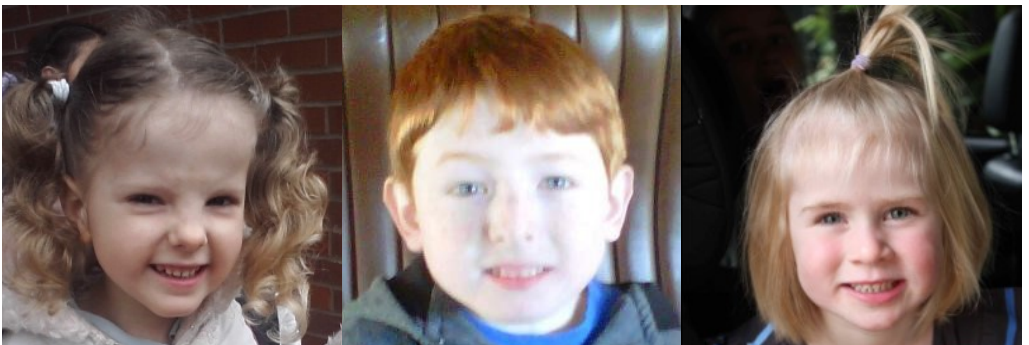




Understanding Chromosome & Gene Disorders

# 2q23.1 microdeletion syndrome



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

## Sources and references

The information in this guide is drawn partly from the published medical literature. The first-named author and publication date are given to allow you to look for the abstracts or original articles on the internet in PubMed (<http://www.ncbi.nlm.nih.gov/pubmed/>). If you wish, you can obtain most articles from Unique. In addition, this leaflet draws on information from a survey of members of Unique conducted in 2013, referenced Unique. When this guide was written in April 2013 Unique had 15 member families with a microdeletion at 2q23.1 ranging in age from a 1-year-old to a 13-year-old.

## 2q23.1 microdeletion syndrome

A 2q23.1 microdeletion is a rare genetic condition caused by a tiny missing part of one of the body's 46 chromosomes – chromosome 2. For healthy development, chromosomes should contain just the right amount of material – not too much and not too little. Even a tiny piece of missing material can disrupt development.

## Background on Chromosomes

Chromosomes are structures found in the nucleus of the body's cells.

Every chromosome contains thousands of genes which may be thought of as individual instruction booklets (or recipes) that contain all the genetic information telling the body how to develop, grow and function. Chromosomes (and genes) usually come in pairs with one half of each chromosome pair being inherited from each parent. Humans have 23 pairs of chromosomes giving a total of 46 individual chromosomes. Of these 46 chromosomes, two are the sex chromosomes that determine gender. Females have two X chromosomes and males have one X chromosome and one Y chromosome. The remaining 44 chromosomes are grouped in 22 pairs, numbered 1 to 22 approximately from the largest to the smallest. Each chromosome has a short or petit (p) arm (shown at the top in the diagram on page 3) and a long (q) arm (the bottom part of the chromosome).

## Chromosome Deletions

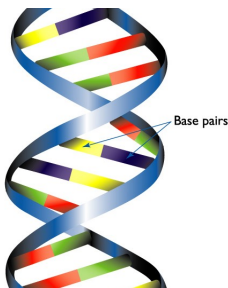
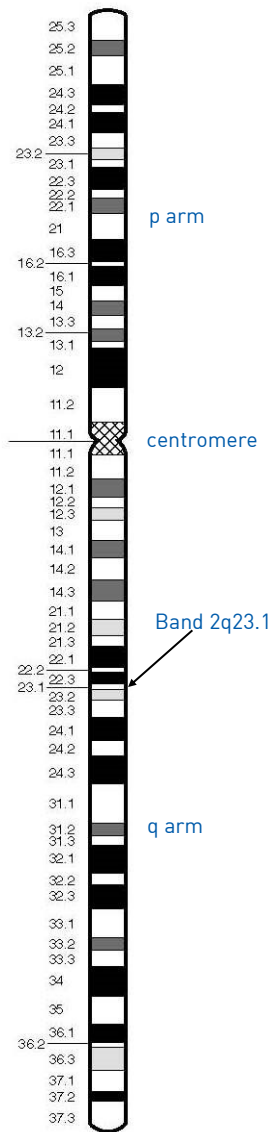
A sperm cell from the father and an egg cell from the mother each carries just one copy of each chromosome. When they join together they form a single cell that now carries two copies of each chromosome. This cell must make many copies of itself (and all the chromosomes and genetic material) in order to make all of the many cells that form during human growth and development. Sometimes during the formation of the egg or sperm cells or during this complicated copying and replication process, parts of the chromosomes can break off or become arranged differently from usual. People with a 2q23.1 microdeletion have one intact chromosome 2, but a piece from the long arm of the other copy is missing. Therefore it is believed that most of the clinical difficulties are probably caused by having only one copy (instead of the usual two) of a gene or number of genes from the missing piece. We are still learning the about the specific jobs or functions of the genes in

this region. It is important to keep in mind that a child’s other genes, environment and unique personality also help to determine future development, needs and achievements.

