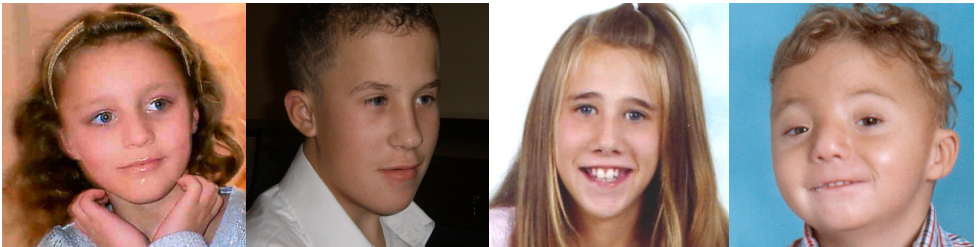


# 10p deletions



## 10p deletions

A chromosome 10p deletion means that part of one of the body's chromosomes has been lost or deleted. If the missing chromosome material contains important instructions for the body, learning difficulties, developmental delay and health problems may occur. How serious these problems are depends on how much of the chromosome has been lost and where the deletion is.

### Genes and chromosomes

Our bodies are made up of billions of cells. Most of the cells contain a complete set of tens of thousands of genes. Genes act like a set of instructions, controlling our growth and development and how our bodies work.

Genes are carried on microscopically small, thread-like structures called chromosomes. There are usually 46 chromosomes, 23 inherited from our mother and 23 inherited from our father, so we have two sets of 23 chromosomes in 'pairs'.

Apart from two sex chromosomes (two Xs for a girl and an X and a Y for a boy) the chromosomes are numbered 1 to 22, generally from largest to smallest.

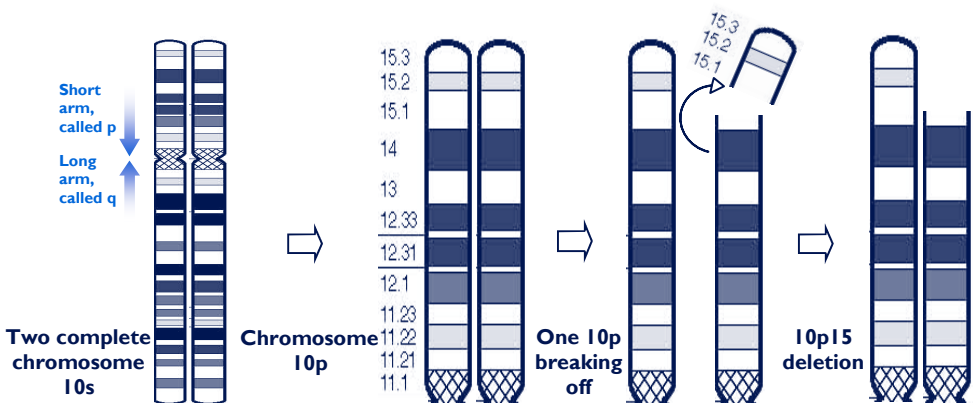
Each chromosome has a short arm (at the top in the picture below) called p from petit, the French word for small, and a long arm called q (at the bottom). In a 10p deletion, material has been lost from the short arm of one of the two chromosome 10s.

You cannot see chromosomes with the naked eye, but if you stain them and make their image about 1,000 times larger with a computer or under a microscope, you can see that each one has a pattern of light and dark bands.

A small piece or a large piece of the chromosome can be missing. Sometimes it can be identified under a microscope or on a computer. The missing piece may be so tiny that it can only be identified using new technology with tests such as FISH or array-CGH. It is then called a **microdeletion**. These tests are sometimes used to check if certain genes are missing and to be more exact about where the chromosome has broken.

One type of deletion is called **terminal**. The chromosome has broken in one place and the part of the chromosome from the breakpoint to the end of the arm is missing.

Another type of deletion is called **interstitial**. There are two breakpoints on the same arm that have rejoined and the part of the chromosome between them is missing.



## How do we know about the effects of a 10p deletion?

Researchers have described around 50 people with a 10p deletion in medical publications, although there are certainly many more. When *Unique* wrote this leaflet, we also had details of 28 members with a 'pure' 10p deletion, without any other chromosome change. *Unique* collects regular reports from its member families so we can see how children and adults develop.

Your genetic specialist can tell you more about the chromosome material that has been lost. You will almost certainly be given a **karyotype**, a shorthand code for your child's chromosomes that shows the points where the chromosome has broken and rejoined. People with a 10p deletion may have the same break in their chromosomes or a similar one but they do not all have the same problems or features. There will be differences between your child and others with apparently similar chromosome changes and these differences can be quite marked. It is very important to see your child as an individual and not to make direct comparisons with others. After all, each of us is unique.

