Understanding Chromosome & Gene Disorders

10q11.22q11.23 Deletions and Microdeletions

rarechromo.org

10q11.22q11.23 microdeletions

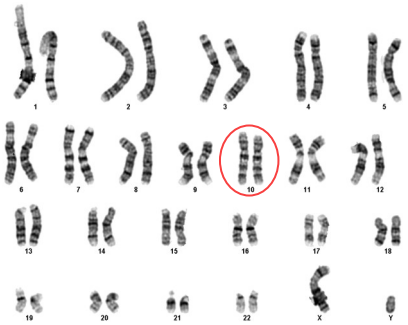
A 10q11.2q11.23 microdeletion is a rare genetic condition caused by the loss of a small piece of genetic material from one of the body's 46 chromosomes – chromosome 10.

For typical development, chromosomes should contain the expected amount of genetic material. Like many other chromosome disorders, having a missing piece of chromosome 10 may affect a child's health, development and intellectual abilities. The symptoms observed in people with a 10q11.22q10.23 microdeletion are variable and depend on a number of factors including what and how much genetic material is missing.

Background on chromosomes

Our bodies are made up of many different types of cells, almost all of which contain the same chromosomes. Each chromosome consists of DNA that codes for our genes. Genes can be thought of as individual instructions that tell the body how to develop, grow and function.

Chromosomes come in pairs with one member of each chromosome pair being inherited from each parent. Most of our cells have 23 pairs of chromosomes (a total of 46) as shown in this image. → Eggs and sperm, however, have 23 unpaired chromosomes. When an egg and sperm join together at conception, the chromosomes pair up to make a total of 46.



Chromosomes pairs 1-22, X and Y (male)
Chromosome pair 10 is circled in red

Chromosome pairs are numbered 1 to 22 and the 23rd pair comprises the sex chromosomes that determine biological sex. They can be viewed under a microscope and arranged roughly according to size as the image shows. Males usually have one X chromosome and one Y chromosome (XY), and females usually have two X chromosomes (XX).

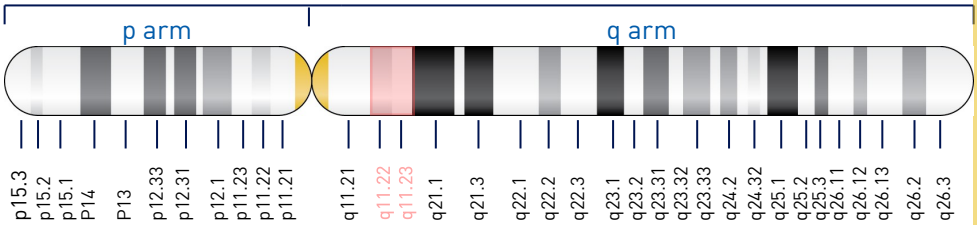
Sources

The information in this booklet is drawn from published medical literature, databases and *Unique* members. The first-named author and publication date from articles 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*. Information gathered from DECIPHER (DatabasE of genomiC varIation and Phenotype in Humans using Ensembl Resources) is open access and can be found at https://decipher.sanger.ac.uk. Five families with a 10q11.22q11.23 deletion competed a detailed *Unique* survey in 2019.

Looking at 10q11.22 and 10q11.23

Chromosomes can't be seen with the naked eye but if cells are prepared in a specific way, the chromosomes can be stained and viewed under a microscope. Each chromosome has a specific 'banding pattern' made of light and dark bands. You can see the typical banding pattern for each chromosome in the image on page 2, and a more detailed version for chromosome 10 in the image below.

Chromosome 10



Each chromosome has a short (p) arm and a long (q) arm and the point at which the arms meet is called the centromere (coloured yellow in the image above). Bands are numbered outwards starting from the centromere. Regions q11.22 and q11.23 (shaded pink in the image above), where the deletions lie, are located next to each other on the long (q) arm of chromosome 10.

Deletions in region 10q11.22q11.23

A number of different deletions have been identified in regions 10q11.22 and 10q11.23 of chromosome 10. The deletions are classified according to their possible affects:

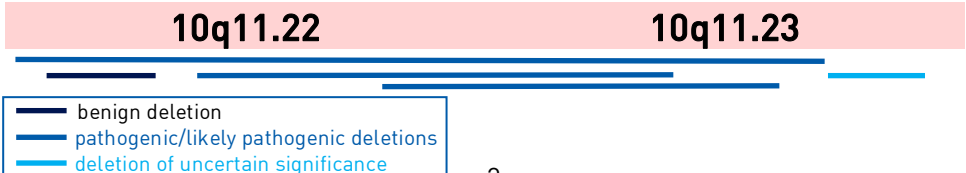
Benign: if a deletion is described as benign, this means it is not expected to have an affect on the person with the deletion.

Pathogenic (or likely pathogenic): if a deletion is described as pathogenic, this means a person can show symptoms thought to be associated with the deletion.

VUS (variant of unknown/uncertain significance): when it is difficult to establish whether the symptoms seen in some people with a particular deletion are directly related to the missing piece of genetic material, the deletion is described as a VUS.