## Looking at 2q23.1

You can’t see chromosomes with the naked eye, but if you stain them and magnify them under a microscope, you can see that each one has a distinctive pattern of light and dark bands. You can see these bands in the diagram of the long arm of chromosome 2 on the right. Band 2q23.1 contains around 1.2 million base pairs. This sounds a lot but it is actually quite small and is only 0.04 per cent of the DNA in each cell and only half a per cent of the DNA on chromosome 2. Base pairs are the chemicals in DNA that form the ends of the ‘rungs’ of its ladder-like structure.

Even if you magnify the chromosomes as much as possible, to about 850 times life size, a chromosome 2 with the microdeletion at q23.1 looks normal. People who have missing material on a chromosome are said to have a deletion but when the amount is so small that it can’t be seen even under a high-powered microscope, it is called a **microdeletion**. The 2q23.1 microdeletion can only be found using molecular or DNA technology, in particular a technique using microarrays (array-CGH), that shows gains and losses of tiny amounts of DNA throughout the genome and can demonstrate whether particular gene(s) are present or not. One gene, *MBD5*, has been suggested to be responsible for most, if not all, of the features of 2q23.1 microdeletion syndrome (see Research involving 2q23.1 on page 17). This guide includes descriptions of people who have a 2q23.1 microdeletion and also people who have a mutation or deletion of the *MBD5* gene.



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

Your geneticist or genetic counsellor will be able to tell you about the points where the chromosome has broken in your child. With a 2q23.1 microdeletion, the results are likely to read something like the following example:

### **arr[hg19] 2q23.1(148,867,234-149,172,531)x1**

arr	The analysis was by array (arr) comparative genomic hybridisation (cgh)
hg19	Human Genome build 19. This is the reference DNA sequence that the base pair numbers refer to. As more information about the human genome is found, new “builds” of the genome are made and the base pair numbers may be adjusted
2q23.1	The chromosome involved is 2 and the position of the deletion is in band q23.1
148,867,234-149,172,531	The base pairs between 148,867,234 and 149,172,531 have been shown to be deleted. Take the first long number from the second and you get 305,297 (0.305 Mb or 305kb). 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 2 – as you would normally expect

## **2q23.1 microdeletion syndrome**

The first published description of a person with a 2q23.1 microdeletion was in 2009. There have since been around 100 cases reported in the medical literature worldwide. When a particular set of developmental features occurs in a recognisable and consistent pattern in enough people, as a result of a single cause, the condition is called a syndrome. The features of a 2q23.1 microdeletion do occur in this way, so the disorder is often known as [2q23.1 microdeletion syndrome](#). The deletion occurs equally often in boys and girls (Waggenstaller 2007; Jaillard 2009; van Bon 2010; Williams 2010; Chung 2011; Noh 2012; Chung 2012; Bonnet 2013; Hodge 2013).

## **How much do we know?**

Comparing different children and adults with 2q23.1 microdeletions shows that some effects seem to be very broadly similar. This information guide tells you what is known about those effects. Comparing your child’s array results with others, both in the medical literature and within Unique, can help to build up a general picture of what to expect. But there will still be differences, sometimes quite marked, between your child and others with an apparently similar array result. It is very important to see your child as an individual and not to make direct comparisons with others with the same chromosome test results. After all, each of us is unique.

## **Most common features**

Every person with a 2q23.1 microdeletion is unique and so each person will have

different medical and developmental concerns. Additionally, no one person will have all of the features listed in this information guide. However, a number of common features have emerged:

- Children are likely to need support with learning. The amount of support needed by each child will vary
- Seizures
- Speech and language delay
- Behavioural difficulties such as autistic spectrum disorder or attention deficit hyperactivity disorder
- Sleep disturbances
- Short stature



## What is the outlook?

We can't be certain yet but there appears to be no reason why people who are healthy should not enjoy a normal lifespan. However, regression has been reported in three out of more than a hundred people in the medical literature. A 44-year-old experienced behavioural regression with a significant increase in skin picking and obsessive compulsive activities. A 4-year-old girl walked independently at 28 months, but at 4 years had lost some of her vocabulary and the ability to walk, standing only with support. A 6-year-old had progressive difficulties with fine motor skills and balance, worsening behaviour and loss of ability to draw lines and circles (Chung 2011; Noh 2012; Hodge 2013). Sadly, one woman developed seizures from the age of 9 months and died at 26 years because of seizures.

