8p inverted duplication and deletion
Inverted duplication & deletion of 8p

Inverted duplication with deletion of 8p, known as inv dup del 8p, is a rare genetic condition in which there is an extra copy of part of the genetic material that makes up the body’s chromosomes and a missing copy of another part of the genetic material. Like most other chromosome disorders, this does increase the risk of birth defects and developmental delay but the outcome for each baby is quite individual.

The 46 chromosomes are the microscopically small structures in the nucleus of the body’s cells that carry genetic information. They are numbered in pairs from 1 to 22, running approximately from largest to smallest, with one member of each pair coming from the father and one from the mother, in addition to the sex chromosomes, X and Y for a boy and two Xs for a girl. Each chromosome has a short (p) arm, at the top in bright blue in the diagram below, and a long (q) arm. Chromosomes can be stained so that each has a distinctive pattern of light and dark bands when viewed at about 1000 times life size under a light microscope.

One normal chromosome 8 and one chromosome 8 with inv dup del 8p

Key to segments

- del(8)(p23.1->pter)
- single copy segment 8p23.1
- inv dup del(8p)
- dup(8)(p11.22->p23.1)
In people with an inv dup del 8p, one chromosome 8 is normal (n(8) in the diagram on page 2) but there is an extra copy (blue in the diagram) of part of the short arm of the other chromosome 8. This is termed a duplication (dup for short). In addition, the end of the short arm of the other chromosome 8 (red in the diagram) is missing. This is termed deletion (del for short). The extra duplicated part runs in the opposite direction to normal and is therefore termed inverted (inv for short). See how the bands in the top blue section on the inv dup del(8) are the mirror image of those below the yellow band. The duplicated blue segments are separated by most of band 8p23.1 which remains neither duplicated nor deleted (coloured yellow in the diagram).

The size of the duplicated (blue) section is not the same in all people with inv dup del 8p. In some it may be larger and in some smaller, depending on where the chromosome breaks to form the inv dup del 8 chromosome. The diagram illustrates a more common large form of the duplication with a breakpoint in band 8p11.22 (transition from black to blue as you move up the short arm in the diagram). In some people, however, the breakpoint is further up and the duplication correspondingly smaller.

In around half the people with inv dup del 8ps, only the extra duplicated material is reported and not the small deletion * (see facing page). This is because the duplication is larger and easier to see and many cases were reported before the small deletion was discovered. However, it is currently believed that the great majority of people with inverted duplications of 8p have the small deletion as well (Guo 1995).

The precise effects of gaining material from a chromosome vary depending on how large the duplication is, how many genes the duplication contains and what those genes do. The same principle applies to deletions. The effects may not be limited to the genes within a duplicated or deleted piece of chromosome because these genes may interact with other genes on the same chromosome or other chromosomes. In a child with inv dup del 8p, some children have brain anomalies as well as developmental delay with specific speech involvement and the large duplication is believed to cause this. Most, if not all, of the clinical features are caused by the duplication rather than the small deletion. We believe this because small deletions of the end of chromosome 8 have little if any effect when they are found on their own.

How rare is inv dup del 8p?

It is very rare, estimated to occur once in every 22,000 to 30,000 births. Around 50 children have been described in the medical literature (Floridia 1996; Giglio 2001; Masuda 2002).
Main features
Features do vary between individuals but these have been found to be the most common and the most likely to make a difference to a child’s health or development. Facial features that are often similar among babies and children with inv dup del 8p are described in the Appearance section (page 6).

- Developmental delay.
- Some degree of learning disability.
- Speech delay or absence.
- Weakness or floppiness of the skeletal muscles (hypotonia).
- Structural anomalies of the brain. Typically, this includes thinning or absence of the corpus callosum, a band of nerve fibres that connects the two sides of the brain. In some people the ventricles, the fluid-filled spaces within the brain, may be enlarged and the brain itself relatively small (see page 11).
- Heart conditions at birth. Some small problems resolve naturally; others are corrected with surgery.

