4p duplications
Sources
The information in this leaflet comes from the medical literature and from Unique's 38 members with 4p duplications, 15 of them with a simple duplication of 4p that did not involve any other chromosome, who were surveyed in 2004/5. Unique is extremely 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.

4p duplications
A 4p duplication is a rare chromosome disorder in which some of the material in one of the body’s 46 chromosomes is duplicated. Like most other chromosome disorders, this is associated to a variable extent with birth defects, developmental delay and learning difficulties.

Chromosomes come in different sizes, each with a short (p) and a long (q) arm. 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. We have two copies of each of the chromosomes (23 pairs), one inherited from our father and one inherited from our mother. People with a chromosome 4p duplication have a repeat of some of the material on the short arm of one of their chromosomes 4. The other chromosome 4 is the usual size. 4p duplications are sometimes also called Trisomy 4p.

This leaflet explains some of the features that are the same or similar between people with a duplication of 4p. People with different breakpoints have different features, but those with a duplication that covers at least two thirds of the uppermost part of the short arm share certain core features.

When chromosomes are examined, they are stained with a dye that gives a characteristic pattern of dark and light bands. The bands are numbered on each arm from the centromere (the pinched point between the arms on the diagram below) to the tip, known as the telomere. You can see the numbering pattern for chromosome 4p on page 4.
Main features
People with apparently exactly the same chromosome rearrangement can vary widely, even within the same family. This is because of many factors - the unique mixture of their other genes, their environment, the exact breakpoint in the chromosome, any other breaks in the chromosomes and other factors that have not yet been fully explained. Every child is unique – but with a 4p duplication, the likelihood of showing one or more of these symptoms increases:

- Developmental delay.
- Speech delay or absence.
- Unusual genital features in boys, such as a very small penis, undescended testicles or hypospadias, where the hole in the penis is not at the end but on the underside. In girls there is usually nothing unusual about the genital area.
- A typical facial appearance, including a small head and a somewhat bulbous ‘boxer’ tip to the nose (see page 5).
- Slow growth as a baby, usually after being normal weight at birth.
- Joints may be contracted.
- Hand or foot anomalies.

Other features
These features have been noticed in quite a few babies or children. The paediatricians and developmental specialists looking after a child with a 4p duplication can be expected to check very carefully for these. Some features develop after the newborn period.

- Unusual muscle tone. In some babies tone is low and your baby will feel floppy to hold (hypotonia). Other babies feel stiff (hypertonia) or there may be a mix of tones.
- High arched palate (roof of the mouth).
- Spinal curvature.
- Gastrointestinal anomalies (the digestive system).
- Frequent respiratory problems.
- Seizures.

How rare are 4p duplications?
As isolated chromosome rearrangements, 4p duplications are very rare. They occur more often as part of an unbalanced chromosome rearrangement, usually involving loss of material from another chromosome. More than 85 people with a 4p duplication had been described in the medical literature by 2004. Unique’s members have a variety of breakpoints and we can put families in contact with each other if they wish.
Feeding difficulties in the newborn period.

- Very small eyes, sometimes with a developmental defect known as a coloboma. In the iris this looks like a keyhole.

The features in the list that follows have also been noticed in individual babies with 4p duplications. However, having any chromosome disorder makes it more likely that a baby will have birth defects. All of the features are also found in babies without chromosome disorders and may just be coincidental to the 4p duplication: rocker bottom feet with prominent heels (the sole is curved like a rocker); heart defects at birth; hernia in the groin (inguinal); structural anomalies of the brain; missing gallbladder; kidney defects; missing 12th ribs; unusually shaped or proportioned hands and feet, with clenched or curved fingers or with overlapping toes; blockage of the nasal passages (choanal atresia) (Bauknecht 1976; Dallapiccola 1977; Gonzalez 1977; Kleczkowska 1992; Lurie 1994; Petit 1994; Wyandt in Estabrooks 1995; Patel 1995; Mau 2000; Tschernigg 2002; Neas 2003; Gerard-Blanluet 2004; Zahed 2004).

Smaller duplications

People with smaller duplications of 4p may be more mildly affected. This is a list of cases from the medical literature and others known to unique, with their key symptoms.

