



For support,
contact with other families and information

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This leaflet is not a substitute for personal medical advice. Families should consult a medically qualified clinician in all matters relating to genetic diagnosis, management and health. The information is believed to be the best available at the time of publication and has been verified by Dr Nicole van Regemorter, Centre de Génétique, Université Libre de Bruxelles, Belgium and by Unique's chief medical advisor Professor Maj Hultén, Professor of Reproductive Genetics, University of Warwick, 2006. Additional material 7/2011.

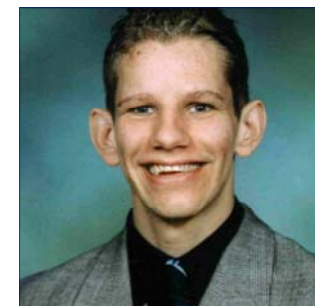
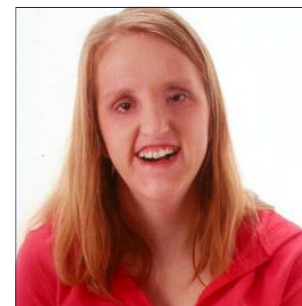
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Duplications of 9p



Duplications of 9p

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

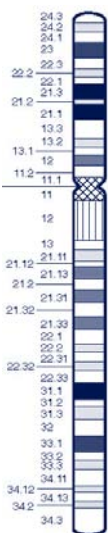
When a particular set of developmental features occurs in a recognisable and consistent pattern as a result of a single cause, the condition is called a syndrome. The features of a 9p duplication do occur in this way, so the disorder is sometimes known as **Dup(lication) 9p syndrome**. It is also sometimes called **Trisomy 9p** or **Trisomy 9p syndrome**.

What is a chromosome?

All our genetic information is contained in the cells in our body. The genetic material that contains this information is DNA, tightly coiled and forming a number of rod-like structures called chromosomes. Each gene is a fragment of the strand of DNA and contains coded instructions for the formation of different proteins that control most of the tasks in our body. So genes make up our genetic blueprint, and there are estimated to be rather less than 25,000 of them located on 46 chromosomes.

These 46 chromosomes occur as 23 pairs. We get one of each pair from our mother in the egg, and one of each pair from our father in the sperm. The first 22 pairs are numbered 1 to 22, approximately from longest to shortest, making chromosome 9 a medium-length chromosome. The remaining pair are the sex chromosomes. Girls and women usually have two X chromosomes (XX) and boys and men usually have an X and a Y chromosome (XY). Each chromosome has a short (p) arm and a long (q) arm, separated by a very important area known as the centromere. On the diagram below this is the pinched point with a long sideways line to the left side. The short (p) arm is above it at the top; the long (q) arm is below the line at the bottom.

Chromosome 9



Trisomy 9p syndrome is well researched and experience shows that people have similar, quite easily recognisable physical characteristics.

Development works with clockwork precision. The right amount of genetic material is needed for normal growth and development. If there is extra genetic material, this is likely to result in problems in growth and development. However, with duplication of 9p, this depends on the segment of the chromosome arm that is duplicated.

There are reports of children with various duplications between 9p11.2 and 9p22.1 who have developed normally. Some have had certain facial and hand features associated with trisomy 9p, while in others these have been too subtle to be noticed. While duplications of 9p11.2 to 9p13.1 are believed to be a natural chromosome variant with no harmful consequences, there appears to be a 'critical region' that must be duplicated for the characteristics to develop. This lies in a short segment between 9p21.3 and 9p22.3. Your child's geneticist or paediatrician should be able to tell you whether all or part of this region has been duplicated in your child.

(Di Giacomo 2004; Bonaglia 2002; de Pater 2002; Stumm 2002; Calabrese 1994)

Does it help to know the exact breakpoints in the chromosome?

It is believed that the 'critical region' for the characteristic features of a 9p duplication lies in a 6 megabase (that is, six million base pairs, or 'rungs' on the DNA ladder) segment between 9p21.3 and 9p22.3, between microsatellite markers D9S267 and D9S1213 (de Pater 2002; Bonaglia 2002; Fujimoto 1998) (see page 3).

This means that people with a duplication that does not include this segment are unlikely to show all, or indeed any, of the typical features. Recently a girl was described with a duplication including the segment between 9p13.1 and 9p22.1 who had very few features of a 9p duplication and no problems with learning. Her only unusual features were slow weight gain, a high arch to her palate and crowded teeth (Bonaglia 2002). 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. More recently, a duplication of the region 9p11.2-p13.1 was shown to be a normal variant with no apparent consequences for development (di Giacomo 2004; Calabrese 1994).