Different deletions in 10q11.22q11.23

Some very small deletions are found in 10q11.22 and others in 10q11.23. However, some deletions span both chromosome bands (hence the name 10q11.22q11.23). These larger deletions are more commonly diagnosed. The size and location of the deletion will influence if and how a person is affected. The blue lines in the diagram below show some deletion examples:



People can have 10q11.22q11.23 deletions of different sizes that include different genes, but most will share a common deleted region. Larger deletions will contain more genetic material which could affect what symptoms they have and how severely they are affected. Over 100 genes have been identified in the entire 10q11.22q11.23 region; further information about a few important genes in these regions can be found on pages 18 and 19.

Some people have small deletions in 10q11.22 or 10q11.23 (rather than spanning both regions). These deletions can vary in position, size and gene content. This means that not everyone with a deletion in 10q11.22 and/or 10q11.23 will be affected in the same way. It's important to establish which part of the chromosome is missing if any comparisons between deletions and symptoms are to be made.

In the past, chromosomal deletion were routinely identified by the basic band staining procedure shown on page 2 but many deletions are too small to be seen using this technique. Another laboratory technique called FISH (fluorescence *in situ* hybridisation) was later developed which enables sections of chromosomes to be analysed in more detail. This technique uses fluorescently labelled pieces of DNA that match the DNA in specific places on a chromosome so is only offered as a test if there is a suspected change in a specific region of a chromosome. A more recent test now more routinely available that allows DNA to be analysed in greater detail is called microarray comparative genomic hybridisation (array CGH). An array CGH test can detect very small deletions even when a specific diagnosis is not suspected. Results provide more precise details of which piece of DNA is missing.

Genome Assemblies

The human genome project, an international effort to sequence the entire human genome and map all of its genes, was announced complete in 2003. However, there were many gaps in the sequence and mapping data, and scientists have since been working continuously to identify the missing information. When new sequence information is identified, the base pair numbers of each chromosome change slightly and therefore deletion coordinates can shift.

Each new version of the genome sequence is often referred to as an 'assembly'. Every few years a new assembly is released. The genetic information in this guide is based on the Genome Reference Consortium (GRC) human (h) genome assembly number 37 (GRCh37), which was released in 2009. You will often see the DNA sequence data for this assembly referred to as hg19 (human genome 19) on a genetic report.

The databases commonly used by clinical geneticists and *Unique* will soon move to a more recent assembly named GRCh38/hg38, which was released in 2014. Genetic reports will at some point also be altered, so genes and genetic changes may have new base pair numbers.

Chromosome test results

Your clinical geneticist or genetic counsellor will have given you detailed information about the piece of DNA that has been deleted in your child (and perhaps also yourself and/or other family members). The information you are given will include chromosomal locations of genetic changes that are thought to be important to your child's condition and which significant genes are in the section of DNA that has been deleted. This will most likely include an array CGH test result such as that detailed below.

Array CGH example:

arr[hg19] 10q11.22q11.23 (46,263,932-51,910,898) x1 dn

arr The analysis used microarray technology

hg19 This is the reference DNA sequence that the base pair numbers refer to, in this case human genome build 19 (for more information, see page 4)

10q11.22q11.23 The analysis revealed a DNA variant on chromosome 10, in regions q11.22 and q11.23

(46263932-51910898) The DNA variant is identified by its base pair numbers (the points where the chromosomal change has occurred). In this example, the DNA variant lies between base pairs (bp) 46,263,932 and 51,910,898. This region covers 531,964 base pairs, or more simply ≈ 5 Mb (1 Mb = 1,000,000 base pairs)

x1 There is one copy of the piece of DNA specified. Since there should be 2 copies of chromosome 10, this shows that the DNA variant is a deletion

dn The deletion occurred *de novo* (as a 'new event'). The parents' chromosomes have been checked and no deletion has been found in this region of chromosome 10

If a deletion is identified as *de novo*, it is very unlikely to have been inherited. If a test result is followed by mat, the deletion has been inherited from the mother (maternal); if it is followed by pat, the deletion has been inherited from the father (paternal).

If a deletion is found to be inherited, other family members may be offered a DNA test such as a microarray, FISH or qPCR (quantitative Polymerase Chain Reaction; a quick test that can be designed specifically for the deleted piece of DNA to identify any change in copy number). A FISH test (see page 4) can confirm if the piece of genetic material is missing and can help indicate somatic mosaicism. Somatic mosaicism is when not all cells in the body are missing the piece of genetic material. In such rare cases, the outcome of having a deletion may depend on which cells in the body contain the deletion.

You may wish to compare your child's results with others who appear to have the same deletion to help understand your child's development. While this may help identify common symptoms, it is important to remember that the same deletion can have very different effects on different people, or no apparent effect at all. Siblings with the same parents and the same deletion can have very different symptoms. A child's own unique genetic make-up, environment and personality help to determine their future development, needs and achievements. It is important to see your child as an individual and not to rely too much on comparisons with others who appear to have the same deletion.

How common are 10q11.22q11.23 deletions?