But some features and health problems are similar in people with a 10p deletion. This leaflet describes the things that are similar.

For some specific 10p deletions, little is known and even *Unique* has few records. It is hard to be certain then about the effects but as more people are diagnosed, the picture will hopefully become clearer.

The oldest child with the disorder known to *Unique* is in her late teens and the group has one affected adult member, but it is likely that there are many older people with a 10p deletion.

## 10p15 deletions

When the breakpoint is in band p15, the deletion may be called **subtelomeric**, meaning that a tiny segment has been lost from very close to the end of the chromosome. A 10p15 deletion appears to be rare as an isolated finding and is more commonly accompanied by another change such as the gain of the end of another chromosome arm. By early 2007 there were only brief notes and no full descriptions in the medical literature of people with a 'pure' 10p15 loss but there were five reports of people with a simultaneous gain (duplication) from another chromosome. Two of these are related – an aunt and her niece – and have additional material from chromosome 12p13.2; another has a duplication of the tip of 13q; the other has additional material from the short arm of chromosome 18 (Battaglia 2007 & 2005; Ravnan 2006; Roos 2006; Caliskan 2005). Within *Unique*'s membership, there are five children and an adult with a 'pure' deletion from 10p15 and five with additional material from another chromosome arm, specifically 2q36; 4p15.3; 6p25.3; and 10q26.1.

With such small numbers, it is not possible to be certain about the effects of a subtelomeric 10p deletion. In particular, no-one can know

## Sources and references

The information in this guide is drawn partly from published medical research papers. We have focused on articles describing people with a 'pure' 10p deletion, without any other chromosome change, and on articles that include a review of 10p deletions.

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. If you wish, you can obtain abstracts and articles from *Unique*.

whether or not there are people who have this deletion but develop normally or almost normally and are never diagnosed with a chromosome disorder. The picture that emerges from those with other additional chromosome material is not consistent. Taking what we know about people who have a 'pure' deletion from 10p15, **birth weight** at term appears to be low. The pattern of growth after birth is not consistent; there may be **growth delay**, as occurs in some other children with chromosome disorders, but one child of 10 years old is 'tall but slim'. **Feeding** problems have been described in one child, with difficulty latching on to the breast at first and a delay in moving on from first stage solid foods to lumpier food. In another child unspecified food intolerances have been described.

Three children with a 10p15 deletion: left, 18 months; inset, baby; right, 11 years.



As far as **development** is concerned, a degree of delay in reaching 'baby milestones' may occur. Babies have learned to roll over between 8 and 12 months, to sit between 10 and 18 months and to walk at around two years, but this may not be possible for all children. At least three children have a degree of hypotonia, low

muscle tone that makes the muscles feel floppy but in one child, this was no longer a major concern by the age of 10. One boy had flat feet and has needed to wear plastic heel splints to align his ankles and support his feet.

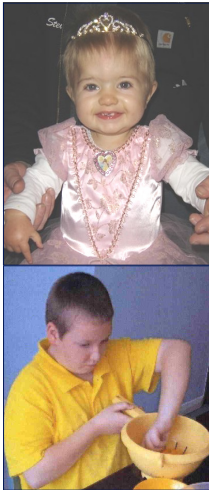
The evidence suggests that these children will need help with their **learning** and in particular may well be late in starting to speak and face **communication** difficulties. First words have emerged at 3 to 4 years and children have benefited from alternative means of communication, in particular signing and using pictures both to communicate needs, ideas and feelings and to signal the sequence of events in a day. At least one child speaks and signs and has progressed to learning to write, at the age of 7, but this may not be possible for all.

In terms of **behaviour**, no particular difficulties have been reported in babyhood. On the contrary, one baby is described as having a lovely, happy personality. In later childhood, it appears that more challenging behaviour has emerged and one child has been described as hyperactive. One child's challenging behaviour reduced dramatically when he moved to a residential school with a highly structured environment, clear routines and a consistent approach.

*Unique* does not have evidence that as a group these children have consistent **medical needs** or birth defects. One child was born with a septal defect (a hole in the heart) that resolved naturally during the first year of life and a degree of hydrocephalus (water on the brain) that also resolved naturally within the first year, and one boy had minor genital problems that could be surgically corrected.

