Understanding Chromosome & Gene Disorders

Trisomy 5p: Duplications of 5p13 & 5p14

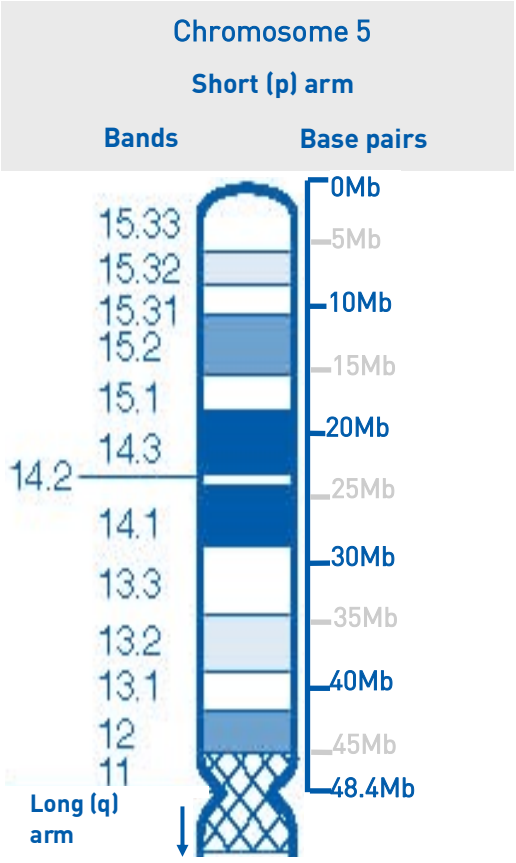
(please refer to our Trisomy 5p: microduplications of 5p13 & 5p14 guide for smaller duplications)

rarechromo.org

5p13 and 5p14 duplications

A 5p duplication is a rare genetic condition that occurs when there is an extra copy of part of the genetic material (DNA) in one of the 46 chromosomes – chromosome 5. This extra copy is known as a duplication. People have 2 copies of chromosome 5 in most of their body cells. However only one of the copies of chromosome 5 in each cell will have the duplication and the other copy will have the usual amount of DNA. This usually affects development, and sometimes health and behaviour as well. But how much it affects individuals, and the ways in which it affects them can vary a lot.

In general, the right amount of genetic material is needed for correct development – not too little and not too much. The precise effects vary depending on how large the duplication is, how many genes it contains and what those genes do. The effects may not be limited to the genes within the duplicated piece of chromosome because these genes may interact with other genes on chromosome 5 or on other chromosomes.



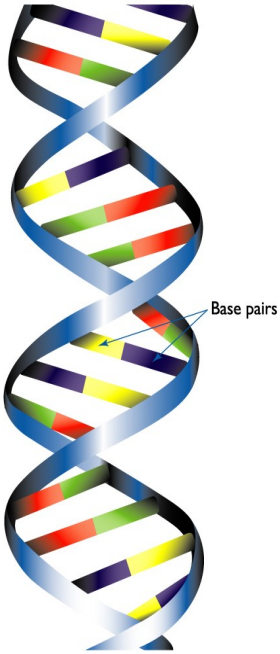
Genes and chromosomes

Our bodies are made up of trillions of cells. Most of the cells contain a set of around 20,000 different genes. The genetic information the genes carry tells the body how to develop, grow and function. Genes are carried on chromosomes. Chromosomes usually come in pairs, and we inherit one chromosome from each parent. Of the 46 chromosomes, two are a pair of sex chromosomes: two Xs for a girl and an X and a Y for a boy. The remaining 44 chromosomes are grouped into 22 pairs and are numbered 1 to 22, approximately from largest to smallest, so chromosome 5 is quite a large chromosome. Each chromosome has a short (p) arm (from petit, the French for small) as well as a long (q) arm (see diagram on page 2).

Looking at chromosome 5p

Chromosomes can't be seen with the naked eye, but if they are stained and magnified under a microscope, each one has a distinctive pattern of light and dark bands. 5p13 and 5p14 are bands in the middle and lower part of the short arm of chromosome 5. You can see in the diagram on page 2 that 5p14 consists of 3 bands: 5p14.1, 14.2 and 14.3. 5p13 also has 3 bands: 5p13.1, 13.2 and 13.3.

Each band of each chromosome contains millions of base pairs of DNA. Base pairs are the chemicals in DNA that form the ends of the 'rungs' of its ladder-like structure that you can see in the image, right. The short arm of chromosome 5 has about 48.4 million base pairs, shortened to 48.4Mb; the 5p14 bands have about 10.5Mb; and the 5p13 bands have about 13.6Mb. The position of each of the 900 or so genes on chromosome 5 is measured in base pairs. On the right of the diagram on page 2 you can see how the base pair numbers relate to the chromosome bands.



