushy or anything with more than one texture combined.

This may also be related to sensory processing disorder (see Behaviour, p 11-15) or a medical concern.

**“ As he got older he only liked soft foods, I didn't think he would ever get off baby food. Sensory integration therapy helped tremendously ” - 16 years**

Two Unique members have chronic constipation; one started having this at 5 years old and still has it at 16 years. Diet and medication are beneficial. One child has been diagnosed with coeliac disease. Another has shown signs of this (Unique).

## Growth

Children may have a short and/or thin stature.

Two people on the Decipher database had a prenatal short stature, partially reflecting the low birth weights that are often a feature. Four Unique members were described as

'failure to thrive', a phrase which describes children whose current weight or rate of weight gain is significantly lower than that of other children of similar age and gender. Growth and height measurements can be plotted on a chart to show the normal range; the average is on the 50<sup>th</sup> centile (percentile), with larger measurements going up to the 99.6<sup>th</sup> centile and smaller measurements going down to the 0.4<sup>th</sup> centile. One child was diagnosed with failure to thrive at three months. At 3½ years she was still off the lower end of the growth charts. By 6½ years she was between the 10<sup>th</sup> and the 25<sup>th</sup> percentile. She appeared small for her age and had thin poor muscle tone throughout her body; medication was started to help build muscle strength.

Another child was below the growth line for children her age at seven years. Although she has grown at her own rate, she's described as muscular and strong.

“ She is very small. Her weight was on the 0.4<sup>th</sup> centile at 3 years 3 months of age. Now, she is slim and has a short stature. Her weight is on the 25<sup>th</sup> centile and her height is on the 9<sup>th</sup> percentile ” – 7 years

“ She is short (4'8") and has not grown in five years ” – 16 years

At the age of nearly five, one child described in the medical literature was between the 3<sup>rd</sup> and 10<sup>th</sup> centile for height and he was between the 25<sup>th</sup> and 50<sup>th</sup> centile for weight (Haberlandt 2012). Similarly, another child was small in stature and weight at 3 years, 8 months (Lysy 2009). In contrast, the third child was morbidly obese from an early age, resulting in gastric band, and subsequently gastric bypass, surgery in her 20s '(Body mass index (BMI) is defined as weight in kilograms divided by height in metres squared; someone is considered morbidly obese if their BMI is over 40). Her obesity was attributed to the deletion of two genes (reistin and the insulin receptor) involved in the processing of sugar in the body. These are found on a part of chromosome 19p13.2 (7.2Mb to 8.0Mb), that was only deleted in this individual and did not overlap with any of the other deleted regions of 19p13.2 described in this Unique booklet (Wangenstein 2013).

Differences in height and weight may reflect the range seen in the population as a whole and individuals with the 19p13.2 microdeletion can be within normal ranges. One 16 year old boy was described as being tall and slightly overweight (5'10" tall, 190lbs). Similarly three people on the Decipher database have a tall stature.

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

There may a degree of delay in acquiring some gross motor skills.

Some parents do not describe any issues with gross motor skills and one stresses that gross motor skills (and fine motor skills) are good. Others report a delay in, for example, learning to walk.

Typically-developing babies, who don't have a chromosome disorder, generally sit unaided at around 7 months and walk on average at 13 months (age range 9-18 months). Where information is available (6 children), the average age of sitting in children with a 19p13.2



microdeletion is 7½ months, with an age range of 6-10 months. Walking happens slightly later than unaffected babies, on average at 17 months, with an age range of 16-21 months.

In other children, a delay in walking is more pronounced. One was not walking at 2½ years. At 19 months, a child who was not yet walking had developed a fear of sitting unaided. He was crawling but walking was delayed until 3½ years old. A walker aided his confidence. At four years old, he is still unstable with a 'dodderly' gait but he is good at climbing frames, stairs, ladders etc which he enjoys.

Hypotonia (low musculature) is not common in Unique members but one child in the medical literature was described as having muscular hypotonia (Lysy 2009).

Another child has been diagnosed with developmental co-ordination disorder (DCD), a condition where children do not develop normal motor co-ordination (co-ordination of movements involving the voluntary muscles). This is usually first recognised when a child fails to reach such normal developmental milestones as walking or beginning to dress him- or herself. Dyspraxia is one type of DCD, affecting movement and co-ordination. As an infant, a Bumbo seat (a moulded floor-based seat) helped this child build trunk strength and stability and she has had physical and occupational therapy since she was three months old (Unique).

A delay in the development of fine and gross motor skills may still be evident in older children.

“ Sitting and walking are done fairly normally except for the use of ankle and foot orthotics (an externally applied device used to modify the structural and functional characteristics of the neuromuscular and skeletal systems) to help her walk. She is much slower and more methodical when it comes to climbing stairs. She also has trouble with walking bridges or ramps; they scare her and she freezes in place, screaming ” – 6 years

“ He has a broad gait. He can walk, jump and run but his running is very immature. He often bangs into things, possibly due to the fast speed at which he moves or possibly his poor spatial awareness. He has a Major Buggy for long distances and also for his own safety when we are outside the home ” – 7 years

“ She is a 'mover and a groover'. She moves almost non-stop (hyper some would say) and she moves fast and often carelessly (bumping into people and things) ” – 7 years

“ He can do what others his age can do but just not as co-ordinated or agile. He runs, walks, hops, balances and rides bikes etc ” – 16 years

In the medical literature, one child has mild motor delay (Wangensteen 2013). Another child started having physical and occupational therapy for developmental delay at 3½ years (Haberlandt 2012). A third individual didn't sit unaided until 15 months and was last reported as standing with help at 33 months (Lysy 2009).

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

Fine motor skills may be more affected than gross motor skills. Children with a 19p13.2 microdeletion may be behind their peers in some but not all skills. Toilet training is one example where children may need extra support.

Developmental delay is described to some degree or other in all Unique members and in the medical literature (Lysy 2009; Haberlandt 2012; Unique). One child has ataxia (a group of neurological disorders that affect balance, coordination, and speech) (Decipher).



Occupational therapy and physiotherapy are reported as beneficial, often from a young age (see 'Therapy' p. 22).