One child had plagiocephaly – an oblique skull shape where one side of the head is longer than the other, giving it the shape of a parallelogram when viewed from one top;

**Different children:**  
**top, 17 months;**  
**below, 11 years.**

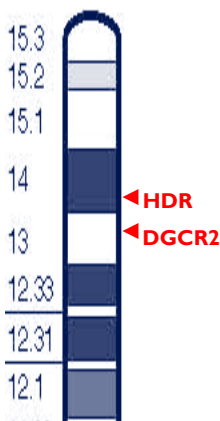


by the age of 10, this was no longer immediately noticeable. Another baby with a deletion from near the tip of 10p was born with early fusion of the join between the plates of the skull that runs down the middle of the forehead (metopic suture) and underwent surgery to re-open the seam to allow more normal head growth. This child also had a blockage in the first part of the intestines at birth, known as duodenal atresia, requiring surgical correction. The thyroid gland was also small and the child has hypothyroidism. Another child with a 10p15 deletion was reported to have a low level of immunity and asthma. Two children developed seizures that were controlled with medication but one of them was able to come off medication at the age of nine without harmful effect.

## Deletions from 10p12, 10p13 or 10p14

Among babies and children with a breakpoint at 10p12, 10p13 or 10p14, features such as some delay in development are consistent and a slow pattern of growth and an unusual look to the face are common. However, individuals vary widely, both in the ways they are affected and the severity of the effects. As a broad generalisation, where the breakpoint is in band 10p14, and especially if the chromosome has broken near to band 10p15, the effects are milder.

Within band 10p14 there is a gene known as *GATA3* and when this gene has been interrupted or is missing, a child is likely to show one or more of the three hallmark features of HDR syndrome (pages 13-14). H stands for hypoparathyroidism. Children often have low calcium levels. D stands for deafness, usually a partial hearing loss that is present from birth and affects both ears. R is for renal. The kidneys may be small, abnormal or one may be missing or there may be urinary tract abnormalities.

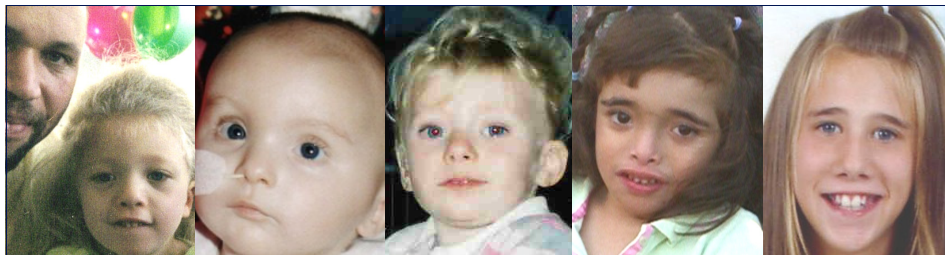


**Approximate position  
of the region for HDR  
syndrome and DiGeorge  
syndrome (see text).**

A little closer to the **centromere** (the point where the short arm meets the long arm) there is a region of 10p known to be important for the normal development of the heart and the cells known as T-cells that help to fight infections. This region is known as the DiGeorge critical region 2 (shortened to DGCR2) because babies and children who have lost important genes from this region have similar clinical problems to babies with a condition known as DiGeorge syndrome. However, DiGeorge syndrome proper is caused by the loss of a tiny amount of chromosome material from the long arm of chromosome 22. The geneticist or paediatrician who tells you about your child's chromosome disorder should be able to tell you whether your child has lost *GATA3* or the *DGCR2*.

## Appearance

To parents, a baby with a 10p deletion may look little different to other babies. Nonetheless, you may see familiar features in the pictures in this leaflet and if you meet another affected family, you may notice some similarities between your child and theirs. Any similarities are likely to be less easy to interpret if your child has a 10p deletion as part of a more complex chromosome rearrangement.