Looking at chromosomes under a microscope, it may be possible to see a large piece of extra genetic material. But changes smaller than 5Mb are very hard to identify, and sometimes even 10Mb changes are hard to see. So if the extra piece is very small, the chromosomes can look normal under a microscope. New techniques, particularly one known as array CGH, are now often used to find the size and position of the extra DNA, helping to identify genes and pinpoint their location on chromosomes.

Has everyone with a 5p13 or 5p14 duplication got the same amount of extra DNA?

No. People have very different amounts of extra DNA, and different extra genes. Some people have very large duplications; others have tiny duplications, known as microduplications when they are smaller than 5Mb. Unique publishes a separate guide to microduplications in 5p13 and 5p14.

Genetic test results: two examples

A person's chromosome make-up is called their karyotype. Someone with a 5p duplication might have a karyotype that looks like one of these examples:

arr (hg19) 5p13.2p15.33 (71704-35463036)x3

The test was by array comparative genomic hybridization (arr). The results follow the Human Genome build 19 (hg19), which is the most up-to-date 'atlas' of human chromosomes. 5p13.2p15.33 shows that two break points were found, the first in band 5p13.2 and the second in band 5p15.33, near the tip of chromosome 5. (71704-35463036)x3 shows that three copies of the material between the break points were found (x3). The normal number of copies is 2, so this means there is an extra copy. 71704-35463036 are the start and end points of the extra copy, measured in base pairs. Take the first long number from the second and you find that there are 35,391,332 extra base pairs. This is about 35.4Mb.

46,XY,der(15)t(5;15)(p14.2;p12)mat

Some people with a 5p duplication have a translocation where DNA has swapped places between two chromosomes. This can create a missing part of one chromosome and an extra part of another chromosome. This example shows someone with the expected number of chromosomes (46). Two different sex chromosomes - an X and a Y - (XY) were found, so this person is male (a boy or man). der(15) means that there is an altered (derivative) chromosome 15. t(5;15) means that there is a translocation (t) - a DNA swap - between chromosomes 5 and 15 (5;15). (p14.2;p12) means that chromosome 5 has broken in the 5p14.2 band, and there is extra DNA from that break to the end of the chromosome 5; chromosome 15 has broken in the 15p12 band, and DNA is missing from that point. mat means that the translocation came from the mother. If it came from the father it would say pat. Unique has a guide to **Balanced translocations**.

I wish I had known .....

"That everything was going to be all right. I wish I had more information. I had to read up a lot of not very relevant literature on eg Down's syndrome."

"I would have liked to be better informed, but mostly I would wish that doctors had treated us with more affection and delicacy. The early years were very difficult in many ways: too many medical tests and hospital visits, and too much anxiety from me to know the future and above all try to change it. Over the years we have stabilized: I have accepted things as they are and that has allowed me to work on building a better future for us both."

Common features of 5p13 or 5p14 duplications

The most common features are:

- Developmental delay
- Learning disability
- Short stature
- Feeding difficulties
- Hypotonia
- Speech delay
- Autism
- Large head
- Brain abnormalities
- Talipes
- Epilepsy
- Heart
- Eye and vision anomalies
- Unusual facial features
- Unusual hands

Sources

The information in this guide is drawn partly from 13 people reported in the medical literature with large duplications of 5p (Brimblecombe 1977; Khodr 1982; Vowles 1984; Overhauser 1986; Chia 1987; Kleczkowska 1987; Gustavson 1988; Harrison 1988; Webb 1988; Rethoré 1989; Zenger-Hain 1993; Chen 1995; Cervera 2005). The first-named author and publication date are given to let you look for the abstracts or original articles on the internet in PubMed (www.ncbi.nlm.nih.gov/pubmed). If you wish, you can obtain most articles from Unique. In addition, this guide draws on a survey of members of Unique conducted in 2014, referenced Unique. When this guide was compiled, Unique had 5 members with a pure 5p13 or 5p14 duplication not involving any other chromosome arm, three with a large duplication. The guide also contains information from 4 cases on the publicly accessible Decipher database (https://decipher.sanger.ac.uk). In all, 20 people are included, aged between newborn and 21 years.

