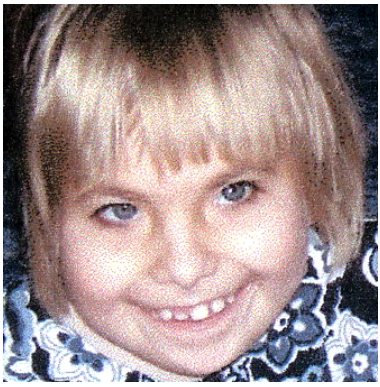
Understanding chromosome disorders

Unique

1p interstitial deletions



rarechromo.org

1p interstitial deletions

A chromosome 1p deletion means that the cells of the body have some genetic material missing from one of their 46 chromosomes, in this case from chromosome 1. For healthy development, chromosomes should contain just the right amount of genetic material – not too much and not too little.

What are chromosomes?

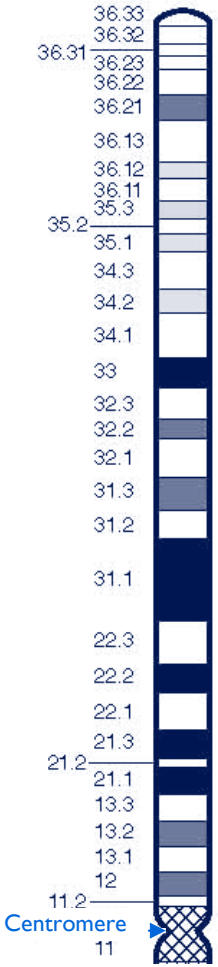
Chromosomes are made up mostly of DNA and are the structures in each of the body's cells that carry the genetic information (in the form of genes) that tells the body how to develop, grow and function. Chromosomes usually come in pairs, with one chromosome from each pair coming from the father and one from the mother. Of the 46 chromosomes, two are a pair of sex chromosomes, XX (two X chromosomes) in females and XY (one X and one Y chromosome) in males. The remaining 44 chromosomes are grouped in 22 pairs, numbered 1 to 22 approximately from largest to smallest. Chromosome 1 is the largest chromosome and contains more than 3,000 of the total of 20-25,000 genes in the human genome.

People with a deletion from 1p have one intact chromosome 1, but there is a piece missing from the other chromosome 1 and this is likely to affect their learning and physical development. Most of their clinical difficulties are probably caused by the presence of only one copy (instead of the usual two) of a number of genes. However, a child's other genes and personality also help to determine their future development, needs and achievements.

Chromosomes have a short arm, named p, and a long arm, named q. The two arms of a chromosome meet at a point called the centromere.

An interstitial deletion means that the chromosome has broken in two places and the broken ends have fused, leaving out the deleted segment. The size of the missing piece varies between different individuals.

Chromosome 1p



Sources and references

The information in this leaflet is drawn from what is known about around 40 people with an interstitial deletion of 1p. Knowledge is still limited, as overall numbers are very small, the great majority of reports are of individuals each with different and sometimes uncertain breakpoints and the oldest individuals were just 30 years old when described. Over twenty people have been described in the medical literature with a pure deletion of material from 1p without loss or gain of material from any other chromosome arm. The first-named author and publication date are given to allow you to look for the abstracts or original articles on the internet in PubMed (at www.ncbi.nlm.nih.gov/pubmed). If you wish, you can obtain most articles from *Unique*. The leaflet also draws on information in the Decipher database of microdeletions and duplications (at https://decipher.sanger.ac.uk). It also draws on *Unique*'s database. When this leaflet was written, *Unique* had 13 members with a pure deletion from 1p.

Looking at chromosome 1p

You can't see chromosomes with the naked eye, but if you stain them and magnify them many hundreds of times under a microscope, you can see that each one has a distinctive pattern of light and dark bands. In the diagram of chromosome 1 on the previous page you can see the bands are numbered outwards starting from the centromere, where the short and long arms meet. A low number such as p13 is close to the centromere. Material closer to the centromere is called proximal. A higher number such as p35 is close to the tip (the telomere). Material closer to the telomere is called distal.

