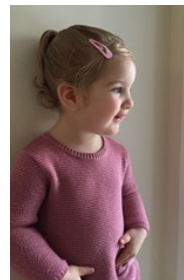
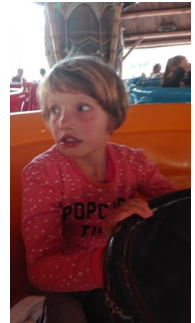




Understanding Chromosome & Gene Disorders

Duplications of 9p



rarechromo.org

Duplications of 9p

A **9p duplication** is a rare chromosome disorder (RCD) in which there is extra chromosome material from the short arm of chromosome 9 (9p) in the cells of the body. The size of the duplication can vary, and the extra material may consist of the entire short arm, part of the short arm or include some of the long arm (9q).

As with other chromosome disorders, having an extra piece of chromosome 9 may affect the development and intellectual abilities of a child, although there is considerable variability in the 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 a 9p duplication do occur in this way, so the disorder is sometimes known as **dup(lication) 9p syndrome**. It is also sometimes called **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).

Co-existing duplication and deletion of 9p

Sometimes an individual may have both a duplication and a deletion of material from chromosome 9p. While these people have features that are associated with 9p duplications, they may also have features that are associated with a distinct **9p deletion syndrome** (*Unique* publishes separate guides to **9p deletions** and **9p24 deletions**). A separate guide to **co-existing 9p duplications & deletions** is available. Both this duplications of 9p guide and the 9p deletions guides will 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.

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.



Chromosome pairs 1-22,
X and Y (male)

Chromosome 9 pair circled in red

Sources

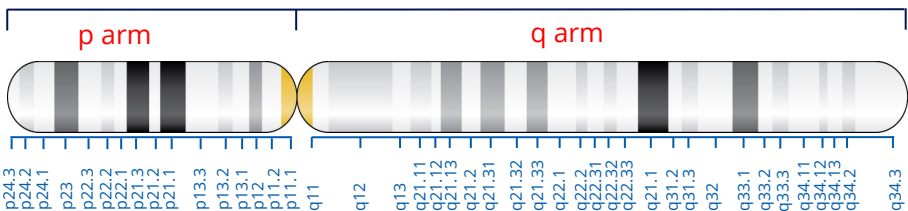
The information in this booklet is drawn from the published medical literature and information from *Unique* members. The first-named author and publication date from articles in the medical literature are given to allow you to look for the abstracts or original articles on the internet in PubMed (<http://www.ncbi.nlm.nih.gov/pubmed>). If you wish, you can obtain most articles from *Unique*. Forty-eight *Unique* members completed a detailed survey in 2017. In addition to this, information has also been drawn from the database records of ~80 further members with a relevant 9p duplication.

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 [Is the size and location of the duplication significant?](#)). Indeed, even exactly the same duplication can have different effects in different individuals within the same family (Unique).

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. 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 is close to the centromere. Material closer to the centromere is called **proximal**. 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, the amount of duplicated DNA can vary. Duplications that are so small that they are not visible under the microscope using standard techniques are called **microduplications**. Many of those with a microduplication may have previously been told their standard chromosome analysis was 'normal'. 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. 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.

Definitions used in this guide

- A **“pure”** duplication refers to a duplication where the entire (or almost entire) short “p” arm has been duplicated e.g. material between 9p11/p12/p13 and 9p24. Duplications of 9p11.2 to 9p13.1 are believed to be a natural chromosome variant with no harmful consequences (Calabrese 1994; di Giacomo 2004).
- A **“small/micro”** duplication refers to a duplication of only part of the short “p” arm of chromosome 9. The duplication may be “small” involving several bands e.g. 9p23 to p24 or 9p13 to p22 or “micro” involving only part of a band or sub-band that is usually one to three megabases (Mb) long, but is sometimes even shorter e.g. arr 9p24.1(6557067_7019424)x3 (0.46Mb).
- A **“large”** duplications refers to a duplication of the whole of the p arm and some of the q arm e.g. material between 9p24 and the q arm up to 9q11/q12/q13/q21/q22.1.

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 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, but it cannot show if the 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/deletions 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).

Chromosome test results

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

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

46,XY,dup(9)(p13p24)dn 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. **dup(9)** means there is a duplication of chromosome 9. **(p13p24)** shows the bands in the chromosome that are duplicated; in this case, there is a gain of a chromosome segment from bands p13 to the end of the chromosome (p24) e.g. almost the entire p arm is duplicated. 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.

46,XX,dup(9)(p23p24)pat This is a girl (XX) with a smaller duplication (**dup**) of the genetic material from chromosome 9 (9) between bands p23 and p24. The duplication has been inherited from the father (**paternal**).

47,XX,+der(15)t(9;15)(p13;q11.2)mat This shows that there are 47 chromosomes, it's a girl or woman (XX), and the extra (+) chromosome is a derivative chromosome 15 (**der(15)**). The derivative chromosome 15 has resulted from an unbalanced translocation (**t**) involving chromosomes 9 and 15 (**9;15**). An extra copy of the short arm of chromosome 9 distal to p13 (e.g. from band 9p13 to the end of the short arm of 9p) is attached to the long arm of chromosome 15 at band **q11.2**. The bands distal to 15q11.2 are missing. This means that the girl has a duplication of almost the whole of the short arm of chromosome 9 with a deletion of almost the whole of the q arm of the extra chromosome 15. Chromosome 15 is an acrocentric chromosome and the presence of the extra chromosome 15 material between 15q11.2 and 15p13 (including the centromere) should not cause any symptoms. The translocation has arisen as a result of a balanced translocation in the mother (**maternal**).

arr9p24.3p13.1(271257_39156954)x3 [hg19] This result shows that the analysis used microarray technology (**arr**). The analysis revealed a DNA anomaly involving bands **9p24.3** to **p13.1**. The DNA anomaly is identified by its base pair numbers (the points where the chromosomal change has occurred). In this example, the DNA anomaly lies between base pairs **271257** and **39156954** (by taking the first number from the second, you can work out that this is 38,885,697 base pairs, or 38.9 Mb). There is an extra copy (**x3**; the normal copy number is two) so it is a duplication. **hg19** tells you which version of the human genome was used for comparison (see **Genome Assemblies** (blue box)).

mos 47,XX,+add(9)(q13)[16]/46,XX[4].arr[hg19] 9p24.3q13(203861_68330127)x3 **Mos**(aicism) means that different cells in this individual have different numbers or arrangements of chromosomes. This is

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.

a girl or woman (XX) with an extra chromosome in some cells (47). Twenty cells have been tested. Sixteen ([16]) cells had genetic material of unknown origin (add). This material was composed of the short arm of chromosome 9 and some of the long arm up to and including band q13 ((9)(q13)). Four [4] cells showed a normal karyotype for a girl or woman (46,XX). Array analysis (arr) has also been carried out using the hg19 ([hg19]) version of the human genome for comparison. This analysis also revealed the DNA anomaly involving bands 9p24.3 to q13. The anomaly lies between base pairs 203,861 and 68,330,127 (68.1Mb). There is an extra copy (x3) so it is a duplication.

Mosaicism

In a few people, the cells containing the 9p duplication chromosome material exist alongside cells with a normal chromosome number and arrangement. This situation, known as **mosaicism**, typically arises after fertilisation and can lessen the impact of the duplication.

Indeed, the medical literature contains two descriptions of people with entirely "normal" development whose mosaic 9p duplication was discovered during other investigations: one a 17-month-old baby; the other a primary school teacher investigated for secondary amenorrhoea (Petty 1993; Cuoco 1982). More recently, there has been a report a 13-year-old girl with mosaicism for a "large" whole p arm duplication extending into q13 with only mild unusual features and "normal" intelligence (Brar 2017). It isn't usually possible to determine exactly which tissues contain the duplicated genetic material (Brar 2017).

How common are 9p duplications?

It is difficult to say. Since duplication 9p syndrome was first described in 1970, over 150 cases of partial or complete duplication of 9p have been reported in the medical literature (Guilherme 2014; Amasdl 2016; Canton 2016). Compared with other rare chromosome disorders, 9p duplications are not uncommon; it has been suggested that this is the **fourth most common type of trisomy**, after trisomy for the whole of chromosomes 21, 18 and 13 (Hannam 1999; Zhou 2015).

In 2017, *Unique* had over 200 members worldwide with the entire short (p) arm, part of the short arm or the entire p arm and some of the long arm (9q) duplicated, of which ~70 members had additional anomalies affecting another chromosome(s), or a duplication and co-existing deletion of 9p (see [Co-existing duplication and deletion of 9p](#)), that could lead to additional features. Nevertheless, this guide should provide useful information for all families affected by a 9p duplication. Many of these additional chromosome anomalies were the result of unbalanced translocations (see [Why did this happen?](#)).

Some members with small duplications and microduplications appear to have been unaffected or so mildly affected by the duplication that they only discovered as adults - when their child was diagnosed and the parents' chromosomes were also tested - that they carried this chromosome anomaly. This suggests that there are other people living in the community who do not know that they carry a 9p duplication.

A survey of *Unique* members with a 9p duplication, and no other chromosome anomaly, was carried out in 2017. We are very grateful to the 48 members who completed this survey and also to those ~80 members whose database information was used to complete this guide.

Why did this happen?

To answer this question, the parents' and affected child's chromosomes need to be tested. These tests may indicate that the duplication has been inherited or, where the parents' chromosomes are normal, the cause of the duplication is then not known but it will almost certainly have occurred as an accident while the sperm or egg cells were being made. Geneticists refer to these events as '*de novo*' (dn), meaning the duplication has occurred as a new event in the child, as opposed to being inherited from a parent. Regardless of whether the duplication is 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.

The medical literature suggests that the majority of duplications arise because one parent, either the mother (mat) or father (pat) has a rearrangement of their own chromosomes (Brambila-Tapia 2014; Oh 2016), although these inherited cases are more likely to be reported than those that arise *de novo* (Schnater 2005). In most cases this rearrangement is a balanced translocation between chromosome 9 and another chromosome, with neither a loss nor gain of genetic material, meaning the parent would not be expected to show any symptoms. A parent with a balanced translocation can have a child who is unaffected and has normal chromosomes; a child with the same balanced translocation who is also unlikely to be affected; or a child with an unbalanced translocation with too much of one chromosome and too little of another (see *Unique's* guide to [Balanced Translocations](#)).

The data from *Unique* families whose data was used for this guide, suggests that where parents' chromosomes have been tested, the bias towards

duplications being inherited may be less marked, but that where a duplication is inherited it is more likely to have been passed on from the mother, a pattern that has also been observed in the medical literature (Brambila-Tapia 2014; Unique).

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 “dysmorphic” (unusual) features or a delay in reaching developmental milestones. While a similar pattern was seen for those with “pure” or “large” duplications, those with “small/micro” duplications were often diagnosed later, in some cases only after testing in adulthood after the birth of an affected child.

The medical literature suggests that duplication 9p is approximately twice as common among girls as boys (Hannam 1999). Among *Unique* members the number of boys and girls affected was roughly equal (Unique).

“ Our daughter had several symptoms that led us to see a geneticist, including: low muscle tone, hip dysplasia and crooked fingers. The diagnosis at such a young age (6 months) allowed us to begin early intervention to help her overcome developmental delays. ” - “pure” dup 9p11.2p24.3

Can it happen again?

The chances of having another child with a 9p duplication 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.

Most common features of 9p duplications

Each person with a 9p duplication is unique and will have different developmental and medical concerns, but the most likely features are:

- A recognisable “look” to the head and face
- 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, often mild
- 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 and respiratory 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)

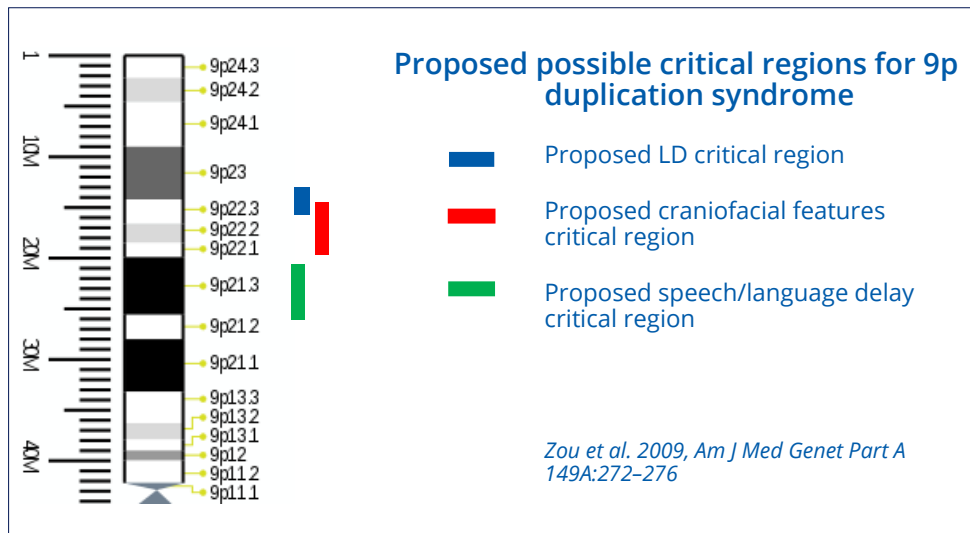
Is the size and location of the duplication significant?

Efforts have been made to determine how the size and location of a duplication affects which features of a 9p duplication are observed. It has become clear that there is a great deal of variability in how individuals are affected regardless of the size of the duplicated region. It would seem obvious to assume that the amount of duplicated material would be the most important factor in determining the range and severity of features - so people with small duplications would be less severely affected than those with larger deletions - but this conclusion would be over-simplistic (Bonaglia 2002; Zou 2009; Abu-Amro 2010; Jelin 2010; Bouhjar 2011; Brar 2017).

We do know that a duplication involving only the region 9p11.2 to p13.1 was shown to be a normal variant with no apparent consequences for development. Also, a mother with a duplication assumed to be 9p11 to 9p12 was found to be carrying a baby with the same chromosome arrangement. Both are healthy and have no developmental difficulties (di Giacomo 2004; Calabrese 1994).

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.

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-Amro 2010; Brar 2017).