- Developmental delay, which can be mild

In 11 babies and children, some degree of developmental delay has been seen, but it is mild in some cases. One girl with a duplication between 5p14.2 and 5p14.1 met her milestones as a baby, but was at a 3½ year developmental level at the age of 4½ years. Another baby showed only slight delay by 12 months, and had a development quotient of 75 (out of 100). Others were more obviously affected, with children of 2 or 3 years having the developmental skills of a 10-12 month old baby, and a girl of 4¾ years having the developmental skills of a 2½-3 year old child. Among Unique members, a 6 month old baby was grabbing objects, but was unable to roll over, chiefly because she had a fixed bar between her feet to correct clubfoot. A 13 year old boy with a p15.1p14.2 duplication showed a spectrum of skills with delay ranging from mild to severe; the delay was obvious even as a young baby, and by 13 years his developmental ability was consistent with a child of 6 or 7 years old.

The developmental delay can affect fine movements like grip and hand function, so a baby of 2 years is only just developing the skills to pick up small things between her index finger and thumb, a skill that you would usually see in a baby of around 9 months; and the 2 older Unique members of 13 and 20 years still have difficulty picking up, holding and using implements. This has an inevitable impact on how a child learns to care for himself, and all 3 Unique members need extra support, or total support for everyday activities like dressing and washing. Toilet training is also affected, with just the child of 13 years dry, but still needing pads for bowel motions, and the young man of 20 years not yet in control of his bladder or bowel (Brimblecombe 1977; Chia 1987; Gustavson 1988; Webb 1988; Rethoré 1989; Zenger-Hain 1993; Chen 1995; Unique).

"He has had problems all his life in grasping objects, holding them, using implements correctly and in handwriting. Although he is aware that he needs to change, wash, dress and undress, he is unable to. There are various components in that I think he is a bit lazy (!) and it's nice to have everything done, but at the moment he is unable to overcome his lack of intellectual ability, his autism, his lack of coordination and his joint stiffness." 13 years

"She is very cute. Every milestone is a big step and a real achievement."

Learning disability

All children old enough for school have needed some support with their learning, but the amount required is variable, depending on the degree of learning problems. A baby girl with a large duplication between 5p15.3 and 5p13.3 had severe learning difficulties by her first birthday; a girl of 4¾ years had a learning age of 3¾ and an IQ of 68; a child of 5 years had an IQ of 45. There is some evidence that the extent of learning disability depends on the size of the duplication. One girl with a small duplication between 5p14.2 and 5p14.1 attended a mainstream primary school, and transferred to a special secondary school. She was reading basic books and writing simple compositions by the age of 15 years. Two Unique members attend schools for children with autism spectrum disorders, in one case the child has associated complex learning difficulties; but their levels of achievement are quite different. A boy of 13 years has mixed abilities, and his learning abilities are at roughly the level of a child of 6 years; while a young man of 20 years has the understanding of a small child of under 2 years (Chia 1987; Gustavson 1988; Webb 1988; Cervera 2005; Decipher; Unique).

"He learns things that he likes a lot better than when he just knows he has to learn."

"He has shown willingness, motivation and keenness to use his computer. Medication to help him concentrate and sometimes the wish to please and help have helped him to learn. He needs clear, short, 1:1 instructions, where possible with visual images, and quiet settings to learn in. He remembers some things with amazing accuracy but others, not at all. He enjoys maps, train timetables, station announcements, and research on Google or websites of interest. He does not recognize all words accurately and his drawing and handwriting are very poor, but he can write his name and short sentences." 13 years

"He can't read, and is in a school with a therapist/teacher and a learning support teacher for every 3 students as well psychology, psychomotor support and a sports coach as extra support." 20 years

Short stature

Generally speaking, babies with a 5p13 or 5p14 duplication are born somewhat smaller than you would expect from their family profile, but their birth weight and length falls within normal limits. The average birth weight at term among 14 babies was just under 3kg (6lb 8oz), the smallest baby weighing 2.4kg (5lb 5oz) and the largest 3.7kg (8lb 3oz). Among 6 babies whose length at birth is known, all babies were below average, measuring between 47-51 cm (18½-20"), but none was unusually short.

Growth in babyhood and childhood continues this trend, with children and adults generally being slightly shorter than you would expect when comparing them with the rest of their family. But children and adults with 5p13 or 5p14 duplications are not typically extremely short, although at least one Unique member is. Among 10 people whose height we have details of, one 2 year old was on the 5th centile for height, and another was below the 0.04th centile; a 3 year old and a girl of 4¾ years were on the 10th centile; one 5 year old was 8cm (3") below average, and another was on the 25th centile. Just two babies were unusually short for their age at 2 months and at 18 months. One child was of average height and attained an average adult height of 1.75m (5'8") (Brimblecombe 1977; Vowles 1984; Kleczkowska 1987; Gustavson 1988; Webb 1988; Rethoré 1989; Zenger-Hain 1993; Chen 1995; Cervera 2005; Unique).