“ Chew toys, TheraTogs (an elasticated undergarment that can help control muscles and improve posture and mobility), weighted blankets, therapy swings and toys that help build fine motor strength and co-ordination have helped immensely ” – 6 years

“ She can hold things fine but struggles to draw, write, cut with scissors and do other fine motor tasks neatly or with accuracy. She has occupational therapy (OT) at school to work on fine motor skills ” – 7 years

“ He is very good at throwing, catching and kicking a ball and at cutting with scissors ” – 7 years

“ At 8 years, he learnt to tie his shoes ”

“ When he was a baby, he couldn't hold his bottle and couldn't use pincher grasp to pick up small objects. He is still clumsy with fine motor skills. Occupational therapy is useful! ” – 16 years

“ Like her gross motor skill, her fine motor skills are developmentally delayed, for example, holding a pencil, holding cutlery properly and using scissors. Pencil grips, dessert fork and a small spoon are useful ” – 16 years

Self care may be challenging for some children with 19p13.2 microdeletion (see Occupational therapy p 23) and is directly linked to their fine motor skill ability.

“ She can brush her teeth a tiny bit, but has a severe oral aversion and doesn't like her mouth to be touched. She can dress herself with the exception of buttons and some zippers. She still needs help with her shoes etc and can't do her own hair ” – 6 years

“ She can dress herself, put on her socks and shoes and brush her hair but she can't brush her teeth thoroughly or carefully ” – 6 years

“ He can clean his own teeth. He needs help with dressing and undressing but can put on his own socks and shoes ” – 7 years

“ She washes herself but needs help washing her hair. She can dress herself but cannot tie shoes ” – 16 years

Children are likely to be toilet trained later than their unaffected peers, although not much information is available.

“ She still wears diapers (nappies) day and night. She can use the toilet but chooses not to most of the time ” – 6 years

“ She is still in diapers at night ” – 6 years

“ He is still in nappies at night but is dry during the day ”- 7 years

## Speech and language development

Communication problems are quite common; many children have delayed speech development and ongoing difficulties making themselves understood. Speech and occupational therapy are beneficial.

Some children with a 19p13.2 microdeletion can begin speaking at 16 months of age. In others, speech is delayed, for a few months to several years, with first words at for example, 2½ or 3 years. In one case, speech began at 5½ years old. Some children may not speak very clearly, with three Unique members reporting that speech has a nasal tone to it. Selective mutism (when a person who is normally capable of speech is unable to speak in certain situations/environments) was reported in one Unique member who was also been taught American Sign Language (ASL) and evaluated for an augmentation communication device (a hardware device, often a handheld computer, that provides speech output for nonverbal users) to aid communication (Unique). Four Unique members use sign language, including Makaton (signs and symbols which help people communicate and designed to support spoken language).



“ She babbled at 2 years and began saying a few words around 3 years old. Now she has partial sentences, with 4-8 words most of the time. She is about 70% understandable to people who are familiar with her. Severe expressive language disorder [difficulty conveying information in speech, writing, sign language or gestures] limits her ability to communicate her knowledge. The quality of her speech is like a deaf 3 year old. She has had speech therapy since she was 3 months old. Communication is mostly using words but she has been immensely helped by sign languages and gestures, pictures (Boardmaker®) and an augmentative communication device ” – 6½ years

“ He can speak in broken sentences of five or more words. He finds some sounds very difficult so it’s not always

easy to understand him on occasions, particularly if it’s out of context. He’s having speech and language therapy for language delay. Two communication aids have been useful and continue to be: PECS [picture exchange communication system, a picture-based method to aid communication] and Makaton ” – 7 years

“ She uses full sentences and has a fairly strong vocabulary but often has trouble retrieving words or names that she knows (memory is a problem for her). She started talking at 3 years but it was difficult to understand her until about age 6. She does have a nasal quality to her speech ” – 7 years

“ His speech is somewhat understandable but has a ‘deaf’ tone about it ” – 12 years

“ He started talking at 16 months and is now very verbal with clear speech. He uses very complicated sentences with difficult words. He has a good vocabulary and a good grasp of proper sentence construction. Correction of speech errors at the time they occur helps the most, although it makes him mad! His speech therapist uses a reading fluency program called ‘Fast Forward’ that has helped his reading, speed, fluency and pronunciation quite a lot ” – 16 years

“ She was verbal from approximately 15 months and now uses full sentences with clear speech. She uses PECS at school to help her visualise her day and what is coming next ” – 16 years

Speech delay or ongoing problems with speech was also reported in the medical literature (Wangensteen 2013). One child, at 3 years 8 months, has no speech (Lysy 2009). Another 3½ year old was having speech therapy to aid communication (Haberlandt 2012).

## Behaviour

Children with a 19p13.2 microdeletion are often described as engaging, lively and humorous individuals. However, the majority have also been diagnosed with one or more behaviour disorders such as autism, ADHD or sensory processing disorder. These can be quite severe, requiring medication and significant support at home and in a learning environment. Anxious and/or aggressive behaviours are also common. Socially, children can be highly interactive or very withdrawn.

Parents regularly report challenging behaviour in children with a 19p13.2 microdeletion. For example, autism, or behaviour on the autistic spectrum, occurs in three Unique members. [Autism](#) is a lifelong developmental disability that affects how a person communicates with, and relates to, other people. People with autism have said that they struggle to make sense of the world - people, places and events - which can cause them considerable anxiety. Understanding and relating to other people is not as intuitive as in unaffected individuals.

Parents of Unique members describe life with autism and ways they have found to help their children:

“ A computer program that showed videos of children in different social situations has been very helpful, helping her to socialise and respond to people in different social situations. She learns better when she sees videos of people, rather than seeing people in real life ” – 6 years

“ Her autism is managed with consistency and routines. She has an after school worker to help her with social/life skills ” – 7 years

“ She tends to be quite rigid in her thinking. Shifting gears and transitions can be very difficult for her ” – 7 years

“ He is very repetitive and asks ‘what time is it?’ fifty times a day ” – 12 years

Attention deficit hyperactivity disorder (ADHD) has been diagnosed in four Unique members with a 19p13.2 microdeletion. This is the most common childhood-onset behavioural disorder and is often diagnosed in children who have no apparent chromosome anomalies. Those affected have a greatly reduced ability: to maintain attention without being distracted, to control what they're doing or saying (because they are impulsive) and to control the amount of physical activity appropriate to the situation, so they are restless and fidgety.

