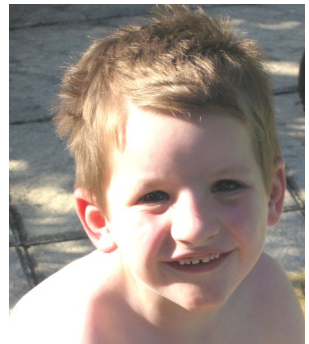




Understanding Chromosome & Gene Disorders

# Co-existing 9p duplication & deletion



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

## Co-existing duplication and deletion of chromosome 9p

Both **9p duplication** and **9p deletion** are clinically-recognised rare chromosome disorders (RCDs). A 9p duplication occurs when there is extra chromosome material from the short arm of chromosome 9 (9p) in the cells of the body, while a 9p deletion occurs when a piece of chromosome 9p is missing.

Sometimes an individual may have **co-existing duplication and deletion** of chromosome 9p, meaning there is both duplicated and deleted material. The size of both the duplication and deletion can vary and, as with other chromosome disorders, having an extra piece and missing piece of chromosome 9 may affect the development and intellectual abilities of a child, although there is considerable variability in these and other individual features that are observed.

When a particular set of developmental features occurs in a recognisable and consistent pattern as a result of a single cause, the condition is called a **syndrome**. The features of both 9p duplication and 9p deletion do occur in this way, so these disorders are sometimes known as **dup(lication) 9p syndrome** (or **trisomy 9p** or **trisomy 9p syndrome**, although the term “duplication 9p syndrome” is usually used since often there is only a partial, rather than whole-arm, duplication of 9p (Fujimoto 1998)) and **del(letion) 9p syndrome** (or **9p minus** or **monosomy 9p syndrome**), respectively. People with concurrent duplication and deletion of chromosome 9p are likely to have features associated with both duplication 9p and deletion 9p syndromes (Di Bartolo 2012; Pedurupillay 2014).

### *Unique's guides to duplications and deletions of 9p*

People with co-existing duplication and deletion of 9p usually have features that are associated with both 9p duplications and 9p deletions. *Unique* publishes separate guides to **9p duplications**, **9p deletions** and **9p24 deletions** that should also provide useful information.

## Background on chromosomes

Our bodies are made up of trillions of cells. Most of these cells contain a set of around 20,000 different **genes** that carry the instructions that tell the body how to develop, grow and function.

Genes are carried on structures called **chromosomes**. Chromosomes (and hence genes) usually come in pairs with one member of each chromosome pair inherited from each parent.



Chromosome pairs 1-22,  
X and Y (male)  
Chromosome 9p pair circled in red

## Sources

The information in this booklet is drawn from 16 cases in the published medical literature and information from *Unique* members. The first-named author and publication date from articles in the medical literature 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*. Nine *Unique* members with co-existing duplication and deletion of chromosome 9p completed a survey in 2017. In addition, information has also been drawn from the database records of six other members with co-existing 9p duplication & deletion.

A normal cell in the body has 46 chromosomes. Of the 46 chromosomes, two are a pair of sex chromosomes: two Xs for a girl and an X and a Y for a boy. The remaining 44 chromosomes are grouped into 22 pairs and are numbered 1 to 22, approximately from largest to smallest.

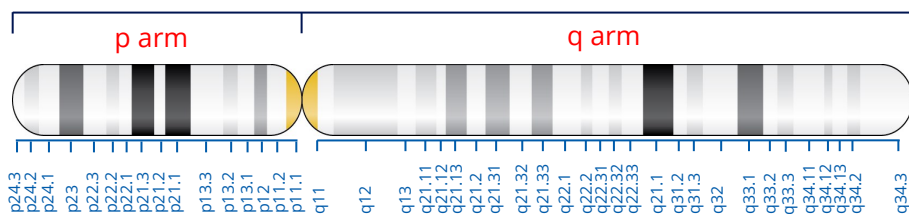
## Chromosomal changes

When a sperm and egg cell join they form a single cell. This cell must continuously make copies of itself and all its genetic material (**replicate**) 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(s) are lost, duplicated and/or become rearranged. The effect of any chromosomal change varies according to how much genetic material is involved and, more specifically, which genes and/or regions that control genes are included, as well as numerous other factors that we are only just beginning to understand (see [Are the size and location of the duplication and deletion significant?](#)).

The term **"dup/del"** that is used throughout this guide refers to a duplication of part of the p arm of chromosome 9 that is accompanied by a deletion of part of the p arm of chromosome 9. A duplication of 9p21.3 to p24.2 accompanied by a deletion of 9p21.1 to p21.3 would be written as **dup 9p21.3p24.2/del 9p21.1p21.3**

## Looking at chromosome 9

Chromosomes can't be seen 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 and sub-bands. You can see the banding pattern for chromosome 9 in the image below.



Each chromosome has a short (**p**) arm (from *petit*, the French for small) and a long (**q**) arm. Bands are numbered outwards starting from the point where the short and long arms meet (the **centromere** (marked in yellow)). A low number such as p12 that is close to the centromere is in a **proximal** region. A higher number such as p23 that is further from the centromere and closer to the tip of the chromosome is in a **distal** region. The term **cen** is used to indicate a location that is very close to the centromere, while **ter** (for terminal) indicates a location that is very close to the end of the p or q arm.

With any duplication or deletion, the amount of duplicated/deleted DNA can vary. Duplications or deletions that are so small that they are not visible under the microscope using standard techniques are called **microduplications/microdeletions**.

A laboratory technique called **FISH** (fluorescence *in situ* hybridisation) enables sections of the chromosome to be analysed in more detail and can help detect a duplication or deletion. This technique uses fluorescently labelled pieces of DNA that match the DNA in specific places on a chromosome so this test will only be offered if there is a suspected abnormality in a specific region of a chromosome.

The more commonly used test nowadays is called **chromosomal microarray (arr)** and allows genomic DNA to be analysed in greater detail. An array test can detect very small duplications and deletions even when this diagnosis is not suspected. It will also identify a more precise position on the chromosome for the piece of DNA that has been duplicated or deleted, but it cannot show if a new piece of DNA has moved to a different place on the same chromosome or to a different chromosome.

Advances in **next generation sequencing (NGS) technologies** offer the promise of ever-more accurate diagnosis and understanding of RCDs. NGS allows multiple genes; the entire protein-coding portion of all the genes in the genome (**whole-exome sequencing (WES)**); or even the entire genome (**whole-genome sequencing (WGS)**), rather than just targeted regions or individual genes, to be sequenced. This allows variation across the entire genome to be assessed and may be particularly useful for detecting microduplications/microdeletions that may be missed by less sensitive microarray analysis. NGS can also more accurately diagnose low-level mosaicism (see **Mosaicism**).

NGS techniques have the potential to dramatically reduce the time taken to give an accurate genetic diagnosis and allow a more tailored prognosis, management regimen and genetic counselling advice to be provided for a particular condition. The need to carry out additional diagnostic tests e.g. biopsies, which may be expensive and invasive, is also reduced.

While the benefits of advances in NGS technologies are undeniable, they do not come without challenges, including: storage of the massive amounts of data that are produced; issues pertaining to who should have access to the data; and how to handle incidental, secondary findings that may impact on the individual who has been tested e.g. unrelated adult-onset conditions. The use of gene panels comprising a more limited subset of genes (from two to >100 genes) that are believed to be linked to a particular RCD, or the feature(s) associated with the RCD, can help to reduce the number of such incidental findings and reduce the amount of data produced (Rabbani 2016; Firth 2018).

Historically, a microdeletion/microduplication co-existing with a larger, diagnosed duplication or deletion may have remained undetected, meaning that there may be more individuals with co-existing duplication and deletion of 9p than we are aware of. The use of microarray technologies, and in particular advances in NGS, offer the promise of detecting more cases of co-existing duplication and deletion of chromosome 9p and could improve our understanding of so-called “critical regions” for certain features, and help allow for the provision of more accurate genetic counselling (see **Are the size and location of the duplication and deletion significant?**) (Di Bartolo 2012; Shi 2017).

## Chromosome test results

Your geneticist or genetic counsellor can tell you more about the genes and chromosome material that has been duplicated and deleted. You will be given the results of your test, which will tell you how much of chromosome 9 has been duplicated and deleted.

Depending on the test that was carried out, someone with co-existing 9p duplication and deletion might have a karyotype that looks like one of these examples:

**46,XY,der(9)del(9)(p22)dup(9)(p12p22)** This result shows that the expected number of chromosomes (46) were observed. It also shows that an X and a Y chromosome were found, so this is a boy or a man. There is a derivative chromosome (*der*), in this case involving more than one rearrangement within chromosome 9 (9). *Del* (9) means there is a deletion of chromosome 9. (p22) shows the band in the chromosome that is deleted. *Dup* (9) means there is also a duplication of chromosome 9. (p12p22) shows the bands in the chromosome that are duplicated; in this case, there is a gain of a chromosome segment from bands p12 to p22. This person therefore has a 9p deletion and a 9p duplication.

**arr 9p24.3p23(203861\_10579116)x1, 9p23(10579116\_12914472)x3 [hg19] dn** This result shows that the analysis used microarray technology (*arr*) and revealed two DNA anomalies. One involves bands 9p24.3 to p23 and the DNA that lies between base pairs 203861 and 10579116 (10,375,305 base pairs, or 10.38 Mb)). There is one copy missing (x1; the normal copy number is two) so it is a deletion. The second involves band 9p23 and the DNA that lies between base pairs 10579116 and 12914472 (2,335,356 base pairs, or 2.34 Mb)). There is an extra copy (x3) so it is a duplication. This person therefore has a 9p deletion and a 9p duplication. *hg19* tells you which version of the human genome was used for comparison (see [Genome Assemblies](#) (blue box)). The duplication occurred *dn* or *de novo* (as a 'new event'); the parents' chromosomes have been checked and no duplication or other chromosome change has been found on their 9p.

**Mos 46,XX,del(9)(p22.3)dup(9)(p11p22.3)[18]/46,XX,del(9)(p22.3)[12]**

*Mos*(aicism) (see [Mosaicism](#)) means that different cells in this individual have different numbers or arrangements of chromosomes. This result shows that the expected number of chromosomes (46) were observed and it's a girl or woman (XX). Thirty cells have been tested. Eighteen [18] cells had a deletion (*del*) of chromosome 9 (9) involving sub-band p22.3 (p22.3) and a duplication (*dup*) of chromosome 9 (9) involving the bands p11 to p22.3 (p11p22.3); these cells therefore have a 9p deletion and a 9p duplication. Twelve [12] cells also showed the karyotype for a girl or woman (46,XX) but the analysis also revealed a deletion of chromosome 9 (*del*(9)) involving sub-band (p22.3). This person therefore has a co-existing 9p duplication and deletion in some cells and a 9p deletion alone in other cells.

## Mosaicism

In a few people, the cells containing the 9p duplication and deletion chromosome material exist alongside cells with either a normal

## 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 hence the numbers for individual genes and duplications can shift.

Each new version of the genome is often referred to as an 'assembly'. Every few years a new assembly is released. The genetic information you are given will be based on the Genome Reference Consortium (GRC) human (h) genome assembly that was the most up-to-date at the time the test was carried out. Therefore, you may see the DNA sequence referred to as hg19 (human genome 19) (on your child's genetic report it may also be referred to as GRCh37), which was released in 2009, or hg 18, which was released in 2006. The lower the hg number, the earlier the release. The most recent assembly is named GRCh38/hg38 and was released in 2014.

chromosome number and arrangement or a 9p duplication or deletion alone. This situation, known as [mosaicism](#), typically arises after fertilisation.

## How common is co-existing 9p duplication and deletion of 9p?

It is difficult to say but we do know that co-existing duplication and deletion of chromosome 9, and no other RCD, has been described in at least 16 patients in the medical literature, [although there are undoubtedly many more people who have either not been described or are undiagnosed](#) (Teebi 1993; Muroya 2000; Krepischi-Santos 2003; Faas 2007; Hauge 2008; Swinkels 2008; Hulick 2009; Jelin 2010; Al Achkar 2010; Chen 2011; Di Bartolo 2012; Neira 2012; Recalcati 2012; Kowalczyk 2013; Schlade-Bartusiak 2013; Pedurupillay 2014).

In 2017, *Unique* had 15 members with co-existing duplication and deletion of chromosome 9. We are very grateful to the 9 members who completed a detailed survey in 2017 and also to those members whose database information was used to complete this guide.

## Why did this happen?

Chromosome disorders can occur either as a result of rearrangements in one parent's own chromosomes that are passed on to the child or out of the blue (*de novo*), so the child with the chromosome disorder is the first person in the family with rearranged chromosomes.

The first step in finding out which mechanism is behind a child's RCD is to check the parents' chromosomes with a blood test. The evidence from the medical literature and *Unique* members suggests that this is most likely to show that the parents both have perfectly normal chromosomes (Neira 2012; Unique). The duplication and deletion of 9p has therefore happened as a mistake during the immensely complex process of DNA copying and assembly that happens when the parents' sperm or egg cells were formed. Geneticists refer to these events as '*de novo*' (dn), meaning the duplication and deletion have occurred as a new event in the child, as opposed to being inherited.

Regardless of whether the duplication and deletion are inherited or *de novo*, chromosome rearrangements affect children from all parts of the world and from all types of background. They also happen naturally in plants and animals. There is no reason to suggest that your lifestyle or anything that either parent did before, during or after pregnancy caused the duplication and deletion.

The data of the nine *Unique* families who completed the 2017 survey, suggests that the vast majority of cases of co-existing duplication and deletion of chromosome 9p are *de novo* events: 6/9 cases were *de novo*; one family chose not to be tested; one family were unsure; and one mother also had a small duplication.

## Diagnosis

The age at which diagnosis occurred is variable. Evidence from *Unique* suggests that the majority of members were diagnosed at birth or within the first year, usually as the result of concerns immediately after birth, a delay in reaching developmental milestones or “dysmorphic” (unusual) features.

One girl with co-existing 9p23p24.1 duplication and 9p24.1p24.3 deletion of chromosome 9p was only diagnosed as a 10-year-old. This case is very much the exception and it should be noted that in contrast to other *Unique* members where the duplication always lies within the so-called “critical regions” for 9p duplication syndrome, the duplication in this case lies outside these so-called critical regions, although the girl still has features of 9p duplication syndrome. The deletion also lies outside the proposed 9p22.2p23 “critical region” for features of 9p deletion syndrome, although this is also the case for more than half of *Unique* members with co-existing 9p duplication and deletion (see [Are the size and location of the duplication and deletion significant?](#)).

While the data is limited, it seems that co-existing duplication and deletion of 9p may be more common among girls than boys: among *Unique* members, nine girls and six boys were affected, while in the medical literature cases involving ten girls and five boys have been reported.

“Our son was tested when he was a couple of days old because he scored a 3 [out of 10] on the Apgar test. The diagnosis was helpful because he had a lot of issues as a baby.” - dup 9p13.1p23/del 9p23p24.3

## Can it happen again?

The chances of having another child with a co-existing 9p duplication and deletion depend on the results of chromosome tests on the parents. Where the test shows that the parents’ chromosomes are normal, their chances of having another affected child are usually no higher than for anyone else in the population. Where the test reveals a rearrangement in the parents’ chromosomes, the chances are very much higher. Each family’s situation is individual and all families should be able to discuss the possibilities they face with their geneticist or genetic counsellor.

(Note: Included in the *Unique* series were two siblings with the same co-



existing 9p21.3p24.2 duplication and 9p21.3p21.3 deletion, despite genetic testing revealing that both were *de novo* events with both parents testing negative. This cannot be explained by the senior geneticist who equated the chances of this happening to "being hit by lightning twice".)

## Features associated with co-existing 9p duplication and deletion

Each person with a co-existing 9p duplication and deletion is unique and will have different developmental and medical concerns, even among those with the same or very similar chromosome rearrangements (see [Are the size and location of the duplication and deletion significant?](#)). Both 9p duplications and 9p deletions give rise to recognisable syndromes, and individuals are likely to have a combination of features associated with both syndromes, although there is a great deal of variability and some features are common to both 9p duplication and deletions.