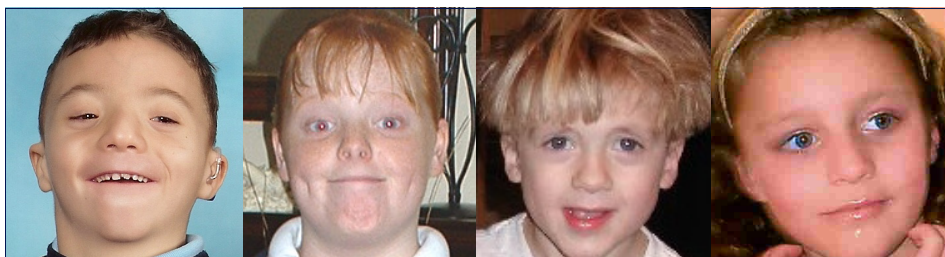
**10p12 deletion:**  
2 to 3 years old

**10p13 deletion:**  
1 year old

**10p13 deletion:**  
20 months old

**10p13 deletion:**  
6 years old

**10p13 deletion:**  
10 years old



**10p14 deletion:**  
6 years old

**10p14 deletion:**  
11 years old

**10p13p15 deletion:**  
5 years old

**10p14p15.3 deletion:**  
7 years old

## Growth

**10p14** It seems that some babies and children with a breakpoint at 10p14 grow slowly and tend to be short, but this is certainly not true for everyone. Some pregnancies are normal and ultrasound scans show no growth delay, while in other pregnancies the baby may be seen to be small for gestational age by the third trimester. Most babies are born at or slightly before term and the range of birth weights at term is broad – from 2.2kg (4lb 14oz) to 3.75kg (8lb 4oz). Length at birth varies a lot, from one baby who measured 40cm (16 inches) at 36 weeks to another measuring 52cm (20 inches) at term. Only one adult has been described – a 26-year-old who was 136cm tall (4' 6") whose small size was noticed as early as the third trimester of pregnancy. Within *Unique's* experience there is one boy whose growth was normal to birth but then tailed off so that by the age of five he was short for his age and a 10-year-old of normal height. One child with an interstitial deletion between 10p14 and 10p15.3 was an average size at birth and remained an average height and weight and was growing well at 7 years of age (Van Esch 1999; *Unique*).

**10p13** Clinical studies report that babies may be moderately underweight at birth, with a mean birth weight of 2.44-2.62kg (5lb 6-12oz). The *Unique* series shows wide variation, with birth weights at term ranging from 1.474kg (3lb 4oz) to 3.26kg (7lb 3oz).



Growth delay appears to continue after birth and most children for whom *Unique* has information are short for their age, although proportionate. There is some evidence that when birth weight is within the normal range, a somewhat faster rate of growth may continue afterwards. One 10-year-old with a birth length and weight in the normal range and no important health problems was in the top 10 per cent of the population for height (Schinzel 2000; *Unique*).

**10p12** The range of birth weights is broad and some babies are born a normal weight. The recorded range is from 1.93kg (4lb 4oz) to 3.23kg (7lb 2oz). One baby weighed 2.14 kg (4lb 11oz) when born at 35 weeks, falling within the 10<sup>th</sup> to 25<sup>th</sup> centiles. *Unique* has information on one child, whose growth in early childhood tracked the lowest curves on the growth chart but followed a normal pattern (Schuffenhauer 1998; *Unique*).

## Feeding

**10p14** Many babies do appear to have feeding difficulties in early childhood, but the severity of any problems varies very much and at least two children with an interstitial deletion (10p14-15.3; 10p13-15) had no significant feeding difficulties, although constipation became a long-lasting problem for one. Typically, some babies have a small lower jaw and receding chin and can find it very hard to latch onto the breast as newborns. Other features may contribute – such as an unusual shape to the mouth (a high arched palate) and a relatively immobile tongue.

If specialist feeding support, adapted teats and enriched milks are not enough to ensure proper weight gain, babies may benefit from temporary feeding direct into the stomach through a nasogastric tube. Occasionally, babies and older children are most appropriately fed for some time through a gastrostomy tube direct into the stomach.

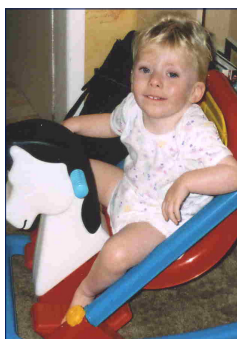
Some babies have quite severe and long-lasting gastro oesophageal reflux, where the stomach contents flush back up the food passage to a significant degree. A baby may inhale milk, which can cause repeated chest infections. Feed thickeners can be added to milk to lessen reflux and propping your baby up after a feed can help. Eventually, some babies outgrow the tendency to bring milk back, but if reflux is severe and persistent, a surgical operation known as a fundoplication can resolve the problem.

Some babies find it hard to move on to solids or chew and in general self feeding skills can be late to develop. Older children may continue to find it hard to chew foods and prefer a soft or mashed diet but *Unique*'s experience is that most of those who have not needed a gastrostomy or other surgical intervention are eating family foods and feeding themselves by school age.

**10p13** Feeding problems may be quite marked and can affect both babies with a heart problem and those without. They may have difficulties coordinating sucking with swallowing, be reluctant to suck or get very easily tired. Reflux may occur and babies are then at risk of choking or of inhaling part of their feeds or stomach secretions, setting the scene for respiratory infections. Some children have much milder feeding problems and others gradually outgrow their early difficulties and progress to eating ground or blended solids and eventually to family foods, albeit with delay. More severely affected babies have benefited in the short or long term from gastrostomy feeding direct to the stomach, eventually with gradual introduction of oral feeding alongside the gastrostomy tube (*Unique*).