Considering only people with a duplication that covers the critical region, there is a broad range of ability among people with 9p duplications and it is often said that the amount of the duplicated material is the most important factor in determining the effects – so people with small duplications are less severely affected than people with larger duplications. In particular, a father-daughter pair with a borderline ability to learn and a small duplication from 9p22 to 9p24 have been described, as has a six-year-old boy with a duplication from 9p21pter who has only a slight degree of learning difficulty and slight delay in growth (Sanlaville 1999; Haddad 1996).

However, this size of duplication: severity effect is not clear from the *Unique* series, where two children with no more than a moderate learning disability, aged 6 and 16, had in one case a complete duplication of the short arm of chromosome 9 and in the other case a very large duplication from band p12 to band p24. Some people with smaller duplications have more far-reaching difficulties with learning (U).





Why did this happen?

To answer this question, the parents' chromosomes need to be tested as well as the child's. In as many as half of all cases, 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' and they are not uncommon. However, it is much less common for the pregnancy to continue right through to birth. Chromosome rearrangements affect children from all parts of the world and from all types of background. They also happen naturally in plants and animals. So there is no reason to suggest that your lifestyle or anything that you did caused the duplication.

In the other cases, the chromosome analysis will reveal that one parent has a rearrangement of their own chromosomes. This rearrangement is generally balanced with neither loss nor gain of material, and the parent would not be expected to show any symptoms.

In a few people, the cells containing the 9p duplication chromosome 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).

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.

Proposed 'critical region' for trisomy 9p



Adapted from Bonaglia et al Am J Med Genet 112: 158

Main features

These features are typical of trisomy 9p syndrome



- A recognisable 'look' to the head and face.
- Short fingers & toes with small or malformed nails (most obviously in babies and young children). The fifth finger may have a single crease or a very short middle joint and curve inwards. Thumbs, big toes and second fingers may have a noticeably short final joint.
- Internal organs are usually normal and as a rule, people are healthy as children and as adults. This is true where the duplicated material is limited to the short arm of the chromosome.
- Some degree of learning disability or difficulty. The level is variable and among adults ranges from moderate to severe.
- Delay in reaching baby 'milestones' for physical (motor) development.
- Growth delay. Children's bones may be late to mature, so that growth continues into late adolescence and even the early twenties, allowing some people to catch up in height.
- Spinal curvature. This typically becomes noticeable in the late teenage years and may either result in a hump (kyphosis), in a sideways twist (scoliosis) or in both (kyphoscoliosis) and may become a serious problem.
- Teeth may be late to emerge and come through crooked.

(de Pater 2002; Schinzel 2001; Fujimoto 1998)

Sources & references

The information in this leaflet is drawn from published medical research. The first-named author and publication date are given to allow you to look for the abstracts or original articles on the internet in PubMed. If you wish, you can obtain abstracts and articles from *Unique*.

Statistical and other information has also been drawn from the records of 94 members with a 9p duplication, together with an in-depth survey of 27 *Unique* members in 2004.

Other features

These features are also found in some people with trisomy 9p. Features involving the heart and bones are usually present only when a part of the long arm of the chromosome is also duplicated. When a larger part of 9q is involved extending to 9q22 or 9q32 (see *diagram on page 2*), cleft lip or palate, a very small lower jaw (micrognathia), talipes (club foot) and congenital hip dislocation are found more frequently (de Pater 2002; Fujimoto 1998; Wilson 1985; Fryns 1979).

- Stiff or, more commonly, loose and easily extendable joints.
- Large anterior fontanelle (soft spot on top of the head) in babies. The bones of the skull are slow to fuse.
- Talipes (club foot) or otherwise unusually angled feet.
- Frequent infections in babyhood and early childhood.
- Short sightedness and strabismus (squint).
- Seizures.
- In boys, small genitalia, with or without undescended testicles.
- High, narrow palate. It is more unusual for a baby to be born with a cleft lip or palate.
- A heart condition.

A very wide variety of other unusual features have been described in individuals in the medical literature.

How common are 9p duplications?

Compared with other rare chromosome disorders, 9p duplications are not uncommon. More than 150 people have been described in medical papers and it has been suggested that this is the fourth most common type of trisomy, after trisomy for the whole chromosomes 21, 18 and 13. Trisomy 9p appears to be approximately twice as common among girls as boys (Hannam 1999; U).