Results of the chromosome test

Your geneticist or genetic counsellor will almost certainly give you your child's karyotype, a way of describing how the chromosomes look that shows the points where the chromosome has broken. It is likely to read something like this

46,XY,del(1)(p21p32) dn

46	The total number of chromosomes in your child's cells
XY	The two sex chromosomes, XY for males; XX for females
del	A deletion, or material is missing
(1)	The deletion is from chromosome 1
(p21p32)	The chromosome has broken in two places. The first breakpoint is in band p21 and the second is in band p32. The segment between p21 and p32 is missing
dn	The chromosome deletion has occurred 'de novo', or as a new event. The parents' chromosomes have been checked and no deletion or other changes found at 1p21 or 1p32. The deletion is very unlikely to be inherited and has almost certainly occurred for the first time in this family with this child.

Instead of a karyotype or as well as one, you may be given the results of a molecular analysis such as FISH or array-CGH (also known as microarrays) for your child. The results are likely to read something like this

46,XX.arr cgh (RP11-100H21)x1.ish del(1)(p34.3p34.3)(RP11-100H21)

46	The total number of chromosomes in your child's cells
XX	The two sex chromosomes, XX for females; XY for males
.arr cgh	The analysis was by array comparative genome hybridisation (CGH)
(RP11-100H21)x1	A DNA marker known as RP-11-100H21 whose position on chromosome 1 is known was present in only one copy instead of the normal two
.ish	A further analysis by FISH w as carried out
del	A deletion, or material is missing
(1)	The missing material is from chromosome 1
(p34.3p34.3)	The chromosome has broken in two places, both in band 34.3
(RP11-100H21)	The DNA marker RP11-100H21 was again shown to be missing.

There is an entirely different rare chromosome disorder caused by loss of material from near the tip of chromosome 1p, known as **1p36 deletion syndrome**. *Unique* publishes a separate leaflet on this syndrome.

How important is the amount of deleted material?

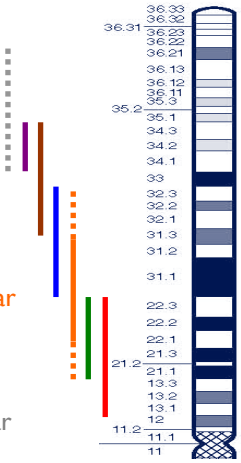
People with a 1p deletion have one intact chromosome 1, but a piece from the short arm of the other chromosome 1 is missing or deleted. Although the exact numbers and types of genes that are included in the deletion are often not known, since some genes are missing there can be effects on a person's learning and physical development.
All the same, children with apparently the same karyotype can develop very differently. One reason for this is that in fact the breakpoints in the chromosome can appear to be the same but on finer analysis turn out to be different. Another reason for the differences is that other genes, environment and personality also help to determine a child's future development, needs and achievements. After all, each of us is unique.

Are there people with a 1p deletion who are healthy, have no major medical problems or birth defects and have developed normally?

There are parts of the human genome that can be deleted without causing any developmental difficulties. These appear to include a small area of band 1p21.1, a small part of band 1p31.1, a tiny part of band 1p36.11 and a part of 1p36.13. There is also a report of a mother with a small deletion at 1p31.1 who was unaffected herself but had an affected baby. In addition, there is a brother and sister pair, each with a deletion between 1p34.1 and 1p34.3 with no problems that could not be explained by their difficult family circumstances. Apart from these, we are not aware of people with deletions from 1p who have shown no developmental delay at all but it is certainly possible that there are individuals scarcely affected by a relatively small deletion who have never been identified or reported by the medical profession (Martínez 1999; Decipher).

What is the outlook?

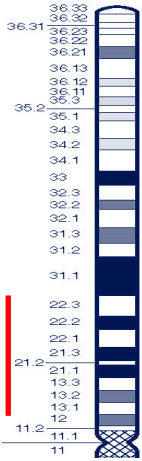
The outlook for any baby or child depends mostly on how the deletion has disrupted early development in the womb. The most important effect is on the major internal organs, especially the heart, kidneys and brain. Historically, babies with heart defects have not thrived as well as those born with a healthy heart but improvements in children's heart surgery and cardiac care mean that today's outlook is generally better than in the past.



