

Unique

9p deletions



Sources

The information in this leaflet comes from the medical literature and from *Unique's* members with a relevant 9p deletion who were surveyed in 2004-5.

Unique is very grateful to the families who took part in the survey.

References

The text contains references to articles published in the medical press. The first-named author and publication date are given to allow you to search for the abstracts or original articles on the internet in PubMed. If you wish, you can obtain abstracts and key articles from *Unique*. Information from the *Unique* survey is marked (U).

9p deletions

A 9p deletion is a rare genetic condition caused by having a chromosome 9 with a piece missing.

What is a chromosome?

The human body is made up of cells. Inside all the cells except the red blood cells, there is a nucleus where genetic information is stored in genes which are packaged into chromosomes.

Chromosomes are large enough to be studied under a microscope and come in different sizes, each with a top (short) arm called p and a bottom (long) arm called q. They are numbered from largest to smallest according to their size, from number 1 to number 22, in addition to the sex chromosomes, X and Y. A normal, healthy cell in the body has 46 chromosomes, 23 from the mother and 23 from the father, including one chromosome 9 from each parent.

A 9p deletion means that the short arm of one of the chromosome 9s has broken. The breakpoint can be almost anywhere, but in many people it is in the region called 9p22. People with a break in this region that deletes a so-called 'critical region' at 9p22-3 are said to have 9p- or Alfi's syndrome, named after the geneticist who first identified a group of people with similar features and this specific 9p loss. Other people with partial deletions of the critical region may have some of the features of 9p- syndrome.

Main features

People with apparently exactly the same chromosome rearrangement are different from each other. This is due to many factors - the unique mixture of their other genes, their environment, the exact breakpoint in the chromosome and other factors that have not yet been fully explained. Every child is unique – but with a 9p deletion, the likelihood of showing one or more of these symptoms increases:

- Developmental delay, particularly speech and language delay.
- Unusual head shape with or large, rounded forehead or a forehead that points forwards like a keel. This is caused by the natural seam in the bone plates that form the forehead joining too early (premature fusion)

of the metopic suture).

- Low muscle tone, making the body floppy.

Other features

These features have been noticed in quite a few children. The paediatricians and developmental specialists looking after a child with a 9p deletion can be expected to check carefully for these.

- Heart conditions.
- Hernias (an organ protrudes out of its normal position) especially near the navel (umbilicus) or in the groin (inguinal).
- Spinal curvature.
- Respiratory problems and frequent ear infections in early childhood.
- Unusual genital features have been described in the medical literature and in a few extreme cases, it may not be possible to assign sex or there may be sex reversal, with babies with male chromosomes having a female genital appearance. However, this is much more unusual than the literature suggests because of a bias towards publishing when a case is found and researchers actively searching for similar cases.
- Long middle joint in the fingers and sometimes toes, sometimes with an extra crease. Square nails.

Families say ...

“Apgar tests alerted the paediatrician who took blood for testing when Thomas was 3 days old. The head shape, low set ears and low muscle tone were the first signs - a 9p22 deletion.”

“We knew something wasn't right, and our paediatrician tested for many things but Charlotte's condition wasn't diagnosed until she was three and a half - a 9p23 deletion.”

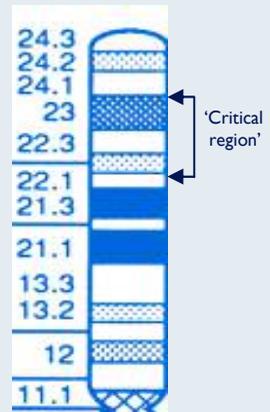
Chromosome 9



9p-



9p



What was the pregnancy like?

Families say ...

“ A very pleasant and uneventful pregnancy - 9p22 deletion.

“ There was very little movement. I had to shake my belly to get her to move - 9p22 deletion.

“ Aimee stopped growing and moving for a short time near the end of pregnancy - 9p22 deletion.

“ Forceps delivery, with hindsight it should have been a caesarean section due to the head shape - 9p23 deletion.

“ Although she was full term, she rated as a preterm baby - 9p22 deletion.

How rare are 9p deletions?