These proposed “critical regions” were largely defined by cases in the medical literature, including: a girl with a duplication including the segment between 9p21.1 and 9p22.3 who had a few unusual features, including weight gain, a high arch to her palate and crowded teeth but no problems with learning (Bonaglia 2002); a man with a 9p12p21.3 duplication who had none of the features of duplication 9p syndrome (Stumm 2002); a 12-year-old girl with a duplication of 9p13.2 to p21.3 segment who had some of the facial features, anomalies of the hands and feet and speech/language delay associated with 9p duplication syndrome but without the expected learning difficulties (Zou 2009).

There are further examples in the medical literature (and some from the *Unique* series) that support a link between the size and location of the duplication and the range and severity of the features observed. In particular, a father-daughter pair with a borderline ability to learn and a small duplication from 9p22p24 have been described; and a six-year-old boy with a duplication from 9p21pter who has only a slight degree of learning difficulty and slight delay in growth (Haddad 1996; Sanlaville 1999).

However, within the *Unique* series this link is sometimes less clear. Two children with no more than a moderate learning disability, aged six and sixteen, both had “pure” duplications: in one case a complete duplication of the short arm of chromosome 9 and in the other case a duplication from

band p12 to band p24. Equally, some people with much smaller duplications had more far-reaching difficulties: a girl with a small distal duplication of 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.

Seven *Unique* members who completed the survey with similar “large” 9p24q13 duplications had learning difficulties and growth delay ranging from mild to severe, while only two had heart conditions and only one had an anomaly of the brain.

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

The reasons behind why people with the same - or a very similar - 9p duplication 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).

Pregnancy and Birth

The evidence from the medical literature and *Unique* suggests that pregnancy and birth are often unremarkable, although some concerns were noted.

In *Unique's* experience a similar picture was seen for duplications of all sizes, with a third to a half reporting concerns during pregnancy, including reduced foetal movements and levels of amniotic fluid. While in most cases mid-pregnancy anomaly scans didn't raise concerns, some families reported unusual findings, such as reduced foetal growth, dysmorphic features and anomalies of the kidneys, brain and heart, which were usually minor. A genetic test during pregnancy may be suggested if there are concerns about foetal development or an anomaly is detected. In the medical literature a few babies had reduced foetal movements, including two unrelated babies with a 9p21p24 duplication (Temtamy 2007).

The vast majority or *Unique* pregnancies and those described in the medical literature went to term. A few babies were born prematurely, but probably no more than would be expected in the general population. Birth weights were usually average or a little below average. A small number of babies grow very slowly in the womb and are tiny at birth.

Birth weights

	"pure" (36*)	"small/micro" (19)	"large" (27)
Average birth weight	6 lb 12 oz (3.06 kg)	6lb 15oz (3.15 kg)	7lb 0.5 oz (3.19 kg)
Range	3 lb 4 oz - 9 lb 10 oz (1.47 kg - 4.37 kg)	3lb 12oz - 9lb 13oz (1.7kg - 4.45 kg)	4 lb 6 oz—9 lb 4 oz (1.98 kg - 4.2 kg)
Average birth weight in medical literature	6lb 5oz (2.86 kg) (12 cases)	6lb 3oz (2.81 kg) (5 cases)	5 lb 12 oz (2.6 kg) (4 cases)

*Number of Unique members who supplied birth weight

Feeding in the new-born period

Feeding difficulties are common.

Feeding problems are common in babies and children with a chromosome disorder. The vast majority of *Unique* babies experienced difficulties with feeding in the new-born period regardless of the size of the duplication, which led to poor weight gain and in some cases failure to thrive; others managed breastfeeding successfully.

Babies may suck weakly and find it difficult to co-ordinate sucking, swallowing 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. Occasionally babies need to be fed directly through a tube to the stomach (a gastrostomy) for some months or years.

Many babies suffer from gastro-oesophageal reflux disease (GERD/GORD), where feeds frequently and forcefully return up the food pipe from the stomach, and some are at risk of inhaling fluid, food and saliva into their airway or lungs (aspiration). 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.

“ My daughter had reflux and struggled to breastfeed. It would take us an hour to feed her each time, but she was gaining weight so there wasn't a lot of concern at that time. ” - “pure” dup 9p13p24, 2 years

“ My son was bottle-fed from birth. He didn't know how to suck and vomited a lot so was admitted into neo-natal care and tube-fed for 13 days. He has always had reflux and has been on Omeprozole since birth. For the first three years he was on a dairy-free diet, but now has all foods containing milk but not milk to drink. ” - “pure” dup 9p13.1p24, 3 years

“ Immediately after his birth he had difficulty gaining weight. We added thickeners to his milk that helped him gain weight. During weaning, he found it difficult to eat small things. Now he eats well and without any difficulty. ” - “small” dup 9p22.3p24.1, 6 years

“ My son's feeding difficulties were due to a cleft lip and palate. He fed from a soft plastic bottle with a spoon rather than a teat and we squeezed gently to control the flow of milk through a plastic diaphragm we made to slow the flow down. He would gulp lots of air, so we had to burp him several times throughout the feed or else he would vomit it all back up. He also had severe, constant gastrointestinal reflux. ” - “large” dup 9q12p24, 42 years

Growth

A mild growth delay is common, whatever the duplication size.

While a slight delay in growth before birth is sometimes observed, a pattern of slow growth in babies and children was more common but was generally deemed to be “mild”.

Children and adults in the *Unique* series were usually described as average or below average height and weight, regardless of duplication size, although this trend was not universal. A similar picture is recorded in the medical literature, although here the trend towards a growth delay was often more

marked. The picture nevertheless remains mixed and a few children are tall and/or overweight. *Unique* families note a range of statures from “short and stocky” to “tall and thin”.

A few children were described as “fussy” eaters, while at least two *Unique* children had sensory issues that made eating and gaining weight difficult. Some children have benefited from attending a feeding clinic where an assessment can be made and advice to help treat any eating and drinking difficulties provided (see [Constipation](#)).

Bone age is typically delayed and because of this, children may continue to grow until their twenties, allowing them to catch up at least partly in height. Some adults are of normal height (Cuoco 1982; Haddad 1996; Fujimoto 1998; Frederico 1999; Sanlaville 1999; Guanciali Franchi 2000; Schinzel 2001; Teraoka 2001; Pater 2002; Krepisch-Santos 2003; Schnater 2005; Temtamy 2007; Vundinti 2007; Zou 2009; Mahjoubi 2011; Brambila-Tapia 2014; Guilherme 2014; Stagi 2014; Martínez-Jacobo 2015; Zhou 2015; Amasdl 2016; Canton 2016; Brar 2017; *Unique*).

Low levels of growth hormone (GH) have been recorded for some children and a growing number of children have been documented in the medical literature as responding well to GH treatment, with some subsequently reaching their target height. Several *Unique* members have also been treated with GH (see below), with limited evidence that treatment with GH may be accompanied by an improvement in gross motor skills (Joy 2017; *Unique*). 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).

“ Due to scoliosis it is hard to measure her height accurately, but she is under 5ft tall and was 8 stone 9 pounds when she could stand on the scales. Her build is short and stocky in the middle as she is sitting in a wheelchair most of the day. Her weight has remained stable since she started using a wheelchair, due to swimming. She likes a limited range of foods, which have varied over the years. We have to introduce new foods gradually and ensure she has a good variety of the healthiest things she will eat. We give her cod liver oil and vitamins to supplement her diet. ” - “pure” dup 9p, 34 years

“ She *had* a delay but now she has caught up to others her age and even surpassed their growth. She has taken growth hormone since she was 12-years-old and that helped her to grow normally. She has a solid stature and is well-proportioned with very long legs. ” - “pure” dup 9p13p24.3, 17 years

“ At 8 years she is short and thin - with height and weight measurements in the 25th centile. There is sometimes a small amount of hypersalivation after eating and sometimes she keeps food in her mouth and doesn't swallow it. ” - “pure” dup 9p12p24.3, 8 years

“ She had IUGR and was very small in the first couple of years, even though she fed well. She is now average height but overweight. She used to regularly gag and vomit with every meal but she outgrew this and eats a good diet, although if food were readily available she wouldn't know when



to stop. She eats a good diet, but weight gain seems excessive. ” - “small/micro” dup 9p24.1p24.3, 8 years

“ He is very tall at 13 years 8 months; he weighs 68.5 kg (>98th centile) and measures 158.7 cm (75th centile). ” - “micro” dup 9p24.3, 13 years

“ He's 8-years-old but in age 5-6 clothing and weighs 20kg. He is gaining weight very slowly and is thin for his height, but very muscular - he has a six-pack and is very strong. He eats adult portions of food but because he's relentlessly active he never fattens up. There is no fat on him at all. ” - “large” dup 9q22.1p24, 8 years

“ His growth was delayed and he was short for his age as a child. He continued growing until his late twenties and is now about 5ft 10in and weighs 70kg. Although slim, he sometimes has a pot belly when his constipation is bad. He underwent bone studies when he was 11¾-years-old, which found that he had a bone age of an 8- to 9-year-old. He was not treated with growth hormones. ” - “large” dup 9q12p24, 42 years

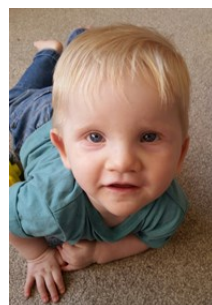
Appearance

Children with a 9p duplication often have a recognisable look.

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 9p duplications.

The most common features are: 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 researchers have noted that children have a ‘worried look’.

Your child's head may have an unusual shape: the head may be unusually small (microcephaly) or have a flattened skull, usually at the back (brachycephaly). In the *Unique* series, new-born babies often 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. The jaw may also be unusually small (micrognathia) and/or receding (retrognathia) (Zou 2009; Guilherme 2014 Canton 2016; Amasdl 2016; Brar 2017; Unique).



“[Our sons are unrelated but] they look so alike we call them twins!”



The evidence from *Unique* suggests that those with “large” duplications are likely to have more of these characteristic facial features, especially compared to children with “small/micro” duplications. There is also some evidence to support 9p22.1p22.3 as a “critical region” for unusual craniofacial features: children with “small/micro” duplications including this region were more likely to have features typical for 9p duplication syndrome than those with duplications outside the region. A small and/or receding jaw and an unusual head shape were notably more common among those with “large” duplications, where a large fontanelle was almost universal.

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

A delay in gross and fine motor skills is near universal.

Babies and children are typically delayed in reaching their developmental “milestones”, including rolling, sitting, moving and walking, and benefit from early intervention with occupational therapy and physiotherapy.

There is a wide range of eventual ability, however, with some children acquiring mobility skills around the same age as “typical” children and others showing more obvious delay (see table). It also appears that those least affected or unaffected in early childhood are most likely to achieve normal mobility and sporting prowess as adults, while those children who have obvious mobility problems early on achieve a more limited degree of mobility (Unique).



Developmental milestones

	“pure”	“small/micro”	“large”
Developmental Delay (<i>Unique</i> survey 2017)	21/21	5/8	13/13**
Rolling	9 months (*n=17) Range: 2m-24m	5.5 months (*n=8) Range: 3m-9m	11 months (*n=13) Range: 4m-2yr 6m
Sitting	13 months (*n=28) Range: 7m-18m	10 months (*n=18) Range: 6m-17m	14 months (*n=14) Range: 6m-4yr 6m
Crawling	1yr 7m (*n=20) Range: 2m-3yr	1yr 2m (*n=16) Range: 8m-2yr 7m	1yr 9m (*n=12) Range: 12m-5yr
Walking	2yr 8m (*n=28) Range: 17m-5yr 9m	1yr 7m (*n=24) Range: 12m-4yr 6m	2yr 11m (*n=16) Range: 18m-10yr
Smile	3 months (*n=14) Range: 2m-6m	3 months (*n=7) Range: 2m-6m	2.5 months (*n=6) Range: 2m-4m

Data from 2017 survey and Unique database. *n = number of Unique members data is derived from. ** - possibly one case of no DD - to be verified.



The data from *Unique* combined with the medical literature, suggests that babies and children with “pure” and “large” duplications are likely to experience more of a delay than those with “small/micro” duplications.

The children we know about without developmental delay all have a “small/micro” duplication (an 8-year-old boy with an almost “pure” 9p13.3p24.3 duplication was assessed as having “normal” intellectual development, although the age at which he reached developmental milestones was not recorded (Bouhjar 2011)). These include a six-year-old girl with a 9p13.1p22.1 duplication (Bonaglia 2002) and a six-year-old boy with a 9p21p24 duplication (he did, however, have a speech delay and a mild intellectual disability) (Sanlaville 1999). The *Unique* database includes details of a girl with a “micro” 9p24.3 duplication who “met all her developmental milestones on time”. Another girl with a 9p22.1p22.2 duplication “rolled at 5 months; sat at 7

months; crawled at 8 months; walked at 13 months; walked alone at 17 months; and climbed stairs at 14 months. At 7 years she enjoys playing, running and monkey bars”. Three children in the 2017 *Unique* survey with a 9p21.1p24.3 duplication, 9p21.3p23 duplication and 9p22.3p24.1 duplication respectively, also reached their milestones without a delay, or showed only a minor delay. It should be noted that most of these children did experience a speech/language delay and some degree of learning disability (Unique).

Hypotonia/hypertonia - Duplications of all sizes are associated with both reduced (hypotonia) and increased (hypertonia) muscle tone or a combination of both, although hypotonia alone is more common. 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; the *Unique* data series suggests babies and children with normal muscle tone reached milestones on time. Muscle tone generally improves with maturity, but for some problems may persist into adulthood.

Some children also have very loose joints or by contrast, tight, contracted joints. Both conditions also have an impact on mobility, as do some anomalies affecting the feet.

Treatment - Regular physiotherapy generally helps, particularly if the intervention is made early, and the use of orthotics such as support boots may also help increase mobility. In some cases a wheelchair may be needed for long distances and outdoors, at least for a time. Eventual walking style also varies. Although some achieve total mobility and learn to climb stairs, to run, ride a bicycle and to swim, others retain an uneven and uncoordinated walking style and some continue to rely on a wheelchair in all or certain circumstances. There are instances of regression, but data on this is limited.