### Most common features of 9p duplications:

- A recognisable "look" to the head and face e.g. low-set, unusually-shaped or prominent ears; a broad nose with a bulbous tip; widely-spaced, down-slanting eyes that may be deep-set or even sunken or with skin folds at the inner corner of the eye; a short space between the nose and upper lip; a mouth with down-turned corners; a low hairline; and a short, broad and sometimes webbed neck
- Some degree of developmental delay
- Some degree of learning disabilities, ranging from mild to profound
- Speech and language delay
- Growth delay, which is usually mild
- Abnormalities of the hands and feet
- Dental issues including late teething, over-crowding, tooth-grinding, weak enamel
- Low muscle tone (hypotonia)
- In boys, minor anomalies of the genitals or undescended testicles are common. Abnormalities in the genitals of girls are less common
- Constipation
- Feeding difficulties, including reflux, which usually resolve after babyhood or early childhood

### Other features

These features are also found in some people with 9p duplications:

- Spinal curvature/skeletal abnormalities
- Loose and easily extendable joints or, less commonly, stiff joints
- Large anterior fontanelle (soft spot on the top of the head) in babies; the bones of the skull are slow to fuse
- Talipes (club foot) or otherwise unusually angled feet
- Short-sightedness and/or strabismus
- Glue ear/frequent ear infections, which usually resolve during childhood
- A high, narrow palate or, less commonly, a cleft lip or palate



- Seizures
- Frequent respiratory infections in babyhood and early childhood
- A heart condition, which often resolves naturally
- Anomalies of the brain
- A very wide range of other unusual features have been described in the medical literature and by *Unique* members

(Fujimoto 1998; Schinzel 2001; Bonaglia 2002; de Pater 2002; Zou 2009; Amasdl 2012; Guilherme 2014; Stagi 2014; Brar 2017; Unique)

## Most common features of 9p deletions:

- A recognisable “look” to the head and face e.g. widely-spaced, up-slanting eyes that may have skin folds at the inner corner of the eye; a long space between the nose and upper lip; under-grown upper jaw, cheekbones and eye sockets; a nose with up-turned nostrils and a flat nasal bridge; a small mouth; a small/receding jaw; low-set, unusually-shaped ears
- Trigonocephaly (a keel-shaped forehead) or a minor ridge on the forehead; a flat occiput (back of the head)
- Some degree of developmental delay
- Some degree of learning disabilities, ranging from mild to profound
- Speech and language delay
- Growth delay, which is usually mild
- Abnormalities of the hands and feet
- Dental issues including late teething, over-crowding, tooth-grinding, weak enamel
- Low muscle tone (hypotonia)
- In boys, minor anomalies of the genitals or undescended testicles are common and in a few cases it may not be possible to assign sex or there may be sex reversal, with babies with male XY sex chromosomes having a female genital appearance; abnormalities in the genitals of girls are less common
- Constipation
- Feeding difficulties, including reflux, which usually resolve after babyhood or early childhood

## Other features

These features are also found in some people with 9p deletions:

- Spinal curvature/skeletal abnormalities
- Loose and easily extendable joints
- Nystagmus (abnormal eye movements)/strabismus (a squint)
- Glaucoma
- Cataracts
- Narrow or blocked nasal passages
- Glue ear/frequent ear infections, which usually resolve during childhood
- A high, narrow palate or, less commonly, a cleft lip or palate
- Frequent respiratory infections in babyhood and early childhood

- A heart condition
- Anomalies of the brain
- Seizures
- Kidney reflux
- Hernias (an organ protrudes out of the normal position)
- Omphalocele (a baby's intestine or other abdominal organs are outside of the body because of a hole in the belly button (navel) area. The intestines are covered only by a thin layer of tissue and can be easily seen)
- Hypopigmentation (light patches) of skin/hair
- Excessive drooling
- Precocious (early) puberty
- Autism spectrum disorder (ASD)
- Sleep disorders

(Christ 1999; Kawara 2006; Swinkles 2008; Recalcati 2012; Onesimo 2012; Güneş 2016; Spazzapan 2016; 9pminus.org; Unique)

## Are the size and location of the duplication and deletion significant?

One of the most common question parents would like answered is: "How will the size and location of the duplication/deletion influence how my child is affected?". It has become clear that there is a great deal of variability in how individuals are affected regardless of the size and location of the duplicated and deleted regions. It would seem obvious to assume that the amount and location of the duplicated and deleted material would determine the range and severity of features - so people with small duplications/deletions would be less severely affected than those with larger duplications/deletions and the duplication and deletion of particular regions would always be associated with particular features - but this would be oversimplistic (Bonaglia 2002; Hauge 2008; Zou 2009; Abu-Amro 2010; Jelin 2010; Bouhjar 2011; Di Bartolo 2012; Pedurupillay 2014; Brar 2017).

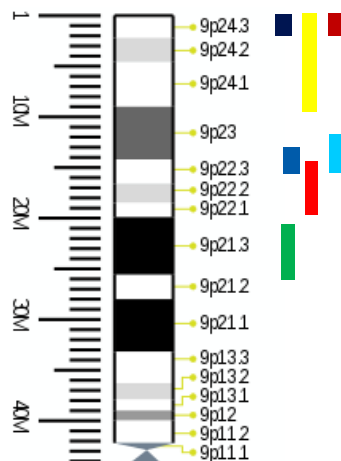
We do know that there can be markedly different outcomes depending on whether a particular, specific region of chromosome 9p is duplicated or deleted: where a duplication involves only the region 9p11.2 to p13.1 there are no apparent consequences for development, while conversely deletions involving only 9p12 to 9p13 are associated with a range of features, including moderate developmental delay, feeding difficulties, ADHD, hand tremors and tooth grinding (Calabrese 1994; Giltay 1994; Eshel 2002; di Giacomo 2004; Niemi 2012; Crone 2016).

## Potential critical regions for 9p duplications

A 'critical region' for the characteristic features of a 9p duplication was previously proposed to lie in a ~6 Mb (that is, six million base pairs, or 'rungs' on the DNA ladder) segment between 9p22.1 and 9p23, between microsatellite markers D9S267 and D9S162 (McGuire 2000). This would mean that people with a duplication that does not include this segment would not be expected to show all, or indeed any, of the typical features.

## Proposed possible critical regions for 9p duplication & 9p deletion syndromes

- Proposed learning difficulties critical region (9p duplications)
- Proposed craniofacial features critical region (9p duplications)
- Proposed speech/language delay critical region (9p duplications)
- Proposed 9p deletion syndrome critical region
- Proposed critical region for more distal deletions (9p deletions)
- Proposed sex differentiation critical region (9p deletions)
- Proposed Autism Spectrum Disorder critical region (9p deletions)



Attempts have since been made to narrow down the “critical regions” for specific features. It has been suggested that for learning difficulties this lies within a 2.6 Mb region of 9p22.3p23; for speech/language delay within a 4.9 Mb region of 9p21.2p21.3; and for unusual skull and facial features within region 9p22.1p22.3. A region predisposing for anomalies of the palate has also been suggested to reside within p22.1p22.2 (Haddad 1996; Fujimoto 1998; Bonaglia 2002, de Pater 2002; Zou 2009; Abu-Amero 2010; Brar 2017).

While there are examples in the medical literature and *Unique* series that support a link between the size and location of the duplication and the range and severity of the features observed, within the *Unique* series this link is sometimes less clear. While two children with no more than a moderate learning disability had duplications involving the whole of chromosome 9p, some people with much smaller duplications had more far-

reaching difficulties: a girl with a distal duplication of only 9p24.1p24.3 had many features of duplication 9p syndrome, including seizures, strabismus, brain anomalies, feeding difficulties, hypotonia, developmental delay, mild intellectual difficulties and a speech delay. Conversely, an adult man with a 9p24.1 duplication had only a few, mild features and had served in the military and held down a number of jobs.

Within families, members with the same duplication can show marked differences in the degree to which they are affected. A brother and sister with a paternally inherited 9p22.3p24.1 duplication had an overlap in some features but also marked differences, while their father was only diagnosed in his forties, but had a speech delay and struggled at school.

“ [My son and daughter have the same 9p22.3p24.1 duplication as their father]. There are things in common but there are so many different things with the same duplication. ” - Mother of two children with a “small” dup 9p22.3p24.1

## Potential critical regions for 9p deletions

A similarly complex picture has emerged when attempting to identify a critical region(s) that when deleted leads to the features associated with 9p deletion syndrome. While a number of research groups narrowed down the potential critical region to within 9p22p23, which it was suggested by one group of researcher could be further refined to a much smaller 0.3 Mb region within 9p22.3, subsequently several groups have described a more distal critical region closer to the tip of 9p that contains genes that are believed to contribute to the features associated with 9p deletion syndrome. Further, deletion of genes in the 9p24.3 region have been implicated in cases of sex reversal and genital anomalies that are sometimes associated with 9p deletions (see [Anomalies of the genitals](#)), while a gene(s) associated with autism spectrum disorder (ASD) is believed to be located within 9p24 (see [Challenging behaviours](#)).

As with 9p duplications, the link between the size and location of the 9p deletion and the features observed is not as straightforward as this suggests. Children with similar deletions can show marked differences in the severity and range of features. To take one example, when a research group compared 12 patients with co-existing 9p duplication and deletion where the deletion included 9p24.3, only one was found to have genital anomalies (Veitia 1997; Christ 1999; Kawara 2006; Faas 2007; Vinci 2007; Hague 2008; Swinkels 2008; Di Bartolo 2012; Yang 2012; Pedurupillay 2014; Güneş 2016; Unique).

## What does this mean for co-existing 9p duplication and deletion?

It is clear from the medical literature that it is also not possible to predict exactly how an individual with both a 9p duplication and 9p deletion will be affected by looking at the size and location of the duplication and deletion alone, although they are likely to have a combination of features associated with 9p duplication and deletions syndromes.

Within the 2017 *Unique* series, the three individuals with deletions including part of the proposed critical region for 9p deletion syndrome had more of the features associated with 9p deletion syndrome than those with deletions outside this region: most notably all had hernias, nystagmus, sleep apnoea and two had trigonocephaly. Two children for whom we had limited information in the *Unique* database, but who also had deletions including this critical region, both had omphalocele – the only children to do so – and one had trigonocephaly.

The overlap in many of the features associated with 9p duplication and 9p deletion syndromes, including developmental delay, intellectual disability, heart conditions, seizures, problems with hearing, skeletal anomalies and genital anomalies, makes it particularly difficult to determine the cause of a particular feature(s).

Further, even two sisters with exactly the same co-existing 9p duplication and deletion showed marked differences in the extent to which they were affected.

“ I have two daughters with the exact same genetic defect of a deletion and duplication of chromosome 9p; however, their presentations are different. One is quite severely affected, and one is quite mild. Every child is unique and there is a huge spectrum of expression even with the exact same genetic disorder. ” - Mother of two children with dup 9p21.3p24.2/del 9p21.3p21.3

## Why is there such variability?

The reasons behind why people with the same - or very similar - co-existing 9p duplication and deletion show such variability in the range and severity of features are complex and not yet fully understood.

Proposed explanations include: the cumulative effects of the variation in the DNA sequence across a person's whole genome; the outcome of interactions between genetic variants across the genome; and the influence of environmental factors (both internal and external) on the individual's genome. For instance, so-called “modifier genes” located across the genome can influence the expression of another gene(s) that may play a role in the development of a particular feature.

Duplications and deletions that result in the gain or loss of a group of genes that are located adjacent to each other can lead to multiple, unrelated features, contributing to the broad range of features observed for a particular RCD. Equally, a particular duplication/deletion may disrupt a gene or genes in a way that a similar but slightly different duplication/deletion does not, leading to the development of a specific feature(s).

Moreover, when you consider that an individual feature may result from variation in any of a number of genes located across the genome on different chromosomes, as is the case for intellectual disability, which can be caused by variants in one or more of >700 genes, it is not surprising that there is often an overlap in features observed across the range of RCDs that affect different chromosomes (Firth 2018).

Ultimately, while it may be tempting to try to compare your child to children with the same or similar co-existing duplication and deletion genotypes (both in the medical literature and within *Unique*), and while this will help to build up a general picture of what to expect, there will still be differences between your child and others with apparently similar genotypes. Your child is a unique individual and will make their own journey.

## Pregnancy and Birth

While many mothers said that their pregnancy was uncomplicated, and the subsequent birth was uneventful, up to one third of parents reported some cause for concern.

A genetic test during pregnancy may be suggested if there are concerns about foetal development or an anomaly is detected. One mother was told of the presence of an omphalocele following an ultrasound scan at 20 weeks, and a subsequent ultrasound found fluid surrounding the lungs, heart, abdomen and neck. These findings led to an amniocentesis to allow genetic testing that revealed the presence of a *de novo* co-existing duplication 9p13.3p22.2 and deletion 9p22.2p24.3. Others reported individual instances of an unusually small head (microcephaly) and intrauterine growth restriction (IUGR); an un-specified abnormal test *in utero*, which doctors believed could indicate Down’s syndrome; an irregular heart beat and bleeding during the first trimester; and an under-sized uterus (womb). The majority of pregnancies described in the medical literature were uneventful.

Five *Unique* babies were delivered by caesarean section: two as the result of breech or transverse positioning, one was scheduled due to a previous history of c-section, and one baby was too large to be delivered vaginally. Only one emergency c-section, due to IUGR, low levels of amniotic fluid and reduced movements was recorded.

A range of birth weights was recorded, with a tendency towards birth weights that were average or below average but within the normal range. A few babies grew very slowly in the womb and were tiny at birth, while several were of above average weight (unusually for an RCD, a trend towards above average birth weight has previously been noted for *Unique* babies with a 9p deletion).

Birth weights		
	Average birth weight	Range
<b>Unique members (12*)</b>	6lb 3oz (2.8kg)	1lb 8oz (0.68kg) - 9lb 2oz (4.138kg)
<b>Medical literature** (7*)</b>	6lb 1oz (2.76kg)	5lb 1oz (2.3kg) - 7lb 11oz (3.5kg)

\* - Number of Unique members/patients with co-existing 9p duplication and deletion for whom we have relevant data. \*\* - Hauge 2008; Hulick 2009; Di Bartolo 2012; Neira 2012; Kowalczyk 2013; Schlade-Bartusiak 2013; Pedurupillay 2014

The majority of pregnancies went to term; a few babies were born prematurely and tended to be those with the lowest birth weights.

## Feeding in the new-born period

Feeding problems are common in babies and children with a chromosome disorder.

The vast majority of *Unique* babies with a co-existing 9p duplication and deletion, including 7/9 babies in the *Unique* 2017 survey, experienced some degree of difficulty with feeding in the new-born period, which led to poor weight gain and in some cases failure to thrive and medical interventions. Two sisters with co-existing dup 9p21.3p24.2/del 9p21.3 appear not to have experienced feeding difficulties and were breastfed from birth.

Babies may find it difficult to latch on; suck weakly; and find it difficult to co-ordinate sucking, swallowing (dysphagia) and breathing, which can also make bottle-feeding time-consuming. Babies with a high/arched or cleft palate (roof of the mouth) may find sucking particularly hard. Some babies need to be fed for a short while by nasogastric (NG) tube, including 5/9 in the *Unique* survey. Occasionally, babies needed to be fed directly through a tube to the stomach (a gastrostomy) for some months or years. A baby with a co-existing dup 9p23p24.1/del 9p24.1p24.3 found bottle-feeding difficult but was able to breastfeed for the first year before moving on to a sippy cup.

Reflux was also prevalent in babies and during the early years; some babies suffer from gastro-oesophageal reflux disease (GERD/GORD), where feeds frequently and forcefully return up the food pipe from the stomach. Two *Unique* children had problems with aspiration (where difficulties with swallowing mean that there is a high risk of food, fluid and saliva entering the windpipe or lungs). These conditions can be helped by holding a baby upright for feeds and letting them sit in a semi-upright position afterwards. Your doctor can prescribe milks that are thickened and easier to keep down, and medicines that help feeds to stay down and act against the acid effect of stomach contents on the food pipe. If these measures do not work, it is possible to strengthen the valve between the food pipe and the stomach with a surgical operation called a fundoplication, in which the top of the stomach is wrapped around the bottom of the oesophagus and stitched in place. At the same time the hole in the diaphragm through which the oesophagus passes is tightened (Hulick 2009; Kowalczyk 2013; Schlade-Bartusiak 2013; *Unique*). Some children and teenagers had on-going problems with constipation (see [Constipation](#)).

Children may benefit from attending a feeding clinic where an assessment can be made, and advice given to help treat any eating and drinking difficulties.