This is not known, but a 9p deletion is reported to occur in one in 50,000 newborn babies, of whom two-thirds are girls. Studies of well over 100 people with a 9p deletion have been published but there are undoubtedly many more people who have either not been described or not diagnosed. The oldest patient described was 61 years old. On the 9p- syndrome network website at www.9pminus.org there are messages about a 50-year-old woman and adults in their thirties (Nielsen 1977).

Unique has 40-45 member families with Alfi's syndrome or a similar deletion from 9p. Twenty families completed a detailed questionnaire in 2004-5.

What was the pregnancy like?

There has been no formal study, but most *Unique* mothers had an unremarkable pregnancy and no advance warning of their baby's chromosome condition. Some mothers noticed a lack of fetal movement in the last month of pregnancy and one baby was shown to have stopped growing. Three out of 20 mothers developed high blood pressure or pre-eclampsia, but this could have happened regardless of the baby's chromosomes. One summary in the medical literature confirmed that 23 out of 28 pregnancies were unremarkable.

The typical keel-shaped forehead was noticed in just one baby at the mid-pregnancy ultrasound scan but then not confirmed at an expert centre for prenatal diagnosis (Huret 1988; U).

How were babies affected at birth and as newborns?

There is no formal series comparing babies with 9p deletions at birth. Most *Unique* babies were born around term. Four were born early, at 35 to 37 weeks, and two babies arrived two weeks late.

At birth, around half the *Unique* babies showed signs that alerted medical staff to check their chromosomes. The others showed nothing out of the ordinary and were diagnosed later when their pace of development fell behind that of other children.

Features that were noted at birth included the typical 'keel-shaped' forehead or an otherwise oddly shaped head, marked congestion in the face, very marked

floppiness, low Apgar scores (0-10 scores of a baby's condition at birth), reluctance to feed, hypospadias (where the hole is not at the end of the penis but on the underside), a heart condition, a very large umbilical hernia or in one case an omphalocele, allowing the liver to protrude through the abdomen wall at the umbilicus, widely spaced nipples, no finger or toe nails or unusually square nails, and unusual facial features. Three out of 16 babies had very irregular blood sugar levels or marked hypoglycaemia (low blood sugar) shortly after birth and a raised blood sugar has been noted by one researcher (Burton 1989; U).

What about food and eating?

Typically, babies with 9p deletions have a high palate and a small, receding jaw and both of these features can make feeding more difficult (Alfi 1976).

Despite these difficulties, half the babies described in the *Unique* series breastfed successfully for between one and five months and most of the others overcame early difficulties latching on, sucking and swallowing to feed well from a bottle. In around one quarter of the babies the difficulties with feeding were enough for tube feeds to be given, usually with expressed breast milk, but this was usually only needed for a few days or weeks. Occasionally it is helpful for a baby to be fed direct through a tube into the stomach (gastrostomy), but this was only needed for one baby in the *Unique* series who also had a heart condition.

Gastro-oesophageal reflux, where feeds and stomach contents return up the food pipe and may be vomited or inhaled, is common among babies with chromosome disorders and affects some babies with 9p deletions. If your baby is very uncomfortable after a feed or brings up very much more of their feed than with normal possetting, discuss it with your health visitor or GP. If measures such as careful positioning after feeds, giving very small feeds and using prescribed medicines or feed thickeners do not work well enough, it is possible to do a surgical procedure called a fundoplication to improve the action of the valve between the food pipe and the stomach.

Many families reported **constipation** that was bad enough to need prescribed medicines and some families noted that this got worse as their child got older. This is

Families say ...

“ I breastfed successfully for one month. She was a very hungry baby so I had to supplement with a bottle earlier than my other children - 9p22 deletion.

“ No feeding problems, eats normally and well - p23 deletion.

“ She would not breastfeed but took to the bottle without problems. She would not chew and just sucks so you have to be careful that she does not choke, as has happened several times. Food still comes down her nose when she sneezes - p22 deletion, age 10.

Families say ...

“ Ailbhe has mild learning difficulties. Her ability with numbers is not too good but she manages money fairly well. She has a good grasp of concepts and ideas. She was in a special class in a mainstream primary school from age 8, and attended a special school from the age of 13 - 9p22 deletion, adult.