"On the small side." 2 years

"Perhaps a little short, but I, his mother, am short too." 20 years

"He is very good, lively, affectionate, and funny... I love him more than anything in the world."

Feeding difficulties

Feeding difficulties are rarely mentioned in the medical literature or on the Decipher database, but they are a universal feature among Unique's members who have a 5p13 or 5p14 duplication. One baby had early difficulties feeding and was readmitted to hospital when she was a month old because she could not feed well enough to maintain her growth rate (failure to thrive). Her feeding difficulties persisted.

2/3 Unique babies were initially breast fed, but there were difficulties with this method of feeding. One baby had difficulties latching on, and was never exclusively breast fed, switching to a bottle from 2 months. Another baby could not coordinate swallowing and breathing while

bottle feeding and often had to pause to rest. One baby who started to vomit milk from 2-3 months was thought to be aspirating (inhaling) milk, and tests showed that the muscles around the top and back of her mouth and throat didn't close the air space at the back of her throat properly, allowing milk to escape: this condition is called velopharyngeal insufficiency.

When babies were weaned (around 6 months), they needed extra seating support, as they were not sitting up yet properly. They could also only cope with thickened foods like purées and yoghurt, and choked on lumps, as well as when drinking liquids. These difficulties were persistent, with uncoordinated swallowing presenting an ongoing risk of choking, and inadequate chewing meaning that smooth foods are usually preferred, even into adulthood (Vowles 1984; Unique).

"She still eats baby food, chewing a bit, but this is very delayed. She is OK if the food is solid or liquid, but not if it is mixed." 2 years

"At 6 months, he would arch his back while bottle feeding as if in some pain and this seemed to ease his stomach. At 4 years, he still had a tendency to choke when drinking water from a bottle without a straw or drinking teat. Today, while he can eat and drink independently, his eating has always needed to be supervised to avoid choking. He has a tendency to gulp food and drink, and swallow food without complete or proper chewing." 13 years

"For 4 or 5 years he only ate purées. It's better now but his chewing is still bad." 20 years

■ Hypotonia

Low muscle tone, making a baby feel floppy to hold, is extremely common, and is known to affect 6 out of 7 children including all of Unique's members. The low tone may not affect the entire body: one child has truncal hypotonia – low muscle tone in his body – but good tone in her arms and legs; another has low tone specifically in the arms and legs. The hypotonia can affect the muscles of the mouth and face, causing feeding difficulties (see Feeding, page 8) and drooling (dribbling), so that specific face exercises have been helpful to tone up the facial muscles (Rethoré 1989; Zenger-Hain 1993; Cervera 2005; Unique).

■ Speech delay

Most reports in the medical literature are of babies too young to establish whether or not they have any speech delay. However speech delay has been a reported feature in two children: a boy of 3 years and a girl of 15 years. It is universal among Unique's members with a 5p13 or 5p14 duplication. Unique babies first smiled later than is usual, between 3-4 months. Babbling (producing strings of word-like sounds) also

developed significantly late, from about 18 months in one child, and was never achieved in another, who as an adult communicates through vocal noises, gestures, and some signing, as well as pictures and a communication device. The development of speech and language in a third child is described below (Webb 1988; Chen 1995; Decipher; Unique).

"She has been making Hi 5s and waving bye bye from about 18 months, and understands words like kiss, cuddle, up, lie down, mummy, daddy and nana – but as yet has no words herself." 2 years

" At almost 4 he was still unable to talk properly but could make many recognisable single words and sounds and some 2/3 word phrases, as well as vocalising, signing Makaton, using picture exchanges, gestures, pulling and pushing, and singing. From about 18 months old, his understanding was quite significantly ahead of his expressive language, so although he talked, he used a language we could not understand, even though the language patterns were the exact replica of the way we speak, with the appropriate intonations, pauses and hand expressions. Later he started using words that I or we could understand, and slowly he built his vocabulary, for example 'car key'. He enjoyed talking and did not appear to be aware that people could not understand him. He tended to seek adults out as they have more time to listen and try to understand.