“ He needed orogastric tube feeds to start - then could not take a bottle as he had a high arched palate and swallowing difficulties. Whilst still in hospital we tried feeding with a soft-edged cup and numerous teats to no avail, and so returned to orogastric feeds. He was eventually fitted with a gastrostomy tube at three years and came on leaps and bounds afterwards. Also suffered from severe reflux and vomiting. ” - dup 9p12p22/del 9p22



“ Our daughter was born with a cleft lip and palate. Had a NG tube for first three days, while in hospital. Then fed with a Haberman feeder teat until cleft palate surgery at eight months. Tried to breastfeed; however, she couldn't due to cleft. She had expressed breast milk (EBM) until she was 15-months-old, via a bottle. ” - dup 9p12p24.2/del 9p24.3

“ He had severe reflux and GERD. We were able to help the problem through reduced flow. While it was originally recommended to place a feeding tube, we found alternative solutions that worked for him. Breastfeeding was challenging. He had severe allergies to just about everything, his stomach was always severely bloated, and he was head-to-toe covered in eczema. ” - dup 9p13.1p24.3/del 9p24.3

“ Severe GERD. Problems with digestion necessitated NG tube feeds. Suspected possible problem with palate since he had difficulty nursing, but this has not been confirmed. Since having much of his ileum and colon removed he has had a central line for providing much of his nutrition. Has a gastrojejunostomy (GJ) button because he can't tolerate anything in his stomach, including his own stomach acid! Fed through this button into his jejunum [part of the small intestine]. Also has a central line to supplement nutrition. ” - dup 9p13.3p21.3/del 9p22.1

## Growth

While a slight delay in growth before birth is occasionally observed, a pattern of slow growth in babies and children was more common, affecting 4/9 children in the *Unique* 2017 survey and many children in the medical literature. In the *Unique* series any delay was generally deemed to be “mild” or “moderate”.

Children and teenagers in the *Unique* series were of below average (6/9) or average (3/9) height and often of average weight (6/9). A further two children were described as being below average weight and one above average weight. A similar picture is recorded in the medical literature, although here the trend towards below average height and weight was more marked. *Unique* families note a range of statures including “short and stocky”, “short and thin/slim”, “proportionate” and “tall and thin”.

A low level of growth hormone (GH) has been recorded for one child with co-existing dup 9p22.2/del 9p21.1. A growing number of children with 9p duplications in the medical literature responded well to GH treatment with limited evidence that treatment may be accompanied by an improvement in gross motor skills (Joy 2017; *Unique*) (see [Duplications of 9p](#) guide). There is some evidence to suggest that treatment with GH can lead to a worsening of scoliosis, which should be monitored carefully if treatment is undertaken in affected children (Stagi 2014; Canton 2016).

Equally, a delayed bone age is likely to account for some of the recorded incidence of growth delay (see [Bones](#)). Children with a delayed bone age may be small for their age but growing at a normal rate, and may continue to grow until their twenties, allowing them to catch up at least partly in height.

“ We thought he might have a growth delay, but it was actually delayed

bone growth, so we are glad we didn't do growth hormone therapy when we considered it. He had severe aspiration of fluids from birth to four years and possible slight aspiration and choking in the last three years. At fifteen he was a bit below average height (9th centile) and 45kg. He is short and slim." - dup 9p13.32p24.2/del 9p24.2p24.3, 16 years



"Very slim and struggles to put weight on even on a liquid diet. He suffers from severe reflux - tried most antacids and still on Omeprazole which is successful. No constipation issues but he does have swallowing issues - aspirates when feeding via mouth and could not take in enough food to sustain himself so gastrostomy fitted. Had tasters up until age 15 but he was aspirating too much so is now nil by mouth." - dup 9p12p22/del 9p22, 19 years

"Our 10-year-old daughter is of short stature: she is four inches shorter than her fraternal twin sister - who does not have any chromosome disorder - at 4ft 2in (1.27m) and 48 pounds. I also don't see any signs of secondary growth characteristics appearing. She is underweight but has followed her growth curve of the 3rd percentile since birth. She tends to be easily constipated. In contrast, her younger sister [who has the same co-existing 9p duplication and deletion] follows the 50th per centile for growth, and is of average height and weight." - dup 9p21.3p24.2/del 9p21.3, 10 years & 4 years.

## Appearance

Features associated with 9p duplications and deletions are common.

You or your doctor may notice what are known as 'dysmorphic features' – facial features that are unusual and may suggest a chromosome disorder. These can be obvious, or subtle and only apparent once they are pointed out. These features do not matter to your child, but they may mean that you see unexpected similarities between your child and others with co-existing 9p duplication and deletion, as well as those with 9p duplication and 9p deletion syndromes.

Looking at the information provided by *Unique* families and in the medical literature, children tended to have combinations of features associated with both these syndromes. Most common were: low-set, unusually-shaped or prominent ears; a thin upper lip; widely-spaced eyes that may be deep-set, up-slanting and with skin folds at the inner corner of the eye; an under-grown upper jaw, cheekbones and eye sockets; a long space between the nose and upper lip; a broad nose with a bulbous tip; and a small mouth. Children may also have widely-spaced nipples and excessive hair growth on the face or body.

Your child's head may also have an unusual shape. In one third to one half of children the head was unusually small (microcephaly) and a few babies had a flattened skull, usually at the back (brachycephaly). Where the co-existing 9p deletion involved 9p22.3, trigonocephaly - where babies are born with a forehead that looks pointed when seen from on top resembling the shape of the keel of a boat - was common. Previous reports have mapped the causative gene(s) involved in trigonocephaly to a region in 9p22.3. This unusual shape develops when the natural seam between the bone plates of the forehead (the metopic suture) fuses too early in development (craniosynostosis), giving the skull a triangular form. A more minor degree of early fusion may leave the forehead a normal shape but with a ridge running down the middle. In mild cases no treatment will be needed, but some children may benefit from helmet therapy to reshape the skull and if necessary the bones of the forehead can be separated in a surgical procedure. Although this sounds alarming, quite a few *Unique* children with a 9p deletion have been operated on with success.



“ He has trigonocephaly. At 16 months considering surgery to his skull. ” - dup 9p13.3p21.3/del 9p22.1p24.3

A few new-born babies had wide gaps between the bony plates of the skull and a very large soft spot (fontanelle) on top of the head that was slow to fuse, which is characteristic of 9p duplications. The jaw may also be unusually small (micrognathia) and/or receding (retrognathia) (Teebi 1993; Muroya 2000; Krepisch-Santos 2003; Faas 2007; Hauge 2008; Swinkels 2008; Hulick 2009; Jelin 2010; Al Achkar 2010; Chen 2011; Di Bartolo 2012; Neira 2012; Recalcati 2012; Kowalczyk 2013; Schlade-Bartusiak 2013; Pedurupillay 2014; *Unique*).

“ We looked into our son having a MARA (mandibular anterior repositioning appliance) fixed brace, which is used to encourage forward growth of the lower jaw but decided against it to avoid more invasive interventions. Still thinking about it. ” - dup 9p13.32p24.2/del 9p24.2p24.3, 16 years

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

A delay in gross and fine motor skills appears to be universal.

A delay in achieving milestones such as rolling is often one of the earliest signs of a chromosome disorder. Babies and children with co-existing 9p duplication and deletion are typically quite delayed in reaching their developmental milestones and benefit from early intervention with occupational therapy (OT) and physiotherapy (PT).

Some children are simply a few months late reaching milestones, including two sisters with dup 9p21.3p24.2/del 9p21.3 and a girl with dup 9p23p24.1/del 9p24.1p24.3, and most of those affected are able to walk eventually. This is not possible for all: a 19-year-old with co-existing dup 9p12p22/del 9p22 “learnt to roll from ~9-months-old [but] has not achieved any other

# Developmental milestones

## Average age

Developmental Delay	21/21
Rolling	<b>10 months</b> (*n=10) Range: 8m-16m
Sitting	<b>1yr 2m</b> (*n=10) Range: 10m-2.5yr
Crawling	<b>1yr 8m</b> (*n=8) Range: 11m-2.5yr
Walking	<b>3yr 6m</b> (*n=13) Range: 20m-5yr
Smile	<b>2 months</b> (*n=3) Range: 2m-3m

*\*n: number of individuals for whom the milestone was achieved and relevant data is available, including Unique members and patients from the medical literature (Teebi 1993; Krepischi-Santos 2003; Hauge 2008; Swinkels 2008; Hulik 2009; Al Achkar 2010; Recalcatti 2012; Neira 2012; Kowalczyk 2013; Schlade-Bartusiak 2013; Pedurupillay 2014)*



milestones to-date”.

A similar mixed picture emerges from the medical literature: two children with mosaicism for a co-existing 9p duplication and deletion walked at two-and-a-half years and two years (with support) (Schlade-Bartusiak 2013; Pedurupillay 2014). A girl with co-existing dup9p13.3p24.1/del 9p24.1 walked at 5 years, while a girl with co-existing dup9p13.3p22.2/del 9p22.2p24.3 walked at 7 years (Swinkels; Recalcatti 2012).

Walking may remain unsteady and children may need support (holding on to furniture, splints, walking aids or a wheelchair) and protection out of doors, particularly as they may lack the ability to save themselves when they fall (Unique).

**Hypotonia/hypertonia**– The majority of co-existing 9p duplication and deletions, no matter the size and location, are associated with reduced muscle tone (hypotonia), sometimes in combination with increased muscle tone (hypertonia). While hypotonia can make the body floppy and may lead to obvious head lag in babies, hypertonia makes the body feel overly rigid. Both hypotonia and hypertonia are associated with difficulties in carrying out gross motor skills. Muscle tone can improve with maturity but for some problems may persist into adulthood.

Many children also have very loose joints that have an impact on mobility, as do some anomalies affecting the feet (Hauge 2008; Swinkels 2008; Hulik 2009; ; Recalcatti 2012 Neira 2012; Kowalczyk 2013; Schlade-Bartusiak 2013; Pedurupillay 2014; Unique).

“ Our son had both hypotonia and hypertonia when he was very young, especially as a baby when he had very clawed feet and fisted hands. Has relaxed over the years, though still very tight in the legs and wrists etc. He walks in a flexed position as a result. ” - dup 9p13.32p24.2/del 9p24.2p24.3, 16 years

**Treatment** - Most children have received regular PT and OT sessions from a young age. Occupational therapists and physiotherapists will work with your child directly and will also be able to suggest games and exercises for you to work on with them at home. One girl persevered with PT until the age of five years before taking up weight training, which she found not only beneficial for her strength and muscle tone but also highly enjoyable!



Competing in the Special Olympics

Orthotics, such as support boots and braces, or insoles in shoes, may also help increase mobility. Eventual walking style is likely to vary and although some children may achieve total mobility and learn to climb stairs, run, ride a bicycle and swim, others will retain an uneven and uncoordinated walking style, and some may continue to rely on a wheelchair in all circumstances.

“ He had physio from birth. He has benefited enormously as without the physio he would have become rigid and inflexible. ” - dup 9p12p22/del 9p22, 19 years

## Development: hand use and coordination (fine motor skills)

The majority of children are likely to have a delay in the development of hand use and hand-eye coordination, and for many these remain poor into the teenage years. Fine motor skills are essential for tasks such as reaching out for and holding objects, transferring objects from hand-to-hand, using cutlery, playing with toys and fastening clothes, and don't necessarily develop in line with gross motor skills. It has been suggested that hypermobile joints in the fingers and thumbs, hypotonia and anomalies of the hands, including unusually bent and shortened fingers, may contribute to difficulties (see [Hands and Feet](#)).

The evidence from *Unique* is that as childhood progresses fine motor skills often improve, but some teenagers still need help to carry out daily personal care tasks, such as brushing their teeth and dressing.

Early intervention with occupational therapy to stimulate hand use can prove extremely beneficial. *Unique* families with children with an RCD have found certain toys especially helpful in promoting their baby's early development, including: maracas; bells on or off a stick; bangles; cellophane; ping pong balls on a resonance board; lights; bright musical objects and toys to encourage reaching; shiny objects such as a big spoon (particularly helpful for improving grasping skills); small bricks; and rusks or rusk-sized toys (Unique).

“ Both her fine motor and gross motor skills are delayed. At 10-years-old, she still can't tie her shoelaces, fasten buttons, floss her teeth, use a knife, ride a bike, and swim. Her writing is poor although legible. ” - dup 9p21.3p24.2/del 9p21.3, 10 years

“ Although he learnt to roll at ~9 months, he has not achieved crawling,

sitting or walking to-date. He does have very good fine motor skills and hand to eye coordination - he can hold anything and transfer from one hand to the other or to his mouth.” - dup 9p12p22/del 9p22, 19 years

## Ability to learn

Some degree of learning disability is to be expected.

Evidence from *Unique* and the medical literature demonstrates that some degree of learning disability (LD) is to be expected and is usually moderate to severe (see table).

A range of learning abilities exist, ranging from a 20-year-old with co-existing dup 9p22p24.2/del 9p24.2pter who was described as having an “IQ at the lower limit of normal”, to a 19-year-old with co-existing dup 9p12p22/del 9p22pter with a profound LD and “a cognitive age of ~18 to 24 months”. Even those with the same genotype can have different levels of disability: an elder and younger sister with co-existing dup 9p21.3p24.2/del 9p21.3p21.3 had a severe and moderate LD, respectively (Al Achkar 2010; *Unique*).



### Range of learning abilities

	<i>Unique</i> 2017 survey	Medical Literature
<b>Learning Disability</b>	<b>9/9</b>	<b>14/14</b>
<b>Mild</b>	<b>0</b>	<b>1</b>
<b>Mild/Moderate</b>	<b>1</b>	<b>0</b>
<b>Moderate</b>	<b>3</b>	<b>1</b>
<b>Moderate/Severe</b>	<b>1</b>	<b>0</b>
<b>Severe</b>	<b>3</b>	<b>4</b>
<b>Severe/Profound</b>	<b>0</b>	<b>0</b>
<b>Profound</b>	<b>1</b>	<b>0</b>
<b>Unspecified</b>	<b>0</b>	<b>8</b>

\* Muroya 2000; Krepisch-Santos 2003; Faas 2007; Hauge 2008; Swinkels 2008; Hulick 2009; Jelin 2010; Al Achkar 2010; Chen 2011; Di Bartolo 2012; Neira 2012; Recalcatti 2012; Kowalczyk 2013; Schlade-Bartusiak 2013; Pedurupillay 2014



While the segment between 9p22.3 and p23 has been suggested to be a “critical region” for the development of intellectual disability for those with 9p duplications and the majority of the available evidence supports this, a few children with a duplication involving this region appear not to have an LD, while some who have duplications outside this region do, including a *Unique* child with a 9p22.1p22.2 duplication with a (mild) LD.



In the *Unique* series, of seven members with a “small/micro” duplication of all or part of the 9p24 band, but including no other bands of chromosome 9, while the majority had a mild LD, a boy with a 9p24.1p24.3 duplication was described as having a moderate or even severe LD. An overlapping location (within 9p22p23) has also been proposed as the critical region for developing the features associated with 9p deletion syndrome, including LD.

Some researchers believe that this critical region needs to be refined as deletions involving distal regions closer to the tip of 9p can contribute to features commonly associated with the syndrome. This is reflected in the experience of *Unique* members, where even for those with a 9p deletion involving only 9p24.3 (without a co-existing 9p duplication), a range of learning difficulties has been reported, from those who appear to have no LD to those with an LD that is generally mild or moderate but can occasionally be severe (Di Bartolo 2012; *Unique*).

Most *Unique* children have struggled with learning to draw, read, write and use a keyboard; some children have some degree of mastery of these skill, although typically following a significant delay. For those with a more severe or profound learning disability this has not proved possible. Most parents believed that their child had specific areas of strength, but these were not consistent across the *Unique* series, ranging from an aptitude for reading to a notable proficiency for carrying out practical tasks. One child had an amazing memory for names and places and paid particular attention to fine details.

Notably, most *Unique* parents felt that their child’s learning ability had improved with age, often in fits and starts. Several children have shown a marked improvement after struggling as toddlers and in early childhood, especially following intervention to improve communication skills. Further, *Unique* parents universally believed that their child was reticent to try new experiences and acquire new skills, but some mention that perseverance and encouragement often led to a successful outcome.

