

4p 8p Translocation



Sources & References

The information in this guide is drawn from what is known about a small number of people with a 4p;8p translocation reported in the medical literature. The first-named author and publication date are given to allow you to look for articles on the internet in PubMed (www.ncbi.nlm.nih.gov/pubmed). There is a literature list on page 19. You can get articles marked **Free access** yourself. If you wish, you can obtain other articles from *Unique*. The guide also draws on *Unique*'s database. When this guide was written, *Unique* had 14 members with this 4p;8p translocation. Four have a chromosome 4 with a piece missing and extra chromosome 8; ten have a chromosome 8 with a piece missing and extra chromosome 4 (Stengel-Rutkowski 1984; Tranebjaerg 1984; Martsof 1987; Wheeler 1995; Kant 1997; Partington 1997; Wieczorek 2000; Tönnies 2001; Giglio 2002; Zollino 2004; Maas 2007; Hollox 2008; *Unique*).

4p;8p translocation

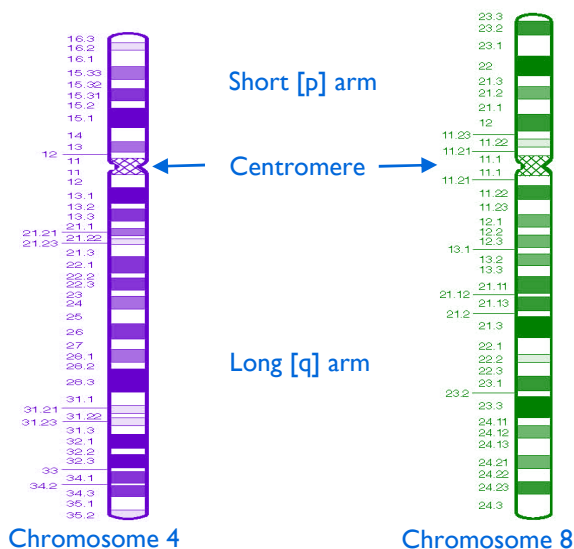
This is a guide to the most common 4p;8p translocation. The break in chromosome 8 is in the band known as 8p23.1. The break in chromosome 4 is in band 4p16.

What are chromosomes?

Our bodies are made of billions of cells. In each cell there is a set of structures called chromosomes. These chromosomes carry all the instructions [genes] for the cells to function. Genes are made up of the chemical called DNA. We generally have 23 pairs of chromosomes, so there are 46 chromosomes in a set. We inherit one chromosome from each pair from our father and one from our mother. Forty-four of the chromosomes are numbered from 1 to 22, approximately from the largest to the smallest, so chromosome 4 is a large chromosome and 8 is medium-sized. The other two chromosomes are the sex chromosomes that determine what sex we are, named XY for a male and XX for a female. Each chromosome has a short (p) arm and a long (q) arm.

Looking at chromosomes

You can't see chromosomes with the naked eye, but if you stain them and magnify them under a high-powered microscope, you can see that each one has a distinctive pattern of light and dark bands. You can see these bands in the diagrams of chromosomes 4 and 8 below. The bands are numbered outwards starting from the point in the chromosome where the short and long arms meet [the **centromere**]. A lower number such as p12 is close to the centromere. A higher number such as p16 or p23 is very close to the end of the chromosome, at the top in the diagrams.





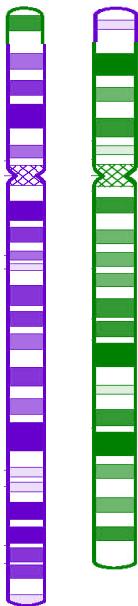
Increasingly, a technique known as chromosomal microarrays or array-CGH is used to examine chromosomes in much greater detail. Microarrays can show chromosome changes down to the numbers of 'base pairs'. These base pairs are chemicals in DNA that form the ends of each 'rung' of DNA's ladder-like structure. Each chromosome has many millions of base pairs.

bp = one base pair
kb = 1,000 base pairs
Mb = a million base pairs

What is a 4p;8p translocation?

In people with a 4p;8p translocation pieces of two chromosomes have changed places. Data from chromosomal microarrays show that in people with the 4p;8p translocation, chromosome 4 has broken in the 4p16 band. People whose chromosomes were examined directly under a microscope may have been told that the break was in 4p15 but this is probably just due to resolution differences between the two techniques.

A 4p;8p translocation can be **balanced** or **unbalanced**.



In a **balanced 4p;8p translocation**, the top bit of the short arm of one chromosome 4 has transferred to chromosome 8 and the top bit of the short arm of one chromosome 8 has moved to chromosome 4. There is no apparent loss or gain of chromosome material.