Features that are not usually obvious at birth but may develop during childhood include:

- Spinal curvature.
- Contracted joints, making movement difficult.

Other features
Many other features have been noted in the medical literature. Some are known to be generally more common in children with chromosome disorders. Others may in fact be unconnected with the chromosome disorder. All the same, because they have occurred in other people with this chromosome disorder, you can expect your child’s paediatric specialists to be especially alert to them.

- High palate.
- Unusual dental development.
- Eye abnormalities such as strabismus (squint) and iris coloboma, a developmental defect of the coloured part of the eye that gives it a ‘keyhole’ appearance. Underdevelopment of the eye, cataracts and developmental defects of the retina have also been observed. Some babies have a hooded upper eyelid (ptosis) on one side or both.
- Anomalies of the arms, legs, hands or feet. A baby may have unusually angled feet, known as club foot (talipes). This can be corrected with therapy or surgery.
- Hernias in the groin or the umbilicus.
- Unusually positioned intestines.
- Anomalies of the kidneys, urinary system and bladder.
- Dislocated hips or hips that dislocate easily.
- Early fusion of bone plates of the skull.
- Precocious puberty.

First signs
Signs may first be detected in pregnancy during ultrasound scanning. However, there is usually no obvious growth delay during pregnancy. Only the most severely affected babies are likely to be noticed and those with less obvious effects will not necessarily be identified until after birth. One baby in the Unique series was observed to have spina bifida, where part of the spinal cord is exposed through a gap in the backbone.
Most frequently, babies in the Unique series were diagnosed when they missed their developmental milestones. No babies were diagnosed at birth with a congenital anomaly that had not been suspected during pregnancy, but one baby was diagnosed as a newborn after he had seizures and episodes where he stopped breathing. Three out of 16 babies were investigated because they had an unusual facial appearance (dysmorphic signs, see Appearance page 6) as well as developmental delay and hypotonia (de Die-Smulders 1995; Macmillin 2000; U).

Families say …
“ I am a nurse and worked with syndrome children when I was studying. When M was born, I thought he had a syndrome-like appearance: a big, square forehead, a big mouth, a short neck, rather big ears with strange earlobes and an incurved fifth finger. His belly was big and he had a banana-shaped body, and he felt so ‘soft’ to hold on to. None of this was significant and the doctors on the maternity ward claimed that he was completely normal even when I said I was worried about him.
“ Initially R was investigated because of delays in walking and speech. But as we look back, there were other signs, one being that she was born with a full extra thumb, which we later learned is part of her del/dup.

Pregnancy
Information on pregnancy in the medical literature is sparse, but it is said that most babies are born at term. In the Unique series, seven out of 18 mothers went into premature labour between 32 and 36 weeks. Three mothers reported high blood pressure or pre-eclampsia and three babies were delivered by emergency Caesarean section. One mother, who went into premature labour at 35 weeks, had pregnancy bleeding between six and 12 weeks. Another had a placental abruption, where the placenta detaches from the wall of the uterus. Two mothers noticed very little fetal movement and one had very little amniotic fluid (oligohydramnios). Eight pregnancies were described as normal and the baby was born at full term; one baby was induced 18 days after his due date (de Die-Smulders 1995; U).

Newborn babies
Seventeen Unique families described their newborn baby’s experiences. Most babies showed some signs of difficulty at birth. Three were unusually inactive. Four babies needed immediate ventilation to help them to breathe but only one needed long term oxygen support. He had an underdeveloped lung and had extra oxygen for 6-9 months. Typically, babies had an immature sucking reflex and had feeding difficulties or experienced episodes where they stopped breathing or their heart rate slowed (bradycardia) during feeds. One baby experienced neonatal fits and was sedated but by
the age of five had had no further seizures. Two babies, neither born prematurely, required phototherapy for severe jaundice. One family commented that meconium first appeared when their baby was a week old (de Die-Smulders 1995; U).