“ Daniel has moderate learning difficulties and can learn easily if it is what he wants, but if not can be quite stubborn. At age 8 his learning targets included numbers to 100, concentrating for ten minutes, writing on the line and drawing in correct proportions, developing understanding of time and sequencing and writing a complete sentence - 9p23 deletion.

not caused by low muscle tone but children's relative inactivity may play a role. As well as giving enough liquid and fibre or fibre-enriched nutritional drinks, many families regularly gave stool softening and stimulant medicines by mouth or enema.

Once past the baby stage, most children ate well and even greedily, but some had difficulty chewing and choked easily and would only suck their feeds or restrict themselves to mashed feeds or first stage baby foods (Bennett 1993; U).

Fair or dark?

Some researchers have commented that a child with a 9p deletion has lighter skin and hair colouring than the rest of the family. Just two *Unique* families noticed this, so if it is true, it only applies to a small number of children (Wagstaff 1995; Muroya 2000; U).

What about growth?

Unusually for babies with a chromosome disorder, most babies with a 9p deletion in the *Unique* series were above average weight at birth. Birth weights for term babies varied between 6lb 8oz (2948g) and 10lb 2oz (4592g). Birth weights in the original research series also fell between the 10th and 90th centiles.

Babies may also be quite long at birth. In the *Unique* series, babies were between 19 and 24 inches (50 - 60 cm) and Alfi noted lengths or heights between the 50th and 95th centiles. However, this is not universal, and some babies are born small (Alfi 1976; U).

How well have children coped with learning?

Formal research into learning styles is sparse apart from one piece of research that showed three children with differing levels of learning ability facing similar difficulties with tasks requiring visual recall (Chilosi 2001).

All the children known to *Unique* have needed some extra help with their learning but in general the eventual outcomes have been good, with some adults in supported work placements. Learning difficulty ranged from mild to severe but the great majority of families described their child's special learning needs as moderate.

Asked what their children's strengths were in the classroom, many families pointed to sociability, personality and their child's wish to please and comply. Other families noted self confidence, a sense of humour, curiosity and a determination to learn. Some families commented on their child's long attention span. Most children learned some reading and writing and could handle numbers, although they may have found it harder to cope with the concepts of number and mathematics. Some children do not achieve at this level and there was no obvious link between the site of the breakpoint on the chromosome and the level of learning difficulty. One of the children with a severe learning disability had an interstitial deletion between p24 and p22.

The excerpts in the box (right) were taken from a paediatrician's description of one child's progress to the age of 4. They illustrate the progress that can be made in an individual case with early intervention.

Schooling

Children in the *Unique* series usually started their education in a mainstream school, either with learning support or in a special unit. Transfer to a special school occurred between the ages of 8 and 13.

Would a child need a statement of special educational need?

The great majority of children were supported by a statement of their special educational need, but where this was not provided, educational psychologists were involved in assessing and monitoring progress.

Speech, language and communication

Typically, children with 9p deletions speak surprisingly well and develop an adult way of speaking. Judging from the *Unique* experience, speech was usually somewhat delayed but communication was a strength and the great majority of children were talking, sometimes quite fluently in short or long sentences, by the time they started school. First words generally appeared between a child's second and third birthdays and were used appropriately, with understanding usually more advanced than expression.

A paediatrician reports ...

“ She initially had moderate developmental delay with feeding difficulties and severe speech delay. However, she made good progress in her overall development, particularly speech and language and social skills, and now shows mild global developmental delay with some significant difficulties in gross motor skills. She is a sociable girl. There are no obvious behavioural problems and she is very motivated and very keen to learn. She is due to start school in reception class and will certainly impress the teachers. However, I am concerned that her difficulties although mild may be overlooked if not carefully monitored - 9p22 deletion, age 4.

Families say ...

“ Ailbhe uses language appropriately and in a normal way. She loves using new big words, usually in the right context - 9p22 deletion, adult.

“ Karly does not always use language consistently. She talks normally but is very repetitive and cannot express her feelings very well. She has made steady progress but is about 3 years behind - 9p23 deletion, age 12.

“ Daniel had very limited speech to the age of 5. He used to pull or hit people to get their attention and even today does not always use the right word. He can say short sentences, and understands a lot if things explained in a very simple way. Sometimes he finds it difficult to access the right word - 9p23 deletion, age 8.

“ Speech is her best attribute - 9p22-24 deletion, age 6.