“ She can be hyper, impatient and angry ” – 6 years

“ She has a short attention span and is hyperactive and loud. She can have trouble slowing down when it’s time – taking care of her is often exhausting because her physical needs are so intense. She is impulsive and can get herself into trouble fast ” – 7 years

“ He is an extremely active child ” – 7 years

One child in the medical literature and one on the Decipher database were described as being hyperactive. One of these children also self-injures (Haberlandt 2012; Decipher). Behavioural difficulties are mentioned for four people on the Decipher database.

Three Unique members have been diagnosed with [sensory processing disorder](#) (SPD). ‘Sensory processing’ is a term that refers to the way the nervous system receives messages from the senses and turns them into appropriate motor and behavioural responses. In individuals who have SPD, there is a ‘neurological traffic jam’ that prevents certain parts of the brain from receiving the information needed to interpret sensory information correctly. A person with SPD finds it difficult to process and act upon information received through the senses, which can make countless everyday tasks difficult. People with SPD can be affected in only one sense – for example, just touch or just sight or just movement – or in multiple senses. One person with SPD may over-respond to sensation and find clothing, physical contact, light, sound, food, or other sensory input to be unbearable. Another might under-respond and show little or no reaction to stimulation, even pain or extreme hot and cold. Other children exhibit an appetite for sensation that is in perpetual overdrive.

“ He is very hyperactive. We have spent a lot of time addressing his sensory process needs and, in combination with medication, this is helping him to be on a more even keel. We have a sensory diet for him, involving regular squeezing, chewing, rolling and carrying of heavy weights ” – 7 years

“ She has always been an extreme sensory seeker – swinging as high and fast as possible and getting angry if you don’t push her high enough on the swing. But she also has a lot of sensory avoidance issues – tactile, oral and she is very sensitive to loud noises. She loves petting animals and just about crawls into their fur. She constantly wears hoods and hats, even if she’s sweating. She can’t stand tags or itchy clothes. She gets very upset when she has to tolerate bad smells and gags easily (even when the smells are not so strong) ” – 7 years

A diagnosis of [obsessive compulsive disorder](#) (OCD) is reported in two Unique members. Obsessive compulsive disorder (OCD) is a mental health condition where a person has obsessive thoughts and compulsive behaviour. An obsession is an unwanted, unpleasant thought, image or urge that repeatedly enters a person’s mind, causing them anxiety. The word “obsession” usually describes something enjoyable, but in OCD the obsession is unpleasant and frightening. A compulsion is a repetitive behaviour or mental act that someone feels they need to carry out to try to prevent an obsession coming true. For example, someone who is obsessively scared they will catch a disease may feel the need to have a shower every time they use a toilet.

[Anxiety](#) and [aggression](#) can be an issue for many children with a 19p13.2 microdeletion and [frustrated behaviour](#) is prevalent. One Unique member has been diagnosed with anger dysregulation disorder and Impulse Control Disorder (NOS).

“ She has very challenging behaviour, including hitting, kicking, biting, scratching and breaking things when she is upset (many times each day) ” – 6 years

“ When things aren’t going her way, she can be explosive – yelling for long periods of time, throwing objects and furniture across the room ” – 7 years

“ He is very loving but can also be very aggressive towards his main carers and continues to exhibit self-injurious behaviours like head banging and biting himself ” – 7 years

“ She is often anxious, has a short fuse and doesn’t tolerate frustration or boredom well ” – 7 years



Challenging or distressing behaviour may start young. At 19 months, one Unique member had developed a fear of sitting unaided which caused him to panic, sweat and grip the nearest thing to him. He seemed frustrated at not being able to do what others were doing in the toddler years.

Another Unique member started having severe rages from nine months, with extreme sensory issues and OCD behaviours. This worsened with age, requiring a period of residential treatment, before things improved with the right school environment and appropriate medication/therapy. In particular, although he was still OCD and oppositional, his rages diminished such that the family were able to go on holiday and he can sit through church.

“ We spend our time trying to keep him under control behaviourally. He seems to become immune to strategies, so we constantly have to come up with new ones. For all his behavioural challenges, psychiatric medications help more than anything else. You can’t reason with him or train him until he is acting more rationally with the medications ” – 16 years.

Children like to play with a range of toys from stuffed animals, puzzles and dolls to model trains, cars and construction kits. They also enjoy dressing up, handicrafts, computer games, watching TV and DVDs. Physical activities may be popular, like playing baseball (special needs league) and robust physical games for children with a need for sensory stimulus:

“ Her favourite, favourite activities are high-action, high-speed, outdoor time with a friend or her family – her dad pushing her on the zip line, spinning on a tyre swing, monkey bars etc. The faster, higher, jerkier the better and she squeals with delight ” – 7 years

Listening to audio books was reported by one Unique member to be a particular favourite. Several Unique members also report a particular love of music and/or animals.

“She enjoys playing with her sister and our mini-schnauzer ” – 6 years

“She loves animals, especially dogs, cats and horses. We have a dog and three cats, all of whom she adores ” – 7 years

**Socially**, children, and often any one child, can have a wide spectrum of behaviour from very withdrawn to overly friendly. Parents sometimes report the child's anxiety about social situations and their ability to handle social interactions. One child has been diagnosed with selective mutism. However, they're able to speak freely to close family and friends when nobody else is listening, for example when they're at home.