“ Rolling and sitting were reached at the typical age but crawling was odd - a "commando" crawl. Walking was achieved at age 3 years 1 month. Our daughter had PT and OT - through early intervention from 8 weeks to 3 years, and then in the public school system until age 21. Both were very, very helpful. ” - “pure” dup 9p12p24, 30 years

“ All her milestones were delayed due to problems with her hips, which required plasters from six months, then surgery. She didn't walk unaided until six years due to early surgery. By 18 years she was using a wheelchair fulltime. She was always active, even in leg braces when mobile, and loved to dance. She still does wheel chair dancing and self-propels when she can. ” - “pure” dup 9p, 34 years

“ My daughter can only walk short distances but gets tired on long journeys. At the age of 9 years, she needed a disabled buggy but loved swimming and dancing. At 11 years she still needs the buggy for long days out but does not need Pedro boots anymore; however, she still needs insoles. She has had physiotherapy and occupational therapy. ” - “pure” mosaic dup 9p

“ She never crawled - went right from sitting to walking but had a hard time standing. She had to keep walking! She walked at 17 months. She's had OT and PT since she was two-years-old. Motor skills have definitely improved because of natural physical development, I think. We found sports that would help with posture and elongating the body as well as strengthening her core e.g. horseback riding, rock climbing and karate. ” - “pure” dup 9p13p24, 17 years

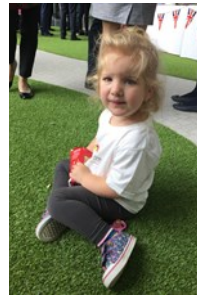
“ At 41 months both locomotor and manipulative skills were at the 30-month level. ” - “small” dup 9p21p24

“ He had poor balance but walked independently; however, by 20 years he no longer walks independently. He had another surgery on his left femur at 20 years to rotate it for a third time and can no longer support his weight on it. ” - “small” dup 9p22p24, 20 years

“ Rolling, sitting unassisted and crawling were all delayed. Low muscle tone made this difficult. She began walking at 3 years 2 months. PT helped strengthen muscles. ” - “large” dup 9q13p24, 9 years

“ At 10 years some activities are still difficult: running, jumping, climbing, stairs. My daughter has severe hypotonia that has delayed all her psychomotor development. She has had many interventions from a young age, including PT, without which I think her delays would be worse. ” - “large” dup 9q21p24, 10 years

“ She showed developmental delay, not reaching milestones at the usual time. At 19 months she was able to stand independently (and at 16 months when holding on to the furniture) but only took a few steps holding on. She walked at 27 months and wears Pedro boots and corrective insoles. At 9.5



years her gross motor skills are good. She can run well, walk backwards, climb up- and downstairs and kick a ball. She attends mainstream athletics and participates in most activities to the best of her ability. ” - “large” dup 9q21p24

Development: hand use and coordination (fine motor skills)



Development of hand use and hand-eye coordination, which are essential for tasks such as holding a bottle, using cutlery, playing with toys and fastening clothes, are frequently delayed and don't necessarily develop in line with gross motor skills. Parents suggest that hypermobile joints in the fingers and thumbs, hypotonia and anomalies of the hands, including unusually bent and shortened fingers, often contribute to difficulties (see [Hands and Feet](#)).



The evidence from *Unique* is that as childhood progresses fine motor skills improve, but some teenagers and adults 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).

“ Our daughter’s fine motor skills are one of her strongest areas of development: she is fantastic at posting objects, feeding herself with a spoon and fork, drinking out of a cup, threading and puzzles. She has received monthly physiotherapy since she was 16-months-old. She also has access to a physiotherapist at her Playskill specialist development centre, where we also work with an occupational therapist during her weekly session. She can put her socks and shoes on and occasionally her trousers. Her current OT target is to put her coat on independently. ” - “pure” mosaic dup 9p13p24.3, 2 years

“ Dexterity isn't great, but he can feed himself and hold a pencil just fine. He finds it hard to pick up a coin, though. ” - “pure” dup 9p, 30 years

“ At 34 years my daughter is in nappies day and night, but was toilet trained before wheelchair use. She can't get dressed, brush teeth etc... ” - “pure” dup 9p, 34 years

“ At 12 years the Movement Assessment Battery for Children (M-ABC) was used to assess our son's manual dexterity, ball skills and dynamic balance. He scored below the 1st centile overall, so he is well below average in motor coordination. Within the M-ABC for fine motor skills, manual dexterity was his weakest component. Tests show he has visual-perceptual difficulties, which impact on his recognition, insight and interpretation of what he sees. Lack of ability to interpret or remember visual information affects his ability to sequence processes such as getting dressed, copying from the whiteboard or remembering and following verbal instructions. ” - “micro” dup 9p24.3

“ His fine motor skills are poor, but he can hold a pen and cutlery. He struggles with zips and cannot tie shoe laces. Has PT and OT. ” - small” dup 9p22p23/dup 9p23p24 mosaic, 26 years

“ Motor skills have taken longer to develop; especially as low muscle tone is involved. The OT helps with holding utensils, grasping a pencil, printing, toileting etc. ” - “large” dup 9q13p24, 9 years

“ Our daughter had PT and OT all through her school years. The best therapy was when the PT/OT required a word from her before doing what she enjoyed the most. She has made all this work in her own unique way. ” - “large” dup 9q11p24, 28 years

Ability to learn

The range of learning ability is very broad, but some degree of learning disability is to be expected.

Evidence from *Unique* and the medical literature demonstrates that most 9p duplications are associated with some degree of learning difficulty (LD) ranging from mild to profound (see table), although there are a few notable exceptions where no LD was recorded.

At one end of the spectrum are a few children with no notable LD, while a number of parents of children with 9p duplications were only diagnosed as adults and achieved a range of school-leaving qualifications - in several cases these parents report that they did struggle at school but were not officially diagnosed with a LD. At the other end are children and adults with a severe to profound LD.

A similar pattern is observed for “pure”, “large” and “small/micro” duplications and has been reported in the medical literature, although of the *Unique* members and six cases in the medical literature with “normal” cognitive development, most have “small/micro” duplications (Haddad 1996; Sanlaville 1999; Guanciali Franchi 2000; Tsezou 2000; Bonaglia 2002; De Pater 2002; Krepischi-Santos 2003; Schnater 2005; Vundinti 2007; Temtamy 2007; Bouhjar 2011; Chen 2011; Mahjoubi 2011; Guilherme 2014; Zhou 2015; Canton 2016; Brar 2017; *Unique*).

The examples of a 9p duplication without a LD to-date are: a report in 2017 of a girl with a “large” 9q13p24.3 duplication that was only detected in certain cell types due to mosaicism (Brar 2017); a report of a boy with a “pure” duplication between 9p13.3 and the tip of the short arm (9p24.3) who had a normal IQ of 95 at the age of 8 years (Bouhjar 2011); a patient with a



9p13p21.3 duplication (Stumm 2002); another with a 9p13.2p21.2 duplication who has speech and language delay but no intellectual disability [Zou 2009]; and a girl with a 9p21.1p22.3 duplication with a normal IQ (Bonaglia 2002). A 9p11.2p13.1 duplication has also been reported without any effects on the patient (Di Giacomo 2004).

While the segment between 9p22.3 and p23 has been suggested to be a “critical region” for the development of intellectual disability 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.

Many *Unique* children learned to draw, read, write and use a keyboard, but for a few children with a severe or profound learning disability this has not proved possible. The data is limited, but many children with a “pure” duplication learned to read and write between the ages of five years and 14 years (the average age for reading was 6 years 8 months and for writing 8 years 6 months). The majority of children with a “small/micro” duplication reached these milestones a little earlier and many began to read and write around six years. Some children with “large” duplications began reading and writing between the ages of five and seven years. For nine *Unique* members with a “large” duplication extending to 9q21 or q22, one was assessed as having a “mild to moderate” LD; two were described as having a “moderate”

Range of learning abilities

	“pure”	“small/micro”	“large”
Learning Disability	42/42	26/30*	21/21
Mild	3	5	2
Mild/Moderate	2	2	2
Moderate	11	5	5
Moderate/Severe	3	1	1
Severe	11	3	6
Severe/Profound	1	1	0
Profound	0	1	0
Unspecified	9	8	5

Data from 2017 survey and *Unique* database. * In two cases the children are too young for an LD to be diagnosed

LD and three a "severe" LD, while three others had an unspecified LD.

"My daughter has a mental age of about five years. She cannot read or count and draws without form, only a circle. She forgets what she has learned easily. She uses a Tablet - only for games or videos." - "pure" dup 9p12p24, 8 years

"He has a mild learning disability with a reading age of 7 years and 4 months at 8 years 6 months. He wrote his name and was good on a computer - a smart chap! Aged 13 years he reads at a 10-year level, and writes his name, address and short notes. He has a very good memory." - "pure" dup 9p11p24, 13 years

"He has an IQ of 48, but he really is smart. He is starting to read but maths comes easier for him. He would likely be doing very well in school if he would behave and focus." - "small/micro" dup 9p21.3p23, 10 years

"His cognitive age varies depending on the task. His understanding of numbers is at about a 3- or 4-year-old level. Some areas are almost normal such as being able to follow a story. He struggles following instructions and answering complex questions and has also been diagnosed as having autism." - "small/micro" dup 9p22p23 mosaic, 26 years

"She has a reading age of 9 years and a comprehension age of 7 years at 10 years. She can learn lots about a subject she loves e.g. geography." - "large" dup 9q12p24, 10 years

"My daughter's ability depends on the area. Her cognitive age is estimated to be between 5 ½ and 6 years at the age of 10 years, with a global reading age of 7 years. She has a delay in all areas. Her visual memory is very good but her immediate memory is bad. She is very good at reading but has a poor level of comprehension. She has dyscalculia and dysphasia. What one thinks acquired must be regularly revised or else she forgets what she has learned. Example: to go down the stairs by alternating the feet, work on the pronunciation of certain double consonants (cr, dr ...) or sentence construction." - "large" dup 9q21p24, 10 years

"She was assessed as having a moderate intellectual disability and presents with an even profile, except for locomotor which is slightly more challenged. At 9.5 years a recent assessment showed her to have an IQ of 46 - moderate to mild LD - with a reading age of 7 years and writing age 6.8 years." - "large" dup 9q21p24, 9 years

Some parents believed that their child's learning ability has improved with age, with several parents mentioning that there has been a vast improvement in their child's ability to learn and acquire new skills as a teenager or adult. Sometimes changes in ability went in fits and starts or an improvement in one area coincided with regression in another. Other parents believed that learning ability had remained consistent throughout childhood, and the parent of a 28-year-old girl with a "large" 9q11p24 duplication felt that she was losing her cognitive abilities.

The picture is mixed, but many parents told us that their child could at times

be scared of trying new things or seemingly reticent to acquire new skills, but with patience and through repetition and encouragement new skills were often mastered.

Most parents also believed that their child had specific areas of strength. For some this might be reading and writing; others favoured maths, numbers and problem-solving. Some children have particularly good memories for dates and places. Many younger children enjoyed stacking bricks, playing with shape sorters and organising their toys.

“A good reader. Also good at math, with a calculator. His best skill is spelling - he's very, very good at that.” - “pure” dup 9p12p24, 30 years

“Math comes easy to him. Reading is OK once he memorises a word but sounding out is hard.” - “small” dup 9p21.3p23, 10 years

“He can identify almost all of the letters of the alphabet and knows more about trains than most adults in the U.S.!” - “large” dup 9q13p24, 4 years

“Counting and colours are better than reading and writing. She is very good at art.” - “large” dup 9q13p24, 10 years

Most children have needed additional support with their learning. Many children attended a regular (mainstream) nursery/day care setting prior to starting school, sometimes with early intervention programmes. The information we have for *Unique* families suggests that once they started their formal education most had 1:1 dedicated support within the mainstream classroom or transferred to a special unit within a mainstream school (20/35) or attended a special school (15/35), in order to access the curriculum and develop to their full potential.

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 learning difficulties).

“From eight weeks to three years he attended an early intervention program (at no charge to the family). When he turned three, he transitioned to the public (state) school system where he attended what's called a "self-contained" program (meaning there were no "general education" (mainstream) students). They had shared recess (breaktime), music, and physical education with general education students. This type of program worked well for him, as it allowed him to have lots of extra adult support and made him feel he was with his peers. As parents, we liked this approach, and he thrived. He had good, devoted teachers and support staff. Our family had no issues with evaluations or educational plans. They set realistic goals with realistic timelines and staff were very willing to update plans as needed, even if more frequently than the typical annual update.” - “pure” dup 9p12p24, 30 years, USA

“ Our daughter has been given all the resources she needs. We have worked hand-in-hand with the school district and have been very happy with the services that they have provided. She attended regular (mainstream) pre-school, elementary, middle and high school, with support.

It took us a while to know how to work with the school district. We were always told that "the squeaky wheel gets the oil" from helpful teachers that wanted to see my daughter succeed. Parents need to advocate, advocate, advocate. I have learned to listen to "advice" from educators (who know your child only from a few hours in one setting), but factor in what I know about my own child. You have to be able to fight for your child every single day because there is ALWAYS an issue that arises. Another key element is knowledge. Know the laws that involve students with learning disabilities, etc. Go into meetings informed so that YOU can be in control and not the school. Stay strong, focused and optimistic. It can make a world of difference if you are able to get all the resources your child needs. When you don't have a specific "diagnosis" to tell the school, they don't know what to do. YOU have to guide them. ” - “pure” dup 9p13p24, 17 years, USA

“ Since she was 18-months-old she has attended weekly sessions at Playskill - a charity that runs a specialist group for SEN children. Then at 20 months we also started attending a local authority EYSDC (early years specialist development centre). Our daughter then started at our local mainstream nursery (at 2 years 5 months) and attends three mornings a week without me. We are currently in the process of writing the EHC plan application form. ” - “pure” dup 9p13.1p24, 2 years, UK

“ We are a military family and moved every few years due to my husband's changing duty stations. Our daughter was always put in a special needs class for severely disabled children in the schools she attended. We always made sure she was happy going to school and enjoyed her time in class. That was always our main goal for her. How much the educators could make her learn was secondary to her happiness in class for us. She has had a plan in school since she began pre-school; obtaining this was not difficult for us. ” - “pure” dup 9p13p24, 19 years, USA

“ Our son went to a standard nursery but repeated the year. He attended a mainstream primary school with 1:1 support for two years but then moved to an additional support school. He then moved to a support unit within a mainstream school but did not cope very well with this due to behavioural problems and was subsequently moved to an additional support secondary school. He has gone on to do several adult support learning classes, such as food preparation, life skills etc. and has taken part in the Duke of Edinburgh scheme. ” - “small” dup 9p22p23 mosaic, 26 years, UK

“ While our son attended nursery he always had a support teacher for 12 hours a week. He was an exceptional person who did a great job with our son. Now he is starting elementary school where he will be followed by a support teacher.