“ Jenna has quite adult conversations for her age and forms long sentences, often copying what she has heard from an adult. She has excellent understanding but has difficulty processing information - 9p23 deletion, age 4.

“ Jessie’s progress is slow with stops and starts due to illness. Acquired skills can seem to disappear but will reappear later - 9p22 deletion, age 2.

All children needed speech therapy, generally from age 2 or 3 but starting in babyhood for some, although in some areas the service was judged to be poor. A small number of children learned a sign language to support their communication but this was a stopgap measure until language became more fluent. In some children, progress was steady, in others language skills developed in spurts, while one child showed progress followed by regression. Generally, families did not report difficulties in making the sounds of speech although some said that it was much easier for the family than unfamiliar people to understand their child.

Some children showed particular ability or delay that fell outside this range of achievement.

A group of researchers who recently surveyed children with 9p deletions found that children understood very much better than they could express themselves and this caused a frustration that could be vented as temper tantrums. As speech improved and with it the ability to express their feelings and wishes, tantrums subsided. They therefore stress how important it is to encourage communication using other means, such as sign language until speech emerges (Swinkels, personal communication).

Overall physical development and gross motor skills

For many children in the *Unique* series the delay in reaching their baby developmental ‘milestones’ was the most obvious feature of the chromosome disorder and for six out of 16 families this was the main reason their baby’s chromosomes were tested. All babies were said to be very floppy (hypotonic) from birth and were late to hold their heads steady. A minority were reported to have highly flexible joints (ankles, knees, shoulders, elbows, wrists, fingers) and specifically loose hip joints (developmental hip dysplasia) but only one was

immobilised in a splint or plaster. Rolling was achieved between three months and three years, sitting upright between eight months and two years – often in conjunction with supported seating, such as a giraffe chair, followed by crawling or bottom shuffling between one and three years.

Almost all babies received physiotherapy and those who did not had occupational therapy. Some children also had hydrotherapy. For some, therapy started from birth to address the low muscle tone, in others it was provided from four or six months onwards to encourage achievement of the key mobility skills. One child received physiotherapy from 10 months to strengthen her knees when walking. All families found the service helpful.

Walking was achieved between 16 months and four years three months and some children took a further year or two to walk independently. Almost all needed some form of leg or body support, from shoe supports or ankle braces to a stander or walker. However, once mobility was achieved only one child continued to use a wheelchair and then only for long distances. Some families described a typical gait – leaning forwards from the ball of the foot and not always looking where they were going, so children had a tendency to trip and fall.

A sizeable minority of families reported short, contracted hamstrings and one child had surgery to lengthen the tendons. Other families mentioned that their child moved quickly but unsteadily, putting them at risk of falling. One family reported recurrent knee pain while walking, but investigations and X-rays revealed no underlying abnormality. Another family described the way their daughter throws her foot to one side while walking. Ultimate mobility levels were very varied, with some children swimming and cycling with ease and one taking part in the special Olympics.

For almost all children the characteristic floppiness improved with therapy, exercise and maturity and in some it was only a feature of babyhood and the toddler years. One teenager was still quite significantly affected and tired very quickly when taking exercise.

Almost all families said that their child's feet were very flat and typically they were also long and narrow. Most children needed insoles to correct the foot position but

Families say ...

- “ Gemma had low muscle tone as a baby and tires very quickly - 9p23 deletion, age 14.*
- “ Andrew suffers from knee pain when he walks but x-rays showed no abnormalities. As a young child he walked with a rather stiff, wide gait, moving quickly but a little unsteadily - 9p22-23 deletion, age 13.*
- “ Emily walks with bent knees and is never steady. She does not watch where she is going and trips easily over anything, so she can fall down kerbs if not monitored - 9p22 deletion, age 10.*
- “ Matthew is very unsteady and tends to run with his head down - 9p22 deletion, age 5.*
- “ Anna is still slightly unsteady but getting better all the time - 9p22-24 deletion, age 5.*

Families say ...

“ Some difficulty with all motor skills, all resolved by adulthood - 9p22 deletion, adult.

“ Gemma still has difficulty controlling cutlery. She can hold a pen or marker for short spells but is unable to maintain this and slow - 9p23 deletion, age 14.

“ Andrew had difficulty holding anything for many years but can now hold most things - 9p22-23 deletion, age 13.