Someone with a balanced translocation [a **carrier**] usually has no health or developmental problems, although they may have difficulties when they want to have children. *Unique* has a general guide to

Balanced Translocations.

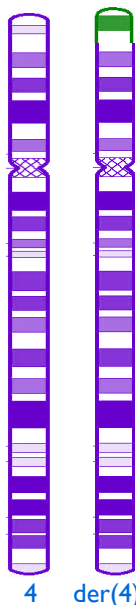
A balanced 4p;8p translocation. The top bit of chromosome 4 has moved to chromosome 8 and the top bit of chromosome 8 has moved to chromosome 4

The photographs in this guide show children with an unbalanced 4p;8p translocation with part of chromosome 8 missing and an extra bit of chromosome 4

In an **unbalanced 4p;8p translocation**, the amount of chromosome material present is incorrect and this can cause difficulties with development and health. There are two main types of unbalanced 4p;8p translocation. In the first, part of chromosome 4 is missing and there is an extra bit of chromosome 8 [pages 4-5]. In the second, part of chromosome 8 is missing and there is an extra bit of chromosome 4 [pages 6-15].

Unbalanced 4p;8p translocation

I: Part of chromosome 4 missing; an extra bit of chromosome 8



As well as one normal chromosome 4, your child has a chromosome 4 with the top bit missing, replaced by a bit of chromosome 8.

When your child is diagnosed, you will very likely be given their genetic test results in the form of a **karyotype**, a way of describing what chromosomes look like under a microscope. It is likely to read something like this:

46,XX or XY,der(4)t(4;8)(p16.1;p23.1)

46 = Total number of chromosomes in your cells
XX or XY = The two sex chromosomes, XX for females; XY for males
der(4) = One chromosome 4 is a 'derivative' chromosome. That means it has a change in its structure, in this case a piece missing, replaced by a piece of chromosome 8
t(4;8) = There is a translocation between chromosomes 4 and 8
(p16.1;p23.1) = The first translocated chromosome, ie chromosome 4, has broken in the p16.1 band. The second translocated chromosome, ie chromosome 8, has broken in band p23.1. You can see the numbering of these bands in the diagrams on page 2.

At the end of the karyotype, you may see one of these words:

mat = The translocation is a family one, inherited from the mother

pat = The translocation is a family one, inherited from the father

dn = The parents' chromosomes have been checked and no changes found involving chromosomes 4 and 8. The translocation is de novo (dn), very unlikely to be inherited, and it is very unlikely that another child will be born with this 4p;8p chromosome disorder.

What will the effects be?

When part of the end of the short arm of chromosome 4 is missing, including a length of DNA in band 4p16.3, Wolf Hirschhorn syndrome [WHS] results. When researchers have compared people with WHS caused by losing a bit of 4p16 with people with a 4;8 translocation form of WHS, some have found no obvious differences between the two groups while others have found a picture of 'atypical WHS'. So it seems that losing a bit of 4p counts more than gaining a bit of 8p.

The typical effects include some degree of difficulty with learning, low muscle tone [hypotonia], seizures or an unusual electrical pattern in the brain and being born very small or extremely small for dates.

Generally, most babies with a 4p deletion are born very small for dates and some are extremely small. But one or two of these babies are an appropriate size for dates. These newborn babies are typically quite unwell and have difficulty establishing and maintaining their breathing. Their Apgar scores [a measure of wellbeing at birth] are typically low. But this is not always the case. One baby in particular who was born a good weight had no problems at birth.

Feeding and sucking efficiently present these babies with real problems so they cannot maintain a good growth rate. Many are diagnosed with failure to thrive, which occurs when a baby cannot take in enough nourishment to grow properly. As children they are typically short or extremely short and adult heights range upwards from 128 cm [4' 2"]. However, one adult man was 165 cm [5' 5"] tall. Typical build is thin and frail and weights among adults range from 35 kg [5 stone 7lb] to 45 kg [7 stone], giving a weight: height ratio or body mass index in the 14.5 [very underweight] to 20 [healthy] range. Apart from the low muscle tone, one reason for the early feeding difficulties is that many babies have either a cleft palate [split in the roof of the mouth], a cleft lip, or both. Sometimes the hard, front part of the roof of the mouth is split, sometimes there is a split in the soft palate at the back of the mouth. A cleft palate makes feeding very difficult and most babies will need adapted feeders until the palate has been surgically repaired.

Wherever dental information is available, there is some dental anomaly. Typically babies are born with a proportionately very small head [microcephaly] and in a rare case where a baby was born with a normal sized head, it grew more slowly than the rest of the body so by the age of 18 months the head was very small.