Our daughter attended a mainstream kindergarten and elementary school like all other children. She also has a support teacher for 12 hours a week.

One family's experience of mainstream education in Canada

"Our 9-year-old daughter and five-year-old son have the same "large" 9q13p24 duplication.

We live in Canada and have chosen to include our children in "typical" classrooms as we feel it both beneficial to our children, and to the peers that they are with. Even if they need to work on subjects at a lower level than their peers, it is more important to us that they remain with their classmates throughout their schooling. Their peers learn to accept and support them naturally. We also support the school if the teacher feels that pulling our children out of class to work on something specific - like guided reading, speech or math - could be beneficial. In our school, all students have an opportunity to work in small groups, or one-on-one. Both of my children have an Individualized Program Plan (IPP). It did help receiving a letter from our Genetics Clinic & Paediatrician's Office, stating that any and all supports necessary should be made available to our daughter, as this genetic condition is rare, and it is uncertain what needs would arise.

Our daughter has always loved school and learning. She is in Grade 4 but works at Grade 2/3 in maths and languages/arts. But she's learning math! She's beginning to write sentences! Skills I wasn't sure she would ever have! She continues to learn at Grade (expected) Level in Science and Social. She is a great speller and can read; however, comprehension is tricky to test as she is non-verbal. She writes sentences with assistance using her communication device, and then transfers them to paper. She enjoys drawing - generally people or abstract shapes. She has keyboard skills on her touchscreen device, but not proper finger-positioning. Word prediction is very helpful.

Part of our vision for our daughter was that she should have the same opportunities that her older "typical" brother had growing up. Our school has been so accommodating to make our vision a reality, in that they will modify and/or adapt programming to meet her specific needs and help her learn and grow from there. We are working on increasing her peers' capacity to support her as, ideally, we want her friends assisting her when necessary, and reduce the adult support. She's doing so much more than we first thought possible from that original diagnosis. We never want her to give up at school; some concepts just take longer for her to learn than others.

Our son attended preschool last year (age four), three days per week for two hours. He now attends kindergarten, five days per week but only half days. We made the choice to not put him into school when we could have so he is, and will continue to be, one of the older children in his classes. This was an excellent decision!

He is becoming more focused, can attend to certain tasks for longer periods of time, and he is now ready to learn with that extra few months to catch up developmentally. We have had an IPP in place for him for three years now. At the moment, our early education provider completes the IPP for us. Next year, in Grade 1, it will be the school who completes it.

He is working on drawing and printing and uses an AAC device to communicate. He is very accurate in selecting the correct cell on a 60-cell page and has a cognitive age of approximately three years at the age of five."

She struggles most with maths, but she also makes many spelling and grammar mistakes.” - “small” dup 9p22.3p24.1, son (6 years) & daughter (8 years) have the same duplication, Italy

Speech and Communication

Speech is usually the most obviously affected area of development.

Information from *Unique* members and the medical literature suggests that speech is typically the most affected area of development (including Zou 2009; Guilherme 2014; Canton 2016; Unique). While a “typically”-developing baby usually coos and babbles by six months, produces speech-like noises in the next few months and says their first understandable words around their first birthday, speech and language development is usually delayed in children with 9p duplications, regardless of duplication size, and a significant minority of children remain non-verbal.

For verbal children, first words often emerged between the ages of one and five years, and often between a child’s third and fourth birthday. While some children progress to speak conversationally in sentences, this is not possible for all and many continue to use single words or two-, three- or four-word phrases with limited grammar. Some families report periods of (usually temporary) regression in speech. Others say that their child eventually learns to speak fluently; a brother and sister with a 9p22.3p24.1 duplication only spoke their first words at three years of age, but, at six years and eight years respectively, spoke “like all the children of his age” and “in long, complex sentences”.

There are a very few, isolated cases of children with no obvious speech delay: in the medical literature an 8-year-old boy with a 9p13.3p24.3 duplication had normal speech (Boujhar 2011); a male patient with a 9p12p21.3 duplication had no apparent speech/language difficulties (Stumm 2002); and in the *Unique* series, a girl with a “micro” 9p22.1p22.2 duplication “babbling at four or five months; spoke her first word ‘dada’ at six months; and at 7 years speaks fluently”. These cases are very much the exception, and even children with duplications involving only 9p24 have a speech delay, which in some cases was severe. Taken together, the evidence suggests that proposed critical region for speech/language delay within 4.9 Mb of the 9p21.2–p21.3 segment may need to be revised (Zou 2009).

Even among more fluent speakers, some lack of clarity in certain speech sounds has tended to persist, with some families remarking on their child’s disordered speech patterns and inability to discriminate between f, d, s and p sounds and consonant sounds at the beginning of a word. For one girl with a “large” 9q13p24 duplication speech apraxia was suspected (a speech disorder in which the person has trouble saying what s/he wants to say correctly and consistently), with the testimonies of other *Unique* families suggesting this may be a more common problem. Others reported difficulties with hearing and a short lingual frenulum (the strip of tissue that connects your tongue to the base of your mouth) as factors that may contribute to speech delay/communication difficulties. There is some evidence to support this from the literature, as well as evidence of an unusually low-pitched voice with a harsh quality.

Where individuals have no speech or very few words, communication has usually still been successful through augmentative/alternative communication (AAC) e.g. Makaton, signing, gesture, facial expression, Picture Exchange Communication System (PECS) and iPad communication.

Understanding appeared to progress ahead of speech in all children, and clear, literal instructions and statements reinforced by gesture were universally understood.

An assessment by a speech and language therapist should be able to identify your child's specific difficulties, allowing regular therapy sessions tailored to your child's specific areas of need. Speech therapy has proved beneficial to many *Unique* families. Similarly, hearing concerns should be acted on early.

“ My son was around two when he started to attempt to imitate words and sounds. He can only say a very few words and they are still unclear, particularly to anyone who is unfamiliar with his speech. He uses Makaton and gestures to support his speech e.g. 'do' (dog) with dog Makaton sign, then 'ee' (sleep) with sleep Makaton sign, and fills in the majority of the gaps with grunts and babble. His receptive understanding is amazing, and he understands pretty much everything; however, his expressive communication is very delayed. He currently sees his speech and language therapist every 8 weeks. ” - “pure” dup 9p13.1p24.3, 3 years

“ Our son prefers to speak rather than use augmentative communication, but he's very difficult to understand if you don't know him and he had speech therapy until the age of 21. We figure things out by paying attention to gestures and context. He never uses more than about three words at a time. This is the only place we have sorrow as we would love to know what he's thinking. His level of understanding is far better than what he can express. ” - “pure” dup 9p12p24.3, 30 years

“ My daughter does not speak, but instead uses noises and babbles. She understands when we tell her “no” or “yes” but she cannot express what she wants clearly. ” - “pure” dup 9p13p24.3, 19 years

“ We were told that our daughter would never speak and would need to use PECS for the rest of her life. She looked at me one day when she was about three-years-old - after not saying anything, and babbling, humming a lot and signing basic needs - and she said clearly, “apple.” She loved songs and watched videos of kids singing and dancing (Barney, the Wiggles and Kids Songs) and that helped her be more engaged.

Early intervention was not going to provide speech therapy to a child that couldn't talk and that was my first real battle. Bottom line, we got her three speech sessions a week. We practised with her all of the time and now, even though she'll mix up a word or two or repeat phrases to “fill the space”, she can carry out regular conversations. Her articulation is not the best but when she slows down and tries, her facial muscles have developed enough now that she can make those sounds she could never make when she was younger. Inference and symbolism is tough to understand. My daughter expresses much more knowledge when she is asked something directly, so I

One little boy's "speech" journey....

Our son has a "micro" 9p21.1 duplication and has severe receptive and expressive language delay, with a phonological delay and oral-motor dysfunction (difficulty controlling the lips, tongue, and jaw muscles, which makes mouth skills - including talking, eating and drinking - difficult to master). He spoke his first words at 14 months but at 2 years 7 months he still had only a few words that he used consistently. He was able to follow some simple directions, communicating mostly with grunts and cries.

At 2 years 11 months, he began pointing and successfully responded to picture cards to indicate choice of food and activity. He could point to all his body parts and retrieve certain toys when asked. It was difficult to get him to respond to his name or follow direction, though I believe he has the ability to do more than he lets on! He still used mostly single words that were not very easy to understand. He would use them and then they would disappear. His vocabulary was definitely over 100 words, but he rarely repeated them and he rarely imitated words on demand. As his mum, I was able to get him to say "cacka" for "cracker" and "etchel" for "pretzel" in his highchair, as a reward system suggested by his speech and feeding therapist, but he usually cried and protested vehemently, pointing to the food item. Consistent words were "gogogo", "car", "clock", "dagat" (the cat), "dagod" (the dog) and many repetitive sounds like "chugachuga" and "choochoo" while playing with his trains. He often talked to himself, but we could not understand him.

By 3.5 years he said his first sentence: "Uh-Oh, it is broken", and referred to "Mommy", "Dada" and his little brother as "baby".

At nearly four years he was still not speaking or communicating very much but used sign language more often. He said "Uh-oh" if something was broken about anything and everything that came apart.

At six years he is talking more in sentences e.g. "Need to find Logan", "Want chocolate milk" etc. He will never answer a question but just ignores it!

One adult's story....

Our daughter, who is in her twenties, has a "large" dup9q11p24.3 duplication. She babbled as a baby then stopped all sounds for an entire year.

When she was three-years-old she started to babble again. Sentences started forming around six years, but she still used sign language to help with understanding.

Now she is an adult it can still be VERY hard to understand her, but she really tries. I can repeat part of what I understand and then she can help finish the sentence again. The more hurried she is, the less success she will have. She can call her van driver in the morning to cancel pick up or check on times. A few people can understand her if they try and don't make her nervous. She might say: "Mom, you and dad going to dinner tonight?"; "Sister does not want to go shopping with us, so it will just be you and me, OK?"; "Brother is silly, he told me I needed to give him 10 dollars to take me shopping". She loves jokes and being silly! e.g. "What time we going to the party on next Saturday? You know brother is not going?". I know for sure that she knows when someone likes her and will help her, or when someone is ignorant and does not want to help her. She understands a person's character very quickly!



KNOW there's a lot in there!" - "pure" dup 9p13p24.3, 17 years

" At 4 years 8 months she used single words, but not sentences, and had difficulty making sounds. At 17 years, she can speak fluently but can struggle to construct a proper sentence. Also, she doesn't always make it clear what the subject is. Speech therapy weekly was no help at all. " - "small" dup 9p24.1p24.3, 17 years

" For the first 18 months our son only grunted and cried. Then he babbled, quit babbling, babbled, quit babbling....

At around three-years-old, he said "Nana, Mama, car and Papa" with no progress for the next year. He would just repeat those words and use signs and crying to communicate. He used over 100 signs before he spoke a single word. At around four-years-old he began to imitate speech and try to say many words every day! His words are unclear and he drops the first consonant e.g. "hain" for "train" and "ai ee" for ice cream, and he doesn't speak in sentences yet. " - "large" dup 9q13p24.3, 4 years

" Aged 9, she is non-verbal and uses an AAC device to communicate. She has 10 intelligible words/approximations and suspected apraxia of speech. Once she had had grommets fitted to help with glue ear she began to babble. There is ABSOLUTELY a difference between what she understands and can express, with a severe expressive speech delay, but mild (if any) receptive speech delay. " - "large" dup 9q13p24.3, 9 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 9p duplication can have strikingly different personalities, but when describing their children, the words most frequently used by *Unique* parents are: loving, happy, fun, caring, gentle, determined, stubborn 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; others may exhibit over-friendliness with strangers. A minority of children display aggressive, destructive and disruptive behaviours and some have been diagnosed with specific behavioural, social, emotional and anxiety disorders (see [Challenging behaviours & Social, emotional & anxiety disorders](#)).

In common with their peers, babies and children with a 9p duplication enjoy a range of activities but seem to particularly relish dressing up; role-play; playing



with and arranging building blocks or other toys; listening to music and singing or dancing to it; and swimming.

“ She is wary of new situations, dislikes change, and is easily overwhelmed. She is shy with strangers, but very friendly and caring of those she knows, and is generally good-natured, cheerful and chatty at home. She can have difficulty interacting in large groups and, due to limited speech, she tends to listen rather than join in, unless she knows people well. ” - “pure” dup 9p, 34 years

“ She is always happy and laughing. She loves people, is tenacious, curious, affectionate and has a strong character. She enjoys being with her siblings. At five years she could be challenging and adapted her behaviour to the social situation; but was very friendly. At 6 years 9 months she is in opposition with her mother, touches everything and loves to decide things by herself.” - “pure” dup 9p12p24.3

“ She is a very strong-willed child; her determination will help her succeed in life. She enjoys being involved in anything and everything that is happening in the house. If you are cooking, she will push her chair to the side of you, climb up and help. She is very sociable and would rather play with someone than play alone. She can be very stubborn e.g. if she is told “no”. We have noticed that she can at times be overwhelmed in large groups of people, such as at parties, even if this is with familiar adults. ” - “pure” dup 9p13.1p24.3, 2 years

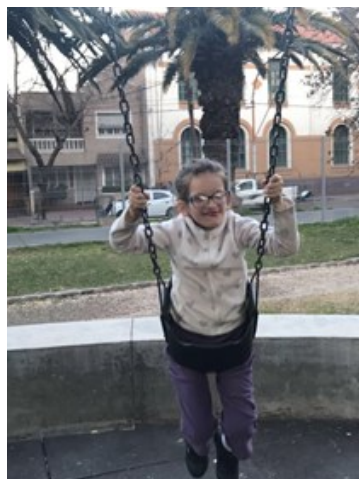
“ At 2 years 8 months he is very active and bright and has a happy disposition. ” - “micro” dup 9p24.3

“ He is stubborn, persistent, funny, energetic, kind, impulsive, a great problem solver, skilled at figuring out how to get a response from people, with a great memory. ” - “small” dup 9p21.3p23, 10 years

“ Empathetic, happy, loving and determined/stubborn/strong-willed, with a good sense of humour. She has a love/hate relationship with her brothers and a love of learning. ” - “large” dup 9q13p24.3, 9 years

“ He is like a whirlwind and is on full power from the minute he wakes up until the minute he's in bed, with no down time. He is cheeky and sometimes gets frustrated when he's not getting your attention. Definitely gets “hangry” before food, after eating he will quite happily “mooch” around, carrying his favourite books, or climbing on the slide. Loves slapstick, like things getting dropped or someone spilling stuff. ” - “large” dup 9q22.1p24.3, 8 years

“ Outgoing and determined, she's our little spitfire. She is reserved when uncomfortable, but once she warms up she's a go-getter. Feisty, sweet, loving, eager to please, funny. ” - “large” dup 9q13p24.3, 5 years



“Challenging” behaviours

Some children and adults with 9p duplications demonstrate so-called “challenging” behaviours (see pages 32/33), which often arise because of frustration at an inability to make their needs and wants understood.