" By now, at 13, he has been diagnosed over the years with several speech disorders and delays. He is however today extremely verbal and has learned that speech is an effective way of engaging adults on his terms. His use of language today is appropriate, but the content of his speech can sometimes be quite mystifying to people who don't know him. As well as speech, he sometimes adds Makaton signing. Visual timetables are in use at school and he responds well to requests supported with images. His speech is very fluent and his sentence structure entirely appropriate: questions and answers, pauses, statements etc. He will also suddenly use quite an unusual word (eg 'ominous') in a context that may or may not be right. He can be very loud and 'shouty' and does not appear to realise just how overwhelming he can be.

" He still seeks adults out to communicate with; children of his own age outside school either keep their distance or laugh at him. There is still a wide disparity between what he can understand and what he expresses, in that he will pick quite relevant topics such as the weather, trains etc but engage in conversation about them entirely on his terms. He remains blissfully unaware that many items/topics/facts are of no interest to others, and therefore operates in his world quite happily, but finds it hard if someone cannot, or doesn't want to relate to his world."

Autism

Autism has been diagnosed in two people on Decipher and 2 Unique members. The diagnosis is not of a classical autism, however, as can be seen below. Many Unique members have said that a diagnosis of autism was more helpful to their child in accessing services than the diagnosis of a chromosome disorder. This has not been the case for this child (Decipher; Unique).

"His eye contact is good, he is polite and courteous, he more or less engages appropriately, although invasion of personal space is still an issue, and he loves talking. The interactions are very much on his terms though." 13 years

Large head

A head that is larger than usual, known as macrocephaly, is a distinctive feature of Trisomy 5p, where an extra copy of most or all of the short arm of chromosome 5 is present. In people with a 5p13 or 5p14 duplication, a large head is also found, but not in all cases. In 7/10 children and adults, the head was larger than average, but usually within normal limits. Just two babies had an extremely large head, and one child actually had an abnormally small head (known as microcephaly). The circumference of a baby's head at birth usually measures 31-38cm (12-15"), but the most typical measurement for babies with a 5p13 or 5p14 duplication and a large head is around 36cm (14"). The newborn baby with the most increased head size had a head measurement of 43cm (17").

Some babies are also born with an unusually shaped head: long (dolicocephaly, turricephaly); short from back to front (brachycephaly) or flattened at the back and longer from front to back on one side than the other (plagiocephaly). The unusual shape usually becomes less obvious with time, particularly after the baby's hair grows, but reshaping with a helmet or even surgery is occasionally considered if necessary (Brimblecombe 1977; Vowles 1984; Kleczkowska 1987; Gustavson 1988; Webb 1988; Zenger-Hain 1993; Cervera 2005; Unique).

"She has a large head, on the 99.8th centile, and has seen a plastic surgeon for her ears and will consult him again about the possibility of a corrective helmet for her plagiocephaly, although as she grows, this has become less obvious." 2 years

Unusual brain features

In the 8 cases where the brain has either been imaged or examined, an unusual feature has been found in 6 children. However, among 3 Unique children, all examined, a significant change was found in only one. The unusual features are quite varied, with the cerebellum (the

main part of the back of the brain that controls balance and coordination) involved most often: it was either very small, partly undeveloped, or contained a cyst (Dandy Walker malformation) that cannot be removed. Dandy Walker carries a risk of fluid build-up within the brain known as hydrocephalus, and this was seen in two babies. The corpus callosum (the broad band of nerve fibres linking the brain's two sides) is often involved, and was either small or malformed, or missing altogether. In some babies the outer layer of the main part of the brain (the cortex) develops abnormally (dysplasia) or contains cells from another part of the brain (heterotopia).

Brain anomalies seen in only one baby included a shrinking of one of the front parts of the brain (frontal lobe atrophy); an unusually thin layer of spongy tissue just outside the brain (subarachnoid space); and an unusual change in the part of the brainstem called the pons.

In 2 out of 3 Unique children a brain scan has revealed no anomalies, but if any are found, interpreting them is a matter for your child's neurologist or paediatrician (Brimblecombe 1977; Vowles 1984; Kleczkowska 1987; Gustavson 1988; Cervera 2005; Unique).

Talipes

Club foot is common, recorded in 4/9 babies in the medical literature and 1/3 at Unique. One foot, or more commonly both, are affected. One baby was born with the calcaneocavus type of clubfoot, where the foot is turned outwards and upwards, but most commonly it is of the talipes equinovarus type, where the foot points downwards and inwards. The foot is usually short and broad and the heel points downward while the front half of the foot turns inwards. The talipes can combine with other unusual foot positions, such as metatarsus varus, where the toes point upwards.

Treatment is individually tailored and aims to straighten the foot so that it can grow and develop normally. First-line treatment can be non surgical and may include manipulation, casting, taping, physiotherapy and splinting, followed by bracing to prevent relapse. Surgery and sometimes splinting are considered if non surgical treatments are not completely successful.