Index

You will find information on:

Deletion between 1p13 and 1p22



Seven people have been described, with one from *Unique* and two from the Decipher database. One of these has a small deletion between 1p13.2 and 1p13.3 and the others very likely have different breakpoints, although as most were examined without molecular techniques (see Results of the chromosome test, *page 3*) we can't be certain. The oldest people were 30-year-old identical twins, each with the same complex chromosome rearrangement including a 1p13.3p22.3 deletion.

No pregnancy problems were reported and babies were born at or near term, with birth weights within normal limits. Each of the four babies described in the medical literature had obvious difficulties immediately after birth: one of the twins took 10 minutes to start breathing independently; another was a 'blue baby'; another had a rapid heartbeat, an unusual high-pitched cry and was floppy, especially in the upper body.

There were difficulties with feeding in every reported case, most often frequent vomiting and gastro oesophageal reflux, where feeds return into the food passage and are often vomited or may be inhaled, causing chest infections, known as aspiration pneumonia.

Babies had some unusual facial features, but these could be quite subtle. A small chin and lower jaw is mentioned in three babies and three others have an unusual eyelid formation that could affect eyesight. One baby was born with a hooded eyelid (ptosis), which can interfere with vision if it obscures the pupil, although on this occasion it was resolving naturally by 16 months; another has very narrow eyes (blepharophimosis) and another was born with a membrane attaching the eyelids to each other.

In terms of minor or more serious birth anomalies, the feet were most commonly affected. Problems included underlapping toes (which can usually be readily corrected with exercises or gentle splinting), bent back toes, a high arch, a wide 'sandal gap' between the first two toes and, more seriously, two babies with club foot requiring correction. This is usually by manipulation, casting, taping, physiotherapy and splinting, bracing and sometimes surgery. A baby boy with a 1p13.2p13.3 deletion also had very short legs below the knee. Unusual hands were less noticeable than feet, but one baby girl kept her hands bent backwards towards the wrist, with the fingers bent down and another had unusually bent fingers.

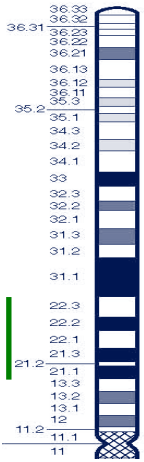
Minor genital anomalies are relatively common among babies with a chromosome disorder, especially boys, and one boy with a 1p13.2p13.3 deletion was born with an unusually small penis.

Most of the babies did not have any major anomaly affecting the body's vital organs but one baby with a 1p13.3p22.3 deletion had a developmental anomaly of the bowel, which caused no problems, but also developed a partial obstruction of the small bowel at four months and needed corrective surgery. Another baby was born with a complex heart condition known as tetralogy of Fallot and sadly did not survive surgery. However, this occurred almost 20 years ago and outcomes for heart surgery in babies are constantly improving. The only other heart defect identified was in a baby with a 1p13.2p13.3 deletion in whom the ductus arteriosus, a channel that takes blood to the

lungs during fetal life, failed to close as it usually does around the time of birth.
In terms of ongoing health, three people developed seizures. Three were found to have a hearing loss, in two cases associated with very narrow ear canals. The boy with a 1p13.2p13.3 deletion went into puberty unusually early. A number of children and adults had varying joint problems, including loose joints, dislocated hips and stiff joints and arthritis.

All seven children and adults showed some level of delay in their development. The most complete description is of the identical twins, aged 30. They sat late at the age of two and walked late at 3½, and as adults had a shuffling gait. By the age of nine, each was speaking quite well but their overall level of delay was considered severe. (Dockery 1991; Tabata 1991; Mattia 1992; Decipher; *Unique*)

Deletion between 1p21 and 1p22



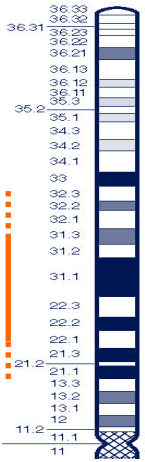
Four people have been described, with one from *Unique* and one from the Decipher database. Breakpoints differed in each case, and the case from Decipher had a small deletion from 1p21.1 which appears to be a natural variant and not to affect development. In all the other cases there were pregnancy problems which included bleeding, less fetal movement than expected, a low level of amniotic fluid and premature birth at 34 weeks. Babies' birth weights were within the normal range apart from the premature baby who was small for dates. Two babies had difficulties as newborns, one with regulating body temperature and the other with a floppy larynx, causing noisy breathing and other difficulties.