There is currently no official estimate of 10q11.22q11.23 deletion occurrence but these deletions are rare. Fewer than 100 people have been reported in databases and medical literature (2019). One research study identified 21 people (out of 58175), referred for genetic testing, as having a 10q11.22q11.23 deletion (Stankiewicz 2012). Nine of these had an additional deletion or duplication. Although no carriers were identified in the 9183 'healthy controls', 10 unaffected parents were found to carry the same 10q11.22q11.23 deletion as their child (as well as two parents who showed symptoms). Another research study that looked at the DNA of 420,247 adults in the general population (UK Biobank; Kendall 2019) identified 57 people with a 10q11.22q11.23 deletion. Although the healthy carriers were not diagnosed with neurodevelopmental disorders, analyses showed that they could be experiencing some mild difficulties. These studies provide some helpful information about inheritance and symptom variation in people with a 10q11.22q11.23 deletion.

Unique members

Unique currently (2019) has 35 members with a 10q11.22q11.23 deletion who live world wide. Three members also have changes to other chromosomes or additional changes on chromosome 10. Only those with a 10q11.22q11.23 deletion, and no other chromosomal variation, are considered in this guide since, for others, the reason for some of their symptoms may be due to additional chromosomal alterations. This guide may however be of use to such families to partly explain their child's difficulties.

Many *Unique* families have provided information about their child with a 10q11.22q11.23 deletion, 5 families also completed a more detailed *Unique* survey in 2019. Survey responses were received for 2 boys and 3 girls, all of whom share a similar deletion.

Why did this happen?

When sperm and egg cells join they form a single cell and this cell must continuously make copies of itself (and all its genetic material) in order to produce the billions of cells that are necessary for human growth and development. Sometimes during the formation of the egg or sperm cells or during this complicated replication process, parts of a chromosome are lost,

duplicated and/or become rearranged. This is a natural process that occurs in everyone; it is only when alterations involve important genetic information that symptoms can occur. It is important to know 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 10q11.22q11.23 deletions. There is nothing that either parent did before, during or after pregnancy that caused the deletion.

Can it happen again?

If a parent is found to have the same deletion as their child, the possibility of having another child with this deletion is 50% in each pregnancy. If neither parent is found to have this chromosomal change, it is unlikely that they will have another child with a 10q11.22q11.23 deletion. Very rarely, parents are identified as having unaffected chromosomes by a blood test, but a few of their egg or sperm cells carry a chromosomal change. Geneticists call this germline mosaicism and it means that such parents can have more than one child with the same chromosome disorder. If they wish, parents can discuss their specific recurrence risks with a genetic counsellor.

If your child with a 10q11.22q11.23 microdeletion goes on to have children of their own, the chances of passing on the deletion to their child is 50%. Your child's ability to look after their own child is very likely to be closely related to their own learning ability and behaviour.

Possible features

Symptoms associated with 10q11.22q11.23 deletions vary greatly, some symptoms appear to be more common than others. The following is a list of features that have been observed in some children with a 10q11.22q11.23 deletion:

- Developmental delay
- Speech and language difficulties and delayed or absent speech
- Learning difficulties
- Behavioural difficulties
  [e.g. autism spectrum disorder (ASD), autistic like behaviour, attention deficit hyperactivity disorder (ADHD)]
- Sensory processing disorder
- Anxiety and/or emotional lability
  (rapid change in type/strength of emotion)
- Hypotonia (low muscle tone)

It is important to note that each person can experience different developmental and medical concerns. Some people with 10q11.22q11.23 deletions, such as parents identified as a result of their child's diagnosis, have no, or very mild symptoms, others experience one or more of the

symptoms listed. Symptoms may also depend on the size of the deletion and which genes are included as well as the unique genetic makeup of each person. The presence of other known or unknown genetic variations may contribute towards the development of more severe symptoms. Other less common features have also been reported in association with 10q11.22q11.23 deletions and are discussed later in this information guide.

The information in this leaflet is gathered from a small number of families and reports published in the medical literature. It may be that some symptoms are not directly or solely associated with 10q11.22q11.23 deletions. At the moment, there is limited information, but further research and information sharing may help explain further. If you have questions about symptoms and whether they are or could be related, you can ask your clinician (geneticist) for advice. The rarity of this deletion can present practical and emotional challenges. Families often feel worried and frustrated by the lack of information and can feel lonely and isolated. Joining a support group such as *Unique* can help with finding further information and connecting with other families.

The following information is summarized from the experiences of a few *Unique* families and those described in the medical literature.

Pregnancy and birth

Unique families did not commonly report complications during their 10q11.22q11.23 deletion pregnancies, most babies were born at or near their due date although two *Unique* babies with a 10q11.22q11.23 deletion were born premature. Three *Unique* families mentioned concerns during pregnancy but each concern was different and can occur during pregnancies of babies without chromosomal deletions.

Newborn

Babies with a 10q11.22q11.23 deletion are not known to commonly have a birth weight outside of the normal range. A few *Unique* families informed us that their babies experienced some difficulties during the new-born period, mainly feeding difficulties; two families mentioned the reason being that their child was 'tongue tied', this is when the connection of the tongue to the floor of the mouth is shortened and sucking is affected. Some families also mentioned food regurgitation and reflux (when food returns up the food pipe from the stomach). Four children with a 10q11.22q11.23 microdeletion and no other known genetic variation described in a research publication (Stankiewicz 2012) were diagnosed with GERD, gastroesophageal reflux disease.