**10p14 deletion,  
2 years old**



**10p13 deletion,  
20 months old**



**10p13p15 deletion,  
5 years old**

“ She still gets respiratory infections due to aspiration of secretions, but much less frequently and recovers more rapidly. We often go for months without nasal suction when it used to be several times a day ” - age 6

“ From the age of eight she has eaten almost anything but only when she wants to. As we believe this is behaviour-related, if she refuses what is served she has to wait for her next meal. She is quickly learning to eat at mealtimes ” - age 10

**10p12** The feeding difficulties described for children with 10p13 and 10p14 deletions appear to affect babies and children with 10p12 deletions, perhaps more severely.

One child began to feed herself from the age of 7.

### **Sitting, moving, walking**

**10p14** Babies can be expected to be delayed in reaching their mobility ‘milestones’, but the evidence from *Unique* is that the delay is not usually great. All children known to *Unique* were walking before school age.

Some children had a mild degree of hypotonia, the low muscle tone that leaves muscles feeling loose and the child holding a ‘floppy’ posture, but none needed support for walking. After wearing splints for a year at age 5 to 6, one child with an interstitial deletion between 10p14 and 10p15.3 walked, ran and skipped like her peers and won her school sports day running race.

Every baby sets his own timetable, but those known to *Unique* rolled over between 4 and 12 months, were sitting by 15 months, were on the move - bottom shuffling, scooting or crawling - by 17 months and started to take independent steps between 22 months and 3 years and 6 months. Climbing stairs, running and dancing generally followed but one family remarked that their son had difficulty integrating both sides of the body and faced difficulties in actions such as jumping and riding a bicycle. Another family remarked that their daughter’s feet and back were painful, despite her good mobility.

“ Somewhat behind his peers, clumsy and cautious ”

**10p13** As a group, children with a breakpoint at 10p13 seem to develop somewhat more slowly than children with a 10p14 deletion. As individuals, some children move ahead as fast as a child with a 10p14 deletion, while others reach their developmental milestones later. The boy (left) with a 10p13-15 deletion has normal mobility. Low muscle tone is common and although this improves with increasing mobility, it tends to persist. Any anatomical anomaly, such as overlapping toes, tends to delay walking. Once mobile, children may be a danger to



themselves due to their limited understanding of their environment but increasing physical ability. *Unique* records show that babies rolled over between 6 and 18 months, sat alone between 10 and 18 months, and in some cases were on the move around their second birthday and walking by age 3 to 5 years (in two cases before their second birthday), although this will not be possible for all. Once children are on the move, mobility continues to improve, with faster, more independent walking, climbing stairs and running becoming possible for some. Although walking is possible, some children will not always walk when required and many families rely on a buggy, stroller or wheelchair outdoors.

**10p12** There is very scant information about mobility in these children. While there is one report of a child not yet standing at 9 years, *Unique* has two members who were walking by the age of 8 (Schuffenhauer 1998; *Unique*).

## Learning

**10p14** Children are very likely to need some support with their learning, but how much help will be needed will only become clear with time. Reports from the medical literature suggest a generally less optimistic picture than *Unique* families, in part because the medical reports are older and children were less likely to receive early stimulation and intervention. Within the *Unique* group, there is quite a range of achievement. Two children are characterised as having severe learning difficulties; one child with a deletion between 10p14 and p15.3 had a mild to moderate delay at the age of four and by the age of seven was writing simple sentences, doing simple arithmetic and reading at an age 5.5 to 6-year equivalent. She was competent with a computer and mouse, having started at 4 years. Two children, both at early primary age, attended mainstream schools but learned best when taught 1:1; one of these moved to a special needs secondary school.

One child had particular facility in reading and was more skilful at writing at a keyboard than by hand.

“ He did not reach for toys as a baby, did not babble and was rather passive. He has presented with sensory dysfunctions from birth: he is oversensitive to movement, loud sounds and touch. At the age of 5, he is very musical, perceptive and affectionate; he can draw a face and is learning to write his name. The weak areas for him are visual/ spatial/ language and memory ” - age 5

“ His developmental delay is particularly apparent in speech and language and he has trouble judging the speed and proximity of objects as well as with spatial awareness. He started to read and write in his sixth year ”

“ She loves reading ” - age 10

## 10p13 & 10p12

Most children appear to need considerable help with their learning. In addition to their cognitive difficulties, many have a low muscle tone and the skills of holding and handling objects develop late. This is not, however, true for all and at least one *Unique* member has a moderate learning disability, no hypotonia and good coordination, while a child with a 10p13-15 deletion was 18 months behind at age 7.