In terms of minor or more serious birth anomalies, one baby had quite significant problems. She was born with a complex heart defect that unfortunately could not be repaired surgically. This baby also had a cleft palate (split in the roof of the mouth) and a cleft lip, small kidneys, anomalies of both the rib cage and some vertebrae as well as a forearm defect that resulted in one missing thumb and one undersized one.

In terms of ongoing health, a three-year-old developed absence seizures, where consciousness is lost for a few seconds. These were successfully treated with a low dose of anti-epileptic medication. Two children had a developmental defect of the eye known as a coloboma, but this affected vision in only one of them.

Development was delayed, and one child had dislocated hips and low muscle tone in the legs. Overall, information at *Unique* has shown slow, steady progress. (Hertz 1985; Stockton 1997; Decipher; *Unique*)

Deletion between 1p21/2 and 1p31/2



Ten people have been described, with three from *Unique* and one from the Decipher database with a tiny deletion from band 1p31.1 inherited from an apparently unaffected mother. Breakpoints are very likely different, although as most were examined without molecular techniques we can't be certain. Descriptions range from newborn to an adult of 30 years.

Most pregnancies were uneventful, but one mother reported a 'low flow placenta' and another had a febrile illness in the first and second months of the pregnancy. Babies were born at or near term apart from one birth at 30 weeks, and birth weights were typically low but within the normal range. Three babies had obvious difficulties after birth: one had a slow heart rate and failed to establish breathing at first; another had a major incident where s/he stopped breathing on day three and another at six weeks; and a third baby had seizures in the newborn period.

Feeding behaviour was variable: one baby fed normally, while two others were affected by a swallowing disorder and one was still fed 'sloppy' foods at eight years. Two babies had gastro oesophageal reflux, where feeds return into the food passage and are often vomited or may be inhaled, causing chest infections, known as aspiration pneumonia. One baby with a swallowing disorder had an operation to improve the action of the valve between the food passage and the stomach (fundoplication) and was fed direct to the stomach through a gastrostomy.

"She has changed my life and made me recognise how everything, no matter how small, is very important

Babies had some unusual facial features, but these could be quite subtle. A small chin and lower jaw is mentioned in five babies and six others have unusually formed ears. In terms of minor or more serious birth anomalies, three babies were born with a heart problem. One had a narrowed aorta (the blood vessel that leads from the heart to the rest of the body) requiring surgical correction; another had a narrowing in the vessel that takes blood from the heart to the lungs but this did not need treatment; while the other had holes between both upper and lower heart chambers.
Three children had a thinned or missing band of nerve fibres between the two hemispheres of the brain (corpus callosum), another had enlarged fluid-filled spaces within the brain, another had lobar holoprosencephaly (incomplete separation of the front part of the brain into two hemispheres) and six had an unusually small head (microcephaly). Two baby boys were born with undescended testicles, both surgically corrected, although one boy had one abnormal testicle removed.

A four-year-old girl had an umbilical hernia. Minor foot anomalies were common. Problems included overlapping toes (which can usually be readily corrected with exercises or gentle splinting), a wide 'sandal gap' between the first two toes, puffy feet, prominent heels, a hammer toe and, more seriously, two babies with club foot requiring correction by manipulation, casting, taping, physiotherapy and splinting, bracing and sometimes surgery. Problems with the hands were less noticeable, but a number of children had long thin fingers and thumbs that joined the hands close to the wrist. Four people had loose joints: one child had hips that easily dislocated; another had dislocated kneecaps; three had a spinal curvature - in one case requiring surgical insertion of rods to keep it straight.