- 4pter - p16 - behaviour difficulties, mild learning difficulties.
- 4pter - p16.3 - mild learning difficulties, tall stature.
- 4p16.3 - p16 - working semi-independently, moderate learning difficulties, delayed puberty.
- 4p16.3 - p16.1 - typical appearance for a 4p duplication, developmental delay, minor heart problem, hernia in the groin, mild ptosis (lowered upper eyelid).
- 4p16.3 - p15.3 - developmental delay, speech delay or absence.
- 4p16.3 - p15.3 - reads, writes, converses, excellent fine motor skills.
- 4p16.3 - p15.3 - significant developmental delay and learning disability, seizures.

A small duplication can occur with a deletion of the region in 4p16.1 that causes Wolf-Hirschhorn syndrome. The effects of the deletion can dominate the effects of the duplication. (Wyandt in Estabrooks 1995; Partington 1997; Zollino 1999; Cotter 2001; Tschernigg 2002; Gerard-Blanluet 2004; Takeno 2004; U).

Families say …

“Her speech was slow to develop, so we asked to see a paediatrician when she was 2½ years old. He had cleared her at a year old but asked for blood tests after noting her single palmar crease - duplication from 4p15.1.
First signs

A minority of families reported that their baby’s small head was noticed at the mid-pregnancy scan or that a later pause in growth in the third trimester of pregnancy alerted doctors. One family with a child with a duplication of the entire short arm reported that multiple small cysts were noticed in one lung at the anomaly scan.

Many babies with a 4p duplication have a recognisable facial appearance at birth. This includes features such as a small head, a prominent forehead, a prominent bone between the eyebrows (glabella), a ridge across the eyebrows, widely spaced eyes with a frequent squint (strabismus), large, low-set ears, a broad bridge to the nose and a bulbous tip, a small mouth, thin lips, a receding, pointed chin, chubby cheeks and often a low hairline. However, these features can be quite subtle and in Unique’s experience, babies diagnosed at birth were those who had evident anomalies, such as a blockage of the nasal passages (choanal atresia), a malformed ear and facial palsy. Most babies on whom Unique has detailed information needed medical or surgical attention at birth, but the diagnosis of a chromosome disorder was not made until later for half of them. Some babies failed to thrive and were excessively quiet, but a group of three children was diagnosed only at school age. There was no obvious relationship between the size of the duplication and health and physical problems (Wyandt HE in Estabrooks 1995; Gerard-Blanluet 2004; U).

Appearance

In addition to the facial features described in First signs children typically have a short neck and when their teeth come through they are frequently misaligned. It is reported that as children mature, their typically round face often lengthens but there has been no formal study and the evidence is mixed. There is a suggestion that some babies have extra hair growth and a minority of Unique families also reported this (Kleczkowska 1992; Frys 2000; Mau 2000; Takeno 2004; U).

Families say …

“Lots of hair growth on her legs and bottom and around her pubic places, in a very masculine pattern - adult.
**Pregnancy and birth**

Beyond recording that babies with 4p duplications are no more likely to be born prematurely or after their due date than other babies, the medical literature has little to say. With a 4p duplication, the rate of birth before 38 weeks is 14.5 per cent and the rate of birth after 42 weeks is 13.5 per cent. *Unique’s* records revealed no consistent patterns during pregnancy either. In two out of six pregnancies, everything was apparently normal; one family reported excess amniotic fluid (polyhydramnios) and fluid retention in the mother while the baby was very small. There was no obvious relationship between the size of the duplication and the likelihood of growth problems or anomalies during pregnancy (Patel 1995; U).

**What about growth?**

One typical pattern described in the medical literature is of normal birth weight, followed by slow growth in childhood and catch-up growth at puberty. A subset of babies, around a quarter of the total, have growth delay in the womb and are born weighing less than 2500g at 38 weeks. Adult height is highly variable. Researchers have also described an overgrowth syndrome associated with a duplication of genes at 4p16.3, with eventual tall and large build. Individual children may depart from this pattern and one adult has been described who is 4’ 3” (130cm) tall. In *Unique’s* experience, most children have been short and have grown into very short adults, some not reaching five foot (150cm), but one young man with a duplication at 4p16.3 reached 5’ 11” (180cm). A young man with a duplication of 4p15.2 - p12 had an unusually long body (Kleczkowska 1992; Patel 1995; Partington 1997; Fryns 2000; Kondoh 2003; U).