These challenging behaviours exist alongside numerous positive traits and are often 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 and some parents mention an increase in challenging behaviours in the teen years. 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 duplication can also be beneficial (see *Unique’s* guide to Behaviours).

“ My daughter is cheerful, capricious and affectionate, also she is sometimes shy. Normally she behaves well, but she can fight with her younger sister. She can be defiant; she cries, and it is hard for her to stop with that behaviour. She sometimes demonstrates some self-harmful behaviour: biting her nails, inducing vomiting when she doesn't get her way, pulling out her hair. Currently she hurts the fingers of her hands. She can also demonstrate some aggressive behaviours: she pulls and sticks her nails into the ears of other children, adults and pets. She has been doing it for years and we haven't been able to stop this behaviour. We think she is trying to show affection because she does not know how to hurt on purpose. She also has no sense of danger and escapes from our home or public places. High windows/stairs and the swimming pool are hazardous. ” - “pure” dup 9p12p24.3, 8 years

“ She has a lovely, gentle nature. She is very much in tune with my emotions but rarely expresses any herself. She is desperate to please, to her own detriment. Her favourite activities are colouring, baking, watching TV and films (repeatedly), cinema and bowling.

Her behaviour has changed since seven years of age. She has become much more aggressive and emotional and has started getting headaches. I feel she is on the autism spectrum, but she has not been tested or diagnosed.

She demonstrates some self-harmful behaviours e.g. picking her finger nails, and can be frustrated if she doesn't understand what is happening. She likes things very orderly and to plan for things well in advance. Things are very literal.

She has difficulty interacting and communicating with others and doesn't have friends, but she doesn't seem to be bothered. She's happy when she's with me. It's been very challenging for my family and her sister; she has

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.

Behaviours and disorders affecting *Unique* members

	"pure"	"small/micro"	"large"
Challenging behaviour	20 cases	12 cases	13 cases
Self-harmful/injurious behaviour	6 cases	2 cases	3 cases
Aggressive behaviour	3 cases	4 cases	4 cases
Destructive behaviour	0 cases	2 cases	0 cases
Disruptive behaviour	0 cases	2 cases	0 cases
Sexually risky/inappropriate behaviour	0 cases	0 cases	0 cases
Intense shyness	4 cases	3 cases	0 cases
Inappropriate friendliness	1 case	1 case	3 cases
ADHD	4 cases	2 cases (+1*)	0 cases
ASD	2 cases (+2*)	2 cases (3*)	3 cases
OCD	2 cases (+1*)	1 cases (+1*)	2 cases (+2*)
SPD	0 cases	2 cases	1 cases
ODD	0 cases	0 cases	0 cases
Other	Severe anxiety (1); phobias (1); no sense of danger (1)		Severe anxiety (1); phobias (1)

Data from Unique's 2017 survey and database. Individuals may display more than one type of behaviour/disorder.

**Cases suspected or undergoing assessment*

required much more of my time and support. I wouldn't change it for a minute. She is a wonderful daughter. I'm very lucky. ” - “small” dup 9p24.1p24.3, 17 years.

Social, emotional & anxiety disorders

A few children have received a specific diagnosis of a social, emotional or anxiety disorder (see pages 32-33). Information from the medical literature is limited, but a 17-year-old girl with a mosaic “pure” 9p13.1p24.3p duplication, and features typical of 9p duplication syndrome, had a diagnosis of autism (Abu-Amero 2010). More recently, a 19-year-old woman with a “large” 9q21.1p24.3 duplication, but only mild features of 9p duplication syndrome, was diagnosed with psychotic behaviour. 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 suggests that more research is needed in this area (Martinez-Jacobo 2015).

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. Some children have been prescribed medication to help with specific disorders following diagnosis - including methylphenidate (Ritalin) for ADHD, which can help with restlessness and inappropriate comments - but with mixed results.

A link between 9p24 deletions and autistic features has 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 been proposed as one possible cause of mental health conditions, including ASDs and OCD. This was suggested as a possible cause of the autism observed in the case of the 17-year-old girl with a mosaic “pure” 9p13.1p24.3 duplication reported in the literature, although it wasn't possible to confirm this as tissues such as the brain cannot be readily tested to assess their chromosome make up (Vinci 2007; Abu-Amero 2010; Kantojarvi 2010; Yang 2012; Güneş 2016).

“ He has recently been diagnosed as autistic. He repeats things a lot and obsesses about thing like calendars, trains, pens etc. ” - “pure” inverted dup 9p24.3p13.2, 25 years

“ He is very sociable, outgoing, amusing and energetic. His behaviour can be challenging e.g. inappropriate friendliness, verbal abuse if plans are changed, self-harming (he pulls his cheeks and bruises them). He has ADHD and OCD and was given Ritalin at 16 yrs, but stopped taking it at 25 yrs. ” - “pure” dup 9p, 37 years

“ He is friendly, playful and lovable and has a mischievous side. He likes to

be with other children and engage in parallel play, and is interested in spinning objects. He does not like loud noises and does not like to walk barefoot on the grass. He is a determined little boy and never experienced separation anxiety. Loves music but does not dance very often.

At nearly four years his behavioural issues were a concern, mostly hitting and pushing his 18-month-old brother and getting up to mischief around the house. At six years he plays floppy if he does not want to go somewhere.

He has many autistic traits, including a lack of eye contact. Early concerns over autism were ruled out during an intensive evaluation at the local evaluation centre at 2 years 9 months, but he has been evaluated many times since.” - “micro” dup9p21.1

“ He has had OCD behaviours from an early age, which have varied over the years. He picks holes in his clothes - but hates to wear anything with a hole in it. Many things have to be “just so”. He makes a number of phone calls (the phone calls are another OCD behaviour which can be up to 30/day). ” - “large” dup9q12p24.3, 42 years

Sleep

Almost half of *Unique* families, with duplications of all sizes, said that their child has experienced some degree of sleep disturbance, although problems were not usually severe and often resolved with time.

It is also worth remembering that “typical” babies and children experience sleep problems.



Some children had difficulty settling, but once asleep slept well; others had difficulty sleeping for long periods and woke frequently through the night. Some parents also said that their child needed their comforting presence at bedtime in order to fall asleep and would reach or call out for them in the night.

Where sleep has been particularly challenging, 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.

A few children experience sleep apnoea, a sleep disorder that is characterised by periods of shallow breathing during sleep. A few have required a CPAP (continuous positive airway pressure) machine at night, usually just for a period of time.

Additional health problems, particularly gastro-oesophageal reflux in babies and asthma, may disturb night-time sleep and parents need to be supported to re-introduce clear regimes after a bout of illness or a hospital stay.

It can be 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.

"She sometimes does not realize when it is day or night. She will wake up in the middle of the night and not go back to sleep for the entire day. She is 19-years-old now and we give her melatonin if she wakes up at night, which sometimes helps her get back to sleep." - "pure" dup 9p13p24.3, 19 years

"When she was a baby she had trouble sleeping during the day, but at night she would sleep through from when she turned four months. She stopped taking naps at two-years-old because it was hard for her to fall asleep and if she did take a nap it was hard for her to fall asleep at night. So we stopped her naps and now she can fall a sleep easier at night and she sleeps for 12 hours." "pure" dup 9p13.1p24.3, 3 years

"His sleep apnoea was very bad. He would stop breathing for a full minute, take several deep breaths and stop for another minute. He wore a BiPAP for over a year. Then, somehow, he learned to breathe while sleeping and he no longer uses it. This was four years ago." - "pure" dup 9p12p24, 48 years

"Up to 18 months she slept badly. She would fall asleep in the middle of the night and wake up for several hours and then sleep again. She is sleeping very well now." - "small" dup 9p22.3p24.1, 9 years

"Takes naps due to terrible sleeping at night but then cannot go to sleep until later in the night. She wants to stay awake until dad gets home. She likes to get his PJs out for him and then spend time with daddy to talk about her day and the upcoming week or two. Her sleep apnoea is severe, but she refuses to wear a CPAP or BiPAP. She just takes it off the minute we leave the room. Nothing has ever been successful." - "large" dup q13p24.3, 28 years

"Severe obstructive sleep apnoea from birth, which resolved by age two years. Wore oxygen for sleep." - "large" dup 9q13p24.3, 4 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 experiences of *Unique* families suggest that for some children toilet training is achieved between the ages of three and seven years. Those with "small/micro" duplications appear to be more likely to achieve toilet awareness at an earlier age, at least during the day, than those with "pure" and "large" duplications.

Many children will continue to need pull-up pants at night with night-time dryness often only achieved in the late teens, and many continue to have "accidents" during the day throughout childhood. Low muscle tone can make toilet training more challenging and, for some children who suffer from constipation, training for bowel movements is particularly difficult.

A 32-year-old adult with a "pure" duplication needs reminding to use the toilet but is otherwise self-sufficient, while a 34-year-old who has required a

wheelchair in recent years has shown regression in this area.

Medical concerns

■ General well being

The majority of *Unique* families described their child's general state of health as "good" or "very healthy".

Although generally in good health, 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. Some parents felt that their child took longer to recover from infections than their "typical" siblings and peers. Chronic constipation is particularly common and often required on-going treatment (see [Constipation](#)). A few parents mention eczema, sometimes requiring treatment with steroid cream. Individual children have specific, on-going health concerns related to a 9p duplication (Unique).

■ Respiratory infections

Children with rare chromosome disorders tend to have a high rate of respiratory infections in early childhood; this seems to be a particular concern for some babies and children with 9p duplications of all sizes. Children may also be prone to allergies and asthma, sometimes triggered by respiratory infections. Evidence from *Unique* suggests that infections and asthma become less frequent with age and maturity, although they can persist throughout childhood.

"Colds go to her chest and then she gets wheezy and needs both brown (preventer) and blue (reliever) inhalers, but she is not asthmatic. We have had to call an ambulance twice and she was hospitalised overnight once." - "small" dup 9p21p24

"Frequent respiratory infections as a baby and young child, but not since." - "large" dup 9q12p24

■ Hands and Feet

Anomalies of the hands and feet are particularly common.

Regardless of the size of the 9p duplication, almost all the children described had at least one unusual feature of the hands and/or fingers (see table). Most common among these were fingers that curved inwards (clinodactyly) or were unusually short (brachydactyly). Fingers that were fused (syndactyly) and underdeveloped (hypoplastic) or misshapen nails were also reported.

A wide variety of specific abnormalities of toe and foot position are also a common feature of 9p duplications. Most notable are pes planus (flat feet), rocker bottom feet (the sole is curved without an instep, like a chair rocker), talipes (club foot, with the foot turned inwards, the soles pointing towards each other), short toes (brachydactyly) that may be curled and overlapping, and under-developed or ridged nails.

Some children are only mildly affected, and any deformity will not require treatment. Others, such as those with club foot, may benefit from massage, physiotherapy and sometimes splinting to help correct in-curved feet. This

Behaviours and disorders affecting *Unique* members

	"pure"	"small/micro"	"large"
Curved finger(s)	91% (15/20)**	100% (10/12)	93% (5/9)
Short finger(s)	41% (11/20)	0% (8/10)	29% (5/9)
Fused fingers	0%	0% (0/10)	7%
Underdeveloped fingernails	27% (11/20)	25% (4/13)	18% (1/9)
Short toe(s)	43% (3/15)	25% (4/4)	21% (3/8)
Curved toe(s)	14% (3/15)	25% (3/3)	43% (2/8)
Flat feet	24% (2/15)	13% (0/4)	57% (1/8)
Rocker bottom feet	14% (3/15)	0% (0/4)	14% (2/8)
Club foot	14%	0%	7% (11/20)
Sandal gap	14% (3/15)	13%	21% (1/8)
Underdeveloped toenails	52% (10/15)	13% (3/4)	27% (5/8)

* Numbers in brackets refer to *Unique* 2017 survey. **Numbers in brackets refer to cases in the medical literature where data is available (Moteji 1985; Wilson 1985; Haddad 1996; Stern 1996; Fujimoto 1998; Frederico 1999; Sanlaville 1999; Guanciali Franchi 2000; Tsezou 2000; De Pater 2002; Krepischi-Santos 2003; Morrisette 2003; Schnater 2005; Temtamy 2007; Vundinti 2007; Zou 2009; Abu-Amero 2010; Bouhjar 2011; Chen 2011; Brambila-Tapia 2014; Guilherme 2014; Stagi 2014; Samana 2015; Zhou 2015; Amasdl 2016; Canton 2016) .

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.

■ Seizures

Some babies and children experience seizures, regardless of duplication size.

Seizures, including epilepsy, affect some babies and children with 9p duplications, including a girl with a small 9p24.1p24.3 duplication.

Seizures are caused by a 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.

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.

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-ataxic: 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; may be obvious or subtle.

Seizures may be focal (partial) or generalised (affecting both sides of the brain). The *Unique* series suggests no particular type of seizure is typical, and an individual may experience more than one type (see [Types of seizure](#)).

Cases of absence seizures (11 cases); tonic-clonic (grand mal) seizures (3 cases); myoclonic seizures (2 cases); and febrile convulsions (1 case) were reported by families. In four other cases the type of seizure was unspecified. Data from the medical literature is limited, but we do know that several cases have been reported, including in individuals with “pure” and “small” duplications.

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 (Zou 2009; Abu-Amero 2010; Stagi 2014, Unique).