Outlook

Most children with pure trisomy 9p syndrome are healthy and life expectancy is unusually good for a chromosome disorder, with lifespan usually unaffected where the duplicated material involves only the short arm of the chromosome. Many older people are described in medical texts, including a gentleman of 53. When part of the long arm of the chromosome is also duplicated, heart conditions are more common and this affects life expectancy (Jones 1997; Zadeh 1981).

At the time of writing, *Unique* had nineteen adult members with trisomy 9p syndrome.



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

Living as an adult with a 9p duplication



All the *Unique* adults who have told us about their life are either living at home or in a group home with caregivers. They help around the home, either with household tasks such as loading machines and setting the table or shopping for the rest of the family. After leaving school, most people attended college to acquire skills for independent living and skills that would be useful in the workplace. One

young woman is working as an administrative assistant in an office, one is working as a volunteer in a library and another is working part-time in an office. Another young woman dreams of being a sales assistant in a clothes or pet shop.

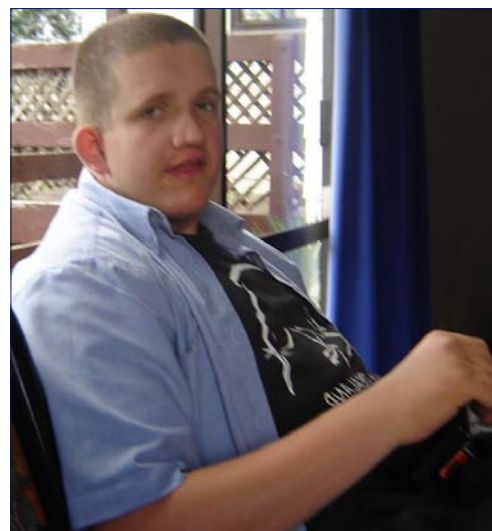
All adults need some supervision with their finances, although in one case this followed a period of independent control.

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 not possible. One young woman recently lost this freedom after going missing twice, leading to police searches.

Women describe their own temperament as adults as nervous and panicky, excitable, happy and loving, helpful, sympathetic and fiery. Although they can be noisy and even aggressive when thwarted, their mood can change fast. As a

group they are straightforward and take things literally.

Leisure activities include dancing, football, television and bowling. One young woman is a Sunday school helper at her church. They belong to a variety of clubs, both for people with special needs and for other people. Most women are reasonably sociable and have groups of friends, but none told us that they have a special friend, boy friend or plans to marry or have children.





consistent regime but if they do not, prescribed medication (such as antihistamines with a sedating effect, possibly melatonin) has worked well for some people. 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.

Fun

Young people with 9p duplications enjoy what other young people enjoy. Top of the list is listening to music, dancing and singing to it. Young children frequently enjoy pretend and dressing up games. As a group, children are happy to imitate others. Those with particular memory skills enjoy games that build on that strength and many children enjoy the company of others.

Growing up



Evidence from nine teenagers and adult women in *Unique* with a 9p duplication shows that puberty is typically slightly delayed and may remain incomplete. Periods started between age 12 and 19 but at least one woman developed secondary amenorrhoea (periods ceased) and two women with otherwise normal sexual characteristics have never had periods. Puberty may be accompanied by mood disturbances that may prove hard to handle. One girl was sterilised at the age of 14 and had a hormonal coil fitted to stop further bleeding. There is some evidence from the medical literature that ovarian function may be affected by a 9p duplication and that periods may start late (Cuoco 1982; U).

Information on pregnancy

The evidence from *Unique* suggests that pregnancy and birth are usually unremarkable. A few babies have been born prematurely, but no more than would be expected in the general population. In *Unique*'s experience, the mid-pregnancy anomaly scan has rarely raised concerns. As the major organs such as the heart are usually healthy, this is to be expected.

Unique's records show that average birthweight at 2715 grams (6 pounds) is below what is expected in a full term baby. However, while most babies are smaller than average, their weight still falls within the normal range. A small number of babies grow very slowly in the womb and are tiny at birth (U).