Families say …
“T was very placid as a baby, rarely cried and after initial difficulties with breastfeeding fed well.
“K’s head shape was very asymmetrical and he was blue. He was to keep a blue-grey skin colour for the first three months of his life.

Appearance
Typical facial features include a high, rounded forehead, a round or square face, an upturned nose, a somewhat ‘pouting’ lower lip, a small lower jaw and large ears with an unusual shape. Some children have skinfolds across the inner corner of the eye (epicanthic folds). Some children also have dry, curly hair that appears to recede from the temples. Some of these typical facial features may not be obvious at birth but develop during the first year of life. Among adults they become less pronounced. Children typically also have a short neck, a long upper body and slender arms and legs, with long, tapering fingers (Barber 1994; de Die-Smulders 1995; U).

Families say …
“C had excess skin on his neck at birth, slightly large, low-set ears, brown curly hair and big blue beautiful round eyes.

Growth
Most babies are said to have a normal or slightly low birth weight. There is no evidence of growth delay before birth, but typically, babies are slender for their length at birth and feeding difficulties in the early months can lead to a slowing of weight gain relative to length. Birth weights at term in the Unique series ranged between 4lb 6oz (1984g) and 9lb 11oz (4082g) but growth rates were slow for most children in the first year of life. Children may be slightly short but typically they appear to grow into adults of average or tall stature (Taylor 1977; Mitchell 1994; de Die-Smulders 1995; Masuda 2002; U).

Families say …
“At birth G’s head circumference was on the 90th centile curve on the growth chart, his length on the 75th and his weight in the low normal range between the 25th and 50th centiles. By 11 months, his head circumference was on the 50th centile, his length was between the 25th and 50th centiles and his weight was below the 5th centile.

Food and eating
Early feeding difficulties were universal in the Unique series. Although the difficulties in a few baby: mother pairs were mild, they were a consistent marker of the need for early, skilled specialist infant feeding support. Many mothers attempted breastfeeding but usually their baby could not latch on, was too sleepy, tired quickly, had no sucking reflex or was not yet able to co-ordinate sucking, swallowing and breathing. Some mothers did succeed in breastfeeding, but weight gain tended to be disappointing. Four babies were fed at first through a naso-gastric tube passed through the nose into the
stomach and four children had a temporary period of being fed direct into the stomach through a gastrostomy tube.

Most babies fed from a bottle, although one baby with tongue-tie (where the tongue is attached to the floor of the mouth by a bridge of tissue) needed an adapted (Haberman) feeder. Choking, coughing and spluttering can make even bottle feeding a trying experience and typically children graduated late from a bottle to a cup with a soft spout, or a spoon using thickened liquids and might not achieve this until mid-childhood.

Four babies had noticeable reflux, where the valve between the stomach and the food pipe allows the stomach contents to be brought back. In some babies, the problem was severe enough to halt weight gain for many months. There are many simple measures to control reflux, including positioning semi-upright for feeds and using a cot with a raised head end, and your doctor can prescribe medication to help feeds stay down and counteract any effect of acidity on the food pipe. If this is not enough, a surgical operation called a fundoplication can improve the action of the valve.

Most children found chewing difficult and avoided hard and lumpy foods. Regardless of their age, many needed to have food pureed or mashed. Families should be offered occupational or speech therapy to address the problems but it is likely that the diet will remain mostly soft. One 16-year-old was able to finger-feed herself and use a spoon with support but still disliked chewing lumpy or hard foods.

Feeding for babies without a chromosome disorder is usually a pleasurable experience. For babies with early feeding difficulties, it can become stressful and some children who have overcome their difficulties with swallowing, reflux or chewing nonetheless become food-averse. Ask your GP, health visitor, speech therapist or paediatrician about specialist feeding clinics to help with the ‘can eat, won’t eat’ scenario that can then develop.