## Pregnancy and birth

Many pregnancies were uncomplicated, and babies were born at or near their expected due date

Many mothers (13/22) carrying babies with a 2q23.1 microdeletion experienced no pregnancy problems, had a normal delivery and only discovered their baby was affected after the birth. However, pregnancy complications in mothers carrying a baby with a 2q23.1 microdeletion have been reported. Two babies were delivered by emergency caesarean (C-) section at 35 and 36 weeks; one due to a placental abruption (the placenta separates from the wall of the uterus before birth) at 30 weeks and the other due to pre-eclampsia (a sudden increase in blood pressure and the presence of excess protein in the urine. If left untreated, pre-eclampsia can have serious complications for both the mother and the baby). Two babies were described as having intrauterine growth restriction (IUGR). This is a term used to describe babies whose growth in the womb has slowed resulting in babies that are smaller than expected for the

number of weeks of pregnancy. This led to one baby being induced at 36 weeks. The other baby with IUGR was diagnosed with kidney reflux during an ultrasound scan. These issues together with his mother's pre-eclampsia resulted in him being induced at 32 weeks. One mother was very sick throughout her pregnancy due to undiagnosed coeliac disease (gluten intolerance). Another mother had a low amount of amniotic fluid and high blood pressure. Pre-term labour began at 28 weeks so she was put on bed-rest. One baby showed less fetal movement than expected while in the womb. A Unique baby had an enlarged right kidney detected at the 20-week ultrasound scan. The baby was delivered at 38 weeks by C-section due to mother's high blood pressure (Jaillard 2009; van Bon 2010; Williams 2010; Noh 2011; Bonnet 2013; Unique).

## First signs and age at diagnosis

For many children the first signs of 2q23.1 microdeletion syndrome were delays in reaching developmental milestones such as sitting and moving or speech or growth delay. Others were diagnosed due to learning or behavioural problems.

Quite a few children were first tested for other syndromes that have similar characteristics such as Angelman, Rett and/or Smith-Magenis syndromes, which are all well known for their specific behavioural characteristics (van Bon 2010; Unique).

The age of diagnosis varies from a baby of 6 months to a man in the medical literature being diagnosed at the age of 44 years (Hodge 2013; Unique).



## Feeding and growth

Feeding and growth can be affected in children with 2q23.1 microdeletion syndrome

Around half of those with 2q23.1 microdeletion syndrome have growth restriction and/or short stature. The majority of birth weights recorded at Unique were within the normal range, with an average of 3.28 kg (7lb 4oz), suggesting that for most the growth delay does not start before birth. However, four out of 26 babies reported in the literature and members of Unique had a low birthweight (below 2.6 kilos) at term. Four other babies were born early (before 36 weeks) (Jaillard 2009; Chung 2010; van Bon 2010; Williams 2010; Motobayashi 2011; Talkowski 2012; Bonnet 2013; Hodge 2013; Unique).

### Range of birth weights (at or near term):

1.134 kg (2lb 8oz) to 4.3 kg (9lb 8oz)

After birth, babies tend to grow more slowly than their peers, with a small minority of babies described as “failure to thrive”. This term is used to describe a baby who has poor weight gain and physical growth failure over a period of time. Feeding problems in babies can also be a problem. The hypotonia (low musculature) that is common in babies with 2q23.1 microdeletion syndrome can lead to difficulties with sucking and swallowing, and/or latching onto the breast. Babies with a high palate can also find the action of sucking and swallowing difficult. The floppiness can also affect their food pipe and contribute to gastro-oesophageal reflux (in which feeds return readily up the food passage). This can generally be well controlled by giving feeds slowly, positioning a baby semi-upright for feeds and where necessary raising the head of the end of the bed for sleeping. If these measures are not enough, feed thickeners and prescribed medicines to inhibit gastric acid may control reflux but some babies benefit from a fundoplication, a surgical operation to improve the valve action between the stomach and food passage (Jaillard 2009; Chung 2010; van Bon 2010; Williams 2010; Motobayashi 2011; Talkowski 2012; Bonnet 2013; Hodge 2013; Unique). Obesity associated with hyperphagia (increased appetite) has been reported in around a quarter of those in the published medical literature but has not been reported in any members of Unique (van Bon 2010; Talkowski 2012; Hodge 2013; Shichiji 2013; Unique).

“She won’t feed herself, not even picking something up. She gags at even a mashed banana and won’t eat a cracker or anything like that” – 18 months

## Motor skills (sitting, moving, walking)

Children with 2q23.1 microdeletion syndrome are often delayed in learning to sit and walk.

Almost all 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, rolling over is mastered between 3 months and 15 months (at an average of 8 months); sitting unaided is mastered between 8 months and two years (at an average of 1 year); crawling is mastered between 10 months and 4 years (at an average of 19 months) and walking is mastered between 1 year and 5 years (an average of 2 years and 4 months). A 10-year-old boy in the medical literature could stand independently for short periods of time but did not walk (Chung 2010; van Bon 2010; Williams 2010; Motobayashi 2011; Noh 2011; Talkowski 2012; Bonnet 2013; Hodge 2013; Unique).