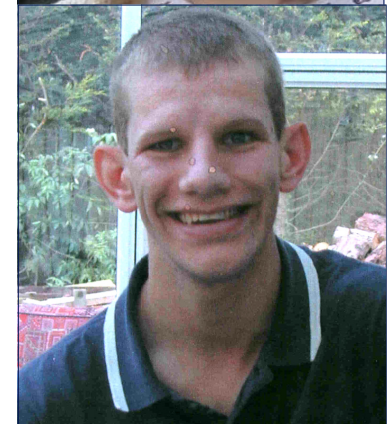
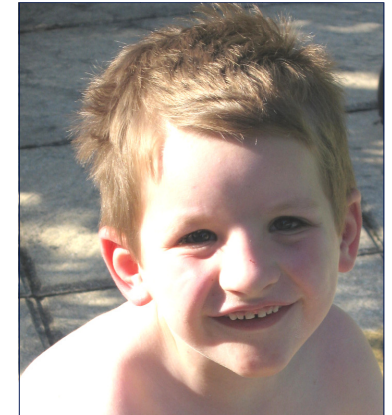
Appearance

Doctors may notice certain features about the face, hands and feet that suggest the need for a chromosome test. Some of these features may be obvious, while others are more subtle. Certainly, a child's facial appearance would not usually make them stand out in a group of other children.

Typical features include: a small, disproportionately broad head, a prominent forehead with a low hairline, deep, widely spaced and downslanting eyes, low, cup-shaped ears that stick out, a thick nose with a chunky tip, a short space between the nose and the upper lip, a mouth with downturned corners that is sometimes asymmetrical, a prominent lower lip, and a short, broad and sometimes webbed neck.

The prominent ears are the one feature for which parents may seek cosmetic surgery: three *Unique* children have had surgery to make them less obvious.

Some researchers have noted that children have a 'worried look'. Others have remarked on a tendency to be slightly hairy. Typically, the forearms and legs from the knee down are slender and a child's hands and feet are small, the toes and fingers particularly short. This was the feature that most new *Unique* families remarked upon (Hacihanefioglu 2002; Fryns



Growth

After the slight delay in growth before birth, the pattern of slow growth continues and most children are short for their age. Some children have been investigated for growth hormone deficiency and at least two *Unique* members have been treated with growth hormone. Partial growth hormone deficiency has also been recorded in the medical literature.

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 (Schinzel 2001; Teraoka 2001; U).

Food and eating

Some babies and children with 9p duplications feed well and easily, but this is not the rule and most families benefit from expert support with feeding. Among breastfeeding babies, intake may not meet the baby's needs for energy and growth. Difficulties in swallowing and in co-ordinating sucking with swallowing make bottle feeding time-consuming as well and some babies need to be fed for a short while by nasogastric tube. In the longer term, fitting a gastrostomy tube to allow feeding direct to the stomach may ease these difficulties and relieve families of the constant worry that their child is not drinking or eating enough. Many babies and children also experience gastro-oesophageal reflux, when the contents of the stomach flush back up the food passage. Prescribed medicines can help to reduce the acidity and ease discomfort and feed thickeners can help to ensure that feeds stay down. Careful positioning for feeds and sleeping also helps to control reflux but some babies need a fundoplication. This is a surgical operation 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.

Feeding problems ease for some babies once they are spoon fed and move on to pureed or mashed food. However, it is quite common for children to continue to experience chewing difficulties and to be reluctant to take any food with lumps. Finger



“ In a new situation, she is either very shy at first or inappropriately friendly before normalising. We have received no treatment or behaviour management advice age 5

“ An easy-going, loving boy age 13

“ She refuses to enter large rooms full of people unless she is in a familiar situation, such as the hospital. Even a known situation like a disco at college can become too much and she will then lock the wheels on her wheelchair and refuse to move age 20

“ She has always been hyperactive and aggressive. As the boss and a disciplinarian, she will deliver a fast whack on the head or back accompanied by a loud snarl one minute and then be sweet as pie the next age 24

Personal care and transition to independence

Young people with a 9p duplication are typically late to learn the skills of personal care that underpin independent living. Toilet awareness may emerge by the age of 5 or so and some children have been successfully toilet trained during the day in mid childhood. However, many children suffer from constipation and this can make training for bowel movements difficult. Even the most mildly affected adults appear to only achieve night time dryness in their late teens.