Constipation is a common problem in children with chromosome disorders, exacerbated by children’s relative inactivity and their small food and fluid intake. There was no evidence of underlying abnormalities of the bowel but most children in the Unique series regularly took medication to soften faeces and stimulate bowel action.

Families say …

“I had lots of milk and M drank what came out but could not suck hard enough to keep the flow up. I was in deep stress, and eventually my milk disappeared so I started to feed him with a bottle and spoon 12-14 times a day when he was 8-9 days old. Feeding him became a full time job.”

“I was slow to learn to breastfeed but after a fortnight he fed very well and has done so ever since. He will still not take hard foods by choice – age 7.”

“When G was two, he had a gastrostomy tube put in. We would feed him throughout the night and at intervals (bolus) during the day. Now he drinks enriched formula from a sippy cup with a valve so it doesn’t spill or come out too fast. He can eat pureed baby-type foods, and apple sauce and yogurt right out of the refrigerator. We use his gastrostomy tube for water, prune juice and any medications – age 7.”

“When K was very small she had really had colic. When she stopped screaming, in the moments when she was calming down, her arms would twitch. Once she was calm
this would stop, but it could happen several times an evening. We went for an EEG but she would not sleep and they could not get a reading. By the time we saw the doctor again she seemed to have grown out of whatever it was and so this was never pursued.

**Learning**

Children with inv dup del 8p will typically need support with their learning and in some cases may need considerable support. There are children who have a mild learning disability, but they seem to be unusual. Most children do best with special education, either within a unit in a mainstream school or in a special school, but a small minority of Unique families had a child in a mainstream class.

Early intervention was important to improve responsiveness and alertness, and consistency and regular daily or weekly practice was needed so that skills were retained.

Families reported similar strengths in their children: their sociability, sense of humour and curiosity and determination helped them to learn. As a group they were more interested in interacting with people than with objects. Some children were musical and especially good at singing, so that music therapy was helpful. One severely affected child sang in a choir (Nevin 1990; Yenamendra 1999; Masuda 2002; U).

Families and schools say …

"Measured against a developmental chart, L’s development would be between 12 and 14 months. Yet she has a wonderful sense of humour, loves her family and friends, is sociable, loves music, reading books, multi-sensory activities, cooking and painting. She can be very determined and both fun and pleasure help her to learn. She enjoys positive praise and shows a good sense of achievement when she does something new – age 16.

"G is a happy first grader who attends a typical first grade classroom for morning calendar. He continues to be an observer but is beginning to recognise children from the classroom and will participate in activities with 1:1 assistance and modifications. He enjoys his time on the computer and will pull up to it to play one of his favourite games. He loves the playground and explores the area both in his wheelchair and out. He responds to people who say ‘Hello’ by smiling, snapping his fingers and sometimes saying ‘Hi’. G laughs a lot and loves music and animal sounds – age 7.

"T is severely delayed in all areas but she is also very sweet natured, placid, loves walking with support, the pool, swinging, watching TV, being talked and sung to. Her strengths are that she is very healthy, beautiful and sweet – age 4.

"K appears to thoroughly enjoy music therapy and responds very well to this. In her sessions she becomes animated, vocalises and will reach for and bang the guitar and tambourine - age 2.

**Communication and speech**

Speech and language are specifically delayed in children with inv dup del 8p but communication is typically good. Understanding is also limited and children need time to process incoming information and compose their response. Children draw on a rich
variety of other means of communication, such as pointing with their eyes, gestures, facial expression, signing, pictures and vocal noises, and often do well with communication devices. In many children, some words do emerge but typically they do not develop into phrases or fluent speech. Children with inv dup del 8p therefore present a paradox of being typically highly communicative but non-verbal. Many families commented that their child learned through nursery rhymes and at the age of 11, one child in the Unique series could hum more than 50 tunes, but had almost no words.