“As a baby he showed very little promise and he seemed to have quite severe learning difficulties as toddler, but then exceeded expectations in learning reading and writing. He was non-verbal till 10 years of age and didn’t take to sign language (Makaton). If we hadn’t unlocked his communication from four years with a communication book and symbols I don’t think he would have made much progress and would have been



underestimated and remained underchallenged. He now has a moderate to severe learning disability, which is probably more on the severe side. Drawing, reading, writing and keyboard skills have not been fully achieved but he reads at the age of a five- to six-year-old; reading is way ahead of the rest. He can write with hand-over-hand support, so at a very early stage, and can write his first name independently. He can type on an iPad using hand-over-hand and can operate an iPad independently e.g. open apps, scrolling etc. He is very resistant to acquiring new skills but loves it if you persevere.” - dup 9p13.32p24.2/del 9p24.2p24.3, 16 years



“ She has very high levels of support at school and is currently in year 7 (first year of high school in Australia) but working at a year 3 level. She is able to draw, read, write and use a keyboard. She loves helping and has a very practical brain; give her a task to do in a practical situation and she will thrive. She can be resistant to acquiring new skills, especially if it is hard. It takes her four times as long as someone else to learn the same skill. If it's something she enjoys she will persist and often achieves.” - dup 9p12p24.2/del 9p24.3, 13 years

“ She is working at the level of a ~5-year-old and is just beginning to learn to read. She knows her letters and sounds and is learning to sound out consonant-vowel-consonant (CVC) words. She learns best with music and through repetition.” - dup 9p21.1p22.3/del 9p22.3p24.3, 7 years

Education - *Unique* children have needed additional support with their learning. While children often attended a regular (mainstream) nursery/day care setting prior to starting school (one girl attended an early development program for one year before starting her primary education at the mainstream school she continues to attend), in order to access the curriculum and develop to their full potential once they started their formal education (either state or private), 3/9 had 1:1 or dedicated support within the mainstream classroom or transferred to a special unit within a mainstream school; 2/9 attended a special school; and 2/9 transferred from mainstream education to a special school. One 9-year-old boy was being home-schooled and a girl had not yet reached school age. Several parents mentioned that they felt their child responded particularly well when singing and/or music was incorporated into their learning.

Early intervention can prove particularly beneficial and formal testing to assess specific, individual needs is recommended. In the UK a tailored education, health and care (EHC) plan can be issued after a child has undergone an EHC needs assessment. This legally-binding document ensures that the educational, health and social provisions deemed necessary to support the child's needs are delivered to the child (previously, a statement of special educational needs was issued to children with LDs). Parents report that the process of obtaining an EHC plan (or equivalent) can be challenging and some have hired SEN lawyers to help with this process.

“ Our son has attended a special needs school all throughout his education - he is currently attending a special needs further education college. My advice for other parents would be to do what is best for your child not you. I have seen a lot of parents put their child through mainstream schools and it has been obvious that is not the best setting for them. Do not dismiss special needs schools, as they cater for a wide range of needs/abilities and adapt the teaching accordingly. Obtaining a Statement was easy, from ~ three years of age. He still has a statement of educational needs even though he is 19 years of age and has not had any contact from the SEND team for four years now and no EHC Plan to date (although I am constantly chasing it). ” - dup 9p12p22/del 9p22, 19 years, UK

“ He attends a mainstream primary school that has a specific class for children with mild to moderate intellectual disability. There are 8 children in his class with a wide variety of issues. He has one teacher and an assistant. He goes to the general education class for homeroom (registration). He takes an adaptive Physical Education class, adaptive art and adaptive music and also receives occupational therapy and speech therapy (individual and group). He receives hearing tests from the school annually. We are fortunate to live in a good school district that is very supportive of special education. ” - dup 9p13.1p24.3/del 9p24.3, 9 years, USA

“ She repeated kindergarten (preschool) twice - the entire team was in agreement, including myself. This year she will go into first grade. Although they pushed for her to go into a self-contained special education classroom, I refused because she is so incredibly social and her skills are very delayed but coming. Her nurse serves as her one-on-one support.

My advice is to advocate for as many services as possible. Make sure that everything is spelled out in the IEP and that the child gets to be a part of the general (mainstream) education, even if it is part-time. Our kids learn very well with music, so that might be an avenue to explore. ” - dup 9p21.1p22.3/del 9p22p24.3, 7 years, USA

## Speech and Communication

As with other areas of development, speech and language development are typically delayed.

For some children first words appeared between the ages of two and three years, while for others a more significant delay was observed, and a few remain non-verbal. This pattern is reflected in both the medical literature and *Unique* children. Even where children said individual words closer to the “typical” age of the first birthday, more complex language development and the ability to communicate effectively often lagged behind their peers.

Where speech does develop, a broad spectrum of eventual communication ability exists. Some children continue to use two- or three-word sentences, even in later childhood, while others go on to speak more fluently in long, complex sentences, although grammar and sentence construction often remain challenging.

Children often find it difficult to make clearly intelligible speech sounds,

## One family's experience of the education system in the USA....

“ Our 17-year-old daughter has co-existing duplication 9p23p24.1/deletion 9p24.1p24.3. Academically she is in a 'mild-to-moderate' special education class. At nine years the school stated that she was performing at grade (expected) level; she was reading at the 3rd grade (nine-year-old) level - with the assistance of a one-to-one reading tutor for one hour every day - and she could add and subtract (with regrouping) and had just learned her multiplication tables.

Understanding money was difficult for her, as was telling the time on a conventional clock. Her comprehension of what she heard and read was excellent and she always had something to contribute to the discussion – when she was comfortable with the audience; however, writing was very difficult for her and she had occupational therapy to try and improve it.

Since she was doing well in this environment, and with the school budgets in such dire straits, the plan was to continue with mainstream education for the following year, which worried us as her speech and writing were not progressing.

At eight years, we sought a full-scale evaluation, which provided a lot more information. Four of the doctors that were consulted all believed her to be on the autism spectrum. Socially, she was challenged for a long time as she was the only girl in her classes. To remedy this, I found a local Girl Scout troop and that was very helpful in having her meet girls and to learn some social skills. In crowds, she withdraws and has poor eye contact, but her time spent interacting with the group helped. I also found a social group locally that takes special needs kids on excursions each Sunday to encourage social skills and interactions. She was prone to tantrums and NEVER stopped moving. She needed A LOT of redirection and prompting so we would give her no more than a one- or two-step task. Initially, this earned her a diagnosis of ADHD at the age of six years. After trying behaviour modification, she started stimulant medications at the age of seven-and-a-half years, which helped: after she started the medication she went from a kindergarten reading level to the 2nd (eight-year-old) grade level in about six months.

At nine years she could skip awkwardly and ride a bike with training wheels but at times would forget to brake. She has always been a bit clumsy and is prone to tripping and falling. I did find a gymnastics teacher who was willing to take her on where they worked on balance and coordination and she LOVED it; she was almost doing a cartwheel.

At 17 years, her current IEP assessed her as at about the age of 12 years. She attends an NPS (private) school that specifically addresses special education. Initially, she was on a diploma but for this next year we moved her to the transition and independent living track. If she were to continue on the diploma track, all services would end when she turned 18 and she would be expected to function in our community as any other member who possessed a high school diploma and that is just not realistic.

I had to hire an attorney/advocate to help us navigate the process of obtaining an IEP. No one volunteers information to the parents and, unfortunately, I did not know what questions to ask all the time. She has also had speech therapy since the age of three years, vision therapy, OT and adaptive PE since she was five-years-old.

Our daughter also attended a two week special needs camp over the summer and that was a wonderful experience for her to develop her independent living skills. ”

which can make communication with strangers particularly challenging. Conditions that affect the cleft and palate; hearing difficulties; and speech disorders, including speech apraxia (also referred to as developmental verbal dyspraxia (DVD)), where an individual has trouble saying what s/he wants to say correctly and consistently, may contribute to speech delay and communication difficulties and should therefore be investigated promptly (Teebi 1993; Krepischi-Santos 2003; Faas 2007; Hauge 2008; Swinkels 2008; Hulick 2009; Jelin 2010; Neira 2012; Kowalczyk 2013; Schlade-Bartusiak 2013; Pedurupillay 2014; Unique).

Almost universally, parents believed that their child could understand a lot more than they could express and even those children who developed more sophisticated speech still experienced difficulties expressing themselves on occasion, which could result in frustration and temper tantrums. Where individuals have no speech or very few words, communication may be enhanced through augmentative/alternative communication (AAC) e.g. Makaton, signing, gesture, facial expression, Picture Exchange Communication System (PECS) and iPad communication, which can reduce frustrations.

An assessment by a speech and language therapist can identify your child's specific difficulties. This will allow the therapist to identify the best ways to support speech and language development, through regular therapy sessions with your family, which have proved beneficial to many *Unique* families.

One *Unique* family recommended myofunctional therapy to help improve speech. This treatment involves facial/tongue exercises, and behaviour modification techniques, aimed at improving tongue placement, speaking, breathing, swallowing and chewing.

A critical region for the speech/language delay associated with 9p duplications involving 9p21.2–p21.3 has been proposed (Zou 2009). Evidence of several children with a speech delay despite having 9p duplications and/or deletions that do not involve this region, including duplications and deletions involving only 9p24, suggests that more research is needed in this area (Stumm 2002; Boujhar 2011; Unique).

“Speech has always been a challenge and she started speech therapy when she was 2.5-years-old. While her family understands her most of the time, new people have a difficult time understanding. She talks very fast, so when she is asked to slow down, her speech is much clearer.

Initially she would make noises and developed a special language with her younger brother. We had to separate them when he was two so that he could develop proper language.

She now uses long and complex sentences. When I just asked her to say something she started to talk about our dog: "He is cute and the best puppy ever. He is noisy and very impatient. I am trying to make these comments fast, so I can get back to my homework." The phrase "still waters run deep" is an apt description for her.” - dup 9p23p24.1/del 9p24.1p24.3, 16 years

“I cannot remember when she actually "started speaking"; however, it was

significantly delayed. She said mum at six months and then the next word was dad at three years. She would babble constantly with different tonal inflections to get her point across when she was little, before she had other words.

A combination of dyspraxia and cleft lip/palate have made it hard for her to speak clearly.

She had speech therapy for many years but has stopped all of these now as they had not been having much impact. She still has problems with speech and sentence construction e.g. "I go work. What you do today?". She can have long conversations with people now, but there are still joining words e.g. in, on, missing. She understands everything but cannot express herself properly due to the miscommunication between her brain and her body. " - dup 9p12p24.2/del 9p24.3, 13 years

" Her speech was delayed. She started putting a couple of words together around two years and is still receiving speech therapy for intelligibility. She now speaks in longer sentences e.g. "What are you doing?", "What time is it?", "Who's going to be there?", "What nurse is coming tonight?". She is extremely funny and she knows it. She understands much more than she can communicate. " - dup 9p21.1p22.3/del 9p22.3p24.3, 7 years

" My eldest daughter's actual speech is not delayed, but the effectiveness of her communication is poor compared to her peers. Often her sentences are filled with words that are poorly organised and out of context, resulting from distracted thoughts. She uses a normal sentence structure, albeit made of simpler words, but the thoughts behind those sentences are most often out of context and illogical. Unfortunately, her problem is her understanding and speech therapy cannot change her random thought processes.

Although my youngest daughter was able to say over 150 words by 13 months, her sentence structure is much delayed now in comparison to her peers. She still occasionally just makes noises or says two- to three-word sentences, with the exception of the occasional longer sentences (six to seven words) repeated based on memory. She tends to use shorter sentences e.g. "Mommy, can I?". When asked to speak properly or I ask her what she means by "can I?", she'll say, "Can I come to your room?". When asked why, she'll say, "I want to sleep with you.". I feel she understands a lot more than she expresses. When she was younger she had speech therapy but since she was able to say so many words at a young age, speech was not a concern and she was dismissed from early intervention. We are currently assessing her for speech therapy again. - dup 9p21.3p24.2/del 9p21.3p21.3, 10 years & 4 years

" At first, he communicated more through signing and could sign five words between the ages of two and four years. He said "gaga", "mamma" and "babba" for one month at six months, then speech completely disappeared until he said "mamma" again at three years. Between the ages of four and ten years he said two made up words for pyjamas and lunch and used a communication book almost exclusively throughout this period. He started trying to say words at 10-11 years and gradually began to say more words

and use more clear speech.

From the age of 15 he has communicated mainly through speech with the back up of a communication book. Now, he is beginning to be clear enough for strangers to understand him and can speak in sentences of up to six to seven words, but he doesn't use correct grammar.

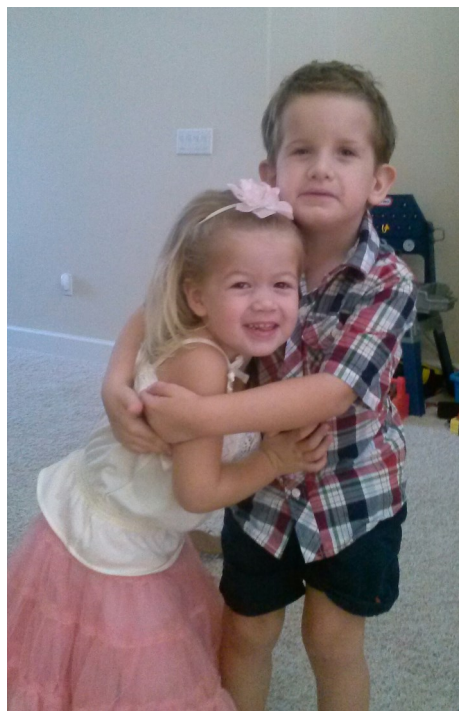
He understands far more than he can communicate, and this was especially evident between the ages of three and ten years when he couldn't speak but I knew he could understand. Speech and language therapists didn't believe he could understand until I set up the communication book.

Speech and language therapy (SALT) helped me become a good speech and language teacher to my son but had little effect on him directly. Other things that did help: sing and sign classes (with a franchise music group aimed at "typical" kids but which was still great), and a little speech and language group therapy class we did from three to five years for children with Down syndrome that was run by Symbol UK. " - dup 9p13.32p24.2/del 9p24.2p24.3, 16 years

## Personality

Every child is an individual and not all personality traits will be related to the chromosome disorder.

Even children with the same inherited co-existing 9p duplication and deletion can have strikingly different personalities, but when describing their children, the words most frequently used by *Unique* parents are: sweet, loving, happy, fun, stubborn, cheerful, caring, gentle, self-centred and sociable (Unique).



Difficulties in communicating needs or completing tasks can lead to frustration, outbursts of temper and "challenging behaviours". Some children and adults can find social situations over-whelming or find it difficult to communicate due to speech or expressive delays.

In common with their peers, babies and children with a co-existing 9p duplication and deletion enjoy a range of activities but seem to particularly relish playing with other children; playing with balls, trains and buses etc.; completing puzzles; and listening/singing/dancing to music. Older children and teenagers enjoy video and board games; socialising and visiting people and places e.g.



bowling, roller-disco, eating out at cafes and restaurants; getting catalogues and reading them; and swimming.

“ Sweet, loving, resilient, patient, persistent; obsessive, rough with others, self-centred. ” - dup 9p13.32p24.2/del 9p24.2p24.3, 16 years

“ She has the absolute best personality of anyone I have ever met. She is happy, funny, friendly and loving. She loves everyone and talks to everyone constantly. I cannot get through the grocery store without her talking to everyone and asking what they're doing, what their name is etc. She has nothing negative to say or think about anyone. She will be friends and talk to anyone. If she is ever crabby I know that something is wrong physically, like low blood sugar or sometimes she is extremely over-tired. Other than that, she is constantly smiling. She affects everyone around her - even strangers - with her contagious laugh and smile. The world would truly be a better place if there were more people like her. She is very, very stubborn, but it is more to play a game - she's not trying to be mean.

Sometimes she will pinch to get a reaction but it's not malicious. She is definitely overly friendly, which is obviously a concern for strangers. But at this point I cannot or will not try to squelch that. ” - dup 9p21.1p22.3/del 9p22.3p24.3, 7 years

“ Our 10-year-old daughter is a cheery, pleasant child who is easily distracted, which makes staying on task frustrating. She is mentally immature and would prefer to play all day long with no consideration for anyone else or anything that is important or urgent. She stills struggles with autonomy issues, often being stubborn, defiant and unwilling to do what she's told. Left alone she is an unmotivated child.

Our four-year-old daughter is a very happy kid who loves to please. She fights for autonomy and strives to be independent with self-care tasks. She is flexible with clothing, food and changes in her environment. She tends to be more adaptable than her sister with the same condition. She is just as affectionate and empathetic as her sister; however, she is much more feisty in nature and can hold a grudge or be vindictive. Overall, she is a very sweet, good-natured child who carries an incredible smile. She does tend to have slight anxiety around crowded places or unfamiliar faces. She often asked to be carried in those environments and would start to fondle my belly for comfort. She can also have uncontrollable melt downs or poor control of her emotions, needing a much longer time to settle. ” - dup 9p21.3p24.2/del 9p21.3, 10 years & 4 years.

## “Challenging” behaviours

Around half of *Unique* children with co-existing 9p duplication and deletion demonstrate so-called “challenging” behaviours.

These range from temper tantrums and more aggressive or destructive behaviour to extreme shyness and an inability to adapt to new situations. Most often, children may exhibit over-friendliness with strangers. Several parents say that they have experienced no problems with behaviour.