“ Emily still has difficulty using both hands together, was delayed holding toys and never held a bottle. But she used a spoon early, has just learned to cut food and could hold a pen from an early age - 9p22 deletion, age 10.

“ Aidan mirrors when doing an action, his pincer grip was late coming - 9p22 deletion, age 9.

only one family reported needing special footwear (U; Hoo 1982).

Fine motor and co-ordination skills

Most children in the *Unique* series were late to use their hands appropriately and to develop hand-eye co-ordination. Other skills that developed late identified from family reports were uncurling of baby fists, developing a pincer grip, using both hands together and independently of each other and gripping two objects at the same time. The degree of delay was quite variable, and in some children was slight.

Occupational therapy was available to most children and many families found it advanced their child's ability to reach and grasp for toys, to hold pens and markers correctly, their hand-eye co-ordination, their ability to feed and dress themselves and their sensory integration.

Typically, the middle section of the fingers of people with 9p deletions is unusually long, but there is no reason to believe that this will affect function.

According to research, the nails are also square, but this was only confirmed by half of the *Unique* families. One family commented also their daughter's nails were ridged (Alfi 1976; Young 1983; Al-Awadi 1988; U).



Age 6, 9p24 deletion

Medical concerns

No two children are affected in exactly the same way by a 9p deletion. The medical problems described here have affected a proportion of children with this chromosome disorder but do not affect every child. The doctors who look after your child will examine him or her very thoroughly and may pay particular attention to these areas.

■ Head

Many babies are born with a forehead that looks pointed when seen from on top and is often described as being shaped like the keel of a boat. This unusual shape develops when the natural seam between the bone plates of the forehead (the metopic suture) fuses early, giving the skull a triangular form (trigonocephaly). It is believed that the metopic suture usually joins in the first year of a baby's life but some babies with 9p deletions are born with it already fused. A more minor degree of early fusion may leave the forehead a normal shape but with a ridge running down the middle. If this affects your baby, he or she will be assessed by a craniofacial team and if necessary the bones of the forehead can be separated in a surgical procedure. Although this sounds alarming, quite a few children within *Unique* have been operated on with success (Alfi 1976; Shapiro 1977; Young 1983; Huret 1988; U).

■ Heart conditions

Heart defects or murmurs have been reported to occur in around half the babies born with 9p deletions and a sizeable minority of *Unique* members were born with one. The most common defects were holes between the lower chambers of the heart (ventricular septal defects, VSDs) or between the upper chambers (atrial septal defects, ASDs). However, in the great majority of children, these resolved naturally with time. Only one child in the *Unique* series needed heart surgery. She was born with a complex collection of problems: coarctation of the aorta (narrowing of the main vessel that takes blood from the heart around the body), a VSD and persistent ductus arteriosus (PDA), a carryover from the fetal circulation that allows blood to go to the lungs instead of around the body. After surgery at the age of eight weeks to close the PDA and widen the narrowing of

Some medical terms

Trigonocephaly

Triangular head shape when viewed from above, caused by premature fusion of metopic suture.

Metopic suture

The join between the two bones that form the forehead and front of the skull. It runs from the soft spot (anterior fontanelle) to the nose.

Craniosynostosis

Premature joining of bone plates of the skull.

Craniotomy

A surgical procedure to separate the bone plates in the skull.

Dolichocephaly

A long skull with a prominent forehead.

Plagiocephaly

The head shape is flattened at the back and longer from front to back on one side than the other, so it looks like a parallelogram when viewed from on top.

the aorta she has thrived. She has a 9p22 deletion (Huret 1988; U).

■ **Hernias**

Hernias have been reported to be more common in children with 9p deletions and *Unique's* experience is that hernias of the umbilicus or in the groin (inguinal) have occurred in over 20 per cent of children. Less commonly, a defect in the abdominal wall may allow part of the contents of the abdomen to bulge out. This is known as an omphalocele and affected one *Unique* child with an interstitial deletion between 9p22 and 9p24. Following two surgical repairs at birth and one year of age, she is thriving but still has abdominal weakness (Huret 1988; Shashi 1994; U).