“My daughter was diagnosed with epilepsy at 11 years of age, with absences prior to this, although no treatment was given. She had myoclonic and tonic-clonic seizures for 10 years after that, which were well controlled with medication. She was given Epilim (sodium valproate) from 18 years but her weight increased by 10 kg so she was put on Lamictal (lamotrigine) a few months later. The dosage was increased at 20 years of age when she was also started on Keppra (levetiracetam), in addition to Lamictal and Clobazam. Her seizures are now well controlled with only very occasional episodes and some absences.” - “pure” dup 9p, 34 years

■ Heart

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

While heart problems are by no means a universal feature of 9p duplications, among *Unique* members ~20% of those with “pure” and “small/

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.

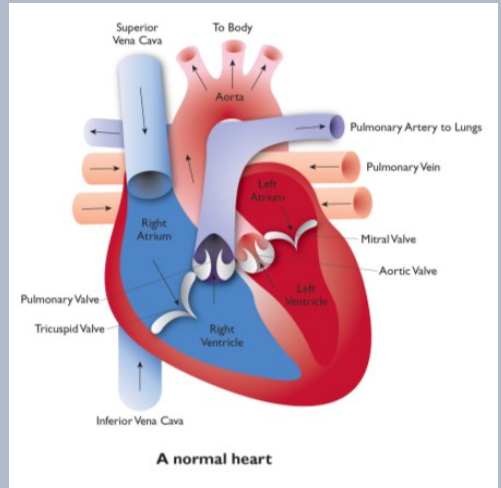
Specific treatment for VSD is determined individually. A baby with a VSD will be evaluated periodically. Small VSDs may close spontaneously; a larger VSD usually needs surgical repair to prevent lung problems that would develop from exposure to extra blood flow.

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.



micro" duplications had a heart condition, rising to ~40% for "large" duplications that extended to include a part of the long arm of chromosome 9 (9q). Some children were affected by more than one condition.

A heart murmur was the most commonly reported condition (7 cases), which in the vast majority of cases was benign (not harmful) or corrected itself naturally. Other more complex heart problems included: persistent ductus arteriosus (PDA) (5 cases); atrial septal defect (ASD) (4 cases); ventricular septal defect (VSD) (4 cases); an unspecified hole in the heart (3 cases); cardiomyopathy (3 cases), including hypertrophic cardiac myopathy; and a patent foramen ovale (PFO) (2 cases). Various other structural anomalies of the heart were reported in individual cases, including an enlarged heart and vascular sling (see [Types of heart condition](#)). It appears that even these more complex heart conditions resolved naturally or were successfully treated.

A similar picture emerges from the medical literature, with a range of heart anomalies, including ASD, mitral valve prolapse (MVP), and Ebstein's anomaly reported for duplications of varying sizes (Wilson 1985; Haddad 1996; Nakagawa 1999; Canton 2016; Oh 2016; Brar 2017).

Although those with "large" duplications are more likely to have a heart defect, even those with much smaller duplications, including a father and daughter with the same 9p22 to p24 duplication but with different heart conditions (Haddad 1996), and a heart defect in a patient with a "micro" 346kb 9p24.1 duplication (DECIPHER), exemplify the difficulty in identifying a critical region for cardiac defects. The data from the medical literature and *Unique* supports the idea for the involvement of a combination of multiple genetic and environmental factors in the development of the recorded heart defects (Oh 2016).

A number of children with anomalies of the heart were also diagnosed with anomalies of the brain (see next section).

[“Large VSD but by 19 months had healed spontaneously.” - “pure” dup 9p](#)

[“She has a congenital heart defect - a valve is not big enough, so a balloon needed to be inserted. It is working well at two years but will need replacing as she grows.” - “small/micro” dup 9p24.2p24.3](#)

[“She had a hole in her heart at birth, which repaired itself. She also has left side vena cava. She still has a heart murmur, but it is benign.” - “large” dup 9q13p24, 10 years](#)

■ Brain anomalies

Anomalies of the brain have been reported, many of which were minor and resolved naturally in time without any need for treatment or surgery.

While anomalies of the brain are not a consistent feature of 9p duplications and the majority of children have apparently normal brains under brain scans such as CT scans and MRI scans, the 2017 survey of *Unique* members found that ~25% (4/17) of those who provided information relating to anomalies of the brain with “pure” duplications, 50% (4/8) with “small/micro” duplications and ~43% (6/14) with “large” duplications had some type of anomaly.

The most commonly observed anomaly and affecting 5/14 of those with “large” duplications extending to chromosome bands q11,q12 q13 or q21, was an enlargement of the fluid-filled ventricles within the brain, which was sometimes diagnosed before birth. This may interfere with the body's ability to drain cerebrospinal fluid (CSF) from the brain resulting in hydrocephalus - a build-up of fluid within the brain. In many cases no treatment was needed as the pressure rebalanced spontaneously, but a few children required surgery to introduce a shunt (a thin tube that is implanted in the brain and drains away excess fluid). A girl with a “large” 9q13 to 9p24 duplication had communicating hydrocephalus, where CSF can flow between the ventricles. No treatment was required, although the situation was being monitored to check for obstructions. Her younger brother with the same duplication was unaffected. A girl with a “small” duplication including only 9p24.1 to p24.3 was diagnosed with the same condition.

There are several reports in the medical literature of children with “pure” or “large” duplications with the Dandy Walker Malformation (DWM). This is a cyst in the balance control part of the brain (cerebellum) that is involved with the fourth ventricle, one of the fluid-filled spaces within the brain. DWM can also lead to hydrocephalus and the need for a shunt (Chen 2005; Temtamy 2007; Vundinti 2007; Brambila-Tapia 2014; Samanta 2015). Whether some of the cases of fluid-filled ventricles reported by *Unique* families are actually DWM is unclear.

Partial absence (agenesis) of the corpus callosum was also reported for a number of *Unique* children and in the medical literature, including children with “small” 9p12p22, 9p21p24, 9p22p24 duplications and a “micro” 9p22.1p22.2 duplication. The corpus callosum is the largest connective pathway in the brain, linking its two hemispheres in a broad band of nervous tissue containing about 300 million nerve fibres. When the corpus callosum is undeveloped, 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 each hemisphere specialises in processing certain types of information (such as language or spatial patterns). Thus, to coordinate movement or to think about complex information, the hemispheres must communicate with each other. The corpus callosum is the main, although not the only connector, that allows that communication (Temtamy 2007; Stagi 2014; Samanta 2015; Unique).

A range of other conditions affecting the brain were reported for individual children, including cerebral palsy; bilateral striatal vasculopathy (affecting a boy with a 9p22.3p24.1, but not his sister); left cerebellar hypoplasia; and a small, benign cyst (Tsezou 2000; Unique).

“Enlarged ventricles before birth.” - “pure” dup 9p11.2p24, 1 year

“MRI scan revealed larger than normal ventricles.” - “small” dup 9p23p24.1

“Hydrocephalus was diagnosed at six months and a shunt inserted at 8 months - resolved by late teens. A brain CAT scan demonstrated dilated lateral and 3rd ventricles, a normal 4th ventricle, giant cisterna magna (considered a normal variant) and a moderate sized arachnoid cyst in the right middle cranial fossa.” - “large” dup 9q12p24.1, 42 years

“Hydrocephalus diagnosed at 13 months by ultrasound. No treatment was needed because pressure relieves itself.” - “large” dup 9q21p24.1, 29 years

■ Kidneys

Several *Unique* families reported minor anomalies of the kidneys, including seven cases of an enlarged kidney(s) (hydronephrosis) due to a build-up of urine inside, which was sometimes diagnosed during mid-pregnancy anomaly scans. Usually this was mild and required monitoring but no treatment. More serious cases can cause urinary tract infections, which 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. This anomaly was described for “pure”, “small/micro” and “large” duplications.

Two cases of babies born with only one kidney; individual cases of a duplex kidney, where one or both kidneys have two ureter tubes to drain urine rather than a single tube; horse-shoe kidney, where the bottom points of the two usually separate kidneys are joined, creating a U (horseshoe) shape; and benign renal caliectasis, where there is a slight ballooning of part of the kidney, were also reported (Unique).

■ Minor anomalies of the genitals

Among boys minor anomalies are common.

The experience of *Unique* duplication 9p families and the number of cases documented in the medical literature suggests that minor anomalies of the genitals are common, regardless of the size of the duplication.

The 2017 *Unique* survey found that 6/10 boys with a “pure” duplication, 3/5 boys with a “small/micro” duplication and 5/5 with a “large” duplication had unusual genital features. Typically, these were either undescended testis/testes (cryptorchidism), a very small penis (micropenis), or 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. 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.

Many boys were born with a small penis and one boy had a buried (hidden) penis. The evidence from *Unique* suggests that while this condition may persist throughout childhood, the penis may grow to a “normal” size during puberty (Motegi 1985; Frederico 1999; De Pater 2002; Krepischi-Santos 2003; Schnater 2005; Temtamy 2007; Vundinti 2007; Guilherme 2014; Unique).

Girls are much less likely to be affected. One girl with a “pure” duplication had under-developed internal genitalia and labia minora. A girl with a “large” 9q21p24 duplication was born with a bicornuate (heart-shaped) uterus and without a clitoris (Unique).

“ He had a micropenis as a child but at puberty it became normal size. ” - “pure” dup 9p12p24, 48 years

■ Constipation

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

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 9p duplication, whatever the size, 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, or laxatives such as Lactulose and Senna. Some children have benefitted from enemas when symptoms were particularly severe.

“ He has had horrible constipation his entire life, which causes major problems. Nothing has helped with this problem except very expensive colonic hydrotherapies, which physically remove the stool for him. This is not covered by medical here in the US. MiraLAX (aka Movicol or Macrogel) helps keep his stools soft, but he still can’t pass them without laxatives and even they often stop working. I give him daily magnesium/calcium supplements as well. ” - “pure” dup 9p12p24, 48 years

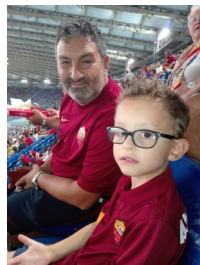
“ He has frequent constipation. Bran muffins and lots of water are very helpful. It’s gotten better as we’ve become better at being more aware of his schedule and we make him sit on the toilet on a regular basis. ” - “pure” dup 9p12p24, 30 years

“ She has always had chronic constipation with very slow transit. She eats little in quantity and very few vegetables and fruits because of the texture so I have to cook to optimise calories. She has Movicol treatment every morning and an enema occasionally if there is no stool for 15 days. ” - “large” dup 9q21p24, 10 years

■ Eyes and vision

A range of eye and vision problems are common.

Strabismus (a squint) where one eye or both turns inward, outward, up or down is relatively common among individuals with duplications of all sizes, including two children with duplications involving only 9p24. Strabismus may be constant, or it can occur intermittently, especially when tired. Among *Unique* members interventions like patching, exercises or glasses generally worked well to correct the squint, but for some strabismus was only corrected following a surgical operation. At least one child developed a “lazy eye” (amblyopia), which can be a consequence of a constant squint in one eye (Brambila-Tapia 2014; Cuoco



1982, Unique).

Other problems with vision include long- or short-sight, although short-sightedness was more common, with some evidence from *Unique* families that this could be linked to delayed visual maturity. In a few cases problems with vision resolved during childhood. For most they seemed to persist but were described as “mild” and were generally corrected by glasses. Several families described more pronounced impairments, with several children considered to have a severe visual impairment or be blind in one eye. One adult is registered blind (Zou 2009, Unique). Astigmatism, where the eyeball is rugby ball-shaped rather than round like a football, is also a cause of blurred vision and was relatively common.

Five *Unique* members (four with “pure” duplications and one with a “large” duplication) and a seven-year-old boy with a “small” 9p21p24 duplication (Temtamy 2007) had nystagmus (repetitive, uncontrollable movement of the eye(s)).

Several children with “pure”, “small/micro” and “large” duplications had ptosis - drooping of the upper eyelid so the eye is not fully open (Haddad 1996; Zhou 2015; Unique). The approach to ptosis depends in part on how severe it is, but if there are possible complications with eyesight, a surgical operation can be carried out to ensure the eyelid does not obscure vision.

A few parents mentioned that their children had difficulty closing their eyelids completely. This condition, called lagophthalmos, can lead to dry and irritated eyes. In the *Unique* series the condition was more common among those with “large” duplications.

There are a few reports of children who developed cataracts affecting central vision; one case of Duane syndrome – a problem with turning the eye; one case of mild optical albinism; and one case of an unusually-shaped pupil. One youngster developed keratoconus in his late teens/early twenties. In this condition the cornea at the front of the eyeball thins at the centre and vision becomes more short-sighted and irregular.

“His left eye is considered “blind”. He has worn glasses since he was 18-month-old.” - “pure” dup 9p, 30 years

“Strabismus in right eye was corrected with glasses. She also has myopia (short-sightedness) and astigmatism. As a child, her eyelids did not close completely.” - “pure” dup 9p12p24, 8 years

“She has a divergent squint. Patching, glasses and operation to correct. Wears distance glasses.” - “small/micro” dup 9p24.1p24.3, 18 years

“He is long-sighted and has a squint. He wears glasses and has a small cataract in one eye (very poor vision in one eye).” - “small/micro” dup 9p23p24/p22p23 mosaic, 26 years

“She required glasses when very young but does not need them now.” - “large” dup 9q11p24, 28 years

“Very short-sighted (-10 right eye, -13 left eye). He has a squint, which

becomes more pronounced with tiredness. Patching was discussed but I refused due to little benefit for what would be a big ordeal for him (he hates plasters and things on his face). He hated wearing glasses, possibly due to sensory issues. We tried contact lenses, but they were a complete failure as he hated having them put in. He will now wear his glasses in school and at certain times at home, but will only wear wire frame as they are less irritating to him. ” - “large” dup 9q22.1p24, 8 years

■ Hearing

A mild to moderate hearing loss due to a combination of glue ear, unusually narrow external ear canals, and excess wax in the ear canal, was noted in ~50% of *Unique* children across the range or “pure”, “small/micro” and “large” duplications, with some cases also reported in the medical literature. Some babies and children were also particularly prone to ear infections (Vundinti 2007; Mahjoubi 2011; Zhou 2015; Brar 2017; 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; 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.