## Types of behaviours and social, emotional and anxiety disorders

**Self-harmful/injurious behaviour** e.g. self-biting, head banging, gnawing fingers, scratching, inducing vomiting.

**Aggressive behaviour** towards others e.g. verbal abuse, threats, physical violence.

**Destructive behaviour** e.g. breaking or destroying furniture and other objects and setting fires.

**Disruptive behaviour** e.g. repetitive screaming, smearing faeces, setting off fire alarms when there is no fire, calling the emergency services when there is no emergency.

**Sexually risky/inappropriate behaviour** e.g. inappropriate touching, explicit sexual behaviour.

**Attention Deficit Hyperactivity Disorder (ADHD):** ADHD is usually diagnosed between the ages of 6 and 12 years. The disorder is characterised by a range of behaviours including hyperactivity, inattentiveness and impulsiveness that make it difficult for children to concentrate and control their actions and speech. Children are often described as “restless”, are easily distracted and may talk or interrupt a lot.

**Autism Spectrum Disorders (ASD):** ASDs include autism and Asperger’s disorder and are associated with impaired social skills, problems with communicating, and a need to carry out restricted repetitive and restrictive behaviours, interests and activities, from which an individual derives comfort.

**Obsessive Compulsive Disorder (OCD):** A related but distinct disorder, which may co-exist alongside an ASD or manifest separately, those with OCD experience anxiety that can be relieved to some degree by carrying out specific, repetitive rituals e.g. obsessive hand-washing, repetitive counting/checking. Those with OCD don’t derive pleasure from these routine behaviours, but fear that something bad will happen if they don’t complete them.

**Sensory Processing Disorder (SPD):**

A child with SPD finds it difficult to process and act upon information received from the world around them through their senses e.g. sound, touch. This makes carrying out everyday tasks and responding to different environments challenging. Typical features of SPD include heightened reactions to sound, movement and touch; clumsiness; behavioural and social problems; difficulties with concentration; and disrupted sleep patterns.

**Oppositional Defiance Disorder (ODD):** A child with ODD becomes annoyed easily and is liable to frequent temper tantrums. They will also challenge authority, refusing to obey rules. This behaviour can appear to be deliberate and can present problems with social interactions.

It is important to bear in mind that these challenging behaviours exist alongside numerous positive traits and may well be transient: children typically experience difficulties with social interactions, both with adults and with other children (often manifested as extreme shyness or inappropriate friendliness) in mid-childhood. Some parents of children with 9p duplications have also mentioned an increase in challenging behaviours in the teen years. Many of these behaviours arise due to frustration at an inability to make their needs and wants understood. Nevertheless, they can be distressing for the child and their family and may have a significant impact on social interactions, schooling and other aspects of life.

Early access to advice and therapy will help those families who find themselves in difficulties with their child's behaviour. Children usually benefit from consistent routines, boundaries, rewards and other behaviour management techniques. Efforts to take into account and introduce strategies to tackle communication and other difficulties specifically associated with the co-existing duplication and deletion can also be beneficial (see *Unique's* guide to Behaviours).

“ My daughter is personable, social, friendly, caring, loving, compassionate, helpful, genuine and loves to interact with people. She has perfect behaviour. There is never a problem, other than when she has to do something that is hard, and she procrastinates and tries to distract you by talking about something else. She also gets frustrated at herself if others can't understand her, and she doesn't always try new things. ” - dup 9p12p24.2/del 9p24.3, 13 years

“ If I had my time again I would do ABA therapy from two years onwards. Our son isn't autistic, but I think the structured step-by-step learning is great and really helps kids like him.

He used to demonstrate self-harmful and destructive behaviour from five to seven years, but no more. He is aggressive now intermittently. A little sexually inappropriate in the first years of puberty but not serious, just discrete inappropriate self-stimulation! ” - dup 9p13.32p24.2/del 9p24.2p24.3, 16 years

“ He doesn't really have good or bad days or challenging behaviour; he has the same temperament all the time. The only difference is some days he will interact with us and some days he does not want to (but I don't think that is so different from us all). ” - dup 9p12p22/del 9p22, 19 years

## **Social, emotional & anxiety disorders**

A few children have received a specific diagnosis for a social, emotional or anxiety disorder and four children had a diagnosis of autism. These included a five-year-old girl in the medical literature with a deletion from 9p23 to 9p24.3 and duplication from 9p21.2 to 9p23 (Yang 2012). One more case of a girl who had sensory issues and exhibited ASD-, ADHD- and OCD-associated behaviours, but who failed to meet diagnostic criteria for these disorders on several counts, was reported by a *Unique* parent. A 16-year-old *Unique* member had a confirmed diagnosis of ADHD, for which she was prescribed medications, as did a five-year-old boy with dup 9p22.2/del

9p21.1 (Unique).

There is evidence from the DECIPHER database (Database of genomic Variation and Phenotype in Humans using Ensembl Resources; <https://decipher.sanger.ac.uk>) that “challenging” behaviours, such as aggression; autism; and, more rarely, psychosis, have been observed in children with 9p duplications of various sizes. A link between 9p24 deletions and autistic features has also been reported, leading to the suggestion that a gene(s) associated with ASDs may be located in 9p24. Low-level mosaic aneuploidy (an abnormal number of chromosomes) in the brain, where some of the brain cells (neurones) are chromosomally abnormal, has also been proposed as one possible cause of mental health conditions, including ASDs and OCD. More research is needed in this area (Vinci 2007; Abu-Amero 2010; Kantojarvi 2010; Martinez-Jacobo 2015; Yang 2012; Güneş 2016).

Where a parent believes that their child may have a specific disorder - such as ASD, ADHD or OCD - they should consult their general practitioner/ paediatrician who can refer then to a behavioural or clinical psychologist to undergo assessment. Depending on the outcome, further evaluation by a specialist such as a developmental paediatrician, neurologist, psychiatrist or psychologist may be offered. Children may be prescribed medication to help with specific disorders following diagnosis - including methylphenidate (Ritalin) or Lisdexamfetamine (Vavanse) for ADHD, which can help with restlessness and inappropriate comments. One family felt that neurofeedback therapy, which aims to train brain activity, was instrumental in improving their son's cognitive abilities.

“ She has OCD-tendencies meaning things have to be organised a certain way, although she's generally messy. She also has sensory issues and enjoys the vibrations of massage chairs and airplanes and will insist on wearing long pants, long sleeves and socks in hot summer. She pays attention to meaningless details, such as hearing barely audible background songs amidst other louder noises or even someone speaking directly to her. She finds it difficult to transition between tasks and struggles with change, such as getting new shoes.

She was assessed for ASD but even though her behaviours are similar to ASD, doctors ruled it out. She has also been assessed for ADHD and although she received medications for ADHD to help her focus in school tasks, she is not an ADHD child. Taking Vivance seems to help her stay on task a bit more and has rendered her more co-operative; however, her focus is also much higher for random things. ” dup 9p21.3p24.2/del 9p21.3, 10 years (older sister)

“ My daughter is very shy, has ADHD and is prone to tantrums during unexpected transitions. She has a desire to be really friendly but is unsure how to “break the ice”. We have her in Applied Behaviour Analysis (ABA) therapy with weekly community excursions. She also belongs to a special needs theatre group that gives her the opportunity to meet and socialise with like-minded peers. She also takes Concerta (Ritalin), Dextroamphetamine and Zolof; mornings go a lot better if the ADHD medicine is given to her at 5:00am. ” - dup 9p23p24.1/del 9p24.1p24.3, 16

years

“ I knew he was autistic at an early age, but the doctors didn't want to diagnose him with ASD. He finally got diagnosed when his paediatrician noticed some ASD behaviours and sent us to see a developmental paediatrician. He's very active, gets into everything, is very curious and loves to explore. He likes to do things with lots of structure and enjoys playing on his phone and adding videos to his YouTube channel. On a bad day, he cries, bites, and pinches himself or others because he's frustrated with one or more things. He usually needs to be alone for a couple of minutes or hide under the covers like a tent to calm down. ” - dup 9p13.1p23/del 9p23p24.3, 9 years

## Sleep

More than half of *Unique* co-existing 9p duplication and deletion families (5/9) said that their child has experienced some degree of sleep disturbance.

While for some families these problems were minor or resolved with time, for others issues with sleep were long-lasting and had a significant impact on family life. Some children had difficulty settling, but once asleep slept well; others had difficulty sleeping for long periods and woke frequently through the night.

Where sleep has proved particularly challenging and conventional behaviour management techniques were unsuccessful, some families have favoured the use of prescribed medicines, including antihistamines with a sedating effect or the naturally-occurring hormone melatonin, which can help synchronise the body clock. These treatments should only be undertaken after consultation with a medical professional. Evidence from the *Unique* series suggests that these medications were largely ineffective.

In the *Unique* series, 4/9 children experienced sleep apnoea, a sleep disorder that is characterised by periods of shallow breathing during sleep, lasting from seconds to several minutes. For some this has proved a transient problem or has been “mild”. More serious cases may require the use of a CPAP (continuous positive airway pressure) machine at night.

Additional health problems, particularly GERD in babies and asthma, may disturb night-time sleep. Parents are recommended to re-introduce clear regimes after a bout of illness or a hospital stay.

Sleep disorders are common among children with 9p deletions and have also been reported by parents of children with 9p duplications. It can be extremely challenging for all the family when a child does not settle well to sleep or is not getting enough good quality sleep. Our [Sleep problems in children with chromosome disorders](#) guide, in the practical guides for families section of our website, has further information.

“ Sleep is one of the worst problems. He needs very little sleep - cat-naps through the day and does not sleep for more than 30 minutes at a time, ever. Tried everything: baths before bed, relaxing music, aromatherapy. You name it, we tried it. We also tried melatonin capsules at a high dose to no avail and saw a specialist who completed a sleep study - we kept diaries of

his sleep pattern for months at a time and she could not see a pattern to them other than he needs little sleep and cat-naps to refresh his energy. She also put it down to active brain activity meaning that he does not have the ability to switch off. He also had sleep apnoea up until he had his tracheostomy fitted aged 11 years. ” - dup9p12p22/del 9p22, 19 years

“ It wasn't until around the age of seven that he started consistently sleeping through the night. He was up on and off all night for at least the first couple of years. His seizure medication helped. Once we got his allergies and sinus issues under control, he could sleep better. ” - dup9p13.1p24.3/del 9p24.3, 9 years

“ She often has trouble falling asleep as she is too interested in what is going on around her. But when she is asleep she generally sleeps really well. She was recently diagnosed with sleep apnoea after her recent pharyngoplasty. ” dup9p12p24.2/del 9p24.3, 13 years

“ He hardly sleeps. He also has brain apnoea. We tried sleep medication and melatonin but they didn't work. The only thing that helps him is a weighted blanket. ” dup 9p13.1p23/del 9p23p24.3, 9 years

## Toilet training

The evidence from *Unique* suggests that a delay in toilet training is to be expected, and may not be achieved by all.

The picture is mixed but the experiences of *Unique* families suggests that for some children toileting was achieved between the ages of five and eight years, sometimes only during the day and not for bowel movements. At the extremes, a girl with a co-existing dup 9p23p24.1/del 9p24.1p24.3 was fully toilet trained at five years, while training had been attempted for a 19-year-old with a co-existing dup 9p12p22/del 9p22 unsuccessfully.

Children may also continue to need nappies or pull up pants at night and may continue to have “accidents” during the day throughout childhood. One family tried giving Desmopressin at night (a drug that reduces the amount of urine produced by the body) but this was not effective enough to achieve full night-time dryness. Low muscle tone can make toilet training more challenging and for some children who suffer from constipation, training for bowel movements is particularly difficult.

## Medical concerns

### ■ General well being

*Unique* families' descriptions of their child's general health ranged from “generally healthy” to “fragile”.

Although generally in good health, within the *Unique* series a trend towards being particularly prone to ear infections, colds and other respiratory infections in the winter - particularly as babies and young children - was noted, regardless of the size and location of the 9p duplication and deletion. Where the deletion included the proposed “critical region” for 9p deletion syndrome, concerns over the child's general state of health were more common. Chronic constipation is particularly common and often required

on-going treatment (see [Constipation](#)), while individual children had specific, on-going health concerns, including seizures and sleep apnoea that required treatment (*Unique*).

“Generally sturdy. In good health once the silent aspirations were treated; resolved itself around five years of age. Only on-going severe problem is chronic constipation. He has been sick with normal bugs less than “typical” children.” - dup 9p13.32p24.2/del 9p24.2p24.3, 16 years

“When she was younger she was very prone to pneumonia as soon as she got a cold. She is quite healthy now and doesn't get sick very often. She grew out of the pneumonia when she was around five to six-years-old. She still has asthma although it is very mild. She has complex medical issues, including being legally blind in her right eye, low muscle tone and she has just been diagnosed with moderate/severe sleep apnoea.” - dup 9p12p24.2/del 9p24.3, 13 years

“His immune system is weak; he gets sick very often especially when he's around other children. He has asthma and seizures.” - dup 9p13.1p23/del 9p23p24.3, 9 years

## ■ Respiratory infections

Respiratory infections and/or asthma are common in children with co-existing 9p duplication and deletion.

Children with RCDs tend to have a high rate of respiratory infections in early childhood, which are a feature of both 9p duplication and 9p deletion syndromes. Children may also be prone to allergies and asthma, sometimes triggered by respiratory infections. Evidence from *Unique* suggests that infections and asthma often become less frequent with age and maturity, although they can persist throughout childhood. Some children have required hospital treatment.

“She did have asthma for the first five to six years but she seems to have grown out of it. Treatment has not been needed for at least five years.” - dup 9p23p24.1/del 9p24.1p24.3, 16 years

## ■ Seizures

Some individuals experience seizures, which are usually successfully controlled with medication.

Seizures are caused by a sudden, abnormal change in electrical activity in the brain. Depending on the part(s) of the brain affected, symptoms vary but include temporary confusion, uncontrollable jerking movements and loss of consciousness or awareness. Seizures may be focal (partial) or generalised (affecting both sides of the brain) (see [Types of seizure](#)).

Electroencephalograph (EEG) and video telemetry (video EEG) are medical tests that can be used to measure and record the electrical activity of the brain and are tools that, when used alongside other tests, can help diagnose the type of seizure experienced.

The 2017 *Unique* survey revealed that 3/9 children had been diagnosed with

## Types of seizure

**Absence seizure:** A change in behaviour as if the child 'switches off', sometimes with staring, eyelid flickering or lip smacking. Absences are very brief often lasting less than half a minute.

**Generalised tonic clonic:** At the onset of a seizure, the abnormal electrical activity involves both sides of the brain. The seizure involves a phase of stiffening followed by jerking.

**Myoclonic:** Generalised seizure involving jerky or shock-like contraction of different muscles anywhere in the body but usually the arms or legs. Each myoclonic seizure lasts for a fraction of a second or a second at most.

**Febrile seizure:** Episodes only occur when the child has a high temperature.

**Myotonic:** Seizure involving stiffening of the muscles.

**Myoclonic-atonic:** Seizure involving jerky or shock-like contraction of muscles, followed by a loss of tone so someone standing up falls to the ground.

**Infantile spasm:** Type of seizure usually occurring in clusters in babies between 3-10 months. Seen most often when a baby wakes and may be obvious or subtle.

seizures (information in the *Unique* database revealed one further case); 3/9 were either being investigated for seizures or showed symptoms that led parents to believe that they may be experiencing seizures; while 3/9 were not believed to be affected. The information we have from the *Unique* series also suggests that no particular type of seizure is typical and that an individual may experience more than one type. Absence seizures (2 cases); tonic-clonic (grand mal) seizures (2 cases); myoclonic seizures (3 cases); and unspecified seizures (1 case) were reported by families.

In the medical literature two cases were reported, including a 21-year-old woman with a 9p21.1p24.3 duplication and 9p11.2p13.1 deletion who developed a seizure disorder as a child that was treated with valproic acid and resolved by 13 years (Jelin 2010), and an eight-month-old boy with a 9p13.3p23 duplication and 9p24.3 deletion who developed a severe form of epilepsy called West syndrome that is characterised by infantile spasms, which usually begin within months of birth and are associated with a specific EEG pattern called hypsarrhythmia, and intellectual disability (Neira 2012).

Treatment options, including the use of anti-convulsants, such as valproate acid, sult(h)iame and Keppra, have been successfully used to help reduce the frequency and severity of seizures (Jelin 2010; Unique).