Families and therapists say …
“L understands very basic concepts of yes/no, stand up/sit down with gestures and given time – age 16.
“E has said the odd word over the years but then never repeats it – age 8.
“K has no speech but makes throaty sounds. He does not yet understand speech and does not respond to sign language but he has started touching his bowl of food when he wants more. Big progress for us! – age 7.
“G can say many words such as ‘cup’ when he is hungry. He can also tell you any sound that an animal makes. He says ‘Hello!’ all day! He is very slowly getting more words, learning mainly through singing, nursery rhymes and repetition. They are single words and occasionally two-word utterances, but used appropriately – age 7.
“T understands a lot, for instance what/ which/ who questions at the level of a 2 to 3-year-old, but he cannot express himself. His language and communication have progressed steadily, although he generally tends to have a spurt in the spring – age 5.
“I think T understands that we love her and sometimes I believe she shows her love for us – age 4.
“G said ‘dada’ at 10 months and ‘mama’ at 12 months and uses these words consistently and appropriately. She has used other words on one or more occasions but she will learn a skill, then lose it and come back to it at a later date, and maintain it the second or third time it is learnt – age 3.
“K recognises four words - her name, clap, ball, and her big sister’s name. K will turn her head to her own name and has just this week been able to respond to a request to clap, which I am really over the moon about. Kyra responds well to physical prompts alongside verbal ones and is starting to make better eye contact. She loves to watch other children and has started vocalising – age 20 months.

Activity and mobility
Children are usually late to reach the milestones of holding their head up and sitting. With support, most children have walked short distances in early to mid childhood, although they often needed splints or support boots and used a walker, relying on a wheelchair outdoors and later on as adults. Typically, children had a poor sense of balance and their upper body control stopped them from crawling. Their muscle tone tended to fluctuate and they found it difficult to maintain either unsupported sitting or standing for a long time.

The Unique series showed that children rolled between 5-7 months and 2 years; sat between 9 months and 3 years; shuffled or crawled between 18 months and 3 years 6
months; often preferred to bum shuffle or roll and never crawled; walked, usually with support, between 16 months and 5 years. Underlying the limited mobility is a mixed picture of weakness and floppiness (hypotonia) and excessive tautness of the skeletal muscles. Hypotonia seems to particularly affect the upper body from the waist in children with inv dup del 8p, causing difficulties with trunk and abdominal stability. Hypotonia improves by late childhood but does not usually disappear.

Children may also develop progressively increased tone in the legs and tightly contracted joints over time and need regular physiotherapy and passive stretching to keep as flexible as possible. Some children have tight heel cords and hamstrings and need a minor surgical operation to release them. However, experience with adults does suggest that the problem may persist despite surgery (Gorinati 1991; Barber 1994; de Die-Smulders 1995; Masuda 2002; U).

The Unique sample showed a wide range of eventual mobility skills. Among the more mobile, a 16-year-old was able to walk confidently on flat surfaces; a 6-year-old was able to climb stairs with adult help but not to climb down. Among the less mobile, a boy who walked with support at five years was able to move by rolling or shuffling and come downstairs by bumping on his bottom at 11 years. He would only walk when highly motivated – to stroke an animal or get into the bath. A seven-year-old boy was unable to move except by rolling from stomach to back.

Families and therapists say …

“M gets tired when he sits up and must lie down to rest. If he is unable to get to the floor, he will sometimes just rest his head on his lap (bad for his kyphosis, spinal curve) – age 11.

“R had a little low muscle tone, but once she started walking at 16 months, the rest came okay – age 4.