“ His hearing is satisfactory for speech and language; however, he has very narrow ear canals and some congestion in the middle ear (glue ear). He has follow-up appointments every six months. ” - “pure” dup 9p13.1p24, 3 years

“ She had hearing loss and frequent ear infections that were corrected by the insertion of grommets. ” - “small” dup 9p21.1p24.3, 4 years

“ We always thought she could hear fine, but the audiologists thought that she had hearing issues because the readings on the audiology equipment at the hospital reflected hard ear drums. After seeing a specialist, it was determined that her hearing was fine. She has very small Eustachian tubes, which caused a misdiagnosis of a hearing impairment. She does have extremely waxy ears, which we are supposed to treat with wax softener, but she won't let us. ” - “large” dup 9q13p24, 10 years

“ She had grommets fitted at about the age of three with no hearing concerns since then. ” - “large” dup 9q13p24, 7 years

■ Joints

Loose joints are relatively common for all 9p duplications and can be severe.

Joints are often extremely loose (hypermobility) 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, in which the hip joints are easily dislocated. This may be apparent at birth or develop later. In either case, it is treated with splinting and if necessary immobilisation in plaster and possibly surgery (Guanciali Franchi 2000; Morrisette 2013; Zhou 2015; Unique).

Very occasionally, individuals may have hypomobile joints that are unusually stiff and may require surgery and tendon lengthening to extend their range of movement (Unique).

“ Knee joints very flimsy, almost double-jointed. Physiotherapy once each month. ” - “pure” dup 9p11.1p24

“ My daughter has hyper-extension of her knee joints. All her joints are hypermobile and unstable. She also has osteoarthritis in one hip. Bilateral dislocation of her hips was treated with surgery (two open reductions; two de-rotation osteotomies). Hyper-extension of the knees was treated by knee braces. At 34 years she is now a full-time wheelchair user and may need hip replacements in the future. ” - “pure” dup, 34 years

“ His joint problems are severe. His femurs did not rotate and he is knock-kneed. By 20 years his left shoulder has also started to dislocate periodically. He has had surgeries on each leg to straighten them, but his left leg has rotated back. ” - “small” dup 9p22p24

“ The neuromotor clinic noted that at 11.5 years our daughter had a level pelvis, excellent gait, full range of motion, and a straight and flexible spine. At 12 years there are no signs of joint deformity. ”- “large” dup 9q21p24, 12 years

“ All her joints seem to be affected. Causes problems with fine motor skills. She has very hypermobile ankles that cause her feet to turn in. ” - “large” dup 9q13p24, 7 years

■ **Skeletal anomalies**

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

Scoliosis (a sideways curve of the spine), kyphosis (an outward curve resulting in a hump) and kyphoscoliosis (a combination of kyphosis and scoliosis) were reported in teenagers and adults, while some younger children with the early signs of an unusual curvature were being monitored. A spinal curvature seems to be more common in those with “pure” and “large” duplications but has also been reported in children with “small/micro” duplications (see table) (Schinzel 2001; Krepischi-Santos 2003; Brambila-Tapia 2014; Guilherme 2014; Stagi 2014; 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

Skeletal anomalies affecting *Unique* members

	"pure" (13*)	"small/micro" (3)	"large" (8)
Scoliosis	8 cases	2 cases	5 cases
Kyphosis	3 cases	0 cases	1 case
Kyphoscoliosis	2 cases	1 case	2 cases

** Number of Unique members with the duplication who reported having a diagnosed skeletal anomaly. Some additional members were being assessed for possible spinal curvature at the time of taking the survey.*

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.

A sacral dimple (dimple or hole in the skin just above the crease between the buttocks) has been observed very occasionally. A sacral dimple may be shallow, so you can see the base, but stools can collect there before your child is toilet trained, so keeping it clean and protected is important. A sacral pit may be deep and even connect to the spinal canal or the colon. If there is any concern about this, your baby's spine will be imaged, usually with ultrasound or an MRI scan.

"My daughter can walk only a few steps without support and received physiotherapy and hydrotherapy at school. She uses a wheelchair outdoors, spending increasing time in the wheelchair from 19 years. By 21 years she had developed scoliosis and at 34 years has scoliosis and kyphosis." - "pure" dup 9p, 34 years

"He has kyphoscoliosis with congenital scoliosis of 57 degrees. To have his scoliosis reviewed and checked at three years to see if the curve is progressive and if he will need spinal fusion surgery." - "micro" dup 9p24.3, 2 years.

"He has a congenital sacral dimple with normal spinal ultrasound. A CT scan of the spine at 16 months was normal." - "micro" dup 9p21.1

"He has a slight 'roll' to his back, so we will be going for an x-ray soon to establish a baseline. No diagnosis as of yet." - "large" dup 9q13p24, 5 years

"He has scoliosis and has had three surgeries on his back." - "large" dup 9q21p24, 23 years

■ Palate

Abnormalities of the palate affect some babies with 9p duplications.

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 - have been found among *Unique* members and in the medical literature. The incidence is similar across the range of 9p duplications.

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 small cleft in the palate resolved before birth in one baby (Moteji 1985; Wilson 1985; Stern 1996; Bonaglia 2002; Hacıhanefioglu 2002; Schnater 2005; Vundinti 2007; Martínez-Jacobo 2015; Unique).

“ We believe he has a high palate, although it is not specifically diagnosed. He has issues with feeding and with speech. He will pack food to the top of his mouth and finds it difficult to chew and move food around his mouth. ” - “pure” dup 9p, 2 years

“ High/cleft palate. ” - “small” dup 9p22p24

“ He had palate spreading prior to braces - collapsed back in adulthood. A cleft palate contributed to difficulties with feeding as a baby (he was unable to breastfeed). ” - “large” dup 9q12p24, 42 years

■ 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 9p duplications, where problems may persist into adulthood.

A number of problems were described by parents (several of which were also reported in the medical literature, although information is limited): unusual dental development; unusual size of the jaw, leading to overcrowding or widely-spaced teeth; feeding difficulties and delayed eating and chewing activity; 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 almost 100% of parents mentioned dental issues (14/14 for “large” duplications, 19/22 for “pure” and 7/8 for “small/micro”), often citing more than one issue. Of particular concern were tooth grinding, overcrowding and late teething.

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 (Cuoco 1982; Frederico 1999; Bonaglia 2002; Unique).

“Late teething and still has one baby tooth. Grinds teeth so enamel worn, but no fillings to-date.” - “pure” dup 9p, 34 years

“She has severe dental decay, very weak enamel and has had many extractions. All treatment must be carried out under sedation.” - “pure” dup 9p, 42 years

“My son teethed on time and had no dental caries until about age 20. Gums are the bigger issue. We see a special care dental service three times a year.” - “pure” dup 9p12p24, 30 years

“He has bad teeth. Due to sensory issues, he would vomit if we tried brushing his teeth early on...when he gets cavities he has to have surgery to fix them. Has had two surgeries (15 cavities first time and four the next).” - “small” dup 9p21.3p23, 10 years

“She has ground her front teeth to stubs. She didn’t get her first tooth until the age of 18 months and she has only lost two teeth at the age of 10. She has some crowding as well - the dentist pulled two baby teeth to combat that.” - “large” dup 9q13p24, 10 years

“Weak enamel and poor dental hygiene as an adult resulted in loss of quite a few teeth.” - “large” dup 9q12p24, 42 years

■ Skin growths

Benign (non-cancerous) skin lesions known as pilomatricomas, pilomatrixoma, ‘calcifying epithelioma of Malherbe’ or trichomatricoma have been found in a few people with 9p duplications, including some *Unique* members, most commonly with “large” duplications (they are also 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. Several *Unique* members have had pilomatricomas surgically removed (www.bad.org.uk, Unique).

Three *Unique* children had skin tags that either fell off naturally or were surgically removed, and a six-year-old girl with a “small” 9p13.1p22.1 duplication 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) at the base of the spine (Bonaglia 2002).

“My daughter had three skin tags on her right ear, which were removed during her hernia operation.” - “pure” dup 9p13.1p24, 2 years

“ She has lots of small pilomatricomas on her scalp; many of these developed in the first few months of life. They don't cause any problems. Since the age of three, she has been developing some on her face and neck, which have grown to be quite large and have been painful. She has had four surgically removed. Currently, she has one on her leg. ” - “large” dup 9q13p24 - 7 years

“ She had a pilomatrixioma on her face, which was removed by a plastic surgeon. She also had a funny little ear tag that the same surgeon snipped off - it wasn't very big. ” - “large” dup 9q13p24 - 10 years

■ Hernias

A few babies were born with a hernia, where an organ or fatty tissue pushes through a weak spot in a surrounding muscle or tissue. The majority were umbilical (at or near the belly button), but there were also instances of inguinal (inner groin), abdominal, diaphragmatic (the muscle that separates the chest cavity from the abdominal cavity) and hiatal (upper stomach) hernias.

In several cases the hernias healed naturally without the need for treatment, but in the majority of cases surgical repair was required (Temtamy 2007; Martinez-Jacobo 2015; Unique).

“ She was born with an umbilical hernia, which was operated on this year. ” - “pure” dup 9p13.2p24.3, 2 years

“ She had a hernia when she was born, but it went away after time without treatment. ” - “pure” dup 9p13.1p24.3, 7 years

“ My son had an inguinal hernia that has been repaired surgically. ” - “micro” dup 9p24.3

“ When the surgeons were operating to bring down the right testicle, they found a hernia and repaired it. ” - “pure” dup 9p, 34 years

■ Blocked tear ducts

Tears normally drain from the eye through small tubes called tear ducts. When a tear duct becomes blocked, tears cannot drain properly, and the eye can become red, watery, swollen, inflamed and sometimes infected.

While not mentioned in the medical literature, blocked and small tear ducts were reported for both “pure” (6 cases) and “large” (6 cases) duplications. In some cases, the blockage resolved spontaneously, but in at least three cases surgery was required (Unique).

■ Bones

Instances of missing or underdeveloped bones have been reported, including several cases of short femur length, underdeveloped shoulder blades and delays in bone maturation (see [Growth](#)) (Cuoco 1982; Stagi 2014; Brambila-Tapia; Canton 2016; Unique).

“ Her bone age is about two years behind. ” - “pure” dup 9p13p24, 17 years

“ Her bones were VERY slow to harden. We couldn't see the ball of her femur on an X-ray until she was about six-years-old. ” - “large” dup 9q13p24, 10 years

■ Tracheomalacia/laryngomalacia

A few cases of tracheomalacia and laryngomalacia have been described, where the cartilage that supports the trachea (windpipe) or larynx (voicebox) is soft meaning that the trachea partly collapses, especially during increased airflow. These include a boy with a 9p21.1 microduplication. In most cases the condition resolved itself within the first few years of life (Oh 2016; Unique).

“ She has a weakness of the windpipe and has always had a consultant anaesthetist for surgery, but otherwise no treatment. ” - “pure” dup 9p, 34 years

■ Other medical concerns

Type 1 diabetes: two cases (one “pure” dup; one “large” dup).

Hypersalivation (excessive drooling): 8 cases (two “pure” dups; two “small/micro” dups; four “large” dups).

Diastasis recti (the stomach muscles do not meet in the middle): 1 case (“pure” dup).

Hypohidrosis (an inability to sweat): two cases (one “small” dup; one “large” dup).

A high pain threshold: one case (“large” dup), although this is likely to be more common and any concerns should be discussed with your doctor.

A cyst on stomach *in utero*: one case (“large” dup: “surgically removed when new-born and had a gastrojejunostomy. Taking Omeprazole for life because she is now at risk of stomach ulcers.”)

Kawasaki disease (a rare childhood illness that affects the blood vessels and causes them to become inflamed): one case (“large” dup at 5 years).

Puberty

There is a trend towards delayed puberty for all duplication sizes.

The information we have relating to puberty is limited, but among *Unique* families there is a trend towards children going through puberty later than is typical, although for a few puberty began at the expected age and, in one case, started early. There is some evidence from the medical literature that ovarian function may be affected by a 9p duplication and that puberty is usually delayed, as was the case for a boy with a 9p21p24.3 duplication and a girl with a 9p12p22 duplication. One adult *Unique* member with a “pure” duplication started her periods a little later than expected at 15 years but started the menopause prematurely at 39 years (Cuoco 1982; Mahjoubi 2011; Stagi 2014; Unique).

For most it seems that although often delayed, puberty then proceeded as expected with no real cause for concern, although mood swings could be

hard to handle. Several families have found that having a hormonal intrauterine device (IUD) fitted to stop periods has been beneficial for girls who find menstruation challenging, and at least one girl was sterilised.

“ She went through puberty late, but it went smoothly. ” - “pure” dup 9p13p24, 17 years

“ She started her menstrual cycle when she was 12-years-old. She didn’t have any trouble.” - “pure” dup 9p13p24, 19 years

“ Showed the first signs of puberty at 15 years 10 months: pubic hair, breast changes etc. She started her periods at 19 years 10 months, but still had no regular periods at age 21. ” - “pure” dup 9p, 34 years

“ Her breasts began to develop at 14 years. Periods have not started at age 21 years. ” - “small” dup 9p13p22

“ She went through puberty early. She handled the practicalities of periods very well, although it’s thought that her epilepsy was triggered by puberty. ” - “small” dup 9p24.1p24.3, 4 years

“ She didn’t appear to have any cramping but was not good with hygiene. At 28 years she is now on continuous birth control in order to have fewer periods per year. LOVE IT! ” - “large” dup 9q11p24, 28 years

“ He had a micro penis before puberty, but it is normal size now.” - “pure” dup 9p12p24, 48 years

“ He has acne but his testicles aren’t quite down yet and he is only just getting pubic hair, but no hair yet under the arms or facial hair. ” - “large” dup 9q13p24, 21 years

Adulthood

Almost all the *Unique* adults who told us about their life either live at home or in a group/residential care home with caregivers to provide support. A few have made the transition to living independently, but have required some on-going support.

Adults need some supervision with their finances, although in one case this followed a period of independent control. Most people travel by public transport and none drives a car. Some need supervision on transport and for those in a wheelchair this level of freedom is probably not possible. One young woman lost this freedom after going missing twice, leading to police searches.

After leaving school, of the few



Sisters with duplication 9p in their 30s and 40s

adults we know about (see testimonies below), most have gone on to attend college to acquire skills for independent living and that would be useful in the workplace. Subsequently, they have often gone on to undertake work, either in a voluntary or work experience setting, or in the workplace with support: a woman with a “pure” 9p13p24.3 duplication has had several jobs, including working as an office assistant, with the support of a charitable organisation; a 30-year-old man with a “pure” 9p duplication works as a custodian at a high-end furniture building company with the help of a job coach; a 25-year-old woman with a “pure” 9p duplication volunteered at a library. Several adults with “small/micro” duplications only discovered that they had a 9p duplication when their child was diagnosed and have had jobs, including working in the military.