> "He has a beautiful smile and brightens our days. Although he doesn't really use speech, he has a range of useful signs and conveys his message with gestures like waving, hugging and shaking hands. He loves looking at pictures and books, playing with the family's dogs, watching TV, riding horseback and bowling. He can walk if you hold his hand or with his walker but has a wheelchair and is working in physical therapy on walking independently - *11 years*

In terms of ongoing health, two children and possibly another baby developed seizures, but these were controlled with medication; and one boy was found to have low thyroid levels, corrected with thyroxine. One boy had lymphoedema (puffy accumulation of fluid) on one side of the body; an eight-year-old had puffy hands and a four-year-old was also found to have oedema of the hands and feet. Two children had repeated respiratory infections and one has low oxygen levels at night. Six have a structural or functional eye problem but the degree to which vision is affected is not known. Three were found to have a hearing loss, in one case associated with very narrow ear canals. Four have dental problems, with late-erupting, small, missing or poor quality teeth. Two teenagers went into puberty late, one at a normal time, one early.

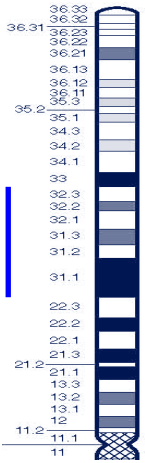
In terms of development, six children or adults were very short for their age (one adult woman was 128cm/ 4'2", an adult man was 150cm/ 4'11"), two were overweight by adolescence and all showed some level of developmental delay, ranging from mild to severe. Children were generally able to sit unsupported in their second year and were walking, perhaps with a walker, by 3 or 4 but one eight-year-old was not walking yet. Increased muscle tone was found despite lax joints in four children, one of whom needed repeated tendon release surgery. Support was generally needed with learning and where IQs were given they were in the 42-50 range but one child has profound and multiple learning difficulties. One child was speaking in sentences by the age of four, while others experienced greater language delays but social interactions were good, with children using gestures, facial expressions and signs to communicate their emotions and needs.

(Bene 1979; Petersen 1987; Lai 1991; Mircher 2003; Callier 2008; Decipher; *Unique*)

"She is a very, very, very happy, loving and sociable girl and always has to be the centre of attention. She's co-operative, so she opens her mouth for her teeth to be brushed and co-operates with dressing by pushing her arms into the sleeves. She's not yet toilet trained.

"She doesn't talk but she has lots of babble and repetitive phrases and can sign words like Yes, No, tired and happy. She also understands a lot and responds appropriately to simple questions and instructions. She's at a special school and enjoys listening to stories, especially the rhyming type - *8 years*

Deletion between 1p31 and 1p32



Seven people have been described, with four from *Unique*. Breakpoints are very likely different, although as most were examined without molecular techniques we can't be certain. Descriptions are of very young children.

Two pregnancies were uneventful, but in one pregnancy there was repeated bleeding and in another the baby was born prematurely at 35 weeks. Only two birth weights are known and one was low, the other normal. One baby had obvious difficulties after birth, with episodes of turning blue within 12 hours and seizures starting on day two; another developed severe jaundice.

Where feeding behaviour is known, it generally - but not universally - failed to meet the baby's nutritional needs. One baby was fed expressed breast milk from a bottle, while another had a fortified formula to encourage growth and weight gain.

Babies had some unusual facial features, but these could be quite subtle and varied between individual babies.

In terms of minor or more serious birth anomalies, two babies were born with a missing band of nerve fibres between the two hemispheres of the brain (corpus callosum) and three had enlarged fluid-filled spaces within the brain. No babies were reportedly born with an unusually small head but two had a large head and one an average-sized head. One baby had multiple holes between the two lower pumping chambers of the heart, requiring surgical correction, and two had a spinal anomaly known as a tethered cord, where the normally free spinal cord is held at one point, causing pulling on the cord and a decreased blood supply. If necessary the cord can be surgically released so that it can hang freely. One of these babies also had a condition known as a Chiari malformation, in which part of the brain protrudes into the spinal canal.

One baby boy was born with undescended testicles and an inguinal (groin) hernia on one side and he also had a small extra thumb on one hand, which was removed when he was four months old. He also had one unusually positioned foot, which was corrected by plaster casting, as did another baby. A baby girl was born with an umbilical hernia and another with the anus somewhat displaced. One baby was born with dislocated hips, requiring surgical correction.