Hand use - fine motor skills

The Unique experience showed that most children, although not all, had delayed hand control. One two-year-old had fine motor development in line with her actual age. Most children had a full range of passive movement in their hands (their joints moved if someone else bent and straightened them) and some showed unusual flexibility of the finger joints. Their arms and hands typically had low tone and for some, splints were helpful for daily activities such as feeding. At the age of 16, one girl could grip and squeeze with her palm but had no tripod grip between her forefinger and her thumb. She used her hands to feel and touch or the flat of her hand to activate objects by slapping movements. Other children showed a reluctance to use their hands or a preference for a pincer grip and one child had extreme sensitivity of the palms. The typical delay in fine motor skills meant that children needed to have their bottle held and to be fed for longer than expected.
Medical concerns

Brain
Current evidence suggests that eight out of 10 babies with duplication of 8p will be born with an underdeveloped or missing corpus callosum (ACC). On its own, this anomaly may not be significant but in a child with inv dup del 8p it may add to the learning difficulties. A magnetic resonance imaging (MRI) scan may also show that the ventricles inside the brain are large, while the head size is average, suggesting that there is less room taken up by brain tissues. Other structural problems have occasionally been found in children with inv dup del 8p, including a cystic enlargement of the cerebellum (the hindbrain) and underdevelopment of this area at the back and base of the brain. Generally speaking, these anomalies do increase the possibilities of learning difficulties and problems with movement and balance, but they should be individually interpreted by a paediatric neurologist.

A minority of children may develop hydrocephalus (an increase in cerebrospinal fluid within the brain) which can be treated if necessary with a shunt to drain the fluid (de Die-Smulders 1995; Tonk 2001; Masuda 2002; U).

Heart
Some babies with an inv dup del 8p will be found at birth to have a heart defect. Typically, this involves one or more holes between the upper and lower sides of the heart (atrial septal defects, ASDs; ventricular septal defects, VSDs) with a narrowing of the artery and valve that takes the blood to the lungs (pulmonary stenosis). These defects can form part of a more complex heart anomaly called Tetralogy of Fallot. Small ASDs and VSDs may be allowed to close naturally with time, while more severe or complex heart conditions can be corrected surgically. A further heart anomaly that has been found in one or two children with inv dup del 8p is dextrocardia, where the heart is in a mirror image of its normal position. In itself, this usually poses no risk to health. It may occur in combination with situs inversus, where the appendix and liver lie to the left of the abdomen and the stomach lies to the right (Guo 1995; Kostiner 2002; Masuda 2002; U).

Spine
Spinal curvature has been reported in four out of 10 people with inv dup del 8p, but in Unique’s experience it may occur more commonly, affecting around three quarters of children, regardless of age. The curve is either a sideways S-shape (scoliosis) or a forwards hump (kyphosis) and appears to be exacerbated by muscle weakness. All children are monitored carefully for curvature, but only three out of 20 children in the Unique series have needed treatment. One child has worn a brace to correct the curve, another has a specially adapted wheelchair and a third has had a spinal fusion to hold the back straight (Feldman 1993; de Die-Smulders 1995; U).

Joints
The medical literature describes a marked tendency for children to develop progressive hypertonia (increased muscle tone) in the legs which, if untreated, can
lead to contracted joints. This is an important reason for encouraging children to be as mobile as possible and for stimulating passive movement by stretching and physiotherapy. Among Unique’s members, the contractions have been noted from babyhood and one family noted that they developed from the feet upwards. More than half the children over seven have developed joint contractures in the legs and hips which limited normal activity and movement. Additionally, two children had surgery for hamstring and adductor release, with varying success (see below). Three children were described as having feet that were curved and angled inwards in a typical position for talipes equinovarus (club foot), which can also be corrected with surgery. The upper body appears to be unaffected by the increased tone and arm and shoulder joints remained unusually flexible (Hongell 1978; Jensen 1982; Fryns 1985; Klczkowska 1987; Barber 1994; de Die-Smulders 1995; U).

**Adductor release**

The adductor muscles are responsible for bringing the legs together. They attach to the inside of the pelvis and the upper thigh bone. If they are too tight your child will scissor when he stands so his legs cross over or his hip may come partly out of joint (sublux) or completely dislocate. In adductor release, the tendons that join the muscles to the pelvic bone are lengthened. After surgery children usually wear a cast for some weeks and a splint for around some months.