Most babies have seizures and are diagnosed with epilepsy during childhood. Around half the babies have a heart problem, most typically a hole between the two upper collecting chambers of the heart [atrial septal defect/ASD], although other problems have been found including a hole between the two lower chambers [ventricular septal defect/VSD] and a narrowing of the artery that takes blood to the lungs [pulmonary stenosis]. Kidney problems are seen in some, one baby had a developmental anomaly of the intestines and an abnormal lung structure. Half the babies have poorly developed genitals, with boys having hypospadias, where the hole normally at the end of the penis is sited on the underside instead.

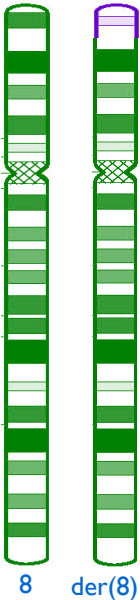
Half of the babies have a vision problem, most commonly a squint [crossed eyes/strabismus] or a developmental defect of one eye or both. Other vision defects include glaucoma [raised pressure within the eye] and one baby was born with complex eye problems leaving him effectively blind.

Developmental delay is marked, with babies reaching milestones such as sitting between 13 and 60 months and walking between 2.5 and 6.5 years. However, walking is not possible for all.

The range of learning difficulties is from mild to profound. Speech and language development ranges from one adult woman with only mild speech delay, who spoke her first words at the age of 2 and developed a rich vocabulary by the age of 24; as an adult, this woman was able to hold down a job. At the other end of the spectrum are others with no speech at all. [Stengel-Rutkowski 1984; Martsolf 1987; Wheeler 1995; Kant 1997; Partington 1997; Wiecezorek 2000; Tönnies 2001; Zollino 2004; *Unique*]

Unbalanced 4p;8p translocation

2: Part of chromosome 8 missing; an extra bit of chromosome 4



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der(8) = One chromosome 8 is a 'derivative' chromosome. That means it has a change in its structure, in this case a piece missing, replaced by a piece of chromosome 4

t(4;8) = There is a translocation between chromosomes 4 and 8

(p16;p23.1) = The first translocated chromosome, ie chromosome 4, has broken in the p16 band. The second translocated chromosome, ie chromosome 8, has broken in band p23.1. You can see the numbering of these bands in the diagrams on page 2.

At the end of the karyotype, you may see one of these words:

mat = The translocation is a family one, inherited from the mother

pat = The translocation is a family one, inherited from the father

dn = The parents' chromosomes have been checked and no changes found involving chromosomes 4 and 8. The translocation is very unlikely to be inherited and it is very unlikely that another child will be born with a 4p;8p chromosome disorder.

What will the effects be?

These pages tell you what is known about the effects of both losing the end of the short arm of chromosome 8 from the p23.1 band and having an extra piece of chromosome 4p from the p16 band. Four people have been reported in the medical literature and *Unique* has 10 affected members [Tranebjaerg 1984; Wheeler 1995; Partington 1997; *Unique*].

Need for extra support with learning

Among children with an 8p23 loss and 4p gain due to an unbalanced form of the most common 4p;8p translocation, the information we have suggests that the spectrum is quite broad but some children are likely to need a significant amount of learning support. Among six youngsters whose level of learning difficulty has been measured, two have an IQ between 50 and 65 [mild intellectual disability], two are moderately affected, one has moderate to severe difficulties and one has severe difficulties.

Typically, these children learn at the level of a child half their age. Children's learning is supported by a statement of need or an individual education plan and pre-school children generally qualify for early home-based intervention and special needs early

education. Many start their education in a mainstream [regular] school, usually shifting to a more supportive special needs environment for secondary school. Most children do learn to read, write and to operate a computer.

Families say that their children learn best with patience, repetition, and, obviously, when their interest is aroused. Some children respond positively to music, learning songs easily; others learn best with computer-based approaches. Other families counsel to try every therapy on offer [Partington 1997; *Unique*].

“ It is difficult to say at this age what her learning abilities will be but at present she is far behind other 2 year olds. She remembers people, places and things we teach her. Often it takes a lot of repetition over many, many weeks to teach her something though - 2 years

“ Some things he remembers really well, like doing things in a certain order; others, like going to the toilet, he forgets all the time. He also learns vocal things better than physical things and when he is in a good mood, not tired, hungry or unwell. He can now scribble and works well with pictures to back up words and actions and a picture timetable so he knows what is going to happen next. He has a 1:1 support teacher 100% of the time - 5½ years

“ She can draw but holds pencils awkwardly and scribbles but does not write. Her memory is OK, great at remembering music and songs. She loves books and being read to but can't read or use a keyboard yet. With 25 hours 1:1 support a week and following an adapted curriculum, she attends her very small local mainstream village primary school (only 19 kids) and is very happy there after a fight with the education authority to allow her education to be deferred by a year - 6½ years

“ He is very focused and more apt to pay attention and retain the information if he's interested in the subject, such as Thomas, trains, Batman, Kipper the dog and computers. He has a great memory for places, anything to do with trains, directions and people. But he can also get obsessive and stubborn. Reading is emerging. He is putting letters and words together, identifying the first and last letter in a word. He is very close to writing his first name with little assistance and likes to scribble. He loves hand-held devices and the computer for learning and games.