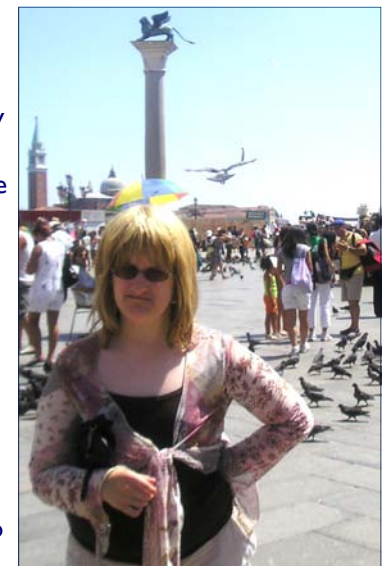
Children seem to be relatively successful at undressing and, later, dressing, learning these skills by mid childhood so long as fastenings are kept simple.

Self care skills such as washing and tooth brushing are usually mastered but many youngsters need reminding about habits of daily living.

These difficulties mean that some level of ongoing support will usually be needed for adults.

Sleep

The evidence from *Unique*'s members is that sleep is not usually a severe problem for families. Children may be hard to settle in the evening, but once asleep they usually sleep well. However, anxiety can disrupt even good sleep habits. The minority of children who do not sleep well usually respond to a firm and



Vision

Eyesight problems appear to be common, occurring in at least one child in three among *Unique's* membership. A squint (strabismus) is found fairly frequently. While the eyes may align better with increased maturity, some children need corrective surgery. There is evidence in the *Unique* series that delayed visual maturity may occur and some children experience persisting problems and remain short-sighted. 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 shortsighted and irregular. One adult is registered blind.

Behaviour



Unique's experience is that young children are typically both friendly and placid. An inability to communicate their wishes can frustrate them and lead to aggressive or self-harmful behaviour, but this only affects a minority. A typical character trait seems to be determination and when this turns into stubbornness it can be hard for parents to manage.

Children typically experience difficulties with social interactions in mid-childhood, both with adults and with other children. This may manifest itself as extreme caution and shyness or as inappropriate friendliness. Insecurity and frustration may also trigger challenging and aggressive behaviour.

A minority of children show hyperactive behaviour and if this is not controllable with behaviour management techniques, drugs have been used with success. These negative behaviours exist alongside positive traits, and children by and large remain loving and friendly.

The teen years bring a noticeable increase in challenging behaviour in some, even children who have presented no difficulties before. Children may show a fear and dislike of change. Some children become noticeably anxious and fearful, while others can show a fiery temper.

Unique's experience is that these behaviours are not extreme and experience with hard-to-handle youngsters shows that they respond well to consistent behaviour management techniques and social skills training.

“Frustrated by lack of communication. In frustration he either head butts a wall or hard object or throws himself against it. To stop him, we hold him tight and talk him down until he is calm and then try to figure out what he wants age 2

foods may increase the range of tastes and textures that a child will try, but chewing difficulties can be persistent and some older children are still partly fed by gastrostomy. *Unique's* records show that feeding is one of the most consistently problematic areas for families of children with a 9p duplication. All families facing feeding difficulties should have access to the expertise of a feeding specialist or clinic.

“Mila is a poor eater. We had no success with breastfeeding and she was tube fed for the first three months. She has remained fussy and stubborn to feed and doesn't like lumps but will eat crunchy food Mila, at 2½

“As a newborn baby Juliette was too weak to drink milk and was hardly awake. She gained so little weight that I stopped trying to breastfeed after 2 or 3 weeks. Once she was fed with spoons and soups in a bottle, things got easier but she still has a poor appetite Juliette, at 7

Learning

“She had to be taught by repetition. Understanding came later.

Families can expect that most children will need some support with their learning. The exceptions to this rule include some children with a duplication between 9p11 and 9p21 and some who have a mosaic form of the duplication (see page 18). In a recent paper [American Journal of Medical Genetics 2011 Part A 155 pp 1735-1739], Dr Inesse Bouhjar has drawn attention to a small number of people with a duplication of 9p and no cognitive disability. She reports on a boy with a very large duplication between the tip of the short arm and the 9p13.3 band who has a normal IQ of 95 at the age of 8. She also mentions three others: a patient with a 9p12p21.3 duplication [Stumm 2002]; another with a 9p13.2p21.3 duplication who has speech and language delay but no intellectual disability [Zou 2009]; and a girl with a 9p13.1p22.1 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].

The medical literature suggests that while some children show a mild to moderate learning disability in their early school years, the eventual level of difficulty may be greater. It also suggests that children with larger duplications have greater learning difficulties.