Many adults enjoy attending a day centre/social support group and undertaking a wide range of leisure activities, in common with their “typically”-developing peers, including: football, swimming, basketball, competitive games and quizzes, music, dancing, gardening, TV, cinema, computer games, reading, shopping, going out for meals, and family parties and events.

There is very limited anecdotal evidence that four adult members may be experiencing some of the signs of premature ageing (Unique).

“Enjoys line dancing and country music, going to Church and helping with Sunday School. Attends a day centre five days a week and they encourage her to try new things, which she finds difficult as she is very nervous, but will try with their encouragement. Doing volunteer work in a computer software company.” - “pure” inv ins dup 9p13p24.3, 52 years

“Attended a college for young adults with physical or learning impairment as a residential student from 19 - 22 years. Now lives at home and attends a local day centre 3 days/week, which she enjoys, and goes out with carers two part-days for swimming and shopping. Have considered supported living. Loves swimming, shopping and going out for meals. Likes TV or music but does not enjoy the cinema. Likes being with her family and favourite carers.” - “pure” dup 9p, 34 years

“He enjoys assisting with the gardening, DIY and is a “buddy” in a care home for the elderly a few hours a week. He lives in his own home with 24-hour support.” - “pure” dup 9p, 37 years

“Being with family is his favourite thing. Likes routine and traditions (he wants us to drive the same road to our vacation site every year) and enjoys bowling with a very large group of adults once a week. He's in charge of

picking up all the pencils afterwards. He is very cooperative and easy going. He's very happy in his Adult Family Home (been there for nearly 10 years) and works as a custodian with a job coach at a high-end furniture building company. We like to get out of the house every weekend when he's home and go for walks along the waterfront, where we can also watch for trains to come by. He also loves to go to bookstores where he buys word search magazines. He subscribes to a train magazine and knows when it should arrive in the mailbox each month. ” - “pure” dup 9p12p24, 30 years



“ Has become more settled and less impulsive in adulthood. Loves swimming and, when in the right mood, going for walks. He attends a social support group once a week where he gets to “chill out” with friends. He loves music and TV. Family parties and events are a favourite and he is always first up to dance. Volunteers at a hospital cafe once a week and has a supported work placement as a cleaner in a local nursing home two mornings a week. ” - “small” 9p22p23/9p23p24 dup mosaic, 26 years

“ Can be left alone in the house for an hour unsupervised, cook food in the microwave, dress and bathe, and use a computer. Has a significant learning disability but is pretty high functioning and graduated from high school with a special diploma (life skills). Looking for a community program where he can possibly work a few hours a week. ” - “large” dup 9q21p24.3, 23 years

“ Only likes attending activities where she has an adult for support. She loved bowling in the special Olympics. We are looking for more activities for her since she is becoming bored with her adult program and we know she has more to offer with her job skills. She volunteered at various places in high school, but less now that she has finished. Now she volunteers at an animal shelter and church. Lives at home and says she is NOT moving out - probably because she is the eldest of four children. ” - “large” dup q11p24.3, 28 years

One adult's story....

"D" is now in his forties and has a "large" 9q12p24.3 duplication. He is average height and slim. For the vast majority of the time, D is a friendly outgoing person and loves socialising. His favourite activities are listening to music and watching sport on TV. In years gone by, D used to play soccer and basketball. He learned to ride a bicycle and we ditched the training wheels when he was about 10- or 11-years-old. He stopped riding his bike about 10 years ago after a couple of near misses.

D has had OCD behaviours from an early age, which have varied over the years. He picks holes in his clothes but hates to wear anything with a hole in it. Many things have to be "just so". He had a gambling addiction, but he was eventually convinced to attend a help group and is proud that he no longer gambles. He developed acrophobia (a fear of heights) after a near miss about 20 years ago, but he has managed to overcome that to the extent that he is now able to walk down stairs. He was on Haloperidol for the OCD for a time, but it didn't help much, and he no longer takes it.

D had physiotherapy (for general motor skills), occupational therapy (for fine motor skills) and extensive speech therapy. His tongue movement is markedly limited, and he is unable to voluntarily lift it or poke it out of his mouth, and he can't spit. He has a distinctive, loud voice and is unable to whisper, and he loves to sing in his own booming way. He has almost no palatal movement during speech and an attempt to fit a palate training device failed due to his hypersensitive palate. Testing demonstrated that he had difficulties with auditory discrimination of speech sounds, auditory memory difficulties, and spatial and temporal concepts. The results of a Frenchay Dysarthria Assessment were that D's speech was markedly dysarthric and was consistent with lesions on cranial nerves VII, IX, and XII. When young, if people didn't understand him he would spell it out. His use of language is now pretty normal. Hand co-ordination is still not wonderful, but he manages cutlery and pencils fairly well. A surprising anomaly is the fact that his fine hand co-ordination is good for obsessive picking of clothing - he's shredded plenty of clothes and even shoes. He is good at remembering dates, names and sport details.

D attended a mainstream country school until the age of 14 1/2 years. For the first few years he shared a full-time aide with another child with special needs. This reduced to 10hr/week in late primary, and to 6hrs/week in early high school. We then moved to a city and he attended a special school, which had children mainly with physical disabilities, many of whom also had intellectual disabilities. He attended a college for Years 11 & 12 where he was in a special class for students with special needs. From there he went to a Technical and Further Education College, where he attended a life skills course for a couple of years.

He moved out of home in his early twenties, at which time he was finding it more difficult living by the house rules and was finding it harder to get along with his siblings. He has been living with his fiancée for about four years. He is very caring and loves his fiancée very much. When he gets angry it can be extremely difficult to reason with him - I usually try to remove myself from the conflict and say that we'll talk when he calms down. He understands pretty much everything but expressing himself is not always easy, although he doesn't usually allow that to stop him.

On a typical day, they get up fairly early, shower and have breakfast. They catch the bus to a day centre three or four days a week where they undertake various activities. They have help come in twice a week for a couple of hours. At home they like listening to music, watching TV or DVDs, and his fiancée likes doing crafts. They do their housework and cook their meals. On paydays, they go to the hotel and have a few beers. I manage D's finances because money burns a hole in his pocket and he has no money left a couple of days after payday - he has to make sure that he buys all the necessities on payday.

D has undertaken work experience in retail and a pizza pub. He has had a few jobs over the years, including in a Self Help sheltered workshop and at a grocery warehouse, but he didn't manage to stay at any of them for more than a couple of years. He has attended a few different day centres who provide various training opportunities and activities, but he doesn't do a great deal. He does, however, call it "going to work".

On Sundays they come to my house for lunch and we play board games or canasta. D learned to play canasta from watching his grandmother and me play each Sunday for years.

What families say...

“ Both our daughters have unrelated disabilities. It has been very challenging and stressful, but also rewarding as both are unique and gifted, with lovely personalities. Accept help if offered and of the right kind. **Act on instincts as well as seeking advice. Enjoy the good times! ”**

“ When we first received the diagnosis I found it particularly difficult to get my head around the fact my 12-month-old daughter was going to face some enormous struggles in life, and we in turn were going to have some battles on our hands to ensure she received all the support she needed. I have found early intervention a MASSIVE help. We also access two specialist developmental groups for children with special needs weekly, which have taught me a great deal. **I have also managed to connect with another family whose daughter is a year older and also has duplication of 9p. That has been a life line, as they truly understand the journey we are on.** I have definitely struggled at times with acceptance and guilt; her brother who is 18 months older has had to grow up a lot and attend a lot of hospital appointments; however, he adores his sister and he is the most caring loving boy you could imagine because of it. ”



“ I suffered from postnatal depression and still to this day I have anxiety. It's been very challenging and scary not knowing how your child is going to develop and what they are going to be able to achieve. I have found that family and friends don't really know what to say when I need support. I am a nursery nurse and found it very difficult not to compare my son against other children his age; however, I now work in a child development centre nursery at the hospital that my son has attended since he was 9-months-old, and I have found this a lot easier as I am now working with children and families on a similar journey to me and I can support them in a way I would like to be supported. I have also met another family with a little boy who has trisomy 9p and have found the support from his family so helpful. I have found talking about the condition and difficulties helps and I want to spread the word!!! **My advice would be to enjoy your child and embrace their differences.** I have found informing people about the condition really helps my son to be included and loved for who he is. You will really find out who your real friends are along the way and make amazing new friends, too. **Take each day, week, month and year and focus on the small milestones you children are achieving. ”**

“ For her older sister it was difficult because as a child she had to go with us to therapies and many doctors. Now that she is a teenager she is more rebellious and does not want to help and be with her sister. ”

“ **Don't be afraid to ask for help,** both financially and supportive. Use whatever local authorities offer in terms of help, get social work involved early on as they can act as the gateway to accessing extra help. Don't dwell too much on the future, this is something I am guilty of and it does not help. ”

“ **It is scary to find out that your child has a chromosome abnormality, but we could have never dreamed of all the joy that she would bring. ”**

“ I started the Trisomy 9p Families on Facebook to offer others the information and support that was not available to me. I hope that no one else will be mistakenly told

their child will die just because of a T9p diagnosis, UNLESS they have some particularly dangerous medical condition not common to most T9p children and do what I can to stop that. I advise parents to enjoy their baby and assume all will go well. **Yes, problems may arise but wait until one does and then worry. I so regret those lost years that were full of fear but should have and could have been full of love and joy.** Of course, I recommend our Facebook group Trisomy 9p Families where we discuss any and all things T9p and offer support for the good times and the bad times. ”

“ Our son's younger sister also has a balanced translocation and she loves her brother and is very proud of him. My husband had the hardest time. He is a biologist, but still felt a huge amount of guilt that this was his "fault". After about 10 years, he finally realized he needed some help and underwent counselling. It helped a lot, and he now regrets that he didn't do it sooner. He never talked about our son to his co-workers or friends at that time. Now, he can't stop talking about how proud he is of him and what a wonderful person he is. We were so lucky that there were very few physical or health issues. I don't know if I would have believed them, but **I wish someone had told us that life would be OK, and even wonderful.** Talking to other families on Facebook and through *Unique* has been the best thing (things we didn't have in those earlier years). Be an advocate for your child(ren). Don't forget your marriage. Don't forget to laugh. Find some place that provides early intervention or obtain the appropriate therapies. Don't believe the doctor who tells you your child will never do anything. **Find people who will support you emotionally and ignore people who want to bring you down. Take a vacation. Don't ignore your other children. Ask for help. Take care of yourself. ”**

“ The best advice we have is to speak about your concerns and fears to each other. Our family motto is "there is no I in TEAM!!!" Things have not always been easy, but we are a team and we work through things together. My husband and I have learned to grow together to keep our family together and work as partners to care for our special needs child. Our daughter does have a typical sibling who was born after she was, so he knows no other life. You cannot believe everything you are told about your child. The child they sometimes see on paper is not the child you have at home and love every day. **Every child is truly different and will progress differently, that is why your child is special!!! ”**

“ It has completely changed our outlook on life and our family dynamic. In terms of the diagnosis it did feel like a bereavement and it took us a while to come to terms with it. In terms of our physical health we have strangely become more healthy and active. Training for fundraising events and the realization that our son will be living with us longer than planned has meant we have to be more in control of our health. Try not to get hung up on what you child can't do and keep on top of the professionals who are helping your child. The support groups on Facebook - Trisomy 9p family/Trisomy 9p families - are both excellent sources of support and advice from families with children at different stages of development. It gives a safe place to share experiences and look for advice on more sensitive issues. Remember your child is still an individual and their experience of T9p will be different to others; they will have their own ways and difficulties. Take them as they come and remember you know them best, so if you feel you need to go back to a doctor or professional and do something different, do it! **Do not blame yourself if it is an inherited condition, there is nothing you could have done to avoid the genetics. Treat them as much the same as your other children. Accept they may have limitations but don't stop them from trying. ”**

“ It hasn't impacted our family in any negative way. **Our daughter is an incredibly sweet and loving baby who is cherished by her parents, brother and extended family.** There are obvious stresses such as medical appointments and surgeries, but

we have a great deal of social and familial support. Once the shock of her diagnosis was past, we were able to settle into our new normal. ”

“ When they are very young, join them in as many things/organisations as possible, even when they do not understand. The other children get to accept them and the child benefits from being in the company of others. Join clubs, church groups, scouts/brownies or some such similar organisation. ”

“ Our family focused less on 'typical milestones', and really celebrated the milestones when she got there at her own pace. When first diagnosed, anger, resentment and mourning all went through my mind. Get support systems in place e.g. family, agencies, groups, organizations; arrange respite; time for self care; relationships with other families with special needs kids, but also those with typical kids. Now I realise what a blessing this child is! Really puts in perspective what is important - the health and happiness of your child. Her sibling is more empathetic towards others with challenges. Daily life is very challenging but has made me a better person. ”

“ Our son is the third child in our family, and the second with a chromosome disorder. He has been a blessing to our family as his personality is very loving and soft. He smiles easily and lights up a room with his presence. He brings other challenges that I had not experienced before with behaviours, but we are working through them with support. Try to make special time for any typical siblings that may feel left out, take care of your relationship with significant other (go on dates), use natural support systems (grandparents, aunts, uncles, close friends, church, family, etc). ”

“ I've learned she doesn't need fixing, this is who she is. I've learned patience, acceptance, and happiness from her. I don't know if our lives would be as rich without her. One day at a time. Never give up. Encourage, love, and accept as they are. ”

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

<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

The Stables, Station Road West, Oxted, Surrey RH8 9EE, United Kingdom
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Join Unique for family links, information and support.

Unique is a charity without government funding, existing entirely on donations and grants. If you can, please make a donation via our website at www.rarechromo.org Please help us to help you!

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

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This booklet was first compiled by Unique (PM) in 2006 and reviewed by Dr Nicole van Regemorter, Centre de Génétique, Université Libre de Bruxelles, Belgium and by Unique's chief medical advisor, Professor Maj Hultén BSc PhD MD FRCPath, Professor of Reproductive Genetics, University of Warwick, UK. Additional material was added in 2007/2011 (PM). A major revision was made by Unique (CA) and reviewed by Dr Maria Isabel Melaragno, Department of Morphology and Genetics, Universidade Federal de São Paulo, Brazil in 2018.

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