One of the causes of the delay in mobility in children with a 2q23.1 microdeletion is hypotonia, which is common in those with 2q23.1 microdeletion syndrome (30/42). This makes a child or baby feel floppy to handle and generally improves and may disappear with physiotherapy and exercises (Chung 2010; van Bon 2010; Williams 2010; Noh 2011; Talkowski 2012; Bonnet 2013; Hodge 2013; Unique).



A number of people with 2q23.1 microdeletion syndrome are described as having an ataxic (unsteady or uncoordinated) or unusual walk and have difficulties with balance and/or are described as clumsy (Jaillard 2009; Chung 2010; van Bon 2010; Noh 2011; Talkowski 2012; Bonnet 2013; Hodge 2013; Unique).

“She does not roll with purpose to get an object. She cannot get into a sitting position on her own. She can sit for a few minutes and then falls over. She loves playing with blocks” – 16 months

“She is very unbalanced. She crawled at 14 months and clapped at 15½ months. She gets there on gross and fine motor skills so far but at the end of the normal range. She likes to come to a standing position when near furniture. She doesn’t walk yet but side-steps while holding on to the furniture” – 18 months

“She walks and scoots and goes to a preschool gym class. She has trouble with coordination and is clumsy” – 4 years

“She runs, walks, climbs. She LOVES to play at the park – swinging and climbing are favourites” – 5½ years

“He sits, walks, climbs stairs, unable to jump (kind of pushes off on one foot in a hop) is in constant motion. He loves to climb and run” – 5½ years

“She seems off balance, slow and gets tired. To climb stairs she has to hold onto a rail. She likes the playground but mainly to observe” – 7 years

“He wears orthotics and is OK with physical movement but can be clumsy. He can sit, walk, go up and down stairs SLOWLY. He can jump. He walked late, at age 3 and used a walker for several months before walking independently. The physical and occupational therapy he receives has made a huge difference in his ability level and quality of life. He still wears orthotics and will likely wear them for the rest of his life” – 9 years

## Fine motor skills and self care

Fine motor skills may be affected in children with 2q23.1 microdeletion syndrome

Hypotonia can also affect fine motor skills in children with 2q23.1 microdeletion syndrome, 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. A 4-year-old is able to scribble and place two cubes to form a tower but is unable to put clothes on by herself. Two 7-year-olds





are able to dress and feed themselves (Chung 2010; von Bon 2010; Noh 2011; Unique).

Toilet training may also be affected. A 7-year-old boy mastered bladder and bowel control at 6 years. A 9-year-old has bladder control but has not fully mastered bowel control. A 5-year-old and 7-year-old are both in nappies (diapers) during the day and night-time. A 4-year-old is toilet trained during the day but wears a nappy at night-time (van Bon 2010; Unique).

“She started holding her bottle at 14 months but she still tires easily and has to have help about halfway through. She can shake a rattle but drops it easily” – 16 months

“She held her toys at 10 months and her bottle at 13 months” – 18 months

“She finds it hard to control force and uses her whole hand. We help her through play, for example puzzles and Playdoh™” – 4 years

“Her fine motor skills are very delayed and are the equivalent of an 18-month to 2½-year-old. She has occupational therapy, feeding therapy and larger handles on cutlery. She is still in nappies and needs help 98% of the time. The only thing she does herself is put her tennis shoes on” – 5½ years

“He still primarily uses a raking grasp and doesn’t rotate a spoon well so is a messy eater. He is still in diapers [nappies] both day and night. He can brush teeth and wash but not well. Can undress himself easily but needs assistance putting clothes on” – 5½ years

“She has a very hard time using utensils and scissors, and shakes when holding a cup. Whenever she holds something her wrists look weak and her hands have a hard time supporting the object. She has been having physical and occupational therapy” – 7 years

“He has a very hard time with hand writing. It is illegible. The low musculature makes writing very difficult, so this in turn makes schoolwork very challenging. He began using a computer called Alphasmart in 1<sup>st</sup> grade and it’s been helpful. He can dress himself but is very slow” – 9 years

## Learning

Children with 2q23.1 microdeletion syndrome often have learning (intellectual) disabilities

All of the children described so far have a learning disability most often in the moderate to severe range. Out of 16 people with a known level of learning difficulty, one was described as having a mild level of difficulty; two had a mild to

moderate learning disability; four have a moderate learning disability; two have a moderate to severe learning disability and five have severe learning disabilities. Two further children were described as having significant learning difficulties. A number of children are hyperactive or described as being easily distractible or having a poor concentration span which can make learning more of a challenge (see Behaviour page 12). A child with a learning disability is likely to need some learning support and many children benefit from attending a special educational school (Waggenstaller 2007; van Bon 2010; Talkowski 2012; Bonnet 2013; Hodge 2013; Unique).