Unique's experience and some research reports suggest a more varied picture. Children face very different levels of learning difficulty, ranging from none at all to a profound disability. Within *Unique*, brothers or sisters with exactly the same duplication have developed differently in terms of learning ability (Schinzel 2001; Young 1982; U).

Family reports have shown that some children have a good memory, particularly for places and spatial information. This could make them good route-finders, organisers, office filing assistants and able puzzle-solvers. They usually mastered computer skills and showed personal characteristics such as determination and a willingness and ability to copy others that helped to develop their potential. Younger children might explore toys with energy and curiosity.



- “ Jack explores toys in depth Jack, at 3
- “ Juliette’s memory is excellent. She likes all memory games and is very good at them and can memorise journeys Juliette, at 5
- “ Sam’s memory is very good if he is interested, for example, which day the dustbin men come! Sam, at 12
- “ Very determined, very curious, logical Alison, at 18

As far as formal academic learning is concerned, most children learn to read. Some read newspapers and magazines and others read single words and signs, while for some children this is not possible. Many children appear to start reading around the age of 5, but others do not read until the upper primary school years.

- “ Julie’s reading of a simple children’s book was tested by her headmistress at nursery. ‘It does appear she may be able to read,’ her teacher said. Julie, at 4. Her learning difficulties are moderate.



- “ Sophie doesn’t read but she points to pictures in storybooks Sophie, at almost 5
- “ James can read his school reading book, and tries to read magazines and television listings in newspapers James, at 8
- “ Alison reads simple words and stories, probably operating at a 5 year level Alison, at 18

Writing also usually appears to emerge around the age of five. Children were often able to copy but found spontaneous writing harder.

- “ J has been writing since he was 4. He can write his name spontaneously J, at 7
- “ Carrie can write her name and short sentences. She can copy sentences from books and magazines Carrie, at 9
- “ Mark starting writing when he was 13 or 14. He can copy his name and address Mark is an adult. He does not read
- “ Wendy started to write at 5 and can now write sentences and short thank you notes Wendy is an adult

In *Unique*’s experience, all children have needed learning support, but this may be provided in a regular (mainstream) educational setting. Most children started their education in a mainstream nursery or school and transferred during the primary years to a special unit or school. Occasionally the movement was in the opposite direction as unexpected abilities emerged or service provision changed.

A more detailed description of the learning pattern of *Unique* members with 9p duplications is available on request.

investigations of all children with trisomy 9p. Dandy-Walker is a cyst in the balance control part of the brain (cerebellum) that may interfere with the ability to drain cerebrospinal fluid from the brain, resulting in a build-up of fluid within the brain. Partial agenesis of the corpus callosum, the broad band of nerve fibres that link the two cerebral hemispheres has also been reported (Hannam 1999; Stern 1996; Bussani Mastellone 1991).

■ Skin growths

A small number of children with a 9p duplication are reported to grow recurrent small fatty lumps under the skin that are not harmful but require surgical removal. Two children in the *Unique* series have been affected by this.

Other concerns

■ Teeth

Typically, teeth come through late. When they emerge, they may be crooked or unduly crowded and some families have noticed weak enamel resulting in extensive decay (Schinzel 2001; U).

■ Hands

A specific feature of trisomy 9p syndrome is a short fifth finger with a missing or shortened middle joint. Three quarters of *Unique* members had this distinctive feature and in many children the fifth finger also curved inwards. The second finger and thumb might have a very short final joint and you may notice that your child’s nails are tiny and brittle. *Unique*’s experience is that the nails grow better in time but often become thickened and may become ingrown. Other unusual features affecting the hands include clenched or hyperextensible fingers and incorrect positioning of the thumb. Hand splints may be enough to improve finger mobility, but surgery is occasionally needed.

- “ Using gentle massage when she was a baby I managed to straighten the finger.



Hearing

Glue ear is common in young children and among those with a high arched palate. Two *Unique* children with a 9p duplication were also reported to have narrow or kinked ear canals. Grommets (ear tubes) usually restore functional hearing, but repeated sets may be needed and some children have long-term tubes to improve hearing. Among 20 teenagers and adults in the *Unique* series, three had impaired hearing.

■ Seizures

An association exists between trisomy 9p, epilepsy and structural anomalies of the brain. Some children have a seizure disorder and evidence from *Unique* suggests that around half are affected. On magnetic resonance imaging (MRI), the brain may show a variety of unusual formations. One such is known as 'band heterotopia' consisting of collections of nerve cells (grey matter) in abnormal locations. A possible idiosyncratic response to common anti-epileptic drugs in some but not all patients including phenytoin, carbamazepine and valproate has been suggested (Federico 1999; Scalise 1998; Stern 1996).