**Feeding - families say …**

“I succeeded in breastfeeding her though her nose bridge is flat, so she often struggled to breathe and suck and came up gasping for air. She still squashes food with her tongue rather than chewing it - duplication 4p15.1 - pter, now adult.

“She took the bottle well though she never breastfed. Once on solids, she was able to eat smooth solids but she found lumpy food difficult. Now she eats most foods cut small but seems to have weak chewing muscles and is prone to choking. She eats fast, often putting too much food into her mouth - duplication 4p13 - p12, now adult.

“Feeding was OK but he suffered from projectile vomiting from 3 to 10 months - duplication 4p16 - p16.3, now adult.

“As a newborn, he was fed through a naso-gastric tube. He eventually took thickened milk from a bottle but gagged and choked constantly. He still has pureed foods and is often reluctant to eat. He will not eat certain biscuits. I think this is more due to his autism and lack of understanding that other things are biscuits even though they look different. - duplication 4pter - p11, age 11.
**Fine motor skills**

The *Unique* series revealed wide individual differences, with some children developing certain fine motor skills at an appropriate age. In general, children were delayed in holding a bottle, using both hands together and manipulating toys and later in using a marker or pen. Specific difficulty in using both hands together persisted for some, so that catching a ball remained difficult.

Within this general picture, individuals achieved high levels of fine motor control, and at 13 one boy was described as competent with activities such as threading, using small objects like beads and writing and drawing with a pen. All older individuals became competent with a keyboard.

Unusual hand anatomy may contribute to any difficulties: a low-implanted thumb was reported by some families and long, tapering fingers by others.

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**Mobility and activity**

Without formal studies, the evidence on mobility and fine motor control, including handling objects, comes from case reports in the medical literature and from *Unique* families.

The recorded delay in achieving early milestones can be quite marked: sitting at 12 months and walking at 24 months in one case; lifting the head at 6 months, sitting at 2 years and walking at 6 years in another (Tschernigg 2002; Kondoh 2003).

The information from *Unique* confirms this pattern of marked, if variable, delay. Babies have mastered rolling between two and 11 months; sitting upright between nine and 19 months; crawling or bottom shuffling between eight and 20 months and walking between 18 months and five years. Walking alone was achieved between three and six years and children learned to climb stairs between two and six years.

Specific difficulties included persistently low muscle tone, although not usually so low that the child needed the support of splints or braces. Early walkers were described as unstable or clumsy and tending to bump into objects and fall down; they might find running difficult. As childhood advanced into adolescence, gait improved but typically remained unusually wide and adults might have persistent difficulty in walking for a sustained period or co-ordinating actions such as running, hopping or skipping.

Some children had very stiff joints, needing intensive physiotherapy and bracing to maintain mobility. In one case, a child required full mobility aids including a wheelchair, stairlift and bathchair.

Many children had birth defects that affected the feet. These included clubfoot, rocker bottom feet (the sole is curved outwards like the rocker on a chair) causing painful walking, crossed toes that required corrective surgery and severely contracted foot joints requiring multiple surgery, plaster and splinting.

Physiotherapy (physical therapy) was offered to children under five to improve muscle tone and joint flexibility and to encourage walking. Individuals needed further therapy in adolescence or as adults to reduce joint stiffness and pain.
Learning

Most children described in the medical literature have had some degree of learning disability, but in Unique’s experience and that of some researchers this can on occasion be mild, even when the duplication is large.

Most children would be described as having a moderate to severe disability but many will grow into adults who can function in society with support.

There has been no formal study of the learning skills of people with a 4p duplication, so accounts you can read in the box on the right reflect families’ experiences of their child’s ability and what helped them most to achieve their potential (Schwanitz 1973; Petit 1994; Patel 1995; Partington 1997; Takeno 2004; U).