In terms of ongoing health, one baby and possibly another developed seizures, controlled with antiepileptic medication. One of these babies had a thinned corpus callosum. Three babies had urinary tract infections, one had enlarged kidneys (hydronephrosis) and one had a kidney abscess secondary to kidney reflux. One baby was found at four weeks to have gallstones but these caused no symptoms. Another had sphaerocytosis, where the red blood cells have an abnormal shape.

Two children were found to have a hearing loss, in one case cause by a build-up of fluid behind the ear drum, in the other case a permanent impairment for which she wore hearing aids. One child had a squint (strabismus) and long sight.

In terms of growth and development, two children were very short for their age and all showed some level of developmental delay. However, one child was reported despite developmental delays to be of normal intelligence at the age of three years. Children were generally late to sit and to walk. Increased muscle tone was found in two children and low tone in three children, of whom one was only mildly affected. Support was generally needed with learning. Children were slow to talk, one child not producing words until the age of seven. One child did, however, show a progressive loss of skills from the age of seven.

Social interactions were generally good, with children characterised as typically happy and loving.

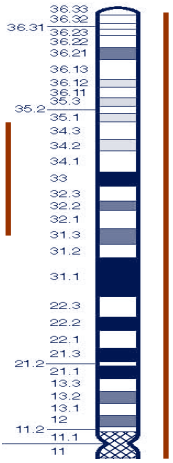
(Barton 1995; Campbell 2002; *Unique*)

> "She has a fantastic sense of humour – quite wicked at times. Everyone who meets her remarks on her strength of character. She is extremely caring, particularly when someone is poorly - *20 years old, with a deletion within bands 1p3 with uncertain breakpoints*

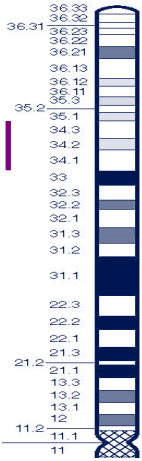
Deletion between 1p32 and 1p34

A single nine-month-old girl has been reported with a 1p32.3p34.1 deletion. After an uneventful pregnancy and a normal term birth, she was born weighing a healthy 3.11kg (6lb 14oz). She had two strawberry birthmarks on her scalp and experienced prolonged jaundice. Her facial features were unusual and she had a high, narrow palate. On CT scan, her brain showed slightly enlarged fluid-filled spaces and areas of low density in the white matter. Her right kidney was swollen, as was the ureter (tube) leading from it to the bladder. She had unimportant unusual features of the hands and feet. She had low muscle tone and her development was slightly delayed - she started walking at 22 months.

(Yoshino 1991)



Deletions within 1p34



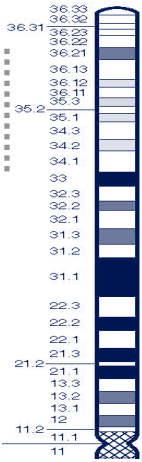
Five children have been described, with one from *Unique* and two from the Decipher database. Two children have the same breakpoints at 1p34.1 and 1p34.3 and are related. Three others have been characterised using molecular techniques, making breakpoints more certain but each has different breakpoints - one in band 1p34.2, one from band 1p34.2 to 34.3 and one in band 1p34.3. Descriptions are up to age 13 but information is very incomplete.

A pregnancy where both breakpoints were in 1p34.3 ended in premature delivery, with the baby weighing 1.446kg (3lb 3oz).
A baby with a deletion from 1p34.2 to 1p34.3 was born with an unusually small head (microcephaly). Apart from some unusual facial features, babies did not have any birth anomalies. A brother and sister with the same deletion between 1p34.1 and 1p34.3 grew normally, at the expected rate for their age.
In terms of development, the brother and sister with the same deletion experienced some learning difficulties but had IQs within the normal range on testing. They each had behavioural and attention difficulties which may have been compounded or caused by difficulties within the family background. Development in two children with a deletion within 1p34.3 and between 1p34.2 and 1p34.3 was delayed, in the first case quite markedly, with rolling at one year and crawling at two.