Hypotonia was also mentioned by a few *Unique* families and by Stankiewicz 2012, this is when a child is described as being 'floppy' and it can lead to difficulties with sucking and swallowing, and/or latching onto the breast. Hypotonia can also result in delays reaching developmental milestones such as rolling, sitting, crawling and walking.

First signs

Since symptoms observed in people with a 10q11.22q11.23 deletion are so variable, babies and children are diagnosed at various stages of development. Babies with a 10q11.22q11.23 deletion are not commonly reported as having physical problems such as hernias that have been associated with other genetic changes. The majority of *Unique* members reported that their child was offered a genetic test due to concerns such as developmental delay, behavioural concerns, delayed speech, hypotonia or delayed motor skills. The age at which a genetic test was offered ranged from one year to 10 years, amongst members who completed the *Unique* 2019 survey. Children described by Stankiewicz 2012 as having a 10q11.22q11.23 deletion as their only known genetic variation, ranged in age from 1 month to 11 years.

Appearance

Children with genetic conditions often have subtle facial features that are not usually obvious to a parent but can be identified by a paediatrician or clinical geneticist. Facial features can be very subtle and children may not look very different to other children and may closely resemble their siblings and/or parents. Professionals looking after children with genetic changes are trained to notice physical features that may suggest a child's difficulties are of a genetic origin. Making a note of these may help establish common features observed in children with the same genetic change and therefore aid diagnosis. Although unusual facial features have been identified in children with 10q11.22q11.23 deletions, there does not as yet appear to be a common or shared feature.

Feeding and growth

A few families who have provided information about feeding have mentioned that their child with a 10q11.22q11.23 microdeletion had feeding problems as a baby. If a baby's nutritional needs cannot be met, they may require supplementation with a high energy formula or in rare cases via a nasogastric tube (a tube leading to the stomach that is inserted via the nose to allow all feeds to be taken directly).

Families mentioned that as their child grew they developed a healthy appetite but a few children displayed an aversion to certain types of food.

“ When she was little all she liked was milk and only soft foods, it wasn't until she was 3 that she started eating properly. She had a bottle until the age of 4 and a half as she would not drink out of a beaker or cup I must have tried every beaker going. I think it was due to her sensory issues. However she is now a really good eater and eats a wide range of foods I have no issues with her eating anymore. **”** - Age 12

“ He tends to stick to the same foods and eat them over and over again. He is a healthy eater but has a lot of sensory issues surrounding food. He has food aversions and feels anxious even when others are eating the food he dislikes if they are eating it in the same room. **”** - Age 8

❝ She had gastro oesophageal reflux and needed thickened drinks and anti reflux medicine. ❞ - Age 4

Sleep

While some families mentioned their child with a 10q11.22q11.23 deletion had no sleeping issues, a few families remarked that their child has some form of regular sleep disruption associated with anxiety.

❝ She has good and bad days, it was only recently that she started going to bed alone, before then I used to have to sit in her room for an hour until she fell asleep, and she would and still does wake up in the night. She gets scared at night time, she usually sleeps better if she stays up later. It's still ongoing with her sleep issues, recently she has started not going to bed alone again and sometimes she wakes in the night and wants to come in my room. ❞ - Age 12

❝ He has insomnia a lot. CBD helps a little. It is all about helping him reduce anxiety during the day. ❞ - Age 8

Child development

Once your child has shown their individual pattern of development it will become easier to predict their abilities and possible difficulties. *Unique* members have reported a range of difficulties in their children with a 10q11.22q11.23 deletion. Developmental delay (when developmental milestones are not reached within an expected time range) was mentioned by most families who shared this information about their child.

Gross motor skills and mobility

A number of 10q11.22q11.23 deletion families for whom we have information regarding motor skills mentioned that their child's gross motor skills are affected, many mentioned their child started to walk late and continued to show some difficulties in early childhood. For some, this may be related to hypotonia and/or joint hypermobility.

❝ She struggles with unfamiliar stairs or climbing equipment. She is a lot more confident as she's got older but still panics with stairs. ❞ - Age 12

❝ Even though he is big for his age and is fit, he struggles to with the skill level of his peers at sport. He complains of tiredness a lot and will often refuse to walk saying his legs are sore. He often injures himself (twisted ankles especially), and had a tendency to fall over a lot. His hypermobility has meant he overstretches muscles which makes him more prone to injury and causes fatigue. He walked at 15 months and crawled at 9 months. His mobility and strength are improving with age. He complained of sore feet a lot and had special orthotic insoles made but due to sensory issues, he refuses to wear them. ❞ - Age 8

❝ She started sitting unaided at 2 1/2 years, has a Kaye walker and uses a wheelchair. ❞ - Age 4

❝ He met his milestones until 15ish months but did not walk until he was 20 months. ❞ - Age 6

Fine motor skills

Some families who provided information regarding fine motor skills mentioned their child with a 10q11.22q11.23 deletion had mild difficulties with fine motor skills. Parents mentioned poor hand use and coordination and delays in meeting milestones.