“ She is often shy with new people; other times she is inappropriately friendly with some people/strangers. On occasions she can go into her own little world where she doesn't want to talk or look at anyone for an entire day (at least 1-2 times per week). She is socially awkward but it helps when she has a peer nearby that she knows. She copies their behaviours in order to fit in ” – 6 years

“ He is very sociable but only if he instigates it. He hates been questioned himself but he questions everybody he sees about their lives and what they're up to. He likes one-to-one adult attention and enjoys helping with family chores most ” – 7 years

“ She loves people and is very outgoing. She will talk to anyone and is charismatic when she feels well but can have difficulty in her social interactions. She has a hard time answering questions or saying she doesn't know the answer to a question (she has deficits in memory and processing skills) so she often ignores a friend who is asking questions. She struggles with friendships – it's hard for her to reciprocate in conversations but she desperately wants to have friends. She gets fixated or 'stuck' in thoughts easily. She spends a lot of time in a fantasy world and it's often hard to 'reach' her. She often yells at me if I ask questions, especially toward the end of the day when she's tired. She tends to talk 'at' her friends more than 'with' them and seems to get easily over-whelmed socially. She prefers to play with one friend at a time. It was recently pointed out to us by a psychologist that she latches on to one friend, who becomes sort of a 'security blanket' for her. I have seen her be a bit smothering to her friends. The psychologist also pointed out that her friends tend to be the ones who are malleable and docile and probably go along with her agenda. He thinks her rigid nature and difficulty seeing another's perspective prevents her from having more friends ” – 7 years

“ She can be quite withdrawn and want to be alone. Although she enjoys adults more than her peers, she is excellent with small children ” – 16 years

“ He is very bossy and obstinate but I think he's just being a normal teenager! He requires me to be involved with him at all times and negotiates everything rather than just accepting my directions, both of which are draining. He doesn't seem to understand or recognise 'his place' when dealing with authority. He is too social and friendly; there are no boundaries for him. Although others seem to find it charming, it is embarrassing for us ” – 16 years

Various therapies and approaches are reported by Unique members to be beneficial in dealing with autism, ADHD, SPD and anxiety (see 'Therapy' p. 22). In severe cases, a hospital stay as a psychiatric patient may be required.

“ The behaviour can be very overwhelming but medication and behaviour therapy can hep immensely ” – 6 years

“ In school they have a reward system for teaching 'flexibility' and 'kindness'. If they get a certain number of stars, the entire class gets 10 minutes of extra recess. We are doing a similar reward system at home – it definitely helps to reinforce desired behaviours ” – 7 years

Although children with a 19p13.2 microdeletion can have challenging behaviour, parents often comment on their children's [endearing characteristics](#):

“ She is a very happy little girl” – 30 months

“ She has a fantastic personality. She is hilarious and can act out the silliest things when she can't use words to relay information. Her imagination is great and she has the biggest heart. She has made me a better mother and is my special gift from God. My life would not be complete without her” – 6 years

“ He has the most wonderful and cheeky smile. He engages people wherever he goes” – 7 years

“ She is so real, raw and expressive and very, very funny. When she loves something, she is full on in love, full of enthusiasm, passion and excitement. She gets excited about things that many of us would not. When she is happy, her enthusiasm can just fill up a room. She is also very sensitive and empathy just pours from her when someone she loves is hurt or distressed” – 7 years

“ He is very difficult to manage but he has made our family members better people through the experience” – 16 years

“ She is the most loving, gentle child we know. She is wise beyond her years and often people tell us she is an old soul” – 16 years

## Learning

Learning disabilities are prevalent in children with a 19p13.2 microdeletion, although the level of impairment may vary. Behavioural disorders can affect children's ability to learn.



Amongst Unique members, all parents report some level of learning disability in their children ranging from mild to severe, although most are on the moderate – severe spectrum. The most frequently-mentioned feature of a 19p13.2 microdeletion on the Decipher database is a learning disability. Learning problems may be accentuated if behavioural issues are affecting a child's learning. Similarly, a delay in language development can be influential. At the age of 30 months, one child had a neurodevelopmental evaluation that revealed a mild learning disability. Intelligence quotient, or IQ, is an assessment of someone's ability to think and reason. A score of 100 means that, compared to people of the same age, you have an average intelligence. At

five years old, this child's IQ was 70, corresponding to an age of 3 years and 10 months (Haberlandt 2012). Another child, at nearly 4 years old, had no speech accentuating a global development delay (Lysy 2009). One Unique member had a verbal IQ of 63 and a non-verbal IQ of 89 at seven years old.

Where reading ability is discussed, parents report that their children started to read at between six and ten years old (Unique). For example:

“ She started reading at 6 years and can read but it is extremely difficult to know how much she knows because she is difficult to understand. She can read a few small words and can recognise large words like ‘adventure’.”

“ At about 7½ years, she is still working towards reading. Her reading is kindergarten level – letters, a few simple words and she has some ‘sight’ words memorised ”

Children are likely to need help with the execution and organisation of writing:

“ She had an advanced grip at young age but her overall strength was poor. We had to build her hand strength with lots of therapy ” – 6 years

“ She started drawing at 5 years and writing at 6 years. She draws people though her drawing is quite messy. She can write letters, though they are pretty disorganised ” – 7 years

Learning support is often described as highly beneficial and parents place emphasis on getting that in place at an early age. Many have an individual education plan (IEP). This is designed for children with special educational needs (SEN) to help them to get the most out of their education. An IEP builds on the curriculum which a child with a learning disability is following, and sets out the strategies being used to meet that child's specific needs.

“ He has a moderate to severe learning disability. He is 2 years behind. We are in the process of getting a statement [of SEN]. He has difficulties with concentration. We have a good amount of learning support from local services ” – 4 years

“ Her cognitive abilities are not affected by the deletion but she has a difficult time learning because of the ADHD. Concentrating is difficult. She is extremely intelligent when it comes to computers and electronics - always wants to know what makes something work. She will attempt to take apart DVD players, computers, etc, to determine how they work. She has a learning disability and has an IEP. She enjoys reading and maths. It is more difficult for her to learn and she learns at a slightly slower pace than others her age. She has a great memory and remembers things through the use of patterns and routines ” – 6 years

“ She struggles with learning and has a moderate to severe learning difficulty. She is on an IEP and receives a lot of individual attention as well as small group learning for all subjects. Understanding and retaining information are difficult. She is well behind peers in reading, writing and maths. Her strengths are perseverance, determination and enthusiasm when she achieves a goal. Memory is an issue - she remembers things that are of great interest to her but struggles with memory in many areas - remembering names of people, places and things is a struggle. Concentration is difficult in all circumstances. She is in a co-teaching classroom where one of the teachers is a special ed. teacher (who is there 30 hours/week). She receives a lot of support in all areas (see also ‘Therapy’ p 22) ” – 7 years

“ He has a moderate to severe learning disability in all areas and has a statement of SEN. He has a good memory for people, names and places we go to regularly.