There are no reports of health problems apart from the child with a 1p34.2p34.3 deletion who had early feeding difficulties and cyclical vomiting (bouts of being sick again and again and feeling tired and nauseated (sick) without any obvious cause).

(Martínez 1999; Decipher; *Unique*)

Deletions from 1p34/5/6 to 1p36



Five children have been described, with one from *Unique* and two from the Decipher database. Three individuals described in the medical literature and within *Unique* have similar deletions from 1p34.3 to 1p36.1; the two from Decipher have smaller deletions that don't overlap from 1p35.2 to 1p36.11 and from 1p36.12 to 1p36.13. The oldest child described is eight years old but overall descriptions are very incomplete.

Overall, these children had more developmental and health problems than those with a more proximal deletion. Three were born with a heart problem, two of them complex and the third a hole between the upper filling chambers of the heart. One baby with a 1p34p36 deletion had a heart defect known as Ebstein's anomaly, where the valve that controls blood flow from the top chamber (atrium) to the bottom (ventricle) is too low down, making the top chamber too big and the bottom chamber too small. This rare heart anomaly has also been seen in children with 1p36 deletion syndrome. Four children also had lung problems or unusual features

of the windpipe (trachea). One had structural anomalies of the brain and underdeveloped optic nerves so that he was visually impaired.

In terms of less serious problems at birth, one baby was born with a membrane over the pupils of the eyes, three had unusually placed thumbs or oddly-shaped fingers and two babies had an unusually small lower jaw. All babies described had an unusually high palate and in a baby with a small lower jaw the combination caused significant early feeding difficulties. It's been remarked that children with a deletion just proximal of the 1p36 deletion syndrome (*see page 3*) breakpoints typically have a lot of body hair and this was seen in a child with a 1p34p36 deletion too. Where development was described, it was relatively severely delayed.

(Howard 1990; Yang 2004; Decipher; *Unique*)

20 years old, with a 1p3 deletion

" Our daughter was born with multiple problems, the most obvious being her cleft lip and palate. This meant that she couldn't feed and for the first three months she was fed by nasogastric tube. She then graduated to the Haberman feeding system and her lip and palate were repaired but even today when she drinks, liquid tends to return down her nose.

" She was also born with a heart defect and today this means that when she exerts herself, her lips turn blue and she gets tired and cold quickly. It has an overall effect on her health in that she tends to be tired all the time and coughs and colds take a long time to clear. With time, she has developed two further conditions – scoliosis, so her back is painful, and a disorder called keratosis pilaris where the skin becomes rough like goose-flesh. She gets thick keloid scarring as well and her skin conditions can make her life a bit of a misery.

" Her development was delayed but she was walking on her own when she was just over two and climbing stairs by three. These days she uses a wheelchair to make life easier when she has to go any distance. Her thumbs are unusually formed and have no joints, which makes feeding herself, washing and so on more of a challenge. But she copes well with prompting from someone else and just needs help washing her hair and with toileting.

" Our daughter is very sociable and amenable and this helps when she is learning new skills. She enjoys swimming, computer activities, craft activities, her dolls and Minnie Mouse and she likes going out to eat or to have a coffee. She's good at remembering directions or, for example, where puzzle pieces fit and generally she's better at hands-on activities when she's been shown how – such as cookery or cutting up fruit and vegetables. She enjoys looking at books and magazines, loves colouring and can draw simple stick people. When she can't express what she wants, she can get extremely frustrated but she makes the vocal approximations of a few words and uses Makaton signs and symbols and gestures. A legacy of her cleft is that her speech is very nasal.