“ She often needs help with buttons, hooks and some zips. She struggles with basic tasks such as opening certain packets of food or opening a can of pop. However she has good neat handwriting now and she uses a pencil grip. She used to go to occupational therapy to help with her motor skills and it did help teach her how to build on her muscle tone and use a knife and folk.**”** - Age 12

“ He writes with his right hand yet the occupational therapist assessed he was left handed. His hand writing was poor but has improved so much in the past few years that he has the best handwriting in the class. **”** Age 8

“ He cannot do buttons or laces. He needs a pencil grip to write, he cannot write small. **”** - Age 6

Self Care

Unique families informed us that self care can be delayed but is eventually achieved. Toilet training is commonly delayed, perhaps more so at night.

“ She was toilet trained at 3 and a half years however it wasn't until she was six that she stayed dry at night. She struggles to wash her hair thoroughly but can clean her teeth well now with prompting. She finds it hard to wipe in the correct way after using the toilet. **”** - Age 12

“ He toilet trained really well at 3 years old (even dry at night). He refused to dress himself for school until age 7, he needed a lot of prompting to dress and clean his teeth until age 7 but he does this really well now. He had great difficulty taking a bath and getting his hair washed. Even now at 8, he needs a lot of reassuring getting his hair washed. He does not like water on his head/face, this is a sensory issue and makes him very anxious.**”** - Age 8

“ She has delay toilet training and regression. She can't brush her own teeth but can wash, well tries, we do it all for her. **”** - Age 4

“ He took a long time to toilet train, he will have an accident sometimes and hide it, he doesn't wipe properly. He cannot cut food correctly and needs a special knife. **”** - Age 6

Ability to learn

Some children, but not all, affected by their 10q11.22q11.23 deletion experience learning difficulties. While some children are identified as having mild to moderate learning difficulties, the learning abilities of others are more severely affected and they have been given a diagnosis of intellectual disability (ID). Two *Unique* children and two children described by Stankiewicz 2012 with a 10q11.22q11.23 deletion and no other known genetic variation have been diagnosed with ID.

Some children attend a mainstream school and do not receive additional help while others have a dedicated support worker. A few children attend a school specifically for children with special educational needs and a few are home schooled. If your child is diagnosed early enough they may benefit from early intervention programmes. Children may also benefit from regular speech and occupational therapy sessions.

“ She went to a mainstream primary school and found school hard, she was many years behind academically and therefore we got her into a special school for secondary school when she started there for year 7. She is better off in her special school as she no longer feels different to other children and the work is suitable for her ability and they teach her life skills. She had always struggled with learning new things, she takes longer than others and often forgets what she has been taught. She is making steady progress in her new specialist school setting.” - Age 12

“ He attends mainstream and is above average compared to his peers. He was slow compared to others with the handwriting and problem solving but has caught up beautifully. He found creative writing very difficult but again is doing much better now. So I guess things were slow, but then he caught up really quick all of a sudden. His main issue with school is the anxiety leading up to going. If an issue arises socially in school, he refuses to go and misses a lot of school. Anxiety about school has led to depression and insomnia. He finds it difficult to communicate boundaries at school. He masks a lot of his anxiety so the school has difficulty understanding why he doesn't want to go. When he is home the anxiety meltdowns occur because of something that happened in school.” - Age 8

Speech, communication and sociability

The abilities to learn and to be sociable are strongly associated with the abilities to understand and use language. Ten *Unique* members with a child with a 10q11.22q11.23 deletion , and no other known genetic change, informed us that their child had or has delayed speech.

An assessment by a speech and language therapist should be able to identify specific difficulties and regular therapy sessions should be tailored to a child’s specific areas of need.

“ She didn't start talking proper sentences until around 2 and a half years. She has only just recently been discharged from Speech and Language therapist. ” - Age 12

While behaviour and sociability are affected by language abilities, other neurodevelopmental behavioural difficulties may also be involved (as described in the following section).

“ She finds it hard to socialize with peers of her own age as she is mentally younger and immature in her mind. She will say unkind words to others and be unaware of others feelings. ” - Age 12

❝ He was diagnosed with autism and he really struggles with social communication. He has experienced difficulties at school regarding this. He is very sociable and friendly and can socialise but only for a set amount of time before he needs to escape and 'defrag'. His preference is to relax on his own to play computer games. He talks very loudly all the time (no volume control). ❞ - Age 8

❝ She uses a laptop, pods book and other aids to communicate. ❞ - Age 4

Behaviour

Not all children or adults with a 10q11.22q11.23 deletion have behavioural difficulties, but as a group, they appear to show a higher incidence of behavioural, social and communication difficulties. It is not yet known exactly what causes this but a known vulnerability in this area means that children should be monitored and families offered early support.

Diagnoses that have been reported in some children with a 10q11.22q11.23 deletion include ASD (autism spectrum disorder) and ADHD (attention deficit hyperactivity disorder) but only a few *Unique* members with a 10q11.22q11.23 deletion have been given these diagnoses. A number of families mentioned that they suspect their child has ADHD but has not been officially diagnosed and others mention their child has not been given an ASD diagnosis since they did not 'tick all the boxes', which means they have autistic like features but lack a behaviour necessary for this diagnosis, such as repetitive behaviour. A few *Unique* families are awaiting an assessment for their child. Some behaviours can be related to other difficulties in areas such as comprehension and communication. Some families also mentioned their child suffers from anxiety.

From birth to at least 3 years of age, most children should be routinely screened for developmental milestones. If there are any concerns about a child's development (either from the doctor or a parent or carer) they should be referred for developmental evaluation, which may include a hearing test and autism specific screening.