“ His seizures (myoclonic, absences and tonic-clonic) developed from 17 years. They are being treated with medication (Keppra and Epilim). So far so good. ” - dup 9p12p22/del 9p22, 19 years

“ He had myoclonic seizures starting at around three-years-old. He was medicated with Trileptal for five years, but we just took him off the seizure medication as he has been seizure free for over two years. ” - dup 9p13.1p24.3/del 9p24.3, 9 years

“ He has experienced myoclonic seizures, absence seizures and grand mal



seizures. He takes Trileptal. It's been effective. He only gets grand mal seizures once a year. ” - dup 9p13.1p23/del 9p23p24.3, 9 years

## ■ Brain anomalies

A range of anomalies of the brain have been reported, many of which were minor.

While not a consistent feature of 9p duplications or 9p deletions, a range of anomalies of the brain have been reported for both chromosome anomalies, and ~1/3 of *Unique* members with a co-existing 9p duplication and deletion and two patients/children in the medical literature were found by MRI or CT (CAT) scan to have a brain anomaly, and in a few cases more than one anomaly. The range of anomalies was notable with no one consistent feature and were associated with duplications/deletions of varying size and location, although in most cases the deletion involved only 9p24 (see table). It should also be noted that in many cases no brain scan had been carried out, so the incidence of further brain anomalies cannot be ruled out (Chen 2005; Temtamy 2007; Vundinti 2007; Hauge 2008; Recalcati 2012; Kowalczyk 2013; Brambila-Tapia 2014; Samanta 2015; Spazzapan 2016; *Unique*).

## ■ Heart

A range of heart conditions have been reported, many of which were minor and resolved naturally without any need for treatment or surgery.

While heart problems are not a universal feature of co-existing 9p duplication and deletion, nor 9p duplication syndrome and 9p deletion syndrome, the 2017 *Unique* survey revealed that 6/9 children had an anomaly of the heart; two further cases of heart anomalies were also recorded in the *Unique* database. A similar picture emerges from the medical literature, with at least 6/15 patients found to have a heart defect(s) (Fass 2007; Swinkels 2008; Di Bartolo 2012; Recalcati 2012; Schlade-Bartusiak 2013; *Unique* ). Some children were affected by more than one condition, while a number of children with anomalies of the heart were also diagnosed with anomalies of the brain (see previous section).

A heart murmur was the most commonly reported condition (6 cases), which generally appears to have been benign (not harmful) or corrected itself naturally. Other more complex heart problems included: atrial septal defect (ASD) (6 cases); persistent ductus arteriosus (PDA) (5 cases); ventricular septal defect (VSD) (3 cases); an unspecified hole in the heart (1 case); sinus arrhythmia (1 case); an enlarged heart (1 case); and a patent foramen ovale (PFO) (1 case) (see [Types of heart condition](#) table). It appears that in most cases these heart conditions also resolved naturally or were successfully treated.

A survey of *Unique* members with 9p duplications of different sizes and locations that was carried out in 2017, found that ~20% of those with a duplication involving the whole or part of the short (p) arm of chromosome 9 had a heart condition, rising to ~40% for “large” duplications that extended to include a part of the long arm, with a similar picture in the medical literature (Wilson 1985; Haddad 1996; Nakagawa 1999; Canton 2016; Oh

# Brain anomalies

Brain anomaly	Description	Cases	Dup/Del
<b>Dandy Walker Malformation (DWM)</b>	A cyst in the balance control part of the brain (cerebellum) that is involved with the fourth ventricle, which is one of the fluid-filled spaces within the brain. DWM can also lead to hydrocephalus and the need for a shunt.	1 case DWM (confirmed)  1 case partial DWM (suspected)	dup 9p21.3p24.2/del p24.2p24.3 (Kowalczyk 2013)  dup 9p13.1p24.3/del 9p24.3 (Unique)
<b>Cerebellar hypoplasia (CH)</b>	Cerebellar hypoplasia is a condition where the cerebellum (located at the back and bottom of the brain and involved in the higher levels of thinking and action) is underdeveloped. CH is associated with developmental delay, speech delay, hypotonia, an inability to co-ordinate muscle movements (ataxia), and abnormal eye movements.	1 case (mild) (suspected)	dup 9p13.32p24.2/del 9p24.2p24.3 (Unique)
<b>Hydrocephalus</b>	Hydrocephalus is a build-up of fluid on the brain, which can put pressure on the brain. In many cases no treatment is needed as the pressure rebalances spontaneously, but sometimes surgery may be needed to introduce a shunt (a thin tube that is implanted in the brain and drains away excess fluid).	1 case	dup p13.3p24.3/del 9p24.3 (Unique)
<b>Arachnoid cyst</b>	Arachnoid cysts are sacs that are filled with cerebrospinal fluid (CSF). Most arachnoid cysts don't cause any symptoms and don't require treatment, but if an individual experiences symptoms, surgery may be needed to remove the cyst or introduce a shunt (see above).	1 case	dup p13.1p24.3/del 9p24.3 (Unique)
<b>Cerebral atrophy</b>	Cerebral atrophy refers to the loss of brain cells (neurones) and the connections between them.	2 cases	dup 9p13.1p24.3/del 9p24.3 (Unique)  dup 9p12p24.2/del 9p24.3 (Unique)
<b>Periventricular leukomalacia (PVL)</b>	PVL is a condition where there is damage (softening) of the white matter (inner part of the brain), which is responsible for transmitting messages between nerve cells, the spinal cord and from one part of the brain to another. PVL can cause problems with movement and other body functions.	1 case (not progressive)	dup 9p21.1p22.3/del 9p22.3p24.3 (Unique)
<b>Hypoplasia (under-development) of the corpus callosum and brain-stem</b>	When the corpus callosum is underdeveloped, the two sides of the brain are poorly connected. Each hemisphere of the brain is specialised to control movement and feeling in the opposite half of the body, and is specialised in processing certain types of information (e.g. language, spatial patterns). To coordinate movement or to think about complex information, the hemispheres must communicate with each other. The corpus callosum is the main connector that allows such communication.	1 case	dup 9p13.1p22/del 9p24.3 (Recalcati 2012)

2016; Brar 2017; Unique). Heart defects or murmurs have also been observed in individuals with 9p deletions, including a girl with a deletion involving only 9p23 who had a VSD, PDA and PFO (Hauge 2008; Schlade-Bartusiak 2013; Unique).

The anomalies of the heart recorded above were seen in individuals with co-existing 9p duplication and deletion ranging from those with a relatively “small” 9p duplication and 9p deletion e.g. dup 9p23p24.1/del 9p24.1p24.3 (PDA) and dup 9p21.1p22.3/del 9p22.3p24.3 (PDA/VSD/PFO/sinus arrhythmia), to those with a 9p duplication involving almost the whole of the short (9p) arm and a 9p deletion e.g. dup9p13.32p24.2/del 9p24.2p24.3 (ASD), dup 9p12p24.1/del 9p24.3 (mosaic) (VSD), or a “large” duplication including the whole of 9p and part of the q arm and a 9p deletion e.g. dup 9q12p22.3/del 9p22.3p24.3 (heart murmur) (Swinkels 2008; Schlade-Bartusiak 2013; Unique).

The data from the medical literature and *Unique* therefore suggests that the combined effect of a 9p duplication and a 9p deletion is likely to contribute to the development of heart anomalies and supports the idea for the involvement of a combination of multiple genetic and environmental factors in the development of heart defects (Schlade-Bartusiak 2013; Oh 2016).

“ He was born with an ASD with an enlarged heart. After surgery at eight months he is pink and breathing much better. ” - dup 9p13.3p21.3/del 9p22.1

“ At nine years we have discovered a congenital heart defect (PDA) that will be repaired soon. ” - dup 9p23p24.1/del 9p24.1p24.3

“ He had a small ASD that spontaneously closed by one year. ” - dup 9p13.32p24.2/del 9p24.2p24.3

“ He has a heart murmur and he was born with two holes in his heart, but they closed up within a month of his birth. ” - dup 9p13.31p23/del 9p23p24.3

## ■ Eyes and vision

Problems with vision were reported by 3/9 *Unique* members: one boy was found to be long-sighted (hyperopia) in the early years but was later assessed as being short-sighted (myopia); another boy was partially sighted, although his peripheral vision was less severely affected; and a girl was classified as legally blind in one eye and short-sighted in the other. Glasses can be used to correct minor visual impairments.

Nystagmus is a recognised feature of 9p deletions that affected 4/9 *Unique* members with co-existing 9p duplication and deletion, three of whom had a 9p deletion involving the critical region for 9p deletion syndrome. The condition is characterised by uncontrollable, repetitive movement of the eye (s), which is usually side to side but may be up and down or possibly in a circular motion. Nystagmus is usually picked up in the first few months after birth and will need to be investigated by an ophthalmologist (eye doctor). Although nystagmus can't be cured, an eye clinic will be able to make a detailed assessment, including how vision is affected, and suggest ways to

## Heart conditions

**Heart murmur:** A heart murmur is an extra or unusual sound that is made by blood flowing through the heart and by the valves in your heart opening and closing. It may indicate an underlying heart problem, such as an ASD (see below), but often there is no cause at all.

Often a heart murmur is “innocent” and no treatment is required but sometimes corrective surgery may be needed.

**Persistent ductus arteriosus (PDA):** This is a channel between the aorta and the pulmonary artery that takes blood to the lungs, which usually closes shortly after birth. When it stays open, the lungs receive more blood than they should, and the heart has to work too hard.

It can be closed using minimally invasive surgery, by inserting a coil via an artery in the thigh. Tissue grows around the coil, closing the gap.

**Atrial septal defect (ASD):** A hole in the muscular wall between the two filling parts of the heart. Some blood flows through from the left to the right side, increasing the amount of blood flowing to the lungs. Treatment depends on the type of defect, whether it closes spontaneously and its size.

Treatment can include medical management, taking medications to help the heart to work better, control of potential infection to the inner surfaces of the heart, and surgical repair with stitches or a special patch.

**Ventricular septal defect (VSD):** A hole in the wall between the two pumping chambers of the heart (ventricles) allows blood to flow from the left to the right chamber, increasing the blood flow to the lungs.

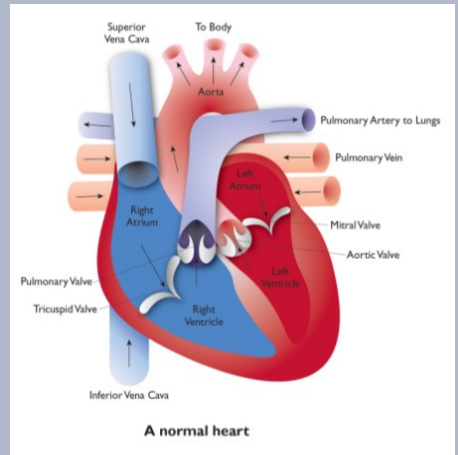
Specific treatment for VSD is determined individually. A baby with a VSD will be evaluated periodically. Small VSDs may close spontaneously; a larger VSD usually needs surgical repair to prevent lung problems that would develop from exposure to extra blood flow.

**Patent foramen ovale (PFO):** An opening between the two upper chambers of the heart does not close in the first year of life, as would normally be expected. When it remains open, this allows extra blood to pass from the left to the right side of the heart.

**Cardiac myopathy:** A disease of the heart muscle that affects its size, shape and structure. There are many possible types of cardiomyopathy, but the most common include hypertrophic cardiomyopathy, where the muscle wall of the heart becomes thickened, and dilated cardiomyopathy, where the heart muscle is stretched and becomes thin. Although all cardiac myopathies reduce the ability of the heart to carry out its function of pumping blood around the body, these changes affect individuals differently.

**Mitral valve prolapse (MVP) and insufficiency:** The mitral valve between the upper left heart chamber and the lower left chamber does not close well enough to prevent back flow of blood when the ventricle contracts. The flaps of the mitral valve allow blood from the left ventricle to flow back into the left atrium.

**Ebstein's anomaly:** A defect affecting the right side of the heart. The tricuspid valve that controls blood flow from the top chamber (atrium) to the bottom (ventricle) is too low down. This makes the top chamber too big and the bottom chamber too small. The valve may also be leaky, letting blood that should be in the ventricle leak back into the atrium.



manage the condition (Unique; [www.rnib.org.uk](http://www.rnib.org.uk)).

Strabismus (a squint) where one eye or both turns inward, outward, up or down is relatively common among individuals with 9p duplications of all sizes, including two children with duplications involving only 9p24, and has also been associated with 9p deletions (Brambila-Tapia 2014; Cuoco 1982, Unique). Strabismus may be constant, or it can occur intermittently, especially when tired.

Interventions like patching, exercises or glasses generally work well to correct a squint, but for some strabismus may only be corrected following a surgical operation. A "lazy eye" (amblyopia), can also be a consequence of a constant squint in one eye. Given this, it is perhaps surprising that among *Unique* members with co-existing 9p duplication and deletion, there was only one report of a squint "when looking at objects close up" and one instance of a pseudo- (or possibly temporary) squint. In the medical literature there was one report of a girl with a squint who was also long-sighted (Schlade-Bartusiak 2013; Unique).

While several children with 9p duplications alone have been found to have ptosis, where there is drooping of the upper eyelid so the eye is not fully open, or lagophthalmos, where a baby or child may have difficulty closing their eyelids completely, no cases of either condition were reported for co-existing 9p duplication and deletion, although one boy did sleep with his eyelids open (Unique).

"For the first few years he had mild long-sightedness but was later found to be mildly short-sighted. At 14 years it was bad enough to require glasses (-1 in both eyes). He doesn't actually wear his glasses as he keeps breaking them, but I don't think it's a problem in practice. There was also much debate about whether he had a squint or pseudo-squint. The conclusion was a pseudo-squint due to wide epicanthic folds, but I think he also had a slight temporary squint that self-corrects under testing. Now all resolved." - dup 9p13.32p24.2/del 9p24.2p24.3, 16 years

"He is partially-sighted but wide vision is better. Also, his vision is better when he looks at things upside down. He has regular eye tests and is believed to have suffered optic nerve damage due to pressure in the skull at age two or three years." - dup 9p12p22/del 9p22, 19 years

"She is classified as legally blind in her right eye (-17 in one eye and -4 in the other eye). She wears glasses. We tried patching as a child but she didn't like it so we used drops to blur her vision. She will likely need surgery in the future as the muscles around her right eye are weak as she really doesn't use this eye at all." - dup 9p12p24.2/del 9p24.3, 13 years



## ■ Hearing

Some degree of hearing loss, due to a combination of glue ear, unusually narrow external ear canals and excess wax in the ear canal, was noted in 6/9 *Unique* children in the 2017 survey with co-existing 9p duplication and deletion, with some cases also reported in the medical literature. The evidence suggests that problems with hearing loss are usually temporary, generally affecting only children in the early years (Hauge 2008; Schlade-Bartusiak 2013; Unique).

Glue ear is caused when a sticky fluid (glue) builds up inside the ear. This can cause the air pressure inside the middle ear to drop and interfere with hearing. Glue ear is typically treated by inserting aeration tubes (grommets) into the eardrum and on occasion this surgical operation may need to be repeated. Normal hearing may not be achieved with aeration of the space behind the eardrum (middle ear) and hearing aids may help as a temporary or longer-lasting measure, although this appears to be uncommon. As children are at risk of speech delay, parental concerns should be acted on early and home- or school-based therapy provided.

“He was born with no hearing but then he started to hear after a few years. I believe he had glue ear.” - dup 9p13.1p23/del 9p23p24.3

“He had multiple ear tube surgeries and also had a small, benign (non-cancerous) tumour removed from his ear drum. He had hearing loss and wore hearing aids, but his hearing has improved as his ear canals have grown. We have been told he has very tiny ear canals and they are kinked - making hearing a problem and also making him more likely to get ear infections.” - dup 9p13.1p24.3/del 9p24.3

“Our son had mild to moderate hearing loss from 4 to 10 years. He had several sets of grommets fitted, which made no discernible difference in practice. Some fell out and one got imbedded and had to be removed.” - dup 9p13.32p24.2/del 9p24.2p24.3

## ■ Palate

Abnormalities of the palate are common.

Anomalies of the palate (roof of the mouth), ranging from those that may be invisible to the casual onlooker such as a high/arched palate, to more obvious defects such as a cleft palate - although this is more unusual - frequently affected both *Unique* children and patients in the medical literature.

A cleft lip and palate is caused by an error in fusion when the foetus is forming: the lip and palate fuse from pieces that start on opposite sides of the head and a cleft occurs when the pieces come round but do not join. Anomalies of the palate, particularly clefting, can cause difficulties in feeding, hearing, teething and speech production. As well as helping aesthetically, surgical repair eases these problems and may even eliminate them altogether.