At school, he is in 1st grade in a Delayed Learning Program with five students, one teacher and two aides. In the afternoon he is in an Applied Behavioural Analysis-type classroom with 1:1 direct instruction. He goes to 'regular' education 1st grade for art, music, and specials and attends field trips with the 'typical' class as well.

Try it all! We have been doing PT, OT, speech and developmental therapy since he turned 2. He has been in hippotherapy with horses and water and massage/ cranial sacral-therapeutic touch has always had soothing and positive effects - 7 years

“ She is in 4th grade and with a high level of learning support can function academically as a first grade can, with the exception of number concepts. She does not understand any addition or subtraction problems at all, and has a hard time with one-to-one counting, even with physical objects such as sweets. She reads

first grade books, can write in capitals, is not a bad speller at all and can use a keyboard. She can learn a song or a dance much better than anything mathematical - 9½ years

“ At 4, he was functioning at the level of a 2-year-old but by the age of 8 was doing much better. He has just started to read and can write his own name and use a keyboard. He attends a special needs secondary school where there are three teaching assistants as well as the teacher in the class - 11½ years

Behaviour

Most families of children with an unbalanced 4p;8p translocation resulting in loss of 8p23 and gain of 4p16 describe their child as loving and helpful and many children are considered sociable, particularly with adults. Speech delays can make it harder to relate to other children. Around half of families describe their child as stubborn and having temper outbursts, usually when thwarted. Children commonly have difficulty in accepting changes of activity and some show some obsessive or compulsive features. Three children have autistic traits but none has a formal diagnosis of autism. Hyperactivity or ‘being constantly on the go’ is also fairly common. Aggression is reported by two of the eight families.

Families say that their child enjoys family pets, music, going out where other people are and above all books [2 years]; helping adults [5½ years]; playing with her rabbit; singing and dancing; watching musicals; pretend play; TV; ski-ing on the Wii; playing with other children at school [6½ years]; cartoons, TV, computers and hand held devices, music, the family dog [7 years]; playing with her friends, with dolls, her favourite books, playing on the computer, cooking [9½ years]; playing with the computer on the Wii [11½ years].



7 years

“ Very happy and very busy. She can be shy or overwhelmed in new situations. It is manageable though: I just make sure she is introduced slowly to new things. When she is comfortable enough to interact, she is friendly and playful - 2 years

“ He is very loving and loves kisses. He used to head butt, can still bite and does still lash out. Some of his behaviours are autistic-like: he lines his toys up and when he goes out he always has to take a small bag with the same toys in it. He has always needed to have the same soft toy in his mouth and also sucks his thumb - 5½ years

“ She has quite a temper due to frustration at not being able to do things or get her own way. She is very sociable, not shy but does not like crowds - 6½ years

“ He is kind and sweet and loving and has the best smile and laugh. He is a joyful person, makes us laugh and wakes up happy every day. He has taught us so much about the world and what is truly important: that one little boy can change how others view the world and that people with disabilities’ lives matter. He has brought so much simple pleasure to our lives and compassion for all children with difficulties. He is also very high energy! Up at 5am and always happy when he starts his day. He has to have his Batman with him or he gets obsessive and keeps asking for it. He can be stubborn and needs breaks at school or he has meltdowns. He definitely has some form of ADHD [attention deficit hyperactivity disorder] and OCD [obsessive compulsive disorder]. We tried Ritalin [methylphenidate] but he became lethargic and didn’t have the same cute little personality. Socially, he is very friendly and is a hugger and a kisser. At 7 this is becoming an issue. We are trying to transition to high fives. He loves other people but always goes back to parallel play. He tries to be social but past the greeting doesn’t know how to interact appropriately - 7 years

“ It is nearly impossible to get her to do something she doesn’t want to do, if she really digs her feet in about it. Consequences make no sense to her. She will sometimes simply decide she’s had enough and either we all leave, or she gets despondent and makes a huge scene. The other thing is that she likes to make awful noises with her vocal cords. Somehow it feels good to her, or she enjoys being impish. These are just the bad parts. She is a wonderful girl and every child acts up sometimes. She has plenty of typical friends and likes to play with them. She is wonderful company and she has a fantastic sense of humor. She is able to turn a bad situation into something at least a little bit funny. Never mind that she may have caused the problem to begin with. She is curious and cheerful, and very self-confident - 9½ years

“ Loving, kind and helpful. He is a hit with adults but some children get weary of him and he can be bad tempered and stubborn - 11½ years

Sleep

Sleep problems are common in young children, probably more common in young children with chromosome disorders and hard to manage. Half of the *Unique* families of children with an unbalanced 4p;8p translocation resulting in loss at 8p23 and gain at 4p16 reported a significant sleep problem, either trouble getting to sleep or frequent night wakings. Although hard to put into practice, sleep programmes designed for typical children are usually successful for children with special needs.