Concentrating is difficult. Learning is helped by one-to-one support, sensory input and medication. He can read his own name, count to ten, knows some colours and shapes and draw circles and squiggles ” – 7 years

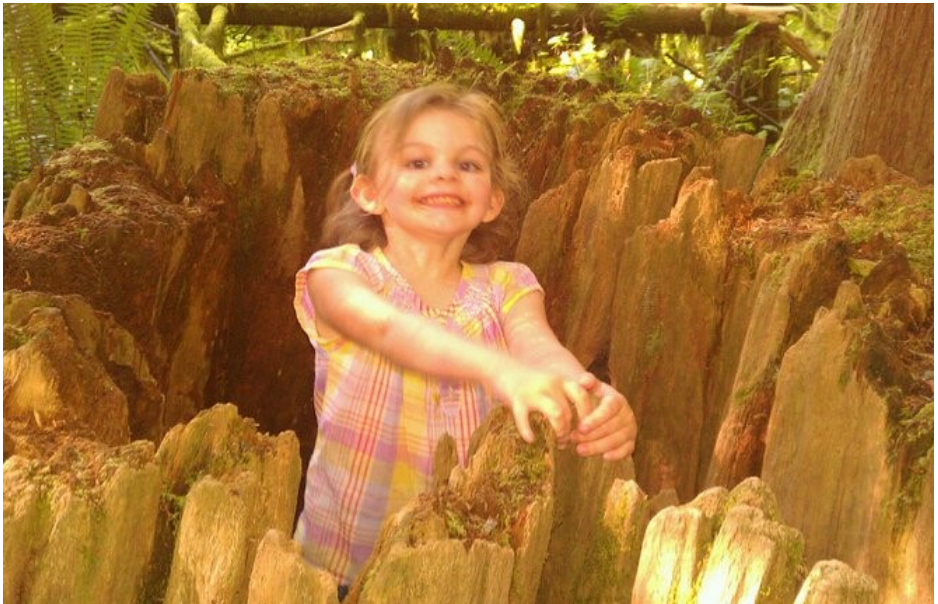
Learning aids can be a great support:

“ Social stories, visual aids, visual daily schedules and a timer, using manipulatives for math, hands-on opportunities, incorporating animals or animal sounds, making the abstract evident in concrete terms, keeping it simple, learning in small groups with peers, including movement and/or song, having frequent motor breaks throughout the day ” – 7 years

“ He learns better when shown something rather than given verbal instructions. He can recite the alphabet when looking at letters but not from memory. He can count to 12 except for number 7 ” – 8 years

“ At 16 years she is going into grade 11 and working at grade 2-3 level. She has an IEP and learning support, one-to-one aide plus a teacher in the classroom. She uses a computer to do school work. Her memory is not good but she is a visual learner. Repetition helps her learn. She is reading books like 'Diary of Wimpy kid' ” – 16 years

“ He has a moderate learning disability - he learns differently, but has the memory of an elephant! He started reading at 10 years old. Now (at 16 years old), he is working at an 8-10 year old level. His learning is helped by small classes, one-to-one instruction, positive teaching style and a firm behaviour management. He loves school and excels at math. He is a perfectionist. He loves calendars and music ” – 16 years



Schooling varies from child to child. Many are in mainstream school with provisions made for extra needs. For example, one teenager is in mainstream high (secondary) school (Grade 11 - equivalent to Year 10, GCSE year, aged 16 in the UK) doing Grade 2 studies (equivalent to Year 3 in the UK, aged 7 years) in a special program:

“ She is in a mainstream school in the regular first grade classroom. She goes to the special education room less than 20% of the time, mostly at snack-time. She has a full-time aide to help her because she has trouble learning without one-to-one support ” – 6 years

“ At aged 10 he went to a new private school. They were very firm with him when he misbehaved. Before that he couldn't read, write etc because he refused and raged. Within two months of starting at the new school he was sitting at a desk, participating, learning kindergarten and 1st grade material and loving school. At 14, he was up to 2nd grade work and loving school, reading, writing and doing 3 digit additions and subtractions. The school works individually with him at his level and speed ” – 16 years



One adult, with an uncommon deletion of 19p13.2, has a mild learning disability and, when given only oral examinations, completed a secondary school education with good grades (Wangensteen 2013).

## Sleep

Difficulties sleeping are an issue with at least half of children with a 19p13.2 microdeletion.

Sleep problems are common in children with this microdeletion, although parents do describe improvements with careful management and over time (Decipher; Unique). Sleeping problems ranged from difficulties falling asleep and staying asleep to getting up very early in the morning.

Regulating sleep patterns was difficult with one child at 3½ years old. Even with medication she was still waking up several times a night. Three years later, the medication is working well and she is more manageable at night:

“ With her doctor's help, we built a special bed with doors that lock, so she is safe at night and can't get out of the house. This turned out to be very soothing and she LOVES her special bed. If we travel and are away from the bed, she can't sleep without it. The insomnia has been one of the most difficult parts of this disorder (from our experience). It can be overwhelming, but there is help. Sleep specialists can help find a medication regime and a routine that can help your child sleep - it will give you peace of mind and help them relax and feel safe as well ” – 6 years

“ As a newborn, she didn't sleep for more than 45 minutes at a time. She had trouble falling asleep and staying asleep. She often swished her head back and forth on her pillow, almost violently, to go to sleep. She screamed when we put her down to sleep

on her back (the recommended sleeping position) and in her car seat. Now, at aged 7 years, she falls asleep easily and sleeps through the night. However, she wakes up between 4 and 4.30am most mornings and cannot go back to sleep. She spends her days very tired and collapses into bed at night. We've been trying to get her to at least stay in bed until 5am, using a clock that lights up when it's time for her to get up. Sometimes she can do this but it isn't really helping because what she really needs is to be able to go back to sleep" – 7 years

"She has always been a poor sleeper. She's been on medication (melatonin) since age 6 but still wakes very early, regardless of the time she went to bed. She sleeps for approximately 7 hours a night but has numerous awakenings" – 16 years

For some individuals, sleep is not an issue:

"He has always been a big sleeper. He sleeps 8-10 hours a night and he sleeps deeply. As a baby, he slept that much along with two 2-hour naps each day" – 16 years

## Medical concerns

Some of these features occur more frequently than in the general population, such as eye problems whilst with other features, such as the 'hole in the heart' and 'seizures, the small numbers involved means it is difficult to be sure that they are associated with the microdeletion.