“She has a moderate learning disability and a scattering of skills equivalent to a 2- or 3-year-old. Her strengths are her happy, affectionate personality and doing puzzles. She can scribble and draw circles. She is hyperactive and gets distracted in a busy setting” – 4 years

“She has a moderate to severe learning disability and learns best when things are set to music or with repetition” – 5½ years

“He has a moderate to severe learning disability. He is two to three years behind in all categories. His strengths are memory, music, his personality and sense of humour. He is very inquisitive about everything and very clever” – 5½ years

“She has a severe learning disability. She is in mainstream school but in a special needs program with classrooms and teachers that are for special needs kids” – 7 years

“He loves to read but struggles with maths and understanding the concept of numbers. He is making progress but at a slower rate than other children. He went through the pre-Kindergarten program twice so he is currently one year older than his classmates. When he repeats the 2<sup>nd</sup> grade next year he will be two years older than his classmates. But hopefully that’s what he needs to succeed academically” – 9 years



## Speech and communication

Speech and language delay is common in children with a 2q23.1 microdeletion. Speech and language development was delayed in most children (37/54), but it is not known whether the delay was in line with the child's cognitive abilities. Speech is variable in 2q23.1 microdeletion syndrome, with some children who speak in short sentences but some who are non-verbal. Most children understand simple language and/or pictograms but struggle with expressive language (speech). Two 3½-year-olds have single words; a 5-year-old has several words but no sentences; a 7-year-old spoke in two or three word phrases and recognised pictograms; another 7-year-old had more than 100 signs, 15 words and could follow simple instructions at 3½ years and by 5 years had 4 to 5 word sentences; a 9-year-old had first words at 12 months, put two words together at 2½ years but did not master speaking in sentences until 7 years; a 10-year-old had a reasonable understanding of simple language but limited speech at 5 years and at 10 years was talkative using mainly single words and 2 to 3 word phrases; another 10-year-old speaks in simple sentences; another 10-year-old had 50 words by the age of two years and 11 months but did not start putting words together until 9 years but at 10 years her speech is unclear but she continues to learn new words and can follow simple commands and a 13-year-old has a hoarse voice and minimal words. Two children had regression of language skills: a 4-year-old with speech therapy was using two-word sentences at 30 months but lost vocabulary by the age of 4. She is able to point to body parts and pictures placing her at a 2-year-old level. She is interactive and able to follow simple commands. Another 4-year-old spoke her first words at 13 months but between 24 and 30 months had regression of language skills. However, four 10-year-olds had no speech and an adult had no speech; one of the 10-year-olds communicates with pictures and can understand some sentences (Jaillard 2009; Chung 2010; van Bon 2010; Williams 2010; Motobayashi 2011; Noh 2011; Talkowski 2011; Bonnet 2013; Hodge 2013; Unique).

“She has no words yet at 16 months. She understands signs but cannot reproduce them” – 16 months

“She wants to be held and will crawl to us or hold her arms out. She will hit the computer if she wants to watch a certain video on it instead of the iPad or TV. Her other communication is more baby-like where she will whine or cry so we know to change her diaper [nappy] or get her something to eat” – 18 months

“She has 4 to 5 word sentences now but pronunciation and sentence structure needs work. There were big changes from 3½ years onwards. She has had speech therapy, uses Makaton signing visuals and the ‘More than words®’ course. The iPad and computer have been helpful and a good application is ‘Busy Beaver’ ” – 4 years

"She has some signs, some words and vocal noises. She mastered her first signs at 20 months and first words at 31 months. She has mostly single words but has some two word phrases" – 5½ years

"He has used words since 2 years old and talks in 5-6 word sentences if he is trying to convey something he wants. He will respond with 2-3 word phrases when asked a question. He definitely needs to work on articulation and enunciation. He uses picture exchange communication (PECs), signing, The Hanen® program (would HIGHLY recommend for 2q parents) and early speech therapy" – 5½ years

"She has words that come and go. She used to say words when she was little that she doesn't say anymore. She has been trying picture communication and PECs at school for the last 4 years. She loves the iPad and we have loaded it with pictures but she has not grasped the concept yet of using it to communicate" – 7 years

"He is verbal and has a large vocabulary but can rush words together and be very difficult to understand. He has been in speech therapy since aged 2. It has helped him with the pronunciation and rate of speech and also understanding word meanings, all of which is very challenging for him. He began signing at aged one and then really began speaking after age 3" – 9 years

## Behaviour

Some children with 2q23.1 microdeletion syndrome have behavioural difficulties such as autistic spectrum disorder or attention hyperactivity deficit disorder

Children with 2q23.1 microdeletion syndrome are often described as having happy, active and social personalities with a good sense of humour. However, a significant number of children – although not all – show a similar pattern of behavioural difficulties.