Pregnancy and Newborn

Among mothers carrying a baby with an unbalanced 4;8 translocation resulting in loss at 8p23 and gain at 4p16, one in three babies was born at term, while two thirds were born early, between 34 and 38 weeks. Reasons for the early delivery varied: one mother had a form of pre-eclampsia, one baby was delivered by emergency Caesarean section after her heart rate slowed and fetal movements lessened.

Four babies needed special care, two because they were premature, one because she was small and had difficulty breathing and one because she stopped breathing 45 minutes after birth. While these babies stayed in hospital for between one and six weeks, other babies left hospital as any typical newborn baby would [Tranebjaerg 1984; *Unique*].

“ Her birth was normal. She had a lot of black hair, which came all the way down over her face at birth. It grew in blonde immediately, so that she had blonde hair with black tips, for a while. She was a very floppy baby. I did not know that was hypotonia. She slept with her limbs splayed, unlike most newborns, who curl up.

Feeding

Of eight babies on whom we have any information, five had no initial feeding problems. Of the three babies who did have feeding problems as newborns, one was tube fed for a week after arriving prematurely but went on to breastfeed successfully. Five babies breastfed well, one for six months and two for a year, but one of them took expressed breast milk at first because she could not latch on properly to the breast without a nipple shield. Another drank slowly and brought some of her feeds back, but not problematically.

Babies moved on to solid and textured foods at the expected age of around six months but while some coped fine with lumpy foods and any textures, others gagged at lumps. Families report that their children generally have a good appetite today and eat a wide variety of foods. Two children tend to overeat; one can become obsessive about food and is somewhat overweight. The major problem at meal times is hand control and hand-mouth coordination, so typically they are very messy eaters, preferring to use their hands to utensils, although this is not always the case [Tranebjaerg 1984; *Unique*].

“ She is a very good eater today and eats almost anything including fruits, vegetables, cereal, bread even spicy foods, meat, fish and of course dessert. She has no problems with textures or chewing although she would prefer to not eat broccoli. She uses a sippy cup because she constantly throws her cup to the floor when she is finished drinking. She uses a baby fork, baby spoon and plastic dishes. She can use the fork and spoon pretty well with easier foods although sometimes she gives up and just digs in with her fingers - 2 years

“ He was breastfed for nearly 6 weeks, and then went on to bottles without problems. He wasn't keen on food he had to chew, such as meat. Today he eats nearly everything and has a good appetite - 5½ years

“ She was breastfed for 3 months, then bottle fed as she was not getting enough milk. Today she eats everything. A Breezi chair supporting her feet is most useful as swinging legs detract from concentration at mealtimes - 6½ years

“ He weighed 30 pounds [14 kilos] at one year and loved to eat. Today he is a good eater but has quite an appetite and overstuffs at times. He will figure out a way to get treats even in the high cupboards - 7 years

“ I did not know she had any problems until she was around 2. Then I started noticing some delays, including the fact that she had trouble feeding herself. Her hands couldn't really find her mouth very reliably. Today she will seek food any time she passes the kitchen and the thought occurs to her. She's a bit overweight - 9½ years

He has started to try different foods but still smells food before eating and if he doesn't like the smell, he doesn't eat it. He is encouraged to use a knife and fork but prefers to use his fingers - 11½ years

Growth

People with extra chromosome material from 4p16.3 may be liable to be unusually tall and that appears to be generally true for people with an unbalanced 4;8 translocation resulting in loss of 8p23 and gain of 4p16.

It has been suggested that the increase in height is explained by an extra dose of the *FGFR3* gene, which is found near the very tip of the short arm of chromosome 4 in the 4p16.3 band.

Information on growth in eight children with this unbalanced translocation shows a marked tendency to be tall. Babies were generally born the expected size and weight for dates; the only baby who was small-for-dates had a significant heart defect.

Six of the children are tall for their age, while two have an average height. Among the tall children, at least two are in the top 10 per cent of the population for height, ranging from 35 inches at 2 years to almost five foot at 9½ years. One child is a twin and much taller than his twin sister who has normal chromosomes. Body build is more variable: some children are tall and lean, others tall and of average or chubby build, others of average height and weight.