The *Unique* series does not suggest any particular type of seizure as being typical. Seizures may occur first in early childhood and remit but then may return in adulthood. *Unique's* experience has not been that seizures are usually hard to control.

■ Heart conditions

Reports show that heart conditions have been found in five to 26 per cent of babies with a 9p duplication, most typically when more than a small part of the long arm of chromosome 9 (9q) is also duplicated. Typical problems include defects in the atrial and ventricular walls (holes between the chambers on the right and left sides of the heart) and the valves that connect the upper and lower chambers of the heart as well as the aortic valve that controls blood flow from the heart around the body.

Unique's experience shows that at least one baby in five was born with a heart condition but that this was usually minor and resolved naturally in time without any need for surgery. The most common problems identified were small holes between the chambers of the heart (atrial septal defect – ASD, ventricular septal defect – VSD). Leaking valves and persistent fetal structures, in particular an open ductus arteriosus (the channel between the aorta and the pulmonary artery that takes blood to the lungs and usually closes after birth) also occurred (Nakagawa 1999; U).

■ Palate and upper lip

The palate (roof of the mouth) is typically high and narrow. Seven out of 18 families who gave information on their child's palate formation had a baby born with an unusual formation of the palate or upper lip – either a high arched palate or a cleft in lip, palate or both. A small cleft in the palate resolved before birth in one baby. A high arched palate may remain unnoticed but can affect feeding and speech while a cleft palate or lip needs surgical repair to achieve a good functional and aesthetic effect (Hacihanefioglu 2002; U).

■ Brain

Recently, growing numbers of children with a 9p duplication have had an MRI scan of the brain and this has led to the suggestion that certain developmental anomalies of the brain may be typical of the syndrome. *Unique's* experience suggests that some enlargement of the fluid-filled ventricles within the brain may be common but this rarely needs more than monitoring. One child in 10 in the *Unique* series showed evidence of enlarged ventricles on an early scan, but only two out of 70 children are known to have a shunt. None of the affected children had a pure 9p duplication.

It has been suggested that partial Dandy-Walker syndrome may form part of the syndrome and that an MRI scan of the brain should form part of the routine

Speech and communication

The medical literature suggests that speech and language are specifically delayed, with delay in understanding consistent with general ability but a specific delay in expression. Children will at most use only single words and rely on gestures or signing and have been noticed to have particular acoustic characteristics of speech (Owens 1981).

Unique's experience is also that 9p duplications are associated with a specific speech and language delay but that many children progress to speak conversationally in sentences. However, this is not possible for all and a few children remain non-verbal while others use single words or 2 or 3-word phrases.

First words tended to emerge late between a child's first and fifth birthdays and children with 9p duplications often used only single words at an age when other children are speaking in sentences. Understanding appeared to progress ahead of speech in all children and clear, literal instructions and statements reinforced by gesture were universally understood. Non-verbal children communicated using vocal noises and gestures and many learned to use picture exchange or signing systems.

It has been *Unique's* experience that children may have difficulty making certain sounds of speech, in particular *f*, *d*, *s* and *p* and consonant sounds at the beginning of a word. There is some evidence to support this from the literature as well as evidence of an unusually low-pitched voice with a harsh quality. These features can make children's speech hard to understand and all children benefited from intensive, high quality speech therapy.

The descriptions that follow give a picture of speech in adults.

“Julie talks in short, stilted sentences and talks even if you don't want to listen. She does not always hear or fully understand questions and then gives inappropriate answers.

“Alison could say three words before she started school, but then lost them. She has a wide understanding and expresses things in her own way, mostly by vocalisation, eye contact and body language.

“Ilana's speech is highly distorted. She understands in three languages and started to speak at 7. However, she misses off opening consonants and her expression and understanding are worlds apart. Speech therapy doesn't work because she doesn't co-operate.

“Pippa expresses herself with vocal noises and has little understanding.

“Ali now uses long and complex sentences but with unusual constructions such as 'Where you went?' She frequently says she can't remember words and needs things explained in a non-idiomatic way as she takes things very literally.



Sitting, moving, walking

The medical literature suggests that children will learn to sit alone between their first and third birthdays and will be walking by 2 to 5 years (Schinzel 2001).