**Hamstring release**

The hamstring muscles connect the pelvis to the back of the knee. If these muscles become too tight a child will not be able to stand up straight. In surgery, the tendons between the pelvis and the back of the knee are lengthened or cut. After surgery, the child is usually in a cast for some weeks and after that splints at night and when resting for some months.

The conditions listed on pages 12-13 have been found to be common among Unique’s members, but are not necessarily part of inv dup del 8p (U).

**Urinary tract infections**

One child in four had frequent urinary tract infections and one child contracted E coli septicaemia from the infection. No families reported structural anomalies of the urinary system, but three children had a dilated kidney and required protective antibiotic treatment in early childhood. One of these children was also reported to have horseshoe kidneys (the kidneys are joined at their base) and an unusual (Christmas tree-shaped) bladder (Guo 1995; U).

**Genitals**

Fifty per cent of boys in the Unique series had a very minor genital anomaly, either undescended testicles that required surgical intervention or a hydrocele (accumulation of watery fluid in a sac around the testes) requiring drainage. Small genitals have also been described in the medical literature (Klczkowska 1987; U).

**Lungs and breathing**

Four children from ten families who reported breathing problems had episodes of apnoea (stopping breathing) that continued after the newborn period. All three children were medicated for this and had a monitor at home and while in one child the episodes ceased by the age of six months unless she was in pain, they continued through
childhood for two other children. The rate of upper respiratory tract infections and chest infections was no higher than in other children with chromosome disorders and no children appeared to have permanent lung damage or defects.

Families say …

“He still has episodes where he holds his breath for a long time and then he will hyperventilate for a few minutes. We don’t know why he does this – age 11.”

- **Hernias**
  Hernias were found in three children, affecting the groin and the umbilicus. They have also been noted in the medical literature. If necessary, hernias can be corrected with surgery (Kleczkowska 1987; U).

- **Seizures**
  Seven families (one in three) reported a seizure disorder, although there was no consistent pattern. Three babies had neonatal seizures but outgrew them by the age of six months; the other children developed seizures in childhood and had not outgrown them. All seizures were reasonably controlled with medication.

- **Hands**
  Small hands with tapering fingers and extremely flexible joints appear to be typical of inv dup del 8p. Features that occurred in the Unique families and may be typical of 8p duplication are deep lines on the palms (and on the soles of the feet) and an extra thumb, which was removed in an outpatient hospital procedure.

- **Teeth**
  Dental problems are common in children with chromosome disorders. Two researchers noted missing or very small teeth in the upper jaw in children with inv dup del 8p and in the Unique series, while no structural defects were found, dental work was one of the commonest reasons for hospital admission (Gorinati 1991; Mitchell 1994; U).

- **Hearing**
  Hearing problems are not a part of inv dup del 8p, although two children in the medical literature have had a permanent hearing loss. In the Unique series, four families out of 10 reported frequent ear infections, glue ear and tube insertion to aerate the middle ear but only one child had a permanent hearing loss and wore a hearing aid (Guo 1995; Masuda 2002; U).

- **Eyes and eyesight**
  Vision problems were reported by seven families (one in three), the most common being a squint (strabismus) and errors of refraction (short or long sight). Other problems have been noted in the medical literature, including microphthalmia (the eye is abnormally small), cataracts, and developmental defects of both the retina at the back of the eye and the iris (Guo 1995; U).
Therapies
Most children need regular physiotherapy from the early months to maintain lower limb flexibility and mobility as well as speech therapy to help with feeding and communication skills and with assisted communication. Occupational therapy is also necessary to develop hand use and co-ordination. Other therapies that families have found helpful are music therapy to stimulate speech and learning, aromatherapy to improve passive extension of hands and feet, active learning therapies to stimulate children's curiosity and encourage them to learn, sensory integration therapy, hippotherapy and aquatics to increase mobility. One family has tried dolphin therapy.

Puberty
The experience of only one young woman is known and puberty proceeded normally (U).