Learning - families say …

“Becky was about 6 and we were in the Yorkshire Dales near a village called Little Beck which was burnt in large letters on a signpost. We couldn’t get her away! I then wrote my own books relevant to her. She adored trains, so ‘Thomas the Tank Engine and Friends’ were a great aid to learning. She has always learned best by repetition - it took me five years to teach her to tie her shoelaces! Until puberty, her level of learning difficulty was mild to moderate and her last recorded reading age was 8.3 years with comprehension at 8.6 years. Then she developed psychosis and her concentration went - duplication from 4p15.1.

“Jennifer learns best with 1:1 support. She has a good memory for past events and this can help her learning. She did read words and simple books with large print and was at her best at about 12 to 13 years. Her eyesight has now deteriorated to the point where she is registered blind and she has lost many skills and is no longer able to write her name - duplication from 4p13 – p12.

“Thomas learns best when he has a personal interest such as trains and when he is in a supportive environment. When he’s enjoying himself he learns much better. At 13, he reads and writes his name and address in a messy fashion and reads easy sentences. He will copy and trace over letters. His reading and writing has really only progressed recently but is still very immature, he finds it difficult - duplication from 4p16.3 - p15.

“James learns best with love and attention and by watching others. At 11, he is very determined and will concentrate on one particular thing - duplication of the entire short arm of 4.

Getting a statement

“She had a statement but it took until she was nine to get it, both her parents were teachers and she unquestionably had a chromosome disorder.
Talking

There have been no formal studies of the speech development of people with 4p duplications. Speech depends on many factors such as understanding, the ability to co-ordinate the actions of speech, gesture or signing and the need to communicate.

Speech therapy

Speech therapy was offered to all children in the Unique series and most families found it helpful. Tom had speech therapy as a baby to help with feeding and all the other children in the series had pre-school therapy to help develop their language. Jennifer had therapy at school age to help her form phrases and sentences and Becky had exercises to tone up her mouth and tongue muscles as her tongue was wide and floppy. Tom had three episodes of speech therapy, most recently private therapy at 11 years to improve his articulation. At the age of 5, Becky ‘began chatting and has never stopped’.

Talking - families say ...

“Becky spoke her first words at the age of 3 but only started speaking more than one word at 4 1/4 years. While on holiday in France she picked up a knife and said ‘Must be careful, end up in hospital’: her first sentence. Her progress was then slow and came in spurts and plateaus. She did have speech therapy and her understanding and comprehension have always been above her reading age.

“Today as an adult, she speaks and can also sign in a limited way because two girls who live with her have speech problems. She can even speak some French. She normally uses words in an appropriate way and has a very good command of vocabulary and when she is well can play on words and make jokes, although reality and unreality can get mixed up! Becky, at 27.

“Jennifer started out using sign language and then words from about 6 years. Today her speech is limited but she can speak slowly in sentences and can ask appropriate, if repetitive, questions. She has an amazing memory for names and events. Overall, she has severe semantic-pragmatic language difficulties and her understanding and use of verbal language are significantly affected - Jennifer, at 25.

“James uses words and sentences and although he cannot converse in a conventional manner, he is improving. Up to 7 years, he used short phrases and single words. Recently he learned to converse and at 22 years he is still learning to express himself better. It is difficult to say how much is understood, nothing too complex. He has progressed very slowly and never regressed - James, at 23.

“James pushes, pulls, gestures and makes vocal noises but uses no speech. I use sign language to him, he doesn’t use it himself. James knows certain things in a routine so if he wants something, he will push my hand there but if I have moved it, he doesn’t understand and will become agitated - James, at 11.

“Rose pushes, pulls and points. She understands very well and has progressed steadily but has now reached a plateau - Rose, at 3.
Medical concerns
Generally speaking, the risk of major birth defects does not appear to be significantly raised in children with 4p duplications. However, joint problems in particular can occur.

**Joints**
Joints can be stiff and contracted and fingers can be clenched. Hip dislocation has been seen, as has radioulnar synostosis, where the two bones that link the elbow with the wrist are fused, limiting certain twisting movements of the forearm.