■ **Genital area**

It is believed that one or more genes that play a role in sex differentiation are to be found very near the end of chromosome 9p in band 9p24.3. Losing these genes is believed to increase the possibility that sex differentiation will not be complete in boys and that development of the ovaries may be disrupted in girls. A very wide spectrum of effects has been observed and some children – in the *Unique* series, most - show no apparent effects. The most extreme effect would be that a baby with male chromosomes would appear to be a girl at birth or a baby would have ambiguous genitals. This has occurred twice in the *Unique* series of 40 and babies of both sexes have usually had only the minor symptoms that are fairly common in other chromosome disorders, such as hypospadias (where the hole usually at the end of the penis is on the underside), undescended testes or, in girls, underdeveloped labia at the opening to the vagina. One of the two girls in the *Unique* series with underdeveloped labia has an interstitial deletion from p22 to p24.

The kidneys and urinary system may also be occasionally involved. The anus may be unusually narrow and the vagina may be close to the anus, making toileting hygiene especially important to avoid introducing infection into the urinary tract (Alfi 1976; Young 1983; Bennett 1993; McDonald 1997; Ogata 1997; 2001; Veitia 1998; Livadas 2003; Fujimoto 2004; Ounap 2004; U).

■ Spine

A minority of children developed a spinal curvature, usually a sideways S-shape (scoliosis) but in one child the curve was forwards (kyphosis). The 61-year-old gentleman diagnosed with a 9p deletion also showed marked kyphosis. In the *Unique* series, no children had yet needed surgery, but they were regularly monitored by an orthopaedic team. One child with a 9p22 deletion was found to have tethered spinal cord, where the end of the spinal cord is attached instead of floating freely in spinal fluid (Nielsen 1977; Huret 1988; U).

■ Nasal passages and palate

A number of children had very narrow passages at the back of the nose and throat (a mild form of choanal atresia) and most had a high arch to the palate (roof of the mouth). Where the nasal passages are narrow, passing a nasogastric tube may be very difficult but if necessary the passages can be surgically widened. Once children are exposed to infections, they may have a particular difficulty with congestion. The high palate, occasionally cleft (divided), or with the flap of soft tissue at the back of the mouth (uvula) split or missing, can cause feeding problems. One family reported that food can get stuck on the palate and then come down the nose (Shashi 1994; U).

The following concerns were raised by families in the *Unique* series but are probably coincidental to the 9p deletion.

■ Tear ducts

Occasionally one or both tear ducts were blocked or missing, causing persistent watering (Funderburk 1979; Huret 1988; U).

■ Ear infections

Ear infections were common, as they are in many children including those with chromosome disorders, and children were at risk of developing glue ear, a form of temporary hearing loss caused by a build-up of fluid in the middle ear behind the ear drum. Long standing glue ear that interferes with hearing is treated by inserting grommets into the ear drum to equalise the air pressure within the middle ear and occasionally children have also needed hearing aids (Young 1983; Shashi 1994; U).

■ Teeth

There is some evidence that irregular dental development may occur, with teeth erupting early or late or coming through at unusual angles. There is no reason to believe that this occurs any more frequently than in children with other chromosome disorders. Two families, both with a child with a 9p22 deletion, reported that their child never developed a full set of adult teeth (Shapiro 1977; Funderburk 1979; Huret 1988; U).

■ Dribbling

Around half of families reported that their child dribbled (drooled) excessively. Most families managed this with simple measures, such as keeping a kerchief round their neck and smearing the skin around the mouth and chin with an emollient protective cream, but one child had his salivary glands reimplanted so that the saliva runs towards the back of the mouth.

■ Persistent chest or respiratory infections

The *Unique* series showed that some children were prone to developing chest and throat infections and persistent wheezing, especially as babies and very young children. When they caught an infection, children might often be more unwell than others without a chromosome disorder.

■ Eyes and vision

A variety of conditions affecting vision has been reported by families, including a squint (strabismus), long sight, nystagmus (rapid eye movements) and optic nerve hypoplasia (underdevelopment of the optic nerve).

Care needs

The care needs described by families were not specific to people with 9p deletions. Families reported that adult children needed help with fine motor actions such as getting dressed and often needed reminding of routine tasks as well as encouragement to speed up. Among teenagers, lack of danger awareness was a concern, as well as toileting and safety because of insecure gross motor skills. Families of younger children mentioned their lack of time-awareness and the need for constant supervision as their key care needs.