Out of 94 children whose behaviour has been described, 67 have been described with autistic spectrum disorder (ASD) or showing autistic traits and 27 with attention deficit hyperactivity disorder (ADHD), hyperactivity or attention problems. Stereotypic repetitive behaviour (such as repetitive hand movements or hand flapping), self stimulatory behaviour (such as teeth grinding and chewing of hands and materials) is also common (van Bon 2010; Talkowski 2011; Hodge 2013; Unique).



Sensory Therapy

Several children have been described as having anxiety and some have obsessive compulsive or routine-bound traits. Some children have shown aggression and several have self-injurious behaviour (including skin and eye picking) and quite a few children are described as having a high pain threshold (Jaillard 2009; Chung 2010; van Bon 2010; Hodge 2013; Unique).

Around 20 per cent of people with 2q23.1 microdeletion syndrome have easily provoked and often inappropriate laughter (van Bon 2010; Talkowski 2011; Hodge 2013; Unique).

It has been suggested that behaviour in some children can worsen at times of increased seizure activity. One child's behaviour improved dramatically after starting a gluten and dairy-free diet (van Bon 2010).

"She loves water play. She has a great belly laugh! She is typically happy but when in new places she develops anxiety especially if people try to interact with her. She loves children but is fearful of adults" – 16 months

"She is generally happy and healthy. She doesn't have any challenging behaviour unless she has a cold or something which is rare and then she just isn't happy. She is very social. She takes a while to warm up to new people and then she is fine" – 18 months

"She loves the TV, computer, iPad, puzzles, dolls, music, playing with older children and games. She has tantrums when she doesn't get her own way. She is hyperactive when taken out in a busy public place and will run off – she doesn't know boundaries and we can't trust her actions in public. We manage her behaviour by being firm and consistent. She will bite her hands when excited" – 4 years

"She loves going to the park, listening to music (children's and classical), watching DVDs, puzzles, looking at books, going to church, going to the library and playing with sisters, cousins and neighbourhood pets. She can have massive temper tantrums when a preferred item is removed. She also throws things. She is over friendly. She cannot be left alone, ever because she will get into things, let strangers into the house, go outside or climb onto things. She gets anxious at night time and in new situations" – 5½ years

"He is very loving and full of joy. He is hyperactive and restless at night (fights sleep). He loves TV, music and dancing, being read to, computers and iPad and climbing and running. He has a lot of parallel play with other kids and loves to talk and say 'hello' to people. He has no separation anxiety. He does not initiate play but will respond if a kid asks. He is not good with personal space or boundaries; gets too close for comfort for typical children his age" – 5½ years

"She loves books and she loves to be pushed around in a stroller [buggy]. She likes to ride in the car. She likes horses, cats and dogs. At home is very different to the way she acts at school. They never see this side of her at

school but at home she is aggressive, throws tantrums, kicks, hits, pulls hair, screams, throws her food, throws anything down when she is frustrated” – 7 years

“He loves playing on the computer and playing video games. He loves sports of all kinds and watches ESPN non-stop. He is very happy and joyful. He can be thoughtful and caring. He has autistic behaviours like flapping, and he chews on his hand until it bleeds. He also loves routine and can freak out if that routine is changed. He goes ballistic when he’s asked to turn off the computer and TV. We are working on giving him limits and having him not freak out so that he’ll be able to continue to enjoy privileges. He is very anxious and needs reassuring constantly that all is OK” – 9 years

## Sleep

Sleep problems seem to be common in children with 2q23.1 microdeletion syndrome. The most common problem is multiple night wakings with some children also suffering from night terrors. Other children struggle to drop off to sleep. Some children take melatonin to help with sleep problems (Jaillard 2009; van Bon 2010; Talkowski 2011; Hodge 2013).

“She goes to sleep fine but typically wakes up around 1am and stays awake until 4 or 5am about three to four nights per week. My solution is to do a pretend physical therapy session in our living room to tire her out. Then we do a warm bath or shower and she is out within two hours instead of three or four” – 16 months

“She has irregular sleep with naps and at night. Night has recently got better but daytime sleep is good some days and some days almost none. She sleeps through the night most nights now” – 18 months

“She won’t settle at night-time but once asleep she is generally asleep for the night. If she sleeps during the day this makes it worse although she struggles not to nap during the day. Melatonin really helps her but makes her clumsy and more tired the next day” – 4 years

“She had sleep apnoea but once her tonsils and adenoids were removed her sleeping patterns improved. She has had painful diaper [nappy] rash which wakes her up. She has trouble going to sleep but reading to her and letting her listen to classical music helps” – 5½ years



“Melatonin has been crucial in achieving sleep” – 5½ years

“She has sleep apnoea and has had her tonsils and adenoids removed. Tried to establish a routine and that helps her to realise that it is time for bed” – 7 years

“He has a lot of sleep disturbances and wakes often during the night. He needs to sleep with someone else. He can fall asleep alone but will wake up terrified if someone isn’t with him” – 9 years

## Appearance

### ■ Facial appearance

Children with 2q23.1 microdeletion syndrome may have a subtle characteristic facial appearance.