Unique's experience is that while most babies are late to reach their motor milestones, delay is not universal and the range of ability is wide. *Unique* babies rolled over between 3 and 18 months and learned to sit alone between 7 months and 5 years. Many babies did not crawl but those who did achieved this between 10 months and 3 years. Children generally started to walk between 18 months and five years, although some were more delayed and only took their first steps at 7 or 8 years. After this late start, mobility in some children developed at the same pace as their peers, but this was not true for all. Co-ordination can remain a difficulty and although most children eventually learn to run, they tend to be unbalanced and to tire easily. Some children progress to jumping, swimming, riding, dancing and playing football but this is not possible for all. Although all *Unique* adults can walk unaided, some rely on a wheelchair for outdoors.

Many facets of the chromosome condition contribute to this delay. At least half of all *Unique* babies were unusually floppy (hypotonic) at birth and low muscle tone could persist through childhood. This is in line with the findings in the medical literature that around 60 per cent of children have low muscle tone. Five out of six *Unique* babies were born with talipes (club foot) or feet that were otherwise unusually angled, needing treatment and in many children surgery. Two thirds were born with loose joints and dislocation of one or both hips at birth was common. Stabilisation in a splint was not always sufficient to ensure proper development of the hip joint and a number of *Unique* babies spent months as babies in plaster. Knee joints were often loose and children needed braces or splints to stabilise them for walking.

Children and adults with a 9p duplication could:

- ... walk with hands held, walk around the room holding onto furniture age 2½
- ... crawl very quickly, climb onto furniture, enjoy being in the swimming pool age 3
- ... walk short distances less than 100 metres age 4
- ... climb up and down stairs alone, run age 5
- ... sit properly on a chair, walk well but get tired, dance, run, swim with armbands, try jumping age 6
- ... walk with no problems age 13
- ... carry full cups of tea to different places in a confined area age 15
- ... ride, trampoline, swim unaided age 19
- ... do wheelchair dancing age 20
- ... play football with his peers age 22

Medical concerns

From a medical point of view, children are usually healthy. Many of the major problems are orthopaedic.

■ Feet

In *Unique's* experience, five out of six babies were born with a foot deformity that needed treatment. This may be in addition to having small feet. The range and severity of foot problems was wide. At the mild end of the spectrum, children were born with incurving feet that could be straightened with massage, physiotherapy and sometimes splinting. At the more severe end, children were born with talipes (club foot) that needed repeated surgical correction. The types of foot problem that were seen most frequently in the *Unique* series were a broad range of talipes, rocker bottom feet (where the sole of the foot is curved like a rocker), curled and overlapping toes, most noticeably the big toe. Toe nails were often small at birth and might be misshapen. Once nails developed, there was a slight a tendency to ingrow.

■ Joints

Typically, some of the large joints in the body are tight and others, particularly the knees, are loose and dislocate easily. The *Unique* sample showed that two out of three *Unique* babies were born with extremely loose joints that might easily dislocate. A much smaller number of children had unusually stiff joints. The joints most commonly affected were the knees and hips, but some families also mentioned a problem with hyperextensible elbows. A high proportion of children had developmental hip dysplasia and might need months of immobilisation in a splint or cast and in a few cases multiple surgery to improve the joints enough to enable them to walk evenly. Some children needed knee braces before they could walk and many also required supports to strengthen the foot and ankle (ankle foot orthoses) (Petty 1993; U).

■ Spinal curvature

Both scoliosis (a sideways curve) and most typically kyphosis (an outward curve resulting in a hump) are reportedly common in teenagers and adults. Among eight adults within *Unique*, seven experienced spinal curvature, resulting in what one mother described as a 'permanent slump'. Early physiotherapy and exercise may be sufficient to straighten the spine but many youngsters needed to wear a brace, at least at night (Schinzel 2001; U).

■ Chest infections

Children with rare chromosome disorders tend to have a high rate of respiratory infections in early childhood. This appears to be a particular concern for children with 9p duplications and the evidence from *Unique* suggests that children may also be prone to allergies and asthma. Among *Unique* members, chest infections were the most common reason for children needing to spend time in hospital. While infections become less frequent with age and maturity, they could persist throughout childhood.

■ Genitals

Boys may be born with a very small penis, undescended testes or both. An additional feature in some boys was hypospadias, when the hole normally situated at the end of the penis is positioned on the underside. This is usually corrected by a surgical procedure. Up to half of all baby boys in the *Unique* series on whom information was given were affected (U).