Other less troublesome foot anomalies are also sometimes seen, including overlapping toes in 3 children. Stretching and strapping from birth can sometimes correct overlapping toes, but occasionally corrective surgery is needed. One baby was born with

her big toes bent upwards; another child wore insoles to correct his flat feet; another has slight webbing between two toes on each foot; one has narrow feet; and two simply have long toes (Brimblecombe 1977; Vowles 1984; Kleczkowska 1987; Gustavson 1988; Rethoré 1989; Cervera 2005; Decipher; Unique).

"Her right talipes was noticed immediately after birth. First she had serial casting to start to correct it, then at 2½ months a tenotomy, and then a fixed bar between her feet. Two years on, she still wears the bar at night, and her foot position is correcting well, with further surgery now unlikely."
2 years

Seizures

Seizures have been reported in 5/17 babies or children with a 5p13 or 5p14 duplication. These seizures differed in type. Two babies had febrile convulsions, which are a type of seizure that can occur in rare cases when a small child has a high temperature. Children who have febrile seizures usually grow out of them after the age of 6 or 7. A Unique member had occasional brief absences and twitches (myoclonic seizures) that resolved without any treatment and had not reappeared by the age of 20 years. One baby experienced tonic-clonic seizures (once called grand mal), by the age of 12 months. Tonic-clonic seizures involve sudden stiffness, followed by repeated, rhythmic muscle contractions. Another child experienced tonic seizures (sudden stiffness) with seizure activity all over the brain (generalised), as well as episodes of loss of awareness with seizure activity limited to one part of the brain. One single seizure does not mean that a child will be diagnosed with epilepsy, but if seizures continue and epilepsy is diagnosed, the first line of treatment is usually an anti-epileptic drug (Chia 1987; Chen 1995; Cervera 2005; Decipher; Unique).

Heart

Most babies with the duplication are born with a strong, healthy heart. However, heart conditions are relatively common, although there is no one particular heart condition, and they range from relatively minor concerns which correct themselves in time to very severe life threatening disorders. Overall, 2/3 Unique members, 1 Decipher patient and 4/11 babies and children in the medical literature were born with a heart condition. Sadly, 3 of the babies reported in the medical literature died of their heart condition within the first month or two of life. However, it is important to remember that these medical reports are almost 30 years old, and the care of babies born with a heart condition is very much better today.

Treatable heart conditions include a persistent ductus arteriosus, where a connection between two blood vessels that usually closes around the time of birth remains open and can occasionally cause symptoms. The connection can be closed using minimally invasive surgery or medications if necessary, although most get better on their own. Narrowing of the blood vessel that takes the blood to the lungs (the pulmonary artery) was seen in one baby, but it was mild, and she needed no further monitoring by the age of 2. One baby was born with a large hole between the two lower pumping chambers of the heart (ventricular septal defect, VSD); holes can be very small or very large, and a very large hole often needs surgery to close it. Another baby was born with a hole between the 2 upper chambers of the heart (atrial septal defect, ASD); again, a large hole usually needs surgical closure, but this may be possible using keyhole surgery. Finally, one Unique child was born with tetralogy of Fallot. After open heart surgery at a specialist hospital when he was 9 months old, this child is in good health today, at the age of 13 years.

Eye and vision anomalies

Most children with a 5p13 or 5p14 duplication have good vision and no eye features. A few have a vision problem, often of a type that is common among all children, whether or not they have a chromosome disorder. Four children have a squint (strabismus, the turning in or out of the eye, also called cross-eye) which is caused by weakness of the muscles that control eye movement. 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. Two babies were born with abnormally small eyes (microphthalmia), which usually means that sight in the affected eye or eyes is limited. Three babies were born with a developmental defect known as a coloboma,

where there is missing tissue in part of the structures of the eye; whether it affects vision depends on which part of the eye is affected and how big the gap is. One baby was born with a drooping upper eyelid (ptosis); treatment depends on whether vision is affected, and can include surgery (Brimblecombe 1977; Vowles 1984; Gustavson 1988; Rethoré 1989; Zenger-Hain 1993; Decipher; Unique).