Many children have a small head (microcephaly). Geneticists trained to note unusual features may find features such as thick, arched eyebrows or a unibrow (abundant hair between the eyebrows so they seem to form one long eyebrow); a large prominent nose or a small bulbous nose; a small chin, widely spaced teeth and thin upper lip with downturned corners of the mouth (van Bon 2010; Talkowski 2012; Unique).

### ■ Hirsutism

Hirsutism (excessive body hair) has been reported in seven people in the medical literature and one member of Unique (van Bon 2010; Talkowski 2012; Hodge 2013; Unique).

### ■ Hands and feet

Hand and feet anomalies appear to be common in those with 2q23.1 microdeletion syndrome and include small hands with short fingers and/or small feet with short toes; incurving little fingers (5th finger clinodactyly); short fifth finger or toe; flat feet and a sandal gap (increased gap between the big toe and second toe). Overall, the pattern is of variable minor hand and feet anomalies (Talkowski 2013; Hodge 2013; Unique).

## Health matters

### ■ Seizures or abnormal EEG patterns

Children with 2q23.1 microdeletion syndrome have an increased risk of seizures

Most children with a 2q23.1 microdeletion have seizures. The age of onset of seizures is variable: from the first days after birth through to 12 years old. The seizure types are also varied, and there are several reports of the seizures being resistant to control with medication. One boy had epilepsy as a child but had outgrown it by the age of 10 years. A 4-year-old is free of seizures since following a ketogenic diet (a high fat, adequate protein, low carbohydrate diet) (Jaillard 2009; Chung 2010; van Bon 2010; Williams 2010; Noh 2011; Motobayashi 2012; Talkowski 2012; Bonnet 2013; Hodge 2013; Unique).



## ■ Constipation

Constipation appears to be common in children with 2q23.1 microdeletion syndrome. Dietary changes and/or medication can help to manage the problem (Jaillard 2009; van Bon 2010; Talkowski 2012; Hodge 2013; Unique).

## ■ Joint laxity

Joint laxity (looseness or instability of the joint also called hypermobility or double jointedness) has been reported in some people (van Bon 2010; Talkowski 2012; Hodge 2013; Unique).

## ■ Spine

Nine people in the medical literature have been described with scoliosis (curvature of the spine) and one child at Unique had a tethered spinal cord (the spinal cord is abnormally attached to the tissues around the spine) which necessitated surgery (Jaillard 2009; van Bon 2010; Talkowski 2012; Hodge 2013; Unique).

## ■ Teeth

Generally speaking, children with chromosome disorders appear to have somewhat more dental problems than their peers, so regular and high quality dental care is important (Talkowski 2011; Hodge 2013; Unique).

## ■ Genital anomalies

Minor anomalies of the genitals are common in babies with chromosome disorders, most often affecting boys. Two boys had a small penis; three had undescended testes (which can be brought down surgically) and one boy had hypospadias (the hole usually sited at the end of the penis is on the underside instead) (Jaillard 2009; van Bon 2010; Motobayashi 2011; Talkowski 2012; Bonnet 2013; Hodge 2013; Unique).

One girl had hypoplastic (underdeveloped) genitalia (Jaillard 2009).

## ■ Eyesight

Seven children have been reported to have a squint where one or both eyes can turn inwards, outwards or upwards. At least six people have astigmatism, which is when the cornea (the clear cover over the iris and pupil) is abnormally curved. The effect on vision is to make objects appear blurred. Sometimes the brain can compensate for astigmatism, although it may be too strong for this to happen without glasses. Three people have optic nerve hypoplasia (a condition present from birth in which the eye does not have all the usual wiring between the eye and brain to transfer information about the visual world). Sixteen people have been reported to have long or short sight (Jaillard 2009; van Bon 2010; Williams 2010; Hodge 2013; Unique).

## ■ Hearing

Generally speaking children have had normal hearing, although young children quite often have the fluctuating temporary hearing loss caused by a build-up of fluid behind the eardrum (glue ear), but they outgrow this naturally. If it is severe or persistent, tubes (grommets) may be inserted into the eardrum to

aerate the space (the middle ear) behind it and improve hearing. Four children within Unique have hearing tubes (Jaillard 2009; Unique).

■ **Heart**

Cardiac problems have been rarely reported. Three children had holes in the wall of the heart (which often close spontaneously but may need surgery) and three children had pulmonary stenosis (where the artery that takes the blood to the lungs has an unusually narrow entrance) (van Bon 2010; Williams 2010; Motobayashi 2011; Talkowski 2012; Hodge 2013; Unique).