There is not a 'medical test' that can diagnose autism, children undergo an autism-specific behavioural evaluation usually carried out by a specially trained physician and psychologist. The evaluation may be multidisciplinary and include a speech and language therapist as well as an occupational therapist, it is also tailored to the age of the child. Depending on the outcome, further evaluation by a specialist such as a developmental paediatrician, neurologist, psychiatrist or psychologist may be offered.

Autism is a spectrum disorder meaning that the same diagnostic 'name' is given for a number of different but closely related disorders. If a child doesn't 'tick enough boxes' to fall into the spectrum they may be described as having autistic like behaviour. The reasons for such behaviour are not always understood but are thought to have a neurological basis.

“ She has many autistic traits such as hand flapping and likes to play alone but had no diagnosis. She does behave inappropriately often and is sometimes unkind to others at school but had no diagnosis for any behaviour.” - Age 12

“ He was diagnosed with ASD, PDA (pathological demand avoidance) and anxiety. He is currently being assessed for ADHD by Educational Psychology.” - Age 6

Some children with a 10q11.22q11.23 deletion have been diagnosed with a sensory processing disorders (SPD). This means they have difficulties processing sensory input which can lead to behavioural difficulties as well as affecting social interactions and learning abilities. While most professionals diagnose and treat SPD nowadays, not everyone is aware of this neurological disorder. If you think your child has an unusual reaction to sight, sound, touch, taste and smell, they may have a SPD that may be affecting their behaviour. Movement, balance and body position can also be affected.

“ She had been diagnosed with sensory processing disorder. ” - Age 12

“ He was assessed by Occupational Therapy and diagnosed with SPD including auditory processing disorder. His sensory issues greatly affect his food, clothing, proprioceptive, sensitivity to touch (avoidance). A little bit of avoidance with noise. Sensory seeking with smells. ” - Age 8

Children with behavioural difficulties may benefit from specialist therapy such as BT (behavioural therapy) and ABA (applied behaviour analysis) therapy. Speech and language therapy (SALT) and occupational therapy (OT) may also be beneficial as well as other therapies such as RDI (relationship development intervention (helping children to develop different aspects of social connections).

“ My child is generally thriving however regression does occur. He gets extremely anxious over any new change (good or bad). When bad change happens it completely unsettles him and leads to periods of depression. This is becoming more apparent as he ages. He has attended a social skills training course. He has also had multiple sessions with a psychologist for emotional regulation help. ” - Age 8

Joining a social skills group may help your child with social difficulties to learn and practise important skills. A parenting course for autism may also help parents to learn behaviour management tools and help to encourage communication and cooperative behaviour in their child to strengthen their emotional wellbeing. Some parents have tried medication to help control their child’s behaviour when it becomes of great concern (such as self harming or aggression). If you think your child’s anxiety has become difficult for them to cope with you could discuss with your doctor the possibility of seeing a child psychologist to help establish some tools to help them deal with their feelings.

“ I attended autism training workshops. I spoke to an Educational Psychologist about his PDA. Trial and error. Have tried it all and have learnt to work around his needs and sensitivity. Usual autism strategies such as reward charts etc

have not worked as he feels pressured. It is a matter of picking your battles with him and working around his anxiety. When things get too much, I reach out for help. ” Age - 8

All children have some days that are better than others, regardless of their genetic make up. A few *Unique* families have shared their experiences:

“ She gets frustrated a lot if she can't do something such as put a dress on her doll, when frustrated she will throw things or try to head but the wall. When out in public she will not be aware of people around her and will try to run off if she gets mad about silly things such as she can't go to the shop she wants to first. She has trouble getting to sleep at night. On school morning's she will get anxiety. ” - Age 12

“ On a good day, he wakes early and likes to cuddle then will happily interact and have breakfast, get ready for school with no real issues. Not much anxiety going to school, will be talkative and his usual hyper self. Will come home, do homework, chatty, have some down time, then want to socialise a little after dinner by playing on the trampoline, running around the house etc, will loudly get ready for bed with no issues and will go to sleep with a quick bedtime routine. On a bad day, he will wake in middle of night with an anxiety nightmare, sleep in my bed, complain of stomach ache and possibly headache in the morning, refuse school completely with multiple anxiety screaming meltdowns, pop out in his rash, feel guilty for not coping and going to school. Will need a lot of reassurances. Will think everyone hates him. Crying, depression outbursts. Refuse food. Insomnia at bed time and will take 1-2 hours sitting with him to fall asleep whilst singing lullabies too. ” - Age 8

Puberty

There is limited information available about puberty in children with a 10q11.22q11.23 deletion although, at the time of writing, *Unique* had 6 members with a child aged between 13 and 17 with a 10q11.22q11.23 deletion and no other known genetic variation. Some families of children with chromosome disorders and behavioural or learning difficulties are concerned at their daughters ability to cope with menstruation, for some, discussing menstrual regulation options with a paediatrician may be beneficial.

Adults

When this information guide was written in 2019, *Unique* had 6 adult members (aged 18 or above) with a 10q11.22q11.23 deletion, three were unaffected or mildly affected parents who had passed on their deletion to their child. No late onset physical or mental health issues have been reported by *Unique* members or in those identified in the general population as having a 10q11.22q11.23 deletion (Crawford 2018).