The experience of Unique members is of unusual stiffness and inflexibility affecting particular joints, such as the knees, ankles and elbows, and limiting activities such as cutting toe nails. Some adults have unusual arm movement patterns, moving their wrists more than their elbows. One child was severely affected by joint limitation, but in most the effects were mild to moderate. One child also developed Perthes disease, a condition in which the head of the thigh bone softens and can deform, leading to stiffness and early arthritis.

Most children received physiotherapy and one adolescent received low level laser therapy, (LLLT), a non-invasive treatment for osteoarthritis and chronic joint pain whose effectiveness remains controversial (for more information on this therapy, you can consult Bandolier at www.jr2.ox.ac.uk/bandolier/band123/b123-5.html) (Kleczkowska 1992; Patel 1995; Schinzel 2001; U).

**Feet**
A minority of children are born with an unusually angled foot or feet, most typically club foot (talipes equinovarus, in which the foot points downwards and inwards) or rocker bottom feet (the sole of the foot is curved outwards so that it resembles the base of a rocking chair). The conditions can be improved or corrected with surgery.

**Respiratory problems**
Researchers have remarked that respiratory infections are common, affecting at least one quarter of children severely enough for them to need hospital treatment. Infections of the respiratory tract may be triggered in the first place by aspiration of food and stomach contents into the lungs and in one child they led to chronic inflammatory lung disease. Unique’s experience broadly supported these conclusions. Children developed respiratory infections at a greater rate than children without a chromosome disorder, but no typical pattern could be seen: bronchitis, asthma, croup and recurrent inflammation of the larynx causing intermittently obstructed airways were all seen (Bauknecht 1976; Patel 1995; Mau 2000; U).
Genital features
For boys, although not apparently for girls, there is an increased risk of being born with one or more unusual genital features. These are typically minor and can be corrected with straightforward surgery or may need no correction. The anomalies that have been seen include hypospadias, where the hole is on the underside of the penis, epispadias, where the hole is on the upper side, undescended testicles, where the testes that usually descend into the scrotum before birth remain high, and an unusually small penis (Schinzel 2001; U).

Seizures
Researchers have estimated that around one quarter of children with a 4p duplication are at risk of developing seizures. Unique’s experience confirmed this rate, with four out of 15 children affected. However, there was no clearly similar pattern of seizure disorder and in one family with two affected children, one experienced seizures, while the other had not developed them by the age of 19 (Patel 1995; U).

Spinal curvature (scoliosis)
Spinal curvature has been described in 38 per cent of people by researchers. The Unique experience confirmed this, but the degree of scoliosis was generally mild, with no children requiring more than monitoring and none needing either special seating, bracing or surgery (Patel 1995; U).

Irregular teeth
Dental irregularities are common in children with chromosome rearrangements and may be a particular feature for those with 4p duplications. Upper teeth have been described by researchers as protruding and overcrowded; the Unique series revealed overcrowding of both jaws in most children, a child with a central plug of bone that required surgery, bracing and a crown and another child with three front teeth (Kleczkowska 1992; U).

Other disorders
The risk of a child having other birth defects or developing other problems is not high, but a wide range of other conditions have occurred in people with 4p duplications. Some may be part of the 4p duplication, others may be coincidental. Percentages are taken from Patel 1995. These include: anomalies of the gastrointestinal tract - 30%; inguinal hernia (in the groin) - 15%; heart conditions at birth, including atrial septal defects (ASD, holes between the upper collecting chambers of the heart), persistent ductus arteriosus (persistent feature of fetal circulation), coarctation of the aorta (narrowing of the main blood vessel from the heart); cleft lip; branchial cyst (cyst that has arisen in the neck from embryonic remnants); Sprengel malformation (complex birth defect in which the shoulder blade (scapula) is deformed and displaced upwards); extra fingers or thumbs or low-implanted thumbs; hernia in the diaphragm that separates the contents of the abdomen from the contents of the chest; absent gallbladder; various brain...
malformations; absent or underdeveloped twelfth rib; diverticula (abnormal pouches) in the urinary system; choanal atresia (blockage or severe narrowing of passage from nostrils to the throat); hypothyroidism (U; full literature list).