■ **Other**

Other health concerns which may or may not be linked with the microdeletion (because they have only been reported in one person) include hip dysplasia (underdevelopment of the hip); inguinal hernia (tissue from the intestine forms a swelling or a bulge the groin); kidney reflux (the urine flows upwards from the bladder back to the kidney, potentially damaging the kidneys) and dolichomegacolon (an unusually long large intestine) (van Bon 2010; Bonnet 2013).

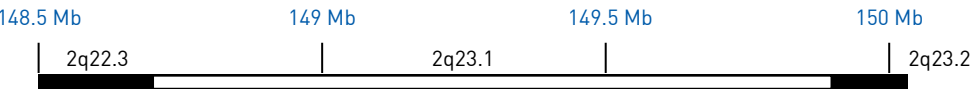
**Research involving 2q23.1**

The microdeletion involving 2q23.1 microdeletion syndrome ranges in size up to about 5.5 Mb. However, recently quite a few people who have either very small deletions which contain only the *MBD5* gene or a single base pair mutation within the *MBD5* gene itself have been described in the medical literature. These people all have a range of features very similar to those who have larger deletions strongly suggesting that the *MBD5* gene may be the gene responsible for these features (Waggenstaller 2007; Jaillard 2009; van Bon 2010; Williams 2010; Chung 2011; Noh 2012; Chung 2012; Bonnet 2013; Hodge 2013).

Although the *MBD5* gene is the predominant gene involved in 2q23.1 microdeletion syndrome, it has been suggested that it is not sufficient to cause all the characteristics of 2q23.1 microdeletion syndrome and that those children whose deletion is larger and includes other genes have further characteristics, such as microcephaly, small hands and feet and growth delay, than those that have either a mutation in or deletion of the *MBD5* gene alone (van Bon 2010; Talkowski 2011).

**Chromosome 2q23.1:**

Position:



Genes:

*ACVR2A*   *ORC4*                      *MBD5*                      *EPC2*

It is important to remember that while identifying the gene(s) responsible for certain features of the 2q23.1 microdeletion syndrome is valuable and may help guide future studies, it does not lead directly to immediate improved treatment. Additionally, even if the supposedly responsible gene is missing, it does not always mean that the associated feature(s) will be present. Other genetic and environmental factors often have a role in determining the presence or absence of a particular feature.

## How did this happen?

In the majority of people described so far, the 2q23.1 microdeletion has occurred out of the blue for no obvious reason. The genetic term for this is *de novo* (dn) and a blood test shows that both parents have normal chromosomes. *De novo* 2q23.1 microdeletions are caused by a mistake that is thought to occur when the parents' sperm or egg cells are formed or in the very earliest days after fertilisation.

There is one report in the medical literature of a child inheriting the 2q23.1 microdeletion from a parent (Talkowski 2011).

What is certain is that as a parent there is nothing you could have done to prevent this from happening. No environmental, dietary or lifestyle factors are known to cause 2q23.1 microdeletions. There is nothing that either parent did before or during pregnancy that caused the microdeletion.

## Can it happen again?

Where both parents have normal chromosomes, it is unlikely that another child will be born with a 2q23.1 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 2q23.1 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. This has been reported in one family where neither of the parents have a 2q23.1 deletion in their blood cells, but they have two children (a brother and a sister) who both have 2q23.1 deletion syndrome (van Bon 2010).

In families where the 2q23.1 microdeletion has been inherited from a parent, the possibility of having another child - either a girl or a boy - with the 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.

## Families say.....

“Once you get past the newborn stage the smiles, kisses and hugs will prove their devotion to you. Hang in there! Work hard and never give up” – 16 months

“She entertains us all and is a joy to be around. We enjoy the small accomplishments she makes” – 4 years

“He has made me less self-centred but a lot more tired!” – 5½ years

“Everyone loves her, kids and adults – she is a very special soul” – 7 years

“People seem to be drawn to him. He is very accepting of things and is an inspiration to me and others. I have learned over time to celebrate each achievement and remember he is always making progress, although it is slower than most” – 9 years



## Support and Information



Understanding Chromosome & Gene Disorders

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



**2q23.1 deletion/duplication disorders**  
2q23.org

There is a Facebook group for families affected by 2q23.1 microdeletion syndrome at [www.facebook.com](http://www.facebook.com):  
[www.facebook.com/groups/260449943985091/](http://www.facebook.com/groups/260449943985091/)

There are also two twitter feeds:  
@2q231 (awareness)  
@2qte\_MDS (research)

### 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!

Unique mentions other organisations' message boards and websites to help families looking for information. This does not imply that we endorse their content or have any responsibility for it.

This leaflet is not a substitute for personal medical advice. Families should consult a medically qualified clinician in all matters relating to genetic diagnosis, management and health. The information is believed to be the best available at the time of publication. It was compiled by Unique and reviewed by Dr Sarah Elsea, Baylor College of Medicine, Houston, USA.

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