Medical concerns

Some children with a 10q11.22q11.23 deletion have experienced medical concerns specific to them, but as yet, there have been no commonly reported medical issues specifically associated with 10q11.22q11.23 deletions. Most families report that their child is generally in good health with minor concerns as reported in the following sections of this guide. No *Unique* family has reported unusual findings following routine blood tests.

Seizures

It is not unusual for children with chromosomal deletions to experience seizures (a sudden change in electrical activity of the brain that causes momentary brain dysfunction), however, seizure activity was not commonly reported by *Unique* families with 10q11.22q11.23 deletions. Only one *Unique* family has informed us that their child with a 10q11.22q11.23 deletion has had seizures, the child experienced absence seizures, which is the momentary loss of awareness of surroundings or actions, and the seizures resolved after time and treatment with medication.

"He had absence seizures starting at age 5, about 50 per day. He was given epilim and I tapered him of it after 1 year and the epilepsy resolved itself."
- Age 8

Another *Unique* child was thought to be experiencing seizures but tremors (involuntary muscle contractions) were diagnosed. Other *Unique* families reported that their child with a 10q11.22q11.23 deletion had no signs of any seizure activity. However, one publication (Stankiewicz 2012) reported five children with a 10q11.22q11.23 deletion (and no other known genetic change) who experienced seizures. It is impossible to determine whether your child will experiences seizures at any stage of their development, but it has been reported in a few children, so if you do observe unusual behaviour that you are unsure about, you should discuss with your child's paediatrician.

Gastrointestinal problems

Food consumption and passage can be affected in a number of ways at any point of this complex process. A few *Unique* members who provided information about feeding mentioned difficulties during the first few months, mainly reflux (when food returns up the foodpipe) and vomiting, but problems resolved during childhood. There are many different reasons why this can occur (e.g. trouble swallowing, delayed emptying of the stomach, tight sphincter, blockage) so it is important the correct diagnosis is made to enable the most appropriate choice of treatment.

Constipation was reported in four children by Stankiewicz 2012 and one *Unique* child with a 10q11.22q11.23 deletion is known to suffer from constipation. It is important to identify the possible cause of the constipation and if treatment is needed.

“ She used to bring a lot of her milk back from her bottle feeds and was always underweight until she was about 2. ” - Age 12

“ He had frequent stomach pains, prone to constipation and reflux.” - Age 6

Eyes and vision

Eye and vision problems are not commonly reported in association with 10q11.22q11.23 deletions. Three *Unique* families reported that their child with a 10q11.22q11.23 deletion has an eye or vision problem. One family informed us that their child was short sighted. One *Unique* member had cataracts in both eyes which were surgically removed at 3 months of age, they are classified as legally blind. Another *Unique* member with a 10q11.22q11.23 deletion has retinol angiopathy (where blood vessels of the eye are affected), myopia (short-sightedness) and astigmatism (an irregular shape of the cornea). There is also a report in the medical literature of a chid with congenital nystagmus [which means they were born with an involuntary eye movement (that can also be voluntary) sometimes called 'dancing eyes'] and unilateral microphthalmos (which means both eyes are smaller than expected and may be malformed). There is another report of a child with opacification of the corneal stroma (when the cornea becomes opaque).

Ears and hearing

Ear and hearing problems are not reported in association with 10q11.22q11.23 deletions. No *Unique* family has reported an ear or hearing problem in their child with a 10q11.22q11.23 deletion and there are no reports in the medical literature.

Teeth

It is not uncommon for children with chromosomal changes to have problems with dentition but there is as yet no information that suggests dental issues are associated with 10q11.22q11.23 deletions. Two *Unique* members mentioned their child had a dental anomaly with one family providing further information regarding baby teeth.

“ Two of her bottom front baby teeth were joined together, however her adult teeth have now come though ok. ” - Age 12

Bones, joints and spine

Bone and joint problems do not appear to be a common feature of 10q11.22q11.23 deletions but a few families mentioned joint laxity and hypermobility which means joints can move beyond the expected range and can be painful.

“ He has hypermobility - he scored 8 out of 9 on the Beighton Scale by a genetics consultant. ” - Age 8

Families say ..... things our children love to do ....

" She enjoys playing outside in the garden on the slide, swing and diddicar. Indoors she enjoys playing with Barbie's, and my little pony figures, and drawing. She also enjoys watching her favourite programmes and DVDs.**"** - Age 12

" He enjoys being on his computer. Jumping on a trampoline. Running and jumping. Playing with his dog. He likes a lot of alone time. He does not like walking. He tends to socialise by himself as his first preference but is sociable and popular at school.**"** - Age 8

" She enjoys reading, playing with her younger sister, teddies, shape puzzles and the park.**"** - Age 4

If you or your child have a 10q11.22q11.23 deletion, please consider joining *Unique* to meet other families and share your information. The more we all know, the better we are able to help!