- **Hearing**

Hearing loss is not common in people with 4p duplications apart from the fluctuating loss caused by glue ear as a result of repeated ear infections in early to middle childhood. This type of deafness, termed conductive hearing loss, occurs commonly in all children and particularly in those with a chromosome disorder. Treatment involves the insertion of grommets, although one family recorded that their daughter’s eardrums were unusually shaped so did not retain the grommets. Earwax, requiring regular syringing, remained a problem for her.

- **Vision**

While strabismus (squint) is common in children with 4p duplications and ptosis (lowered upper lid) also occurs, most have normal vision, although both long and short sight, sometimes severe, have been noted. Serious eye defects affect only a small number of people, estimated at around 15 per cent.

A review of eye defects in people with 4p duplications revealed as the most common anomalies microphthalmos (extremely small eye) and coloboma (a developmental defect that occurs when the cleft that forms to help the nourishment of the developing eye does not close properly), sometimes occurring in the same child. In two babies, one eye failed to form. The researchers suggested that overexpression of a gene or genes near the tip of the short arm of chromosome 4 is responsible for these structural eye defects.

At the time of writing this leaflet, **Unique** had one member with a duplication of 4p13 to p12 severely affected by coloboma. After being partially sighted during childhood, her vision deteriorated in her early twenties, when one retina detached and a cataract formed over the other eye. Although she retained some useful vision, she was registered blind by the age of 25. Another child with a duplication of the entire short arm of chromosome 4 was receiving teaching from a teacher for the visually impaired (Lurie 1994; Schinzel 2001; U).

- **Mental health**

In one **Unique** family the daughter developed psychotic behaviour at puberty. She has a duplication of most of the short arm of chromosome 4 from band 4p15.1 to the tip and a small deletion from the long arm from band 4q35. It is not known whether her mental health problems are connected with her chromosome disorder (U).
Behaviour

A pattern of good social adaptation has been described in a research review, although individual investigators have highlighted increasing aggression and unsociability with age against a background of mild learning difficulties in a father: daughter pair with a small duplication of the end of 4p from band 4p16.

*Unique’s* experience is that in young children there were generally few behaviour problems and parents described their pre-school children as well-mannered, happy, alert & responsive, if timid. A contrary position emerged from some parents who noted marked mood swings and by four years one child was diagnosed with autism. Another young child showed uncontrollable aggression in a pre-school environment.

Behaviour presented greater difficulties during later childhood for some, with attention-seeking behaviour and aggression causing concern. Some youngsters displayed obsessive behaviour and could self harm. As adults, a common feature was that individuals got on better with their carers than with their peers and believed themselves to be generally equable (Schinzel 2001; Garcia-Heras 2002; Takeno 2004; U).

Sleep

Most *Unique* families with a child with a 4p duplication experienced more sleep difficulties than you expect with a typical child. No clear pattern of sleep disorder emerged, but the problems identified by families included:

- Unable to sleep through the night before the age of 7. The family tried all usual remedies, including a sleep disorder clinic. They stripped his bedroom, leaving only a bed, fixed a stair gate across the doorway and ignored him when he was up and shouting.
- Unable to sleep when very anxious. The family used Bach flower remedies, calming oils and appropriate brain gym exercises to reduce anxiety levels.
- A light sleeper who often woke in the early hours. The family found putting her to bed later with a warm drink helped. Her sleep pattern was most disrupted by medication she took for her behaviour. Because of the side effects she stopped taking it after a few months and she now sleeps better.

**People say of themselves ...**

“I am usually very cheerful. I can wake up very grumpy and I think it’s because I feel tired and unwell. But mainly I am very cheerful. I get angry and can shout and become tense but now I try very hard to go straight to someone who can help me discuss it rationally.”

“I get angry when I feel people don’t respect me and my wishes or if I feel people deceive me.”

**Families say...**

“Usually a very calm, easy going personality.”