A region predisposing for anomalies of the palate associated with 9p

duplications has been suggested to reside within 9p22.1p22.2, although not all babies and children with a duplication including 9p22.1p22.2 were affected and a baby with a 9p duplication not involving this region had a high/arched palate. A high/arched palate is also a feature of 9p deletions (Fujimoto 1997; Fass 2007; Swinkels 2008; Hulick 2009; Jelin 2010; Recalcati 2012; Kowalczyk 2013; Pedurupillay 2014; Unique).

“She had a cleft lip and palate at birth requiring surgery at eight-months-old. This caused feeding issues and continues to affect her speech. She has just had a pharyngoplasty at the age of 12 years to try and reduce the excess space in the back of her mouth and improve the clarity of her speech.” - dup 9p12p24.2/del 9p24.3

“It affected his feeding, but he did not have any treatment or surgery for his high palate.” - dup 9p13.1p23/del 9p23p24.3

“Had a high/arched palate that was corrected with orthodontics.” - dup 9p23p24.1/del 9p24.1p24.3

## ■ Teeth

Dental problems are particularly common and often persist into adulthood.

In *Unique's* experience, children with a chromosome disorder generally have a higher rate of dental problems than typically-developing children. This is particularly evident for individuals with co-existing 9p duplication and deletion.

A number of problems were described by parents (several of which were also reported in the medical literature, although information is limited). Of particular concern were: unusual dental development; unusual size of the jaw, leading to overcrowding or widely-spaced teeth; abnormally thin, weak enamel (enamel hypoplasia); and tooth grinding (bruxism), which can prematurely wear down the enamel. Teeth may emerge late and milk teeth may be late to fall out.

In the 2017 survey, 100% of parents mentioned dental issues, often citing more than one problem. Of particular concern were tooth grinding (6/9), over-crowding (4/9), late teething (4/9) and weak enamel (3/9).

A high standard of dental care is important to minimise damage by decay and erosion. Children and adults may also benefit from specialist hospital dental services and may require treatment under general anaesthetic (Hauge 2008; Jelin 2010; Unique).

“Teeth grinding regularly, particularly if he does not like someone new or a new situation/hospital e.g. he is anxious. Very poor enamel on teeth and suffers with tartar, but the dentist says overall his teeth are in good condition.” - dup 9p12p22/del 9p22, 19 years

“Very large gaps in teeth. Teeth were late to fall out.” - dup 9p13.1p24.3/del 9p24.3, 9 years

“Lost her last milk tooth at the age of 14 and the last permanent tooth did not descend until the age of 16.” - dup 9p23p24.1/del 9p24.1p24.3, 16 years



## Anomalies of the hands and feet

Hands	<i>Unique</i> 2017 survey	Feet	<i>Unique</i> 2017 survey
Curved finger(s)	6/9	Curved toe(s)	1/9
Short finger(s)	2/9	Short toe(s)	3/9
Long finger(s)	3/9	Long toe(s)	2/9
Tapering fingers	2/9	Flat feet	9/9
Fused fingers	1/9	Rocker bottom feet	0/9
Underdeveloped fingernails	1/9	Club foot	1/9
Extra joints	1/9	Underdeveloped toenails	2/9
Hyperflexible joints	1/9	Toenails grow upwards rather than outwards	2/9
Brittle/ridged fingernails	1/9	Brittle/ridged toenails	1/9

### ■ Hands and Feet

Anomalies of the hands and feet are common.

Unusual features of the hands and/or fingers are common (see table) and are associated with both 9p duplications and 9p deletions. Most common among these were fingers that curved inwards (clinodactyly) and were unusually long (arachnodactyly) or short (brachydactyly).

Specific abnormalities of the feet and toes were also reported. Most notably, all families in the *Unique* survey said that their child had flat feet (pes planus). One child also had club foot (talipes), where the foot turns inwards and the soles point towards each other. Toes were often either unusually long or short, with under-developed, brittle/ridged toenails that sometimes grew at an unusual angle.

Children are often only mildly affected, and any deformity will not require treatment, although children with flat feet may benefit from insoles to correct the foot position. Others, such as those with club foot, may also benefit from massage, physiotherapy and sometimes splinting to help correct incurved feet, which may reduce the need for corrective surgery and plaster casting. Treatment is tailored to the individual child and in some cases surgical correction will best enhance eventual mobility.

## ■ Skin growths

Benign (non-cancerous) skin lesions known as pilomatricomas, pilomatrixoma, 'calcifying epithelioma of Malherbe' or trichomatricoma were reported by one *Unique* member with a co-existing duplication 9p12p24.2/del 9p24.3 and have also been found in a few people with 9p duplications, as well as being a feature of tetrasomy 9p.

Pilomatricomas arise from the cells at the base of hair follicles, the specialised structures from which hairs grow, and tend to be found on the head or neck, although they can also sometimes arise on the arms, torso or legs. They are skin or purplish in colour, with white areas due to calcium deposits that make them feel surprisingly hard to the touch.

Pilomatricomas are harmless, but occasionally they may burst and release a white and yellow chalky fluid. Very occasionally they can become sore and inflamed if they become infected, so picking and squeezing them should be avoided. Occasionally pilomatricomas may need to be surgically removed ([www.bad.org.uk](http://www.bad.org.uk), *Unique*).

One *Unique* child had a cutaneous hemangioma (an abnormal build-up of blood vessels on or under the surface of the skin that can look like a red-coloured birthmark) that didn't require any treatment (*Unique*).

## ■ Hernias

In the 2017 *Unique* survey, 3/9 members reported that their child had had a hernia. Hernias, where an organ or fatty tissue pushes through a weak spot in a surrounding muscle or tissue, have previously been reported for both 9p duplications and deletions.

Three *Unique* children and at least two children reported in the medical literature had an umbilical hernia (at or near the belly button), which in one case was accompanied by an inguinal (inner groin) hernia. One other child had an inguinal hernia. Hernias may also be diaphragmatic (the muscle that separates the chest cavity from the abdominal cavity), hiatal (upper stomach) or abdominal (belly). Hernias may heal naturally without the need for treatment, but in the majority of cases surgical repair is required (Teebi 1993; Recalcati 2012; Pedurupillay 2014; *Unique*).

## ■ Omphalocele

Omphalocele (exomphalos) is a birth defect that is a rare feature of 9p deletions (Hou 2014), as well as other RCDs including trisomy 13 and trisomy 18.

A baby with omphalocele is born with their abdominal (belly) organs on the outside of the body (sticking through the belly button) and contained within a thin, almost transparent sac. Depending on the size of the omphalocele, some or all of the intestines, liver, or other organs may be contained within the sac. Omphalocele is sometimes detected during prenatal screening tests but may only be diagnosed immediately after birth.

No cases of omphalocele were reported in the 2017 *Unique* survey, but the *Unique* database contains information about two babies with co-existing 9p duplication and deletion who were born with the condition, while two cases

were reported in the medical literature (Swinkels 2008; Pedurupillay 2014; Unique).

Treatment depends on a number of factors. Where the omphalocele is small, surgery to put the organ back into the abdomen will usually take place soon after birth. For a larger omphalocele involving more of the intestine or a number of organs, the repair is usually carried out over a longer period: a clear plastic or silicone pouch (silo) is used to cover the exposed organs and then gradually the organs are encouraged to move back into the abdomen before the opening in the abdominal wall is closed.

“Omphalocele (involving a piece of his liver) was repaired two days after birth.” - dup 9p13.3p21.3/del 9p22.1p24.3

## ■ Constipation

Constipation can cause considerable discomfort and can be a long-lasting problem.

Constipation is common among children with chromosome disorders and can be related to low muscle tone, little exercise, a low-bulk diet and small fluid intake.

The evidence from *Unique* suggests constipation is particularly common among babies and children with a co-existing 9p duplication and deletion (as well as those with 9p duplication and 9p deletion syndromes), and often persists into adulthood. It is important that parents discuss the possible causes with their health visitor or doctor, who may recommend adapting your child's diet, or giving stool softeners such as Movicol and/or laxatives such as Lactulose and Senna. Children may benefit from enemas if symptoms are particularly severe.

“Our son has had constipation from about five years onwards. Treatment with Lactulose worked well for the first few years but then the dentist said to stop as it might rot his teeth. We then tried various alternatives, including sodium picosulphate (a laxative) and Movicol, but he wouldn't drink it. He needed to go to A&E twice with an impacted bowel and was treated there with Movicol. He has only been regular since he was 14-years-old by using French Movicol, which tastes nicer, and sitting him on the loo for one hour every night.” - dup 9p13.32p24.2/del 9p24.2p24.3, 16 years

## ■ Anomalies of the genitals & ambiguous genitalia

Among boys minor anomalies are common, while rarely more severe anomalies are observed.

The experience of *Unique* families and the number of cases documented in the medical literature suggests that minor anomalies of the genitals in boys are very common among those with co-existing 9p duplication and deletion (and are also a feature of both 9p duplication and 9p deletion syndromes) (Muroya 2000; Neira 2012; Recalcati 2012; Unique).

The 2017 *Unique* survey found that 4/4 boys had unusual genital features. Typical anomalies were: undescended testis/testes (cryptorchidism), a very small penis (micropenis), or most frequently, a combination of both.

The testes begin their descent from the abdomen when a baby is still in the womb and have usually arrived in the scrotum by birth. In a significant number of boys without any chromosome abnormality, that journey is not complete by birth but is completed within the next few months of life. When descent does not occur, the testes can be brought down in a surgical operation (orchidopexy) and anchored in the scrotum, as was the case for most boys within the *Unique* series.

While three boys in the *Unique* series were born with a small penis and two boys had a buried (hidden) penis, the testimonies from *Unique* parents suggest that while these conditions may persist throughout childhood, the penis often has a “normal” appearance after puberty (Unique).

One boy also had hypospadias (the hole normally at the end of the penis lies on the underside). If necessary, hypospadias can be corrected with surgery (Unique).

In a few, rare cases (one *Unique* member and two reports in the medical literature) a baby with male XY sex chromosomes appeared to be a girl at birth or had ambiguous genitals - a feature associated with 9p deletions. While those affected all had a deletion including 9p24.3, other boys with 9p24.3 deletions were born with only minor anomalies of the genitals (see above) and a three-year-old boy with mosaicism for co-existing 9p duplication and deletion had “normal” male genitals (dup 9p13.1p22.1/del 9p22.2p24.3 [24]/del 9p22.2p24.3 [14]). Equally, not all boys with a 9p deletion (but not a co-existing 9p duplication) involving 9p24.3 are affected either and many boys with 9p duplications of varying size and location also have minor anomalies of the genitals, although no cases of ambiguous genitalia or complete sex reversal were reported for 9p duplications alone (Muroya 2000; Neira 2012; Pedurupillay 2014; Unique).

The *DMRT1* gene located in 9p24.3 has been identified as being the likely gene responsible for these genital anomalies, although since there is such variability in the occurrence and severity of the anomalies of the genitals, ranging from mild cryptorchidism to complete sex reversal, it has been suggested that a “second hit” may determine the degree to which an individual is affected. For instance, mutations, deletions or duplications of another gene(s) or regulatory elements that affect the expression of the *DMRT1* gene may play a role (Recalcati 2012; Quinonez 2013).

Girls are much less likely to be affected. No girls in the *Unique* series had anomalies of the genitals and only one girl in the medical literature had mildly under-developed labia majora (Hauge 2008 - dup 9p13.3p24.1/del 9p24.1p24.3), while another had normal external genitalia but a small uterus and large polycystic ovaries (Al Achkar 2010 - dup 9p22p24.2/del 9p24.2p24.3).

“He was born with a partially buried penis that was corrected via surgery. He also had surgery to fix his undescended testicle.” - dup 9p13.1p24.3/del 9p24.3

“Our son had two orchidopexy surgeries at around five and six years. They carried out two separate operations as one testicle was very high up and the

operation took too long to do both. He also had what looked like a micropenis before puberty as the penis was hidden by thick, fatty layers surrounding it. I hear this is common from duplication 9p mums. His penis was actually normal-sized. Post puberty there is now normal presentation! ”  
- dup 9p13.32p24.2/del 9p24.2p24.3, 16 years

## ■ Kidneys

Several *Unique* members with 9p duplications have reported minor anomalies of the kidneys, including: an enlarged kidney(s) (hydronephrosis) due to a build-up of urine inside; the absence of one kidney; and individual cases of a duplex kidney, horse-shoe kidney, and benign renal caliectasis.

Kidney reflux, where urine flows backwards from the bladder up the ureter to the kidney, which can lead to urinary tract infections (UTIs), has been reported for 9p deletions (9pminus.org; Unique). UTIs can be treated with antibiotics or, very occasionally, a catheter may need to be inserted to remove the build-up of urine and prevent damage to the kidney.

Individual cases of kidney reflux; small kidneys; and nephrocalcinosis (too much calcium is deposited in the kidney), in otherwise normal-looking kidneys, were reported by *Unique* members with co-existing 9p duplication and deletion. Two further cases of kidney abnormalities were observed in the medical literature: one case of right-sided renal pelviectasis - a mild enlargement of the central area, or “pelvis,” of the kidney (Hulick 2009) - and one case of right renal agenesis, where one of the kidneys is missing (Kowalczyk 2013).

## ■ Liver

Although not previously reported for 9p duplications, 9p deletions or co-existing 9p duplication and deletion, in the *Unique* series two members mentioned that their child had experienced an enlarged liver (hepatomegaly). Although the underlying causes of these diagnoses are unclear, both these children had multiple heart conditions, which can lead to enlargement of the liver (Unique).

## ■ Tracheomalacia/laryngomalacia

Individual cases of tracheomalacia and laryngomalacia where the cartilage that supports the trachea (windpipe) or larynx (voicebox) is soft meaning that the trachea partly collapses, especially during increased airflow, were described for two *Unique* members with co-existing 9p duplication and deletion. This can lead to difficulties with breathing, including: rattling/noisy breathing (stridor), recurrent and prolonged respiratory infections and, in more severe cases, difficulties with feeding (reflux) and a halt in breathing leading to “blue spells” when a child doesn’t receive enough oxygen. Often these conditions resolve within the first few years of life as the child grows, without treatment. Only in rare cases is surgery needed to correct the condition (Unique).

“Mild tracheomalacia. ” - dup 9p13.32p24.2/del 9p24.2p24.3, 16 years

“He had laryngomalacia. Epiglottic fold [three folds of mucous membrane in the oral cavity that pass between the tongue and the epiglottis] was

trimmed approximately five times as it was too big and too floppy, which would result in him stopping breathing numerous times. The treatments worked for a short period then it would grow back. Eventually led to a tracheostomy being fitted age 11 years that remains to date.” - dup 9p12p22/del 9p22, 19 years

## ■ Joints

Joint abnormalities are relatively common and can be severe.

Joints may be extremely loose (hypermobile) (6/9 children in the *Unique* 2017 survey) and elbows, wrists, knees and hips may be affected. This means babies and children can move their limbs into positions others find impossible. While this may cause no problems, hypermobility is sometimes associated with pain and stiffness in the joints and muscles; joints that dislocate (come out of position) easily; and injuries, including sprains.

Children with very loose joints may need physiotherapy, massage or additional braces (supports, splints) before they are able to walk.

Some children have a degree of hip dysplasia (2/9), in which the hip joints are easily dislocated. This may be apparent at birth or develop later. In either case it can be treated with splinting and if necessary immobilisation in plaster and possibly surgery (Huage 2008; *Unique*).

“She was born with hip dysplasia and has very loose joints. She has extra joints in her fingers and very low muscle tone.” - dup 9p12p24.2/del 9p24.3, 13 years

“She prides herself on being double jointed and can bend herself in to unusual positions.” - dup 9p23p24.1/del 9p24.1p24.3, 16 years

## ■ Skeletal anomalies

Some individuals develop a spinal curvature, often as teenagers or adults.

Cases of scoliosis, a sideways S-shaped curve of the spine (4/9 in the *Unique* survey; two patients in the medical literature), and kyphosis, an outward curve resulting in a hump (1/9 in the *Unique* survey; one patient in the medical literature), have been reported. One younger *Unique* child with the early signs of scoliosis was being assessed (Swinkels 2008; Jelin 2010; Recalcatti 2012; *Unique*).

Underlying the curve may be abnormalities of muscle tone, and in some cases the bones of the spine (vertebrae) may be fused together or incorrectly formed. The curvature can be treated with physiotherapy and exercises, or a support brace may be needed. If the curve becomes marked it may be necessary to undergo spinal fusion surgery and straighten the spine using rods. Both conditions may worsen with age and require careful monitoring.