### ■ Heart

Two Unique members had a heart murmur; one is described as innocent (the heart is working normally and there isn't anything to worry about) and the other was investigated but nothing abnormal was found. Heart murmurs are commonly heard, in the population as a whole, as an extra or unusual sound when clinicians listen to a child's heartbeat.

One Unique member had an atrial septal defect (ASD), also known as a 'hole in the heart.' This is a type of congenital (present at birth) heart defect, in which there is an abnormal opening in the dividing wall between the upper filling chambers of the heart. The hole may close on its own naturally, soon after a child is born, or (as is the case here) it can be closed surgically. One person on Decipher, and two of the three people described in the medical literature also had an ASD; one of these was described as not being of clinical relevance (Lysy 2009; Haberlandt 2012; Decipher).

### ■ Seizures

One Unique child has had one seizure, or fit, the cause of which is unknown. Another started having seizures at 18 months and at 16 years has intractable (hard to control) epilepsy. She has had a VNS device implanted to try and help. Vagus nerve stimulation (VNS) is designed to prevent seizures by sending regular, mild pulses of electrical energy to the brain via the vagus nerve.

In the medical literature, the first sign of the 19p13.2 deletion in one child was multiple seizures, although an EEG (electroencephalogram to show brain electrical activity) appeared normal (Haberlandt 2012). In contrast, another child has not had any seizures but a neonatal EEG revealed some abnormalities in brain activity (Lysy 2009).

## ■ Eyesight

Eight of the nine Unique members have eye prescriptions, including four for astigmatism. Eye problems are common in children with a 19p13.2 microdeletion. Four are long-sighted (hyperopia) and four have astigmatism. The main symptom of astigmatism is blurred vision. It occurs because the cornea at the front of the eye is unevenly curved (Haberlandt 2012; Unique). One child has also got ocular albinism (reduced pigment in the eyes causing poor eyesight) and nystagmus (uncontrolled movement of the eyes). Another has nystagmus in both eyes. Glasses are worn by many of these children (Unique).

“ He is very far-sighted and wears glasses. He had ‘lazy eyes’ and has had surgery to tighten the eye muscles, so his eyes are straight ” – 16 years

Two children have strabismus (a squint) (Lysy 2009; Decipher) and two other children are described as having a visual impairment, the precise details of which are not known (Decipher).



## ■ Feet and hands

One child has inward – turning talipes (clubfoot) which had corrected itself by nine months. Another child had ankle and feet orthotics (an externally applied device used to modify the structural and functional characteristics of the neuromuscular and skeletal systems) to help her walk. Two other children have very small hands and feet (Haberlandt 2012; Unique), one has short toes (Decipher) and one has deep skin folds in the feet and hands (Lysy 2009). A single strong line across the palm of the hand (single transverse palmar crease) was found in one child; this is commonly found in 5 per cent of people unaffected by a chromosome disorder (Decipher).

## ■ Facial features

Most children with a 19p13.2 microdeletion will not look different from other children or other family members. Some, approximately half, have slightly unusual features, such as: a prominent forehead, widely-spaced eyes or unusually-shaped/low set ears. One child has plagiocephaly (a flattened area of the head), which has been partially corrected with a DOC band helmet (an outer plastic shell with a foam lining, made specifically for each child. It works by applying mild pressure and directing the growth of the head. This method directs growth to the flat regions and discourages it in any prominent areas (Lysy 2009; Haberlandt 2012; Decipher; Unique).

## ■ Skeletal

One three year child had quite pronounced asymmetric pectus excavatum, a chest that is sunken inwards, such that one side of the chest is higher than the other; this was

reported not to affect their breathing (Unique). In the medical literature, an individual with a deletion extending into the neighbouring 19p13.13 region had a curved upper spine (kyphosis) and craniosynostosis (an irregularly-shaped skull). This child also had microcephaly, a small head, and arthrogryposis of the lower limbs (a neuromusculo-skeletal disorder that affects various joints in the body) (Lysy 2009). A curved upper spine is also reported in another child (Decipher). Scoliosis (a curved spine) and pectus carinatum (pigeon chest – protrusion of the sternum and ribs) occurs in one child, who has frequent fractures (Decipher).

**Other medical concerns** are described with low frequency, or occur quite commonly in the general population, and also may not be related to the microdeletion of 19p13.2.

Four boys have [hypospadias](#) (Decipher; Unique). This is a relatively common birth defect, affecting between 1 in 125 and 1 in 300 male babies. It occurs when the hole through which urine and semen leave the body is not located at the tip of the head of the penis. Surgery is sometimes used to correct the defect. Another Unique member had undescended testicles and double hernias. Surgery was performed at six weeks old.

One Unique member had developed [kidney stones](#) at six years and has about one stone a year. He has haematuria (blood in the urine), lowered kidney function and recurrent urinary tract infections, requiring antibiotic treatment. Small kidney stones (less than 5mm) can be passed in the urine; larger stones may need hospital treatment. For example, lithotripsy, high energy shock waves, can be used to break the stone into smaller pieces which can be passed painlessly in the urine. Another child has had [kidney cysts](#) recently diagnosed (at 16 years old) (Unique).

One child has mild [cerebral palsy](#) (Unique). This is one of a group of neurological conditions (affecting the brain and nervous system) that influence a child's movement and co-ordination. Cerebral palsy is caused by damage to the brain, which normally occurs before, during or soon after birth. A team of specialists, for example, speech therapists, occupational therapists, physiotherapists and a paediatrician may be involved in treating cerebral palsy.

Transient erythroblastopenia of childhood ([TEC](#)) was diagnosed in one child with a microdeletion of 19p13.2 (Unique). This is a slowly developing anaemia that occurs in early childhood and is characterized by an increasingly pale skin. The child was given a blood transfusion. As the name suggests, patients with TEC recover completely.

One teenager has had dysfunctional menstrual bleeding and has been diagnosed with [von Willebrand disease](#) (Unique). People with this condition either have a deficiency of a blood protein called von Willebrand factor, or this protein doesn't work correctly. It means that their blood doesn't clot properly and they are prone to bleeding. It is an inherited condition and 1-2 per cent (1-2 in 100 people) of the UK population has reduced levels of von Willebrand factor; however, only about 1 in 1000 people has symptoms that might require medical attention.