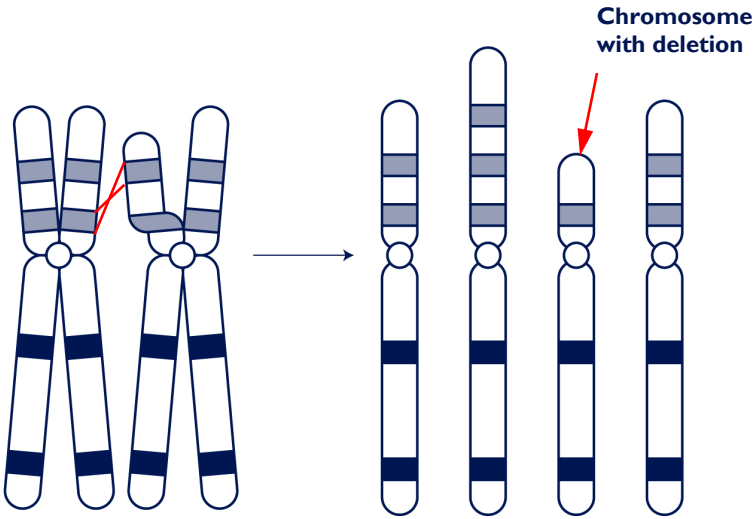
" Her behaviour is mostly determined by how much frustration her communication difficulties are giving her. She can be smiling and laughing one minute and in a major tantrum the next! And she can be very stubborn and defiant – so it's very, very challenging for whoever is looking after her. Added to that, she is always on the go!

How did this happen?

A blood test to check both parents' chromosomes is needed to find out why the 1p deletion occurred in the child. Most 1p interstitial deletions occur when both parents have normal chromosomes. The term that geneticists use for this is **de novo** (dn), meaning 'new'. De novo 1p deletions are caused by a sporadic mistake that is thought to occur when the parents' sperm or egg cells are formed or possibly just after conception. We are still learning about the underlying mechanism but we do know that while chromosomes must break and rejoin in quite a complex process around this time, it only occasionally leads to problems.

When a sperm cell from the father and egg cell from the mother first join together, each carries just one copy of each chromosome. Together they form a single cell that now carries two copies of each chromosome. This cell must make many copies of itself (and all the chromosomes and genetic material) in order to make all of the many cells that form during human development. Sometimes during the formation of the egg or sperm cells or during this complicated copying and replication process, parts of the chromosomes can break off or become arranged differently than usual.

One possible way in which a 1p deletion might occur is by a mismatch between chromosomes. This works as follows: at one point in the formation of the sperm or egg cells, all the chromosomes including the two chromosome 1s pair up and swap segments. To pair up precisely, each chromosome 'recognises' matching or near-matching DNA sequences on its partner chromosome. However, throughout the chromosomes there are many DNA sequences that are so similar that it is thought that mispairing can occur. Although no-one has ever seen this happen, it is believed that when the next step, the exchange of genetic material known as 'crossing over' occurs, it is unequal, looping out or doubling up a length of the chromosome. This process is shown in the diagram below.



What is certain is that as a parent there is nothing you did to cause the 1p deletion and nothing you could have done to prevent it. 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.

Can it happen again?

The possibility of having another pregnancy with a 1p deletion depends on the parents' chromosomes. When a blood test shows that both parents have normal chromosomes, the deletion is very unlikely to happen again in another child.

If either parent has a chromosome change involving 1p, the possibility is greatly increased of having other affected pregnancies. If they wish, parents should have the opportunity to meet a geneticist or genetic counsellor to discuss the specific recurrence risks and options for prenatal and preimplantation genetic diagnosis (PGD). PGD requires the use of in vitro fertilisation and embryo biopsy, and only healthy embryos are transferred to the mother's uterus. If the parents choose to conceive naturally, prenatal diagnosis options include chorionic villus sampling (CVS) or amniocentesis to test the baby's chromosomes. Testing is very accurate, although not all of these tests are available in all parts of the world.

Could my child with a 1p deletion have similarly affected children?

There is one case in the Decipher database of a mother who passed a tiny microdeletion from 1p31.1 to her child. The mother was unaffected but the child had an unusually thin band of nerve fibres connecting the two hemispheres of the brain (corpus callosum). As advances in more sensitive ways of diagnosing chromosome disorders uncover smaller microdeletions, the possibility will increase of discovering more families where the deletion has been passed from generation to generation. Theoretically, someone with the deletion would have a 50 per cent chance of passing it on and a 50 per cent chance of having an unaffected child.

Support and Information

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

Join Unique for family links, information and support.

Unique is a charity without government funding, existing entirely on donations and grants. If you can, please make a donation via our website at www.rarechromo.org Please help us to help you!

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