Behaviour
The personality of children with inv dup del 8p is reported to be one of their strengths. Families consistently described a happy, upbeat outlook and strong sociability. Families of some children have noticed a risk of over stimulation when their child can become hard to manage. In a social situation, children may sometimes grab unpredictably at people or objects within their reach. Tantrums were common in younger children, usually born of frustration or of having their wishes thwarted. Some families remarked on a strong oral tendency, with children sucking fingers or biting for much longer than other children.

Against this sunny background, Unique had one report of an adult with a marked behaviour difficulty. She was prone to depression and had occasional bouts of violence and unpleasant language. This was largely controlled with tranquillisers (U).

Families say …
"E has a lovely personality and aura about her – age 1.
"G listens intently to everything we say and laughs with us, even if she does not understand. To see her smile becomes an addiction, to hear her laugh becomes contagious. We can’t get enough of her smiles and laughs. She gives great cuddles and kisses. The way she dances with her head and hands is amazing – age 3.
"T is very content and sociable and only becomes frustrated when he can’t do something or when I stop doing something he wants me to continue with, such as playing boo – age 5.
"K gets over stimulated very quickly by sounds, movements, lots of people and then becomes very difficult to control. We have to hold him very tight during these outbursts. Sensory integration therapy is helping with this – age 7.
"L slaps people she loves a lot in affection and bites her hand in excitement. Remodelling her behaviour, tapping her legs or giving her something to hold helps – age 16.
Can a child ever live independently?
This is a difficult question that can be better answered as time passes. The evidence from *Unique* and the medical literature suggests that the great majority of people with inv dup del 8p will need considerable support throughout their lives and only a limited measure of independence will be possible. Continence is the exception rather than the rule and feeding remains supervised even among the oldest children. Even the oldest people in our membership have needed full 1:1 support.

Causes of inv dup del 8p
Changes to the structure of chromosomes such as inv dup del 8p occur most often during the cell divisions that lead to the creation of eggs or sperm. 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 crossing points (known as chiasmata).

The chromosome pairs ‘recognise’ each because they are similar. However, where the DNA of the chromosome is repeated at close intervals, the repeat may pair with its partner on the same chromosome instead of the repeat on the other chromosome. On 8p, the DNA is repeated in this way in the form of two clusters of olfactory receptor genes (genes for perceiving smell). These are believed to underlie both the rare inv dup del 8p and an extremely common inversion of 8p in the general population. One in four to one in five people are believed to have this common inversion which involves the same 8p23.1 segment (coloured yellow in the diagram, right) that remains neither duplicated nor deleted in people with inv dup del. This does not affect their health or development and there is no reason why they should know about it unless they have a baby with a chromosome disorder. However, this inversion has been so far been found in all of the small number of mothers of inv dup del children tested for it. It is therefore believed that when a mother with this inversion makes eggs, the inversion leads, on rare occasions, to repeats on the same chromosome pairing with each other and the formation of an inv dup del 8 chromosome after crossing over between the mispaired olfactory repeat sequences.

The presence of this common inversion can be shown by chromosome tests on the parents and means that in theory if you have had a child with inv dup del 8p you could be at risk of having another. However, this has never been known to occur, almost certainly because the sequence of events that leads to the rearranged chromosome is extremely rare, even if the harmless inversion on the mother’s chromosome 8 is common (Floridia 1996; Giglio 2001; Kostiner 2002; Shimokawa 2004).
This information guide is not a substitute for personal medical advice. Families should consult a medically qualified clinician in all matters relating to genetic diagnosis, management and health. Information on genetic changes is a very fast-moving field and while the information in this guide is believed to be the best available at the time of publication, some facts may later change. Unique does its best to keep abreast of changing information and to review its published guides as needed. The guide was compiled by Unique and reviewed by Dr John Barber, Wessex Clinical Genetics Service and by Professor Maj Hultén, BSc, PhD, MD, FRCPath, Professor of Medical Genetics, University of Warwick, 2009.

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