Two Unique members have [hypothyroidism](#), an underactive thyroid gland. This is a condition in which there is a reduced level of thyroid hormone (thyroxine) in the body. Various symptoms result, the most common being: tiredness, weight gain, constipation, aches, dry skin, lifeless hair and feeling cold. Hypothyroidism can be successfully treated by a daily tablet to replace the missing thyroxine.

Two children have high cholesterol. One of these also has low testosterone and coeliac disease (a common digestive condition where a person has an adverse reaction to gluten);

dietary changes are necessary) (Unique).

Two children have had pneumonia, in one case associated with a respiratory syncytial virus (RSV) infection. Recurrent upper [respiratory tract infection and/or ear infections](#) occurred in several Unique members. Grommets (ear tubes to treat glue ear, where the middle ear fills with glue-like fluid instead of air) were fitted to two children. Mild hearing loss is present in two Unique members, attributed to recurrent ear infections as a baby and as young children. One person on the Decipher database has a hearing impairment. In one case, speech development was affected but no sensorineural hearing loss (caused by damage to the inner ear) was evident. One child in the medical literature has a hearing impairment (Lysy 2009; Decipher; Unique).

[Seasonal allergies](#) are quite common and one child is allergic to some food stuffs, for example, nuts and milk protein (Unique).

## What were the first signs?

Some children may not have obvious signs of a 19p13.2 deletion when they are born (see 'Birth' and 'Newborn' sections p 5). In other cases, parents noticed there was something different early on. Within hours of birth, one mother thought something was not right. In several cases, unusual facial features were evident at birth. Birth weights are often low and babies may have feeding difficulties.

One child was unable to suck and had GERD (gastro-oesophageal reflux disease, when gastric acid from the stomach goes up into the oesophagus, causing discomfort and pain, known as heartburn). At three months, no developmental milestones had been met. Another Unique member described a 'stalling' of development at 10 months and deteriorating behaviour.

[“ I thought right from the word go something was wrong. Poor feeding and lack of weight gain led us to seek the doctor’s advice around seven months ”](#)

[“ Our midwife mentioned that she showed signs of being premature, despite being full term. She noticed that her ear cartilage was not fully formed and that the lines on the bottom of her feet were not fully developed. Also, our daughter’s digestive system was not well developed at birth. She was very colicky. Something seemed ‘off’ since she was born because she had trouble sleeping, was often irritable and fussy and seemed to be uncomfortable so much of the time ”](#)

In older children, failure to thrive, language/ developmental delays and challenging social and emotional behaviour may be the first indicators. In affected individuals, the age of diagnosis ranges from 3 months – 16 years old, with an average of 8 years old.

## Therapy/routine appointments

Regular therapy appointments are highly beneficial with ongoing work to develop skills in all environments.

A program of regular therapy appointments is reported by Unique members to be vital in coping with the different features of a 19p13.2 microdeletion. Many of these are covered in more detail in the relevant section above but illustrated below is an amalgam of some of the therapies used, their aims and outcomes and parents' comments on them. Parents often comment on the importance of collaboration between therapists, parents and other adults caring for their children and therefore the continuing development of skills in all settings – home and school etc.

**Speech and language therapy (SALT):** Speech and language therapists work with any child with a communication problem, whether this is linked to deafness or a learning disability. Eating involves similar mouth and tongue control to speaking and so speech therapy also helps if there are feeding issues. Speech therapy can be started as young as 3 months and has been reported by several Unique members to help with reducing the nasal tone of a child's speech.

“ Your child will have a great deal of frustration because people can't understand what they are saying. People automatically treat them like a baby, when they may function at a 'normal' level for their age. Imagine how difficult it would be if people used baby talk with you whenever you tried to talk to them. This is likely to be a lifelong issue for our children and patience and a willingness to try new methods (sign language, PECs , augmentative communication etc) will be key. My daughter could sign a couple of hundred words before she could put two spoken words together. She could sign at 9 months! ” – 6 years

“ She has had speech therapy since the age of two years to improve articulation and organisation/processing of information. Articulation is much better and there is slow, steady progress in other areas ” – 7 years

“ He is still behind but has made huge progress with his speech ” – 16 years

**Occupational therapy (OT):** Occupational therapists work with children to increase their ability to cope with the tasks presented by everyday life. Their work not only covers areas like dressing but also less obvious ones like writing skills and difficulties with perception. Occupational therapy improves fine motor skills, self-care skills and can also help deal with sensory processing disorder and attention span issues. It can be beneficial into the teenage years.

Occupational therapists (and physiotherapists) may use aids such as TheraTogs. These garments are designed to be worn directly on the skin, out of sight under clothes. When snugly applied, the TheraTogs garment comfortably and gently 'grips' the skin surface; the appropriate application of straps influences movement, stability, posture and gait.

“ We used Theratogs, chew toys and sour candy to help calm her down and brushing therapy to help her desensitize her hands and feet. She enjoys a weighted blanket and we also have a therapy swing in our house ” – 6 years

“ For the sensory issues, occupational therapy helps the most. We keep head phones handy for loud noises (movies, concerts, fireworks etc) ” – 16 years

“ He does things I never thought he would, like ride a bike ” – 16 years

**Physiotherapy:** Physiotherapists use exercises to help people gain and keep the best possible use of their bodies. Unique members have reported that physiotherapy has improved gross motor skills and, for example, balance.

**Behaviour therapy/Psychotherapist/Psychologist/Psychiatric nurse/ Psychiatrists:** Challenging behaviours can be addressed with specialist practitioners who deal with behavioural, psychological and emotional problems. There is some overlap between their different roles (although only a psychiatrist, a medical doctor, can prescribe drug-based treatments).

They can help parents understand the underlying reasons for their child's behaviour and teach parents behaviour modification techniques to try to change and improve behaviour.

“ She meets twice a week with a psychotherapist and weekly with a clinical psychiatric nurse to work on social thinking, impulse control and anxiety issues. We also reinforce with social stories and the social thinking vocabulary at home. We just put all this into place, at 7 years old, and are trying to do it across settings, so she learns to ‘generalise’. It seems to be helping her learn a lot of things (especially social thinking) that most kids pick up naturally, but she doesn’t ” – 7 years

**Music therapy:** Music therapy is an established clinical discipline which is widely used to help people whose lives have been affected by injury, illness or disability. It is particularly useful in situations where communication is difficult.