Experience with puberty

Losing the sex determining gene or genes from 9p24.3 may in turn affect the development of the testes in boys and the ovary in girls. If this is the case, the range of effect appears to be very broad, from normal fertility at one end of the scale to ambiguous genitalia at the other end.

There is very little information in the medical literature on puberty in children with apparently normal genital areas, but two girls are described as experiencing a normal puberty, starting at 11 and 12 years and precocious puberty has been described in an 8 year old boy with a breakpoint at p22.

Among *Unique's* membership, one boy with an interstitial deletion between 9p22-p23 developed the earliest signs of puberty at the age of 9. The chromosome material lost did not include the region believed to contain a sex determining gene.

Among the four *Unique* families with daughters who have described their experience with puberty, two girls started puberty early. One girl developed sexual hair and breasts at the age of 8 years. Another baby girl with a 9p23 deletion grew pubic hair at three months but following treatment to arrest her precocious puberty, she went on to experience a normal puberty at the age of 13. Two other girls with a 9p22 deletion and a 9p24 deletion went through a normal puberty starting at 11 and 12 years (Funderburk 1979; Ogata 2001; Ounap 2004; U).

Behaviour

Families generally described their children as affectionate and sociable and this was reflected in the medical literature. A sense of humour was often mentioned and children were described as seeking out both adult and other children's company. Children could want to be the centre of attention and become jealous

Families say ...

- “Ailbhe behaves very well. She has very occasional tantrums when she does not get her own way but these have lessened - adult.*
- “Charlotte gets very jealous of her sisters and wants everybody's full attention all the time. She is getting better now that she is older and wants to be treated as an adult and not a baby. Her behaviour changes daily, so I often improvise accordingly - age 9.*
- “Anna can be demanding. She collapses to the floor if she does not want to do something. She is mostly well behaved but when in the mood will bite and throw tantrums - age 6.*
- “Andrew likes being with other children and with adult support and happily joins in social activities. He particularly enjoys rough and tumble games. His awareness skills are not yet developed and he tends to wander off if not closely supervised. Andrew displays a good sense of humour. He smiles with pleasure, particularly when praised, and at people he recognises, and imitates other children. He also knows the kind of behaviour likely to attract adult attention and his temper tantrums can include throwing or breaking things - age 4.*

and apparently spiteful if they were not. When denied their own way, frustrated or required to do something they did not want, children could have fierce temper tantrums and when in a temper could be destructive. Many families also described a pattern of impatience and some described a need for a fixed routine.

Tantrums generally eased with age and increasing speech fluency, but many families have required professional help for their child's behaviour.

There have been two reports in the medical literature of people with Tourette syndrome, a neurological disorder which causes involuntary noises and muscular tics, although the association with a 9p deletion may be coincidental (Alfi 1976; Singh 1982; Huret 1988; Taylor 1991; U).

Sleep disorders?

The *Unique* series showed that a high proportion of children were poor sleepers, either taking a very long time to settle in the evening or needing only a very short sleep before waking apparently refreshed. Most families tried conventional behaviour management and controlled crying and a sizeable number tried prescribed medication including a sedating antihistamine and melatonin. Once children were able to entertain themselves, sleep management became easier, but the scale of the problem suggested that parents should anticipate it and set firm routines in place early in their baby's first year to prevent sleep difficulties from developing, where possible (U).

Adults with 9p deletions

There are many reports of adults with 9p deletions (see also page 4). A 33-year-old man has been described living in a group home and among *Unique's* membership, three people were working towards a measure of independence. Ailbhe, 27, has attended a day centre and worked at a crèche and in a delicatessen. She goes shopping with her mother and travels on public transport. She lives with her family.

Other *Unique* members in their 20s had attended vocational training courses (such as horticulture) and gained work experience (such as, at a garden centre) and were planning to live independently of their family (Nielsen 1977; U).

50 years old with Alfi's syndrome

This is a description of life at 50 for an adult with a 9p deletion, written by her keyworker.