A 7-year-old girl with co-existing dup 9p21.1P22.3/del 9p22.3P24.3 had a tethered spinal cord. This rare condition occurs when the end of the spinal cord is attached to the spinal column instead of floating freely in spinal fluid, thereby preventing it moving up and down as necessary with growth, bending and stretching. Tethered cord is associated with muscle weakness,

lower back pain, scoliosis and incontinence. Rest, physiotherapy and medications can help to relieve symptoms, but untethering surgery may be the only permanent, successful treatment for more severe cases Unique).

“ Our son had mild scoliosis from six years that suddenly got worse at 14 years. At the last scan he had a more serious, moderate 28-degree curvature. He now wears a Gensingen Brace® that was prescribed privately as a more aggressive treatment than the NHS-prescribed Boston TLSO brace. ” - dup 9p13.32p24.2/del 9p24.2p24.3, 16 years

“ He has kyphosis that has not required treatment to-date. The condition is being monitored as it may have an effect on his breathing/chest. He requires a special seating system and PT. ” - dup 9p12p22/del 9p22, 19 years

## ■ Bones

Individual cases of delayed bone maturation - including a 14-year-old with a bone age of 11 years - and weak, low-density bones have been reported. In reality, these conditions may actually be more prevalent since many parents were unsure whether their child was affected and several children and adults in the medical literature had a bone age that lagged behind their age. Similar conditions have been recorded for 9p duplications (Al Achkar 2010; Kowalczyk 2013; Unique).

“ She has low-density bones and has broken her leg twice. ” - dup 9p21.1p22.3/del 9p22.3p24.3, 7 years

## ■ Hypersalivation and drooling

A significant number of *Unique* parents (6/9) mentioned that their child had experienced excessive saliva production (hypersalivation) and/or drooling (sialorrhea). Drooling can happen without excessive saliva production if there is difficulty keeping the mouth closed or there is an inadequate mechanism or rate of swallowing, as is sometimes the case with neurological conditions such as cerebral palsy and intellectual disability. Various treatment options are available and medication may be prescribed if necessary, although most parents said that the situation improved once their child reached their fourth or fifth birthday (Unique).

“ Continued to drool or wet a shirt until the age of five. ” - dup 9p21.3p24.2/del 9p21.3p21.3, 10 years

“ He experiences severe drooling. We have constantly treated the condition e.g. with Hyoscine (scopolamine) but to no avail as the treatment either dries his mouth out or doesn't work. ” - dup 9p12p22/del 9p22, 19 years

## ■ Narrow or blocked nasal passages

Choanal atresia, where one or both nasal passages is blocked (atresia) by tissue or bone, is a rare condition and an occasional feature of 9p deletions, which affected one third (3/9) of children in the *Unique* 2017 survey. In its mild form the nasal passages may be very narrow (stenosis) rather than completely blocked. The condition is associated with breathing difficulties and is present from birth. Where the nasal passages are blocked a surgical operation is required.



## ■ Other medical concerns

Primary immune deficiency (selective antibody deficiency): One case (dup 9p21.1p22.3/del 9p22.3p24.3).

Weekly infusions for six months to help boost immune system: One case (dup 9p13.1p24.3/del 9p24.3).

Hypoglycaemia (low blood sugar): One case (dup 9p21.1p22.3p/del 9p22.3p24.3).

## Puberty

Although we have only very limited data relating to puberty, among *Unique* members with co-existing 9p duplication and deletion, there was a trend towards children starting puberty within the expected age range, although sometimes at the upper age limit. We also know of one case where the first signs of puberty were noted in a 7-year-old girl. Precocious (early) puberty is characteristic of 9p deletions, while a trend towards delayed (late) puberty has been observed for 9p duplications (Cuoco 1982; Mahjoubi 2011; Cisternino 2013; Stagi 2014; *Unique*).

Anecdotal evidence from families suggests that their children have handled the complexities of puberty well, despite some initial anxiety, and puberty has proceeded as expected with no real cause for concern. It is worth noting that several 9p duplication families have found that having a hormonal intrauterine device (IUD) fitted to stop periods is beneficial for girls who find menstruation challenging.

“She is just starting puberty. She is a little bit anxious about it and I don't think she will really understand it until it happens to her. We talk about it but, because it is a foreign concept that she cannot physically see, she struggles to comprehend it.” - dup9p12p24.2/del 9p24.3, 13 years

Note: At 14 years a scan showed a very small pituitary gland [which has a role in controlling the on-set of puberty], which is being investigated further.

“No issues at all. Most problems were associated with his Adam's apple and the throat area - this changed and made swallowing and breathing more difficult and interfered with his already floppy epiglottic fold, resulting in an emergency tracheostomy (which he stills has to this day).” - dup9p12p22/del 9p22, 19 years

## Adulthood

In 2018, *Unique* had only two adult members with co-existing duplication and deletion of 9p. A 20-year-old with profound ID and absent speech was living in an annex in his parents' home and had carers 24/7. His parents felt that he “would never be able to live independently”, a sentiment that was echoed by another family whose son was in his mid/late teens. A 21-year-old woman with co-existing dup 9p21.1p24.3/del 9p11.3p13.1 “was able to dress, feed herself and use the bathroom independently” (Jelin 2010).

Experiences of adulthood are likely to vary considerably depending on many factors, including the level of ID, any on-going medical concerns and improvements in early intervention. *Unique's* guides to [9p duplications](#) and [9p deletions](#) have more details on adulthood that you may find informative.

## One adult's story...

“ Our 20-year-old son “W” has a co-existing duplication 9p12p22/deletion 9p22. W is a loving, caring, happy person with a wicked, dry sense of humour. He loves people and to be surrounded by his friends and carers. He always has a loving smile for us and charms the ladies and wins people over by blowing them kisses.

W was born 20 years ago with no detection on any scans during my pregnancy. The outlook was very bleak from the beginning, but after the initial shock of having a baby that faced a future of obstacles, we decided there and then that no matter what we would fight all the way for our son.

W developed epilepsy aged 18, is a wheelchair user, and is doubly incontinent but can tell us when he needs “to go” by tapping his pad. He suffers from numerous chest infections that were confined to winter but now seem to be all year round. It doesn't matter what W can and cannot do, he is our son and it is what it is - children come in all shapes and sizes, some do more than others, but W has brought so much joy, love, tears, and pleasure into everyone's life that he touches.

W is non-verbal and uses facial expressions to communicate. He babbles occasionally but uses very few words. He has had speech therapy from birth. This helped with feeding problems and swallowing issues; however, I do not feel they pushed W enough to communicate.

W goes through phases of learning and development: small steps then nothing for ages and ages. Although W cannot read, write or use a keyboard, he can operate a switch (since the age of seven years). From 18 years of age he has become more alert/interested and responsive - so never give up hope. He has attended a special needs school throughout his education and is currently attending a special needs further education college.

He loves music and flashing lights and really enjoys discos, parties and roller disco (using his wheelchair). He also really enjoys ten pin bowling, theatre (if it is musically-themed) and socialising. W is a very sociable person and manages to interact with all his friend at college. They seem to know what he wants and what he likes, and they all fight over who is going to help him in lessons. He knows this and makes the most of it, by playing around with them all – shaking his head to refuse something then five mins later requesting it again; they all find this fun. W has a very high pain threshold and has only ever cried actual tears about five times in his life.

W's sleeping pattern is - and always has been - very poor, which doctors think is due to the level of background brain activity that is going on. He sleeps for five to ten minutes about five times a day but very rarely through the night - he needs very little sleep. We've tried many things to encourage sleep, including herbal, natural treatments then Melatonin at a high dose, but none were effective.

Our biggest challenge since W reached adulthood has been the level of care he requires and the transitional period – we fell out with, argued with, and challenged everyone that thought they knew what was right for W, but eventually he got what we thought was right for him. W has a continuing health care package of 2:1 carers 24/7 (when they can recruit staff). Getting this funding through from the Commissioning Support Unit (CSU)/Clinical Commissioning Group (CCG) was and still is extremely challenging. As everyone knows, having a disabled child/young adult means you have to fight for everything you need for them from equipment to operations, care etc. It is one constant battle and wears you down from time to time but just getting that gorgeous smile from our son makes it all worthwhile. ”

## What families say.....

**“ On balance, my experience of having a disabled child is positive. Certainly, my life these past 16 years has been more interesting and fulfilling than before.**

The diagnosis has affected the whole family - we are probably all more patient and philosophical than our peers. Our lives are somewhat dominated by fitting round my son's needs and interests. My “typical” daughter was forced to be more independent for the first nine years of her life, until our son went to boarding school. On the other hand, I have probably been a more hands on, present, empathetic stay-at-home mum to my daughter than if I hadn't had a disabled child and had continued my career as lawyer. The chromosome 9 Facebook groups are excellent and meeting other families at a get-together in Chicago was great. In the early years, I benefitted hugely from joining the Down's Syndrome Association, reading books aimed at DS and attending excellent training courses from Down Syndrome Education International (previously DownsEd). Our son's social and learning profile matched the DS profile fairly well from birth to 10 years (strengths in social communication, empathy, visual learner) and still does to some extent. He learnt to read using the DownsEd visual method. Discovering AAC (alternative and augmentative communication) in the shape of communication books as well as communication apps like Proloquo2Go was life-changing for him. I don't think he would have made 5% of the progress he has if we hadn't discovered that route at a time when there was no speech and Makaton wasn't working. He was quite frustrated/destructive around four to five years, but once he could communicate with the communication book his behaviour improved and staff at school/therapists realised what he could do.”

“ I'm not going to say it is easy, but our son has enriched our lives (and everyone that meets him) to no-end. His sister is younger, by two years, and adores him and he adores her. He is loving, sweet-natured and people are drawn to him. It has been a journey. There have been moments where we felt devastated and alone, but there have been many more moments that we have felt blessed and amazed by him. Not everyone in the family is going to be on the same page with treatments and therapy etc. **My advice is: trust your instinct as a parent. Be your child's advocate. Look into alternative therapies and find doctors, therapists, family and friends that are supportive of you. Be realistic but be hopeful. Don't stop trying new things or challenging your child (or yourself).** Having a child like our son puts things into perspective. Accomplishments are not just accomplishments, they are triumphs. It's okay to feel sad, mad and disappointed, but relish in those triumphs. I know everyone's experience is different, but for us, our son brings so much joy and life into everyone around him. We were told not to expect much, and we didn't listen. Advice I wish I took sooner: take time for yourself; grieve when you need to grieve; find some people that can ride the ride with you and not necessarily tell you what you should or shouldn't be doing - people that are supportive along the way; don't give up; and invest as much as you can emotionally, financially and physically.”

“ There has been an enormous effect on the whole family, especially his older brother who found it very hard to deal with at school and was teased constantly about having a disabled brother - to this day he still struggles to accept his brothers condition. As a parent it has been very difficult and could have had a detrimental effect on my relationship with my husband as the stress, strain, lack of help and advice was too much. However, we both pulled together and keep each other going. I had a nervous breakdown about six years ago due to the constant fighting with officials/authorities, which is non-stop and continues to this day. The 9pminus (9p-) group based in the USA was a fantastic support to us in the beginning of his journey and we learnt a lot about what was to come - although with our son also having duplication (trisomy 9p) we knew he would not follow their paths as he is affected a

lot more than the 9p- children/adults. They have a brilliant Facebook page for only 9p- parents where you can go and ask other parents about difficulties you may have. **We now let him blaze his own trail and we learn with him as we go through life together.** It is very daunting in the beginning but so worthwhile. Follow your instincts as far as your child is concerned and don't be afraid to ask, challenge and question peoples decisions - we were told our son would not live two hours, then we were constantly told he wouldn't live, but here we are age 19 and **I am proud to call him my son: he never gives up, fights everything and is so loving - his smile lights up the room! "**

" We don't treat our daughter any differently to our other children who do not have a chromosome disorder. We find it very hard to get information and support from professionals and from government agencies as she always slips through the cracks and we feel like we are always a few steps behind in making sure we are doing the best for her. It has also impacted on the extra care and need for extra money to fund all of the doctors' visits. Knowledge is the key. Advice for other families is to not give up. Keep pushing and keep treating your UNIQUE baby as a normal child, **they will achieve so much more if you give them the opportunities to achieve rather than saying they can't do things because of their disorder.** Getting teachers to understand this has been a big thing for us! "

" Try to avoid analysing in detail every single characteristic or drawing comparisons based on similar genetic defects. We have two daughters with the same co-existing duplication and deletion of 9p and their presentations are quite different. There have been many challenges to our parenting skills. A child who doesn't understand the usual logic or read emotional cues brings a lot of frustrations and despair to those trying to help, teach or train her. It is a constant emotional strain on the entire family on a daily basis. In fact, our life is filled with appointments for therapies and never-ending assessments necessitating time off from work. We have lost friends who can't relate to us and we have gained friends who seek comfort in the fact that our child makes their disabled child look normal. Our advice for other parents is to prepare a lifetime of financial support for your child. Do not forsake your employment. Talk openly and freely to others about your struggles. You will find that when you open yourself up, so will others and you will soon realise you are not the only one who doesn't have the "perfect" child. It's okay to feel sorry for yourself; be kind to yourself. Love and be kind to your child. Ignore what others say, whisper or think of your child or you. You are the best chance your child has. Hope for the best, prepare for the worst. Do not let someone else's experience encourage or discourage you. Your child's future has yet to be written. **If someone with a similar genetic disorder has a better outcome, do not kill yourself trying to achieve the same. The opposite is also true. Do not lose hope because someone else's child with the same disorder has a less than desirable outcome. "**

" We have to rely on nurses just to try to get some sleep at night because she needs constant care. I had to take two years off, unpaid from my job, which created a financial strain, and then I had to go back part-time. My work recently forced me to go back full-time and that creates more stress even though financially it is helpful. The stress of it all in addition to other issues led to a divorce. Our son who is turning 13 years is unbelievable with his sister. They absolutely adore each other and although he would have every reason in the world to resent her, he doesn't - he is her biggest cheerleader. Despite all of the stress, and the unknown, I would clone her in a second if I could. She is the happiest, friendliest, most amazing person I have met. "

" There has been a huge impact, but this is our family, and this is the life we were

given. Our daughter is bright and is aware of her challenges; she will use her disability as an excuse to "not carry her weight" and her siblings get frustrated at the unfairness of the situation. **Since we have limited guidelines on what she can actually do, we tend to provide a lot of opportunities for our entire family for exploration and experiences and see what "sticks".** She has hiked around the world and travelled through Europe, Canada, Costa Rica and the US. She thoroughly enjoys the theatre and Broadway shows and even enjoyed a 3 1/2-hour production of Hamlet, which shocked me (but the actors were amazing and engaging). Also, Disneyland is one of her all-time favourites. Wherever we travel, we always have to make a contingency plan to accommodate her when she has reached her limits. We never really know when that will happen and that requires maximum flexibility from her Dad and me. ”

“ At first it was overwhelming because the doctors didn't have answers for us. We didn't know what to expect since his diagnostic was very rare. Family members didn't understand his rare chromosome disorder. It was frustrating at first but as my son got older it was easier. My advice to other people would be to be patient and loving. **At times it might feel like you're the only one who has a special child and that no one could ever understand you and your situation but there are many others with the same issues. You are not alone. At times you will have bad days but as your child gets older it gets easier. ”**

## Facebook Groups

Trisomy 9p Families (194) - <https://m.facebook.com/groups/664602633553853>

Trisomy 9 Family (386) - <https://m.facebook.com/groups/365958293491370>

Chromosome 9 Disorder (417) - <https://m.facebook.com/groups/132806160119488>

Chromosome 9 (795) - <https://m.facebook.com/groups/120832324611655>

(Number of members as at Dec 2018 in brackets)

## Websites

<http://www.9pminus.org/>

<https://patient.info> - information on medical conditions and terms

<https://www.nhs.uk/conditions/> - easy to understand explanations of medical conditions and procedures

<https://www.epilepsy.org.uk/> - Advice on epilepsy & seizures

<https://www.bhf.org.uk/> - British Heart Foundation - reliable, simple information about heart and circulatory disease

<https://www.rnib.co.uk> - Information and support relating to eye conditions

<https://www.actiononhearingloss.org.uk/> - Information on hearing loss and ear problems

<https://www.clapa.com/> - Cleft lip & palate association

<http://www.bad.org.uk/> - British Association of Dermatologist - advice on skin conditions

<https://www.dsdfamilies.org/> - Support group for differences/disorders of sex development

<http://hypermobility.org/> - Hypermobility Syndromes Association

# Inform Network Support



Understanding Chromosome & Gene Disorders

## Rare Chromosome Disorder Support Group

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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 first compiled by Unique (CA) in 2018 and reviewed by Dr V.H.W. Dissanayake, Human Genetics Unit, Faculty of Medicine, University of Colombo, Sri Lanka.

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