“ We make sure she feels love, stimulation and has routines to advance at her own pace ” - age 3

- “ In some ways he is very cute. He doesn't seem to understand commands but for example when dinner is being served automatically sits up at the table ” - age 4
- “ She seems to learn through mobility and her determination, playfulness, physical strength and sweetness. She likes to look at picture books and turn pages, but does not read ” - age 6
- “ An excellent memory for places, loves the social part of school, music, computers and physical education but is unable to focus for long periods. She attends a mainstream school with most of her time in a special education class ” - age 10

## Communication

Many children who have lost the GATA3 gene from 10p14 will have a hearing loss and need to wear hearing aids that they can tolerate. With aids, hearing can be improved and in some cases apparently brought to normal levels.

**10p14** Very young children typically use non-verbal communication, smiling, crying, making vocal noises and pushing or pulling when they want something. Babies and young children usually have some hearing but they face great difficulties in understanding speech. Speech and language therapy is very important and from the age of around three some children learn to sign their needs or use pictures for communication. Speech may develop in some children, particularly once they are wearing hearing aids, and its complexity is likely to reflect the child's general learning ability. One *Unique* member had speech apraxia, that is, difficulty saying what he wanted correctly and consistently and had particular problems with articulation and sequencing. Treatment of speech apraxia is tailored to the individual and usually calls for frequent 1:1 therapy. By the age of 10, one girl was talking in 'short, broken down sentences'. One child with an interstitial deletion between 10p14 and 10p15.3 was communicating in full sentences by age 7 and although repetitive in her speech and tending to favourite topics of conversation, was clear to understand, with a vocabulary probably typical of a 5-year-old. Her understanding improved in early childhood so that by age 7, there was no longer a need to simplify commands. Her vocabulary was still expanding and she could hold conversations including answering and asking questions, although she quite often repeated the question.

**10p13 & 10p12** *Unique's* experience is that older children who have a hearing loss that was not determined in early babyhood have not usually learned to speak. It is too early to know whether early diagnosis and intervention will enable youngsters with 10p13 and 10p12 deletions to acquire more than single-word speech. Despite their lack of speech, children are able to communicate their needs through gesture, movement and in some cases signing and using pictures. One member with difficulty in discriminating sounds rather than a hearing impairment has a three word vocabulary by mid-childhood and communicates chiefly by signing and pictures. At 7 years, a boy with a 10p13-15 deletion can talk conversationally but has difficulty making many sounds of speech.

## Hearing aids: one family's experience



**The aid can be seen in place in the ear.**

“Hearing is as important as vision to a child with severe to profound learning difficulties and with an 80 decibel hearing loss on both sides, our 16-year-old daughter (deletion 10p13 and duplication 5q35.2) needs hearing aids. We started with Behind-the-Ear (BTE) aids when she was 18 months old but as her outer ears (pinnae) are small and soft, the casings would not sit flat against her head and resisted all attempts to restrain them with soft loops or tape. Being small and floppy, our daughter spent her time rolling on the floor or propped up. The aids would catch on carpet or textiles and get pulled out or the tubes would break.

“When our daughter was three, a visit to a 10p- family with an older hearing-impaired child yielded the suggestion of In-the-Ear (ITE) aids and since then, our daughter has never looked back! With

ITEs, the components are encased within the ear mould and if the manufacturers can produce a faithful mould from a good impression using a soft material at the canal end, the aid sits comfortably within the ear. As our daughter is very mobile and still spends much of her life at floor level, her ITEs are ‘low profile’ so that the knobs do not protrude and catch on clothing or furniture. The volume control is screwdriver-adjustable so that she does not adjust the volume when she touches the aid. Drawbacks are that ITEs are more expensive and problematic to manufacture than BTEs, so take longer to replace. Indeed, we have found only one manufacturer able to make successful ITEs for our daughter. Also, we cannot give her an ideal loud volume because with small ears and consequently aids, the close proximity of amplifier to microphone would cause constant feedback.

“However, our daughter loves her hearing aids and is unhappy without them. She tells us when she wants them in by rubbing her ears and once they are in place, she listens well and becomes far noisier herself, since then she can hear what she’s ‘saying’! She does flick them out when tired or irritable or when the batteries go dead and as replacements are not covered by local insurance, we have to guard against losses.

“There are other types of hearing aid available such as body aids where the components are worn in a bag strapped to the body – useful where higher volume is needed but difficult to manage for a child with severe learning difficulties. The internet is a good source of information and you can then discuss the options with your audiologist.