" There does not seem to be any information on this deletion. Doctors don't seem to be very concerned either. I find it isolating having a son with this deletion as not a lot is known about it. I could not see any groups on Facebook about it. **"** - Age 8

Deletions and genes

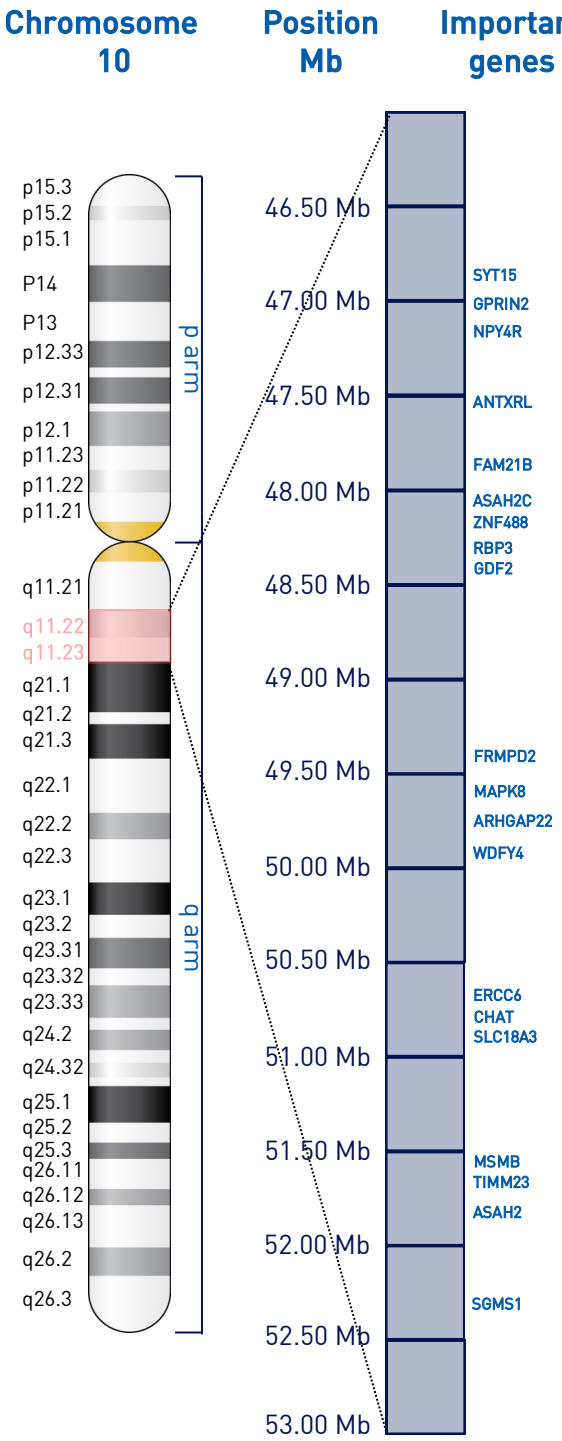
This section provides further information about important genes included in 10q11.22q11.23 deletions. This entire region contains about 120 genes and symptoms may depend on which genes are included in each child's specific deletion. A number of genes in this region are known to be expressed in the brain and have been associated with neurological function.

There is currently limited information known about the relevance of the genes in this specific region. Further information about 10q11.22q11.23 as well as the genes found in this region of chromosome 10 is continuously gathered as researchers study the effects of genetic changes. Gene's of interest may include:

SYT15: Synaptotagmin 15 is a membrane trafficking protein.
GPRIN2: G protein regulated inducer of neurite outgrowth 2.
WDFY4: WD repeat and FYVE domain containing protein 4.
NCOA4: Nuclear receptor coactivator 4.
ERCC6 Excision Repair Cross-Complementing Group 6)

RBP3, *GDF2*, *ERCC6*, *CHAT*, *SLC18A3*, *MSMB*, *MAPK8*, *FAM21B*, *ASAH2C*, *FRMPD2*, *TIMM23* and *ASAH2*.

There are reports of rare cases where children have a gene deleted from region 10q11.22q11.23, and the same gene on their second chromosome 10 is altered in a different way, which means that there is not a copy of that particular gene that is working as it should be. It would therefore be advisable for a child with a 10q11.22q11.23 deletion who has more severe or uncommon symptoms to be reviewed (e.g. referred to clinical genetics) to consider whether further investigations are needed.



This diagram was generated using Human genome build GRCh37/hg19 which was released in February 2009. If your genetic report was issued prior to this (e.g. hg18) or following the publication of this guide (e.g. Hg38) the position of the deletions may have changed slightly.

The yellow bars show example recurrent deletions that have been identified in children with developmental delay and neurodevelopmental difficulties.

Inform Network Support

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

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 http://www.rarechromo.org/donate Please help us to help you!

Facebook groups
www.facebook.com/groups/chromosome10disorder/
www.facebook.com/groups/152331614838414/

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 information guide is not a substitute for personal medical advice. Families should consult a medically qualified clinician in all matters relating to genetic diagnosis, management and health. Information on genetic changes is a very fast-moving field and while the information in this guide is believed to be the best available at the time of publication, some facts may later change. *Unique* does its best to keep abreast of changing information and to review its published guides as needed. This booklet was compiled by Unique (AP) and reviewed by Dr Corrina Powell, Specialist Registrar in Clinical Genetics, and Rosa Spencer-Tansley, Trainee Genetic Counsellor, Leicester Royal Infirmary Clinical Genetics Department ,UK.

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