In a family described in the medical literature with two affected relatives, the increase in height became most obvious in late adolescence and early adult life.

Out of nine people for whom here is information on head size, six have a large head, in one it is of average size and two have an unusually small head. Five out of six people have unusually large feet and four out of seven unusually large or wide hands [Partington 1997; *Unique*].

Appearance

Most children with an unbalanced 4;8 translocation resulting in loss at 8p23 and gain at 4p16 look little different to other children and resemble other members of their family. They may have isolated unusual facial features but we cannot say yet whether these add up to a typical picture for this chromosome disorder. Among five detailed facial reports, the most common recurring features are a slight asymmetry in the face, widely spaced eyes, a small nose and a short neck.

“ She’s adorable!

Speech and communication

Evidence from *Unique* shows that these children communicate well as young babies, smiling responsively at around two months. They continue to communicate well, using a range of methods including vocal sounds and gestures but pre-speech babbling develops later than in typical babies, between one and two years, and children say their first words between 20 months and 2½ years. Learning to sign is helpful to children with speech delay and supports the development of speech in these children. Initially, vocabulary may be limited but gradually extends and children understand much more than they can express. Joining words and signs into 2 or 3-word phrases also develops late but most



1 year

children achieve this by the time they start school. There is variation in children's eventual level of fluency, but conversational speech can develop in children from the age of 7 or 8. Reports from families of older children, however, suggest that children can find maintaining conversation at normal speed stressful.

" She is limited in her vocabulary, both vocal and signs, so she uses the same sign for multiple meanings. For instance, the sign for 'bath' along with the sound 'ba' also means water and swimming and men in magazine underwear advertisements! The sign for 'eat' along with the sound 'eeh' means both eat or drink or snack or just seeing food on TV - 2 years

" He now speaks in 3-4 word sentences ['Mam juice please'; 'Thank you very much'] and sings songs with a repetitive lyric. Sometimes it seems he does not understand things, then a few days later he will do something that shows that he does - 5½ years

" He is talking more and more, in 3-5 word sentences, though they are halting at times and not fully flowing YET! For example, he doesn't say 'Mommy, can I have apple juice?' He says 'Mommy, juice' or 'Mommy, Batman please'. His understanding is emerging, understanding more and more 'wh' questions. He can tell you if asked: he's 7 years old; his address; his town; his school; his sister's name, mom and dad's names along with the dog and extended family members. He can also give you various answers: colours, the names of objects and miscellaneous household items - 7 years

" She has semi-fluent conversation but has a noticeable 'accent' because a lot of sounds are hard for her to pronounce correctly, quickly. It's hard for her to use all of them together at a normal rate of speed. As part of her processing delay, she also repeats herself frequently. She will say, for instance, 'Mom?' and then I'll say, 'Yes?' and she'll say 'Mom?' again, and we can go around many times before she kicks into the next part of the conversation. The other noticeable thing is that if she gets excited or scared of something, we hear about it over and over and over. The exact same words - 9½ years

" He communicates using a lot of gestures and now stutters as he can't get the words out when he tries to say a sentence - 11½ years

Development: sitting, moving, walking [gross motor skills]

Most children with an unbalanced 4;8 translocation resulting in loss at 8p23 and gain at 4p16, if not all, reach their early developmental milestones rather late. The *Unique* experience is that babies started to roll between 6 and 10 months, to sit between 6 and 12 months, to crawl around their first birthday and to walk without help between 12 months and 3½ years. However, many children are unstable on their feet and can trip and fall for many years after learning to walk, needing particular help on uneven ground. One child had repeated casting to improve the position of his feet and wore plastic leg braces to improve his mobility and reduce falls, with good effect as his falls were minimal by the age of seven. They learn to climb stairs between 4 and 6 years.

Part of the delay is explained by unusual muscle tone – either low tone [hypotonia], raised tone [hypertonia] or a mixture of both. Both the pattern and severity of low and raised muscle tone varies from child to child, with some quite obviously affected and others not at all. In any child with abnormal muscle tone, regular early physiotherapy and occupational therapy is very helpful, as are soft play, exercises and stretches to improve muscle tone. The delay can also be partly explained in some children by their

foot position. Many children have flat feet, with no arch. One child with a cavovarus left foot [high arch, inturned heel] and a flat right foot [treated with shoe inserts] has a specific difficulty pedalling and using a scooter.

After a slow start, the outlook is good as most children progress to running, jumping, throwing and catching and climbing and eventually their balance improves. Physical activities enjoyed by *Unique* children include playing on swings, swimming, rock climbing, ballet, cycling, football, basketball.