“One thing: through aids, all sound is amplified, not just the bits you want to be heard and even speech is overlaid with electronic ‘noise’. Don’t expect your child to fall in love with your voice! This could be a reason for trialing the newer, digital hearing aids if you can.”

*Your child’s audiologist will advise on suitable aids. For further information on hearing aids in the UK, contact the National Deaf Children’s Society on 0808 800 8880 [www.ndcs.org.uk](http://www.ndcs.org.uk)  
In the US you can contact the Hearing Loss Association of America at [www.hearingloss.org](http://www.hearingloss.org)*

## Behaviour

There appears to be no typical behaviour pattern associated with a 10p deletion.

Some children show features of autism or have difficulties with concentration but these are generally consistent with their level of understanding of the world around them and in line with their general learning ability.

More than one family has mentioned the emergence of challenging behaviours in middle childhood. In one case, these proved hard to manage as the triggers changed rapidly and medication (risperidone) was taken.



**10p13 deletion:  
10 years old**

In another case the challenging and oppositional behaviour of a child with a 10p15 deletion settled once he was in a highly structured environment with clear routines and a consistent approach.

### **10p14**

“ Slow, cautious and hesitant in his actions. Has a very difficult time with transitions and gets anxious when his routine is disturbed ” - age 5

“ A very independent little girl who knows her own mind. She has challenging behaviour at times though with patience it can be managed. Due to her autistic tendencies her play is immature and repetitive and she can occasionally shout or hit out at her peers or teachers.

She interacts well but loves her own way and if she doesn't achieve this she will scream or hit. Her play is more immature than her peers which can mean she is left out or ignored which upsets her. She loves to dance, likes computer games, jigsaws and playing outdoors ” - age 7

### **10p13**

“ Very placid and gentle. He is oblivious of walking over his younger brother etc but is never deliberately aggressive ” - age 3

“ Our biggest area of concern at present ” - age 10

“ No behaviour problems. She does not get frustrated because she does not try to do very much ” - age 15

### **10p12**

“ Very amiable and happy, loves to be held, hugged and kissed ”



**10p14 deletion:  
11 years old**

## **Medical concerns**

### **HDR syndrome (Barakat syndrome)**

The absence of the GATA3 gene located within band 10p14 is known to cause the three key symptoms of HDR syndrome – hypoparathyroidism, deafness and renal problems. Research studies so far suggest that around half the babies and children who have lost the gene will have each of the three symptoms. So a child may have one, two or all three of the symptoms. Some children, however, have no symptoms of HDR syndrome.

### **H - Hypoparathyroidism**

Embedded within the thyroid gland at the base of the front of the neck are four minute hypoparathyroid glands that release a hormone, PTH, whose function is to regulate the calcium levels in the blood. When the GATA3 gene is missing or mutated, the glands may not develop completely or they may be missing altogether.

This results in hypoparathyroidism and the main effect is an abnormally low level of calcium in the blood, known as hypocalcaemia.

Babies and children known to have a 10p deletion will have a blood test to show whether they have hypoparathyroidism. If the tests are positive, treatment will be started with vitamin D replacement and sometimes calcium. So long as the blood levels of calcium then return to the normal range, any symptoms should vanish and problems should not worsen. The calcium can be given as dissolvable granules (or as chewable tablets) and vitamin D is usually given as drops or capsules of 1-alpha calcidol. This is the form of vitamin D that the body cannot make without PTH and is needed for calcium to be absorbed from the gut. Many people only need treatment with 1-alpha-calcidol and not with extra calcium. Treatment will be needed for the rest of the child's life. The aim of treatment is to keep your child's blood calcium within the normal range and to ensure that the ratio between the calcium in the blood and creatinine (a protein produced by muscle) also stays within the normal range to avoid the risk of calcium deposits in the kidneys (nephrocalcinosis) and eventual kidney impairment.

At first your child will need frequent blood tests, although this will depend on the calcium levels when your child was diagnosed and on his or her age. Once the calcium levels in the blood are stable, blood and urine tests are generally carried out every six months or so.

It is important to treat hypocalcaemia as early as possible to lessen the impact of any long term effects. If calcium levels have been too low for a long time before treatment started there may be some long term effects. Low calcium levels affect the development and functioning of the brain, so there may be some effects on learning. If levels of calcium drop low enough to cause repeated and prolonged fits (seizures, epilepsy), these too can have long-term effects on learning. Low calcium levels can also affect the functioning of the heart and longstanding hypocalcaemia can result in cataracts which may need to be surgically removed.