“ He has had music therapy since the age of six and loves it. He is learning to play the guitar ” – 16 years

Routine medical appointments that form part of the life of a family member with a 19p13.2 microdeletion include: paediatrician, psychiatrist, geneticist, neurologist, gastroenterologist, sleep specialist, and possibly a cardiologist, nephrologist, allergy specialist and/or a nutritionist.

## Helping other parents

Parents of children with a 19p13.2 microdeletion have provided comments and advice that helped them, particularly when their child was first diagnosed:

- It is what it is and giving it a name doesn’t make it suddenly appear. It’s been there all along.
- I wish I had known when she was first diagnosed how much she would grow and learn in just a few years, how much potential she had and that the difficult years (behaviourally) would become more manageable and that medications were out there to help.
- Now, I understand that she can be volatile because she simply doesn’t have the skills (cognitive and or social/emotional) to handle certain situations. I wish I had known that long ago.
- The disorder does not make the child who they are; it is only a piece of them. Continue to live each day to its fullest and treat symptoms as they arise.
- Be patient! They can feel your frustration and it just makes them more frustrated. Don’t feel bad about taking a break (or a lot of breaks!) when you feel overwhelmed. They need patience because they have none. They will learn *it* from you! Once you get the hang of your child’s quirks, they will bless you in ways you never imagine. Every smile, every hug is a gift. They tend to do things on their terms and you will learn to go with the flow.
- This is a marathon, not a sprint. Pace yourself!

## What is the outlook?

We can’t be sure yet but there appears to be no reason why people who are healthy should not enjoy a normal lifespan. Many children who have learning and developmental disabilities in conjunction with behavioural issues do not appear to have major health problems.

## Puberty and Fertility

Only two Unique members have been through puberty and there are no reported cases of children born to someone with a 19p13.2 microdeletion.



One 16 year old girl started menstruating at aged 11 years. Another female, of unknown age, has secondary amenorrhea; this occurs when a woman who has been having normal menstrual cycles stops getting her periods for six or more months. A 16-year-old boy has low testosterone and is on testosterone injections to correct this imbalance (Decipher; Unique).

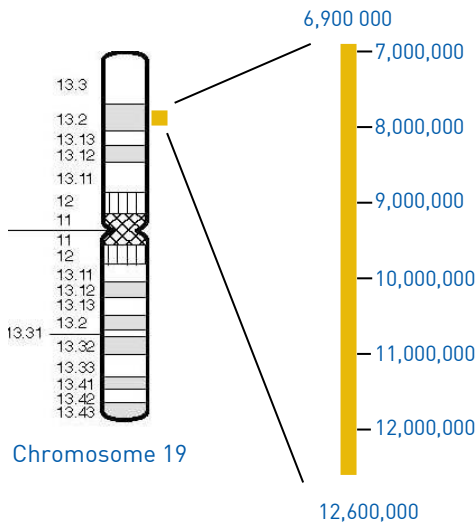
## Ongoing research involving 19p13.2

The 19p13.2 region is located between 6.9Mb and 12.6 Mb on chromosome 19 (see diagram). The variation in size of the microdeletions (0.18Mb – 3.42Mb) within this region can mean anything from 7- 96 genes can be missing (see diagram below). Candidate genes that might play a part in the features associated with 19p13.2 microdeletion include:

Insulin receptor and resistin: genes that could predispose to obesity as they regulate glucose (sugar) metabolism.

*PDE4A* – an enzyme that has been linked to conditions that affect the brain such as: Alzheimer’s, Parkinson’s, bipolar disorder, mild learning disabilities, autism and depression.

*S1RPF*, *CDKN2D* and *AP1M2* – involved in the development of the brain (Haberlandt 2012; Wangensteen 2013)



Some genes (and their base pair position) located on 19p13.2:

*PDE4A* (10,430,645-10,441,307)  
*CDKN2D* (10,538,138-10,540,655)  
*AP1M2* (10,544,347-10,558,991)

As this is a gene-dense region, there are likely to be a number of different genes involved; the precise size and location of the deletion (see diagram) will govern which genes are deleted. It is also important to remember that, while identifying the gene(s) responsible for certain features of 19p13.2 microdeletion is valuable and may help guide future studies, it does not lead directly to immediate improved treatment. In addition, even if a gene is missing it does not always mean that the associated feature(s) will be evident or that there is a direct relationship between an absent gene and a particular feature. Other genetic and environmental factors often have a role in determining the presence or absence of a particular feature.

## Why did this happen?

A blood test to check both parents' chromosomes allows parents to find out how the 19p13.2 microdeletion occurred. The child may have inherited the microdeletion from a mother or a father. However, in the cases where both parents have been tested, the microdeletion occurred when both parents have normal chromosomes. Geneticists call this '*de novo*', which means 'new'. *De novo* 19p13.2 microdeletions are caused by a change that occurred when the parents' sperm or egg cells formed, or possibly during formation and copying of the early embryonic cells when the egg and sperm joined.

All reported cases so far (in the medical literature, listed on the Decipher and Unique databases) are *de novo*, or of unknown genetic origin.

There is nothing that you, as a parent, did to cause the microdeletion, either before or during the pregnancy. Parents should feel reassured that no lifestyle change – environmental or dietary – would have prevented it from occurring.

## Can it happen again?

Where both parents have normal chromosomes, it is unlikely that another child will be born with a 19p13.2 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 19p13.2 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 19p13.2 microdeletion has been inherited from a parent, the possibility of having another child – either a girl or a boy – with the 19p13.2 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.

## References

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# Notes

# Inform Network Support



Understanding Chromosome & Gene Disorders

## Rare Chromosome Disorder Support Group,

The Stables, Station Road West, Oxted, Surrey. RH8 9EE. UK, UK

Tel: +44(0)1883 723356

info@rarechromo.org | www.rarechromo.org

There is Facebook groups for families affected by 19p13.2 deletions:

[www.facebook.com/groups/411622222210614/](http://www.facebook.com/groups/411622222210614/)

## 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/donate](http://www.rarechromo.org/donate)

Please help us to help you!

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.med. D. Kotzot, Sektion Humangenetik, Innsbruck, Austria.

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