"He is very long sighted, has no peripheral vision, and only sees in 2 dimensions." 20 years

Unusual facial features

Your child may look like the rest of your family, but he or she may also have some facial and other features that are common to people with Trisomy 5p. Babies with large duplications starting at 5p13 are more likely to have unusual facial features than babies with a smaller duplication starting from 5p14. The most obvious feature is the large head, but in order of frequency, others are a very low bridge to the nose; tilted back ears; unusually shaped ears; eyes set wide apart; tiny skinfolds across the inner corner of the eyes; a small lower jaw and chin that may also be set back against the upper jaw; slightly upslanting eyes; a high, rounded forehead; and a large, protruding or oddly positioned tongue. Many other slightly unusual facial features have been observed in one or two children, but these features are not specific to 5p duplications and may be very subtle (Brimblecombe 1977; Khodr 1982; Vowles 1984; Kleczkowska 1987; Gustavson 1988; Rethoré 1989; Zenger-Hain 1993; Cervera 2005; Decipher; Unique).

"She dribbles a lot especially when teething, and tends to hold her mouth open, but this is getting better." 2 years

Unusual hands

Your child's hands may also be subtly unusual. In order of frequency, the features noticed most often are long fingers; short 5th (little) fingers; and incurving 5th (little) fingers. Features remarked on in only one child are: small hands; malpositioned thumbs; a single crease across the palm; 4th fingers twisted outwards (Brimblecombe 1977; Khodr 1982; Vowles 1984; Kleczkowska 1987; Gustavson 1988; Rethoré 1989; Zenger-Hain 1993; Cervera 2005; Unique).

"A short fifth finger. All of the distal creases of the fingers are not prominent as usual. He has relatively small hands and fetal fingerpads." Fetal fingerpads are raised pads on the inner surface of the fingertips; these pads usually disappear by 15 weeks gestation.

What do children enjoy?

13 years: Music, trains, and computer.

Pregnancy, birth and the newborn baby.
First signs of the chromosome disorder

Most - 8/11 - pregnancies were uneventful, and babies were born around term, with just one premature birth at 32 weeks. One baby moved less than expected, and when it came to delivery, at least 4/16 babies were born by Caesarean section, 2 because the baby was breech, and 2 because of delay during labour.

Babies' condition at birth as measured by their Apgar score (a measure of the baby's wellbeing at 1, 5 and 10 minutes on a scale of 0-10) was generally reasonable, but 2 babies were distinctly unwell, one with a 1-minute score of 4, the other with a score that dropped at 5 minutes. One baby was found to be very floppy, with low muscle tone, and another needed resuscitation and oxygen for 24 hours after delivery. The baby with tetralogy of Fallot was also very unwell at birth. Feeding difficulties were also common (see Feeding difficulties, page 8).

Babies were generally small, but within normal limits, weighing on average just under 3kg (6lb 10oz), the smallest 2.4kg (5lb 5oz) and the largest 3.7kg (8lb 3oz) (Brimblecombe 1977; Vowles 1984; Chia 1987; Kleczkowska 1987; Gustavson 1988; Webb 1988; Rethoré 1989; Zenger-Hain 1993; Chen 1995; Cervera 2005; Unique).

"In hospital, she couldn't keep her body temperature up, and was placed under a heater. We went home on day 5."

"As a newborn, his health was of great concern."

While the first signs that something was amiss were evident in newborn babies with an obvious problem like clubfoot or a heart condition, this did not always lead to a genetic test. More subtle signs like difficulty breastfeeding or a lack of eye contact were only informative with hindsight. For some babies the realisation that something was wrong was gradual: non-specific signs like squint (strabismus) and slow development meant that the diagnosis of a 5p duplication was reached later, even in the second year of life. For others a single event meant that the baby was referred for further investigations, such as a genetic test: one baby was investigated after having seizures at a year old.

"The first signs were there from birth, but no one picked them up. As a newborn, his health was of great concern and I was constantly reminded 'not to worry' and that all his problems were due to his heart

What do children enjoy?

2 years: Anything like a piano that makes music or lights up when you press a button.

condition. At that point, nothing was known about his chromosome abnormality. The focus was on his heart and this was seen as the main cause of any concerns."

"He didn´t look at anyone or anything; he seemed disconnected. When he was 9 months old he had some infections, and even a vaccination became infected."

General wellbeing & other health issues

Unique's 3 members with a large 5p13 or 5p14 duplication are generally in good health. The baby is prone to colds, in her mother's opinion, catching them somewhat more often than other babies of her age, and has had a bronchiolitis-like chest infection, but the teenager of 13 years and the adult of 20 years are both in good health.

The teenager is rarely ill. The adult is also well, although he is prone to cold sores and herpes infections around the mouth.