- “ The quality of her life is very good. She lives in her own home with one housemate and has 24 hour support. In the past she had different jobs in the community, such as delivering meals on wheels and shredding papers. She lived with her family until she was 14 years old then went into institution. About 12 years ago she moved into her own home with support. She has many medical issues including her learning difficulties, anxiety, seizures, atherosclerosis, osteoporosis, hypertension, asthma, glaucoma, gastro-oesophageal reflux, chronic bronchitis, wasting syndrome (an unintended and progressive loss of weight) and multi-personality. In the last couple of years her psychiatric problems have been very well managed with medication.*
- “ Both of her parents have recently passed away. She had a very difficult time the first couple of months thinking they were going to come back but once she was able to understand and we supported her in her feelings of sadness and loss then she has done very well.*

Families say ...

- “ Expect him to do everything – deal with what happens.*
- “ It's wonderful to see the world as Daniel does.*
- “ Tom is very affectionate, has a sunny disposition and his happiness and enjoyment is infectious.*



26 years old, 9p22

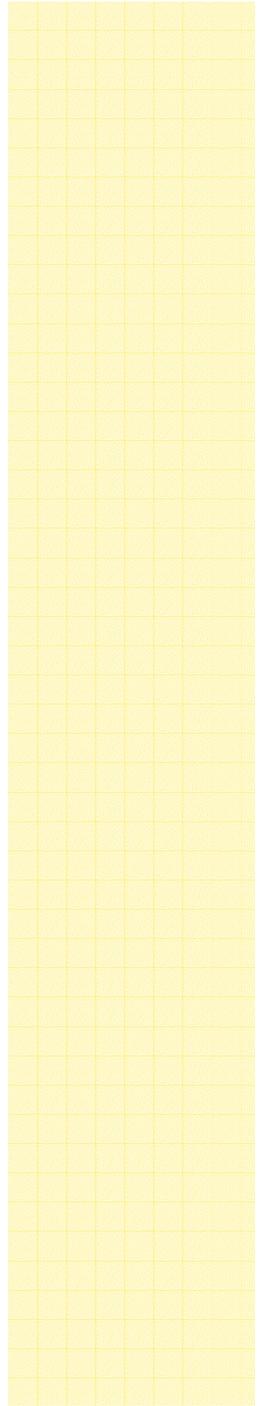
Causes

Changes to the structure of chromosomes such as 9p deletions occur most often during the cell divisions that lead to the creation of egg or sperm cells. Each arm of each of the 46 chromosomes first splits lengthwise into two strands that are held together at the centromere. The chromosomes then arrange themselves in 23 pairs, with pairs lying alongside each other, apart from the sex chromosomes X and Y which attach to each other at one end. Segments of DNA are then exchanged in a process known as crossing-over (recombination) and the chromosome strands are held together at the cross-over points (known as chiasmata). Deletions almost certainly arise during this process when the chromosomes line up incorrectly. An unequal cross-over means that a piece of chromosome can be looped out (interstitial deletion) or lost from the end of the chromosome that then heals over (terminal deletion).

These rearrangements occur in chromosomes as part of evolution and there is nothing you can do to stop them, just as there are no environmental, dietary or lifestyle factors known to cause them. They affect children from all parts of the world and from all types of background.

Chromosome disorders can occur as a result of rearrangements in one parent's own chromosomes or they can happen out of the blue, so the child with the chromosome disorder is the first person in the family with rearranged chromosomes. The only way to know if the disorder is inherited or not (when it is called *de novo*) is for the parents' chromosomes to be checked and the results explained by a geneticist or genetic counsellor. The rearranged chromosome may be the one that came from the mother or the one from the father (Micale 1995; Christ 1999).

When the check reveals a structural rearrangement of one parent's own chromosomes, it is usually balanced so that all the chromosome material is present, and the parent is then almost always entirely healthy. Occasionally the rearrangement will be apparently the same as in the child, and again the parent may be healthy.





Support and Information

**Rare Chromosome Disorder
Support Group,
PO Box 2189,
Caterham,
Surrey CR3 5GN,
UK**

**Tel/Fax: +44(0)1883 330766
info@rarechromo.org
www.rarechromo.org**

9p- Syndrome Network

www.9pminus.org

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

This information 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 the medical content has been verified by Dr Conny van Ravenswaaij, clinical geneticist and cytogeneticist, Dr Marielle Swinkels, University Medical Center, Nijmegen, Netherlands and *Unique's* chief medical advisor Professor Maj Hulten, Professor of Medical Genetics, University of Warwick 2005.

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