“He has certain obsessions and a short concentration span. People comment that he is very pleasant and likeable and he gets on with others if he feels very comfortable.”
Independence

*Unique members’ reports showed that while children had intensive care needs at first, by adulthood they could live away from home in a supported environment.*

One adult left school at 19 and followed an intensive programme in skills for independence at a special needs college. He later followed a course in hotel skills and a vocational qualification in food preparation and was working five days a week in a hotel kitchen. He shopped alone and got around without help. He lived in a flat with three others and a carer and house manager. In his spare time, he went to the gym, watched football, went to the pub, watched DVDs and cooked. He belonged to a gym club and a performing arts club. He would like a long term partner, he told *Unique.* ‘My last girl friend was very nice, placid, jolly and kind when I first met her. She changed suddenly and it was very annoying but in the end with some advice I sorted it out. I feel much more settled now.’

One adult was living in residential accommodation with 1:1 care. After leaving school, she attended a special needs course at college and went to a day centre for adults with autism and did outside activities with her carers. In part due to being registered blind, she was unable to work. One adult lived in a group home with five others since 21, where she was fairly independent, helping with communal tasks such as cooking, shopping and cleaning. There were 24-hour staff available. She visited her family in Spain once or twice a year and had a full and active social life of her own. She attended St John’s ambulance while at secondary school, followed the GCSE (school leaver’s qualification) course in drama and at the age of 20 took part in a Millennium Award recycling project. She worked there one day a week. She did a variety of preparatory courses for vocational qualifications, including independent living skills, computing, fashion and grooming, hair, nails and make-up. She got engaged on her 25th birthday and hoped to marry her partner, who also had special needs.
Causes
To answer the question ‘Why did this happen?’ a geneticist needs to know about the parents’ chromosomes. A straightforward blood test usually gives the answer and in most cases of 4p duplication, it will turn out that one parent has an unusual rearrangement of their own chromosomes. This is no-one’s fault and is not due to anything that anyone has done.

When it’s inherited
Two types of typical chromosome rearrangement in the parent are likely to give rise to a 4p duplication in a baby. The parents themselves are usually healthy and have developed normally because the correct amount of chromosome material is present.

A parent with a balanced translocation has chromosome material switched between different chromosomes. Usually two chromosomes are involved, but it can be more. Chromosome 22 is the other chromosome most often involved with a 4p duplication. If the switch has taken place between chromosome 4 and the short arms of chromosome 13, 14, 15, 21 or 22, the effects on the baby are most likely to just be due to the 4p duplication. In any other translocation, it is likely that there will be additional effects caused by material lost from the other chromosome. A highly unusual situation is for the 4p material to be translocated onto a chromosome X. As one of the two X chromosomes in women is largely inactivated, this may silence the effects of the 4p duplication (Petit 1994).

A parent with a pericentric inversion has one chromosome 4 in which two breaks have occurred, one in the short arm and one in the long arm. The central length of the chromosome has turned 180 degrees and slotted back between the two broken ends. The baby will usually have effects from the duplication of the short arm and loss of material from the long arm.

Very occasionally, the duplication is inherited from a parent with exactly the same chromosome rearrangement. This has only been known to occur with short segments.

In all inherited cases, the risk of having another affected pregnancy is significantly increased. Families can discuss their individual situation with their genetics service.

When it’s not inherited
When the tests on the parents’ chromosomes show they are completely normal, the duplication has arisen as a chance event. Geneticists call this de novo, meaning that it is not inherited and the affected child is the first person in the family with the chromosome disorder. It is then extremely unlikely to happen again. All the same, there is a very distant possibility that in some people the duplication occurred during the formation of the cells that later give rise to the egg or sperm. This can result in a mixture of normal and abnormal egg or sperm cells (gonadal mosaicism or germline mosaicism), with a real chance of another affected pregnancy. However, the chances of this happening are very small indeed.
Inform Network Support

Rare Chromosome Disorder Support Group,
G1, The Stables, Station Rd West, Oxted, Surrey. RH8 9EE
Tel: +44(0)1883 723356
info@rarechromo.org | www.rarechromo.org

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Please help us to help you!

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 the genetic content has been verified by Dr Laila Zahed, American University of Beirut, Lebanon and by Professor Maj Hulten, Professor of Medical Genetics, University of Warwick, Unique’s chief medical advisor, 2005.
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