Frequent respiratory and skin infections have also been seen in a child of 5 years, and one child sadly died of bronchopneumonia when she was just over 2½ years old. Very sadly, 2 other babies with serious heart concerns, one of whom also had hydrocephalus (a fluid build-up in the brain) and small, abnormal kidneys, died within a month of birth (see Heart, page 14). One baby had a sunken chest (pectus excavatum) which is sometimes only a cosmetic concern, but when severe can affect the heart and breathing.

Among more minor health issues, 2 babies had an umbilical hernia, which shows as a swelling near the navel and is caused by weak abdominal muscles where the umbilical cord entered the baby's abdomen. Umbilical hernias are very common in all babies, and usually resolve naturally, as in this baby.

Minor genital anomalies are relatively common in babies with a chromosome disorder, especially boys, and one boy was born with an undescended testicle, which was surgically corrected at the age of 18 months. A baby girl was born with a divided (septate) uterus and a double vagina (Vowles 1984; Kleczkowska 1987; Gustavson 1988; Chen 1995; Decipher; Unique).

What do children enjoy?

20 years: Anything with song: toys, TV, videos, computers, music.

Behaviour

We do not have enough published information to make any general statements about behaviour in children or adults with a 5p duplication. Cameos of 3 Unique children follow.

"She is quiet, an easy child, but does have episodes of hitting herself on the chin that may be self-soothing. Generally she is fine with new people, and with adults and older children, but can get a bit shy." 2 years

"On the positive side he is enthusiastic, engaging, loving and helpful. On the negative side he is defiant, angry, aggressive, and loud. He is entering puberty and his anger levels have noticeably increased: the smallest thing that does not meet with his approval results in tantrums, swearing or outbursts. Routine is the key to maintaining quality of life. There are many aspects of his behaviour that will never change so that I have to change to accommodate his needs. I am constantly risk assessing and weighing up outcomes. He seeks the company of adults much more than of other children. He realizes that he will have a much more pleasurable outcome with an adult than with his peers who have no time or patience for his thoughts or focus. His eye contact is good, he is polite and courteous, he more or less engages appropriately (although invasion of personal space is still an issue) and he loves talking. The interactions are very much on his terms though." 13 years

"Normally he is very quiet, lovely, very affectionate and cheerful. Occasionally he harms himself and he tries to hit me. We don't know why. When he gets upset, I have to speak to him very quietly, and leave him alone in his room until he is better." 20 years

Why did the 5p duplication occur?

If a child has a 5p duplication, often the parents' chromosomes are also checked with a blood test. This most often shows that the parents both have perfectly normal chromosomes. The 5p duplication has then just happened as a mistake in the immensely complex process of DNA copying and assembly that happens in human chromosomes when the parents' sperm or egg cells were formed or in the very earliest days after fertilisation. The duplication has therefore occurred for the first time in this child, an event that geneticists call de novo, shortened to dn. As a parent there is nothing you could have done to change or prevent this, just as there are no known environmental, dietary or lifestyle causes of these types of chromosome disorder.

In a few families, the blood test reveals that one parent has a structural change in their own chromosomes. This is usually balanced so that all the genes and chromosome material are present and the parent is entirely healthy. However, when someone with a balanced chromosome change has a child, the baby can have chromosomes that are unbalanced (with too much or too little DNA) and one result can be a 5p duplication (see Genetic test results, page 4, example 2).

Can it happen again?

Where both parents have normal chromosomes, it is unlikely that another child will be born with a 5p duplication or any other chromosome disorder. Very rarely, both parents have normal chromosomes by a blood test, but a few of their egg or sperm cells carry the 5p duplication. Geneticists call this germline mosaicism and it means that parents whose chromosomes appear normal when their blood is tested can have more than one child with the 5p duplication. This has never been reported with 5p duplications but it is a theoretical risk.

If they wish, parents should have the opportunity to meet a genetic counsellor or genetics doctor to discuss the specific recurrence risks and options for prenatal testing and preimplantation genetic diagnosis (PGD). PGD is a technique which uses in vitro fertilisation and embryo biopsy, and only embryos without the chromosome disorder are transferred to the mother's uterus, although they might still have other conditions. If the parents choose to conceive naturally, prenatal diagnosis options include chorionic villus sampling (CVS) and amniocentesis to test the baby's chromosomes. Testing is generally very accurate, although not all of these tests are available in all parts of the world.

Support and Information

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

Unique is a charity without government funding, existing entirely on donations and grants. If you are able to support our work in any way, however small, please make a donation via our website at
www.rarechromo.org/donate
Please help us to help you!

This 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. This guide was compiled by Unique and reviewed by Dr Jennifer Hague, Specialist Registrar in Genetics, Addenbrooke's Hospital, Cambridge, UK.

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