“ He can be quite clumsy and fall over a lot; he gets easily distracted and loses concentration. Some days he can walk well; others he can fall over fresh air; he is not good on uneven ground. He likes to run around but has an awkward running style - 5½ years

“ She had problems with balance and co-ordination and struggled with steps and stairs if not supported, also to sit comfortably on the floor. But now she needs no supports or aids. She walks well, just needing assistance with obstacles such as steps and kerbs - 6½ years

“ He walks and runs but often gets ahead of himself and falls although he can go far. He enjoys swimming and jumping on a small trampoline - 7 years

“ The effects of her hypotonia are that she falls down all the time, gets tired easily, cannot sit cross-legged or sit on the floor at all without propping herself up with her arms. Her trunk is not strong enough to hold her up. She walks very well. She just cannot recover from any kind of stumble - 9½ years

“ He walks well, then stumbles. He can't walk far before he trips over - 11½ years



6 years

Development: hand-eye co-ordination and dexterity (fine motor skills) and self care

Fine motor skills in children with an unbalanced 4;8 translocation resulting in loss at 8p23 and gain at 4p16 are often affected and children may take longer to reach for and grab toys and hold a cup. This can lead to delays in being able to self-feed and hold a pen to draw or write. Many children prefer to use their hands at mealtimes and only gradually learn to use a fork and spoon alongside. Adapted cutlery helps as do pencil grips when children start to write. Many children have occupational therapy to help improve these skills. An additional concern can be flexible joints: one child has double-jointed thumbs and very flexible fingers. Also, two older children [9 and 11 years] have

a hand tremor that causes constant shaking, and these children wear hand splints or weighted gloves. Mastering a keyboard is often easier than learning to hold an implement to draw or write.

As a result of these difficulties, children are likely to continue to need help with dressing and undressing [zips and buttons can be especially problematic]. They may also continue to need help with tasks such as washing and brushing their teeth for longer than their peers. Toilet training is likely to be mastered late: children in this group became clean and dry between the ages of 4 and 9. Even when toilet trained, children will need help with wiping. Even after a task has been mastered, children will still need help and repeated instructions [*Unique*].

“ Not independent in self care activities yet. She understands washing and dressing and co-operates when being cared for. She brushes her teeth when given her toothbrush and attempts to brush her hair - 2 years

“ Fine motor skills are improving slowly: he now does jigsaws with help but still can't do fiddly things - 5½ years

“ Potty training for urination was much easier than for bowel movements. At 5 years of age we took him to a nurse who runs a potty training boot camp. We spent 8 hours in her home with 3 other children, followed her guidelines for toileting for 1 month and even held him out of school for 1 week – but it worked.

He still sometimes grasps things with his whole hand instead of with his fingers. His writing is getting better: he is close to doing his first name with little assistance or prompting. For personal care he needs assistance. He can put on his socks, underwear and clothes but needs help with buttons, snaps and zippers. He can put shoes on but does not know how to tie laces - 7 years

“ She can wash herself perfectly well if I run her a bath. She cannot get herself dressed. She knows exactly what she needs to wear and how to put it on, but her lack of trunk strength makes it nearly impossible for her to put on her own pants, shoes, and socks. If she bends over without hanging onto something, she simply falls all the way down - 9½ years

“ Dressing is a lot better. Washing he has to be shown or have done for him - 11½ years

General health and wellbeing

Evidence from *Unique* shows that children with an unbalanced 4;8 translocation resulting in loss at 8p23 and gain at 4p16 are generally as healthy as other typically developing children. Some families report that their child seems to be more prone to coughs and colds than typically-developing children and some families try to boost their child's health by giving them multi-vitamins and other supplements. Common conditions such as respiratory infections, eczema and asthma occur, as they do in any group of young children. One child has mild scoliosis [spinal curvature], but will need no treatment unless it deteriorates. One child had a rapid growth on one side of her head as a baby caused by a build-up of fluid on one side of the brain. Surgery to allow the fluid to drain away seemed to solve the problem, although the ventricles [fluid-filled spaces] within the brain are larger than expected. It isn't known if this is connected with the 4;8 translocation or not.

“ She is doing very well. She doesn't have any major health problems. Sometimes I suspect that she gets sick from something that is more of a behavior / hygiene issue. For instance, she puts things into her mouth, and sucks her fingers. Also, her bathroom hygiene sometimes is not everything you would hope for, and then she gets yeast infections - 9½ years

Eyesight

Most of these children have normal functional vision. Among the problems that have occurred the most common is a squint/crossed eyes [strabismus], which is common in young children and especially in those with a chromosome disorder. The crossed eye can look inwards, outwards, up or down. The main effects of a squint are that usually the person will have one eye which is stronger than the other. This is because the brain has to give priority to one eye over the other with the result that the weaker one does not learn to see as well as the stronger one. Treatment of strabismus depends on the cause but can include patching the stronger eye, exercises, glasses to correct a refractive error such as long sight and surgery to realign the muscles that hold the eye in place.

Other eye disorders found in individual children are short sight, long sight and astigmatism, when the cornea (the clear cover over the iris and pupil) is abnormally curved. The effect on vision is to make objects appear blurred. Sometimes the brain can compensate for astigmatism although it may be too strong for this to happen without the aid of glasses [Tranebjaerg 1984; Unique].

Teeth

Generally speaking, children with chromosome disorders appear to have somewhat more dental problems than their peers, so regular high quality dental care is important. Among children with an unbalanced 4;8 translocation resulting in loss at 8p23 and gain at 4p16, 7/8 have some unusual dental feature. However, there is no underlying pattern to the irregularities, which include: too many teeth, too small a jaw to accommodate the teeth, widely spaced, square teeth, deeply grooved-teeth that are susceptible to decay and both early and late eruption of baby teeth [Unique].



7 years

Why did the 4;8 translocation happen?



9½ years, with father

Translocations between chromosomes happen naturally. New translocations occur when sperm or egg cells are forming or just after fertilisation during the copying of the early cells that will become an embryo, then a fetus and then a baby.

To find the cause of the 4p;8p translocation in your family, your geneticist will offer to check the parents' chromosomes.

A small blood sample is needed for the test.

Sometimes one parent is found to

have a balanced translocation between the short arms of chromosomes 4 and 8. This parent is then a carrier.

Sometimes one parent apparently has normal chromosomes but on closer inspection, it turns out that they have rearrangements of their chromosomes 4 and 8 called inversions that makes the translocation just a little more likely. For reasons we don't understand yet, the parent with the inversions has always so far been the mother.

Whether the blood test shows that one parent is a carrier or has inversions on 4p and 8p, as a parent there is nothing you did to cause the translocation and nothing you could have done would have prevented the unbalanced version from occurring in your child. No environmental, dietary or lifestyle factors are known to cause these chromosome changes. No one is to blame when they occur and nobody is at fault.

Will we have another child with an unbalanced 4p;8p translocation?

If either parent is a carrier of a balanced 4p;8p translocation, the chances of having another affected child are fairly high: your genetic counsellor or geneticist can give you a rough estimate. A parent with a 4p;8p balanced translocation can have children with either type of unbalanced chromosomes: part of chromosome 4 missing and an extra bit of chromosome 8; or part of chromosome 8 missing and an extra bit of chromosome 4; or they can have a child with normal chromosomes; or a child with the same balanced 4p;8p translation as the parent.

If neither parent is a carrier, then the translocation is a 'new' one, called **de novo** [dn] by geneticists. Research suggests that one parent, typically the mother, will carry the two inversions on 4p and 8p that make having a child with an unbalanced 4p;8p translocation slightly more likely.

But while having an inversion on chromosome 4, 8 or both is quite common, it's very rare indeed to have a baby with a 4p;8p translocation. So it's true that women with these inversions are more likely to have an affected child, but they are only a little bit more likely. It is important to point out that no family has had two children with a de novo 4p;8p translocation [Giglio 2002; Zollino 2004; Hollox 2008].



“ No family has had two children with a de novo 4p;8p translocation.



Top: 4 years, with sister
Bottom: 8 years, with brother

We wish we had known ...



“ Everything is going to be fine – not that everything is ‘normal’, because it is not; but that we would adjust to our new normal and it is really no different than any other life.

“ I regret spending more than a year arguing with my husband, her doctor and with friends about whether or not there was something going on. I also regret taking it to heart when people reacted badly to the news of the diagnosis. Nobody wants to hear permanent, bad news about a child they love. I felt a lot of pressure from friends and family to avoid

‘believing’ it or ‘labeling’ her. Most people eventually came around, and now I have a lot of support.

“ That we have to take one day at a time.

“ I wish I could have enjoyed him more when he was small and not worried so much and spent so much time trying to find ways to help him. I wish we had gotten to play more and juggle therapies less. I wish there had been someone that had gone before me that could have guided me in helping him.

“ How severe her developmental delay was going to be. It was really played down in the early years and has led to disappointment as she grows up.

Families say

“ To us, she is just our normal child. She may be behind, but she is funny and laughs every day. She is easy to take care of and fits into our family just fine. She makes progress in her therapies and learning and seems proud of her achievements. I think that having her has allowed us to let go of any expectations we had for her future so now every accomplishment is to be celebrated! - 2 years

“ She is very loving and affectionate, very musical and has a great sense of humour. As an only child she has enriched our lives. We think she is fabulous! - 6½ years



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Support and Information



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