Mild hypocalcaemia is usually symptomless but when it is more severe it is likely to produce symptoms. This occurs most often when a child is going through a phase of rapid growth, that is, as a baby and again in adolescence. Symptoms in a baby can be vague and non-specific. Babies may have tremors, spells when they stop breathing (apnoeas) and turn blue; they may be lethargic. Any baby who has fits (seizures, epilepsy), stiffness of the hands or feet and whose breathing is noisy and laboured due to a spasm of the vocal cords (stridor) should have an urgent measurement of the calcium level. Older children may develop muscle cramps, tiredness and spasms but symptoms can also include seizures and stridor.

## **D - Hearing loss**

Of the three hallmark features of HDR syndrome, hearing loss appears to be the most consistent among children with 10p13 and 10p14 deletions. No child with a 'pure' 10p15 deletion has had reported hearing loss, but all children with a 10p12 loss who were tested showed a moderate to severe loss. The cause of the hearing loss is cochlear degeneration and the loss usually starts before birth as newborn babies already have an obvious impairment in both ears. This is most obvious for high frequency sound and is permanent. With time, the hearing loss generally becomes more marked but with aids, it should be possible to achieve normal hearing levels.



Many children also get repeated ear infections that can lead to the long term build up of fluid within the middle ear known as 'glue ear'. Glue ear causes an intermittent deafness that has an add-on effect to any permanent hearing loss caused by the 10p deletion. Glue ear is treated by draining off any excess fluid and inserting tiny ventilation tubes (grommets) into the eardrum. Although some children are fitted with grommets, these will not provide a permanent solution and most babies and children need hearing aids. Most babies also have narrow ear canals which need regular cleaning to ensure they do not block with wax and can make fitting the aids difficult (van der Wees 2004; Van Esch 2000; *Unique*).

## **R - Renal problems**

Once it is known that a baby or child has a 10p deletion, the kidneys and urinary tract will be checked in the first instance with an ultrasound scan of the bladder and kidneys and any treatment will depend on what is found.

The kidneys and urinary tract may show abnormalities although the nature of the defects varies from child to child. The kidneys may be small, one may be missing, there can be a duplex kidney (where the drainage system forms in duplicate), hydronephrosis (kidney enlargement, usually due to an obstruction) or urinary reflux, caused when the urine flushes back from the bladder to the kidneys instead of flowing straight out.

Treatment depends on how severely the kidneys are affected. Very mildly affected children may only need regular monitoring, while a child who is severely affected may need kidney dialysis or a transplant (Skrypnyk 2002; Berend 2000; *Unique*).

## ■ **Heart problems**

Heart conditions have been found in around half of the babies and children with a 10p deletion reported in the medical literature and it has been suggested that there are genes around the border of 10p13 and 10p14 that are important for the development of a healthy heart. This region has been called the DiGeorge 2 region or DGCR2 (CR stands for critical region). Different heart conditions have been found, most commonly holes between the two sides of the heart, abnormally formed valves and a blockage in the blood vessel that takes blood from the heart to the lungs to collect oxygen. The most common abnormality is a hole between the two upper chambers of the heart (atrial septal defect, ASD) and recently researchers have pinpointed a segment of 10p14 that may contain genes important for the development of a normal heart. However even among children who have lost this segment of chromosome 10p, around one baby in three is born with a normal heart (Yatsenko 2004).

Small holes between each side of the heart usually diminish with time and may close naturally, but larger holes generally need surgical repair. *Unique's* experience has been that most families do not report a heart anomaly and that many defects do not interfere with a child's activities so much that surgical correction is needed. Generally speaking, children who do need surgery to correct their heart defects thrive afterwards.

## ■ **Thymus gland and infections**

A 10p deletion can affect the development of the thymus gland. This is a small gland normally at the base of the neck, where T-cells, one of the groups of white blood cell that help to fight infection, mature. Some children with a 10p deletion have a very small

thymus gland, in some children it does not work efficiently and other children may not have a thymus gland at all. Without a properly functioning thymus, a child cannot produce normal numbers of T-cells and children may have lower than normal levels of T-cells. This can mean that infections are slow to clear or are recurrent or both.

Generally as children grow older they are better able to produce T-cells and their immune system becomes more effective. The thymus is most important early on in life and as children get older it shrinks.

Some children do have unusually frequent ear, chest and urinary infections, but without evidence of underlying immunodeficiency.

#### ■ Minor hand and foot abnormalities

These are quite common and varied but they do not usually have a major impact on your child. Researchers report features such as incurved fingers and toes or fingers that overlap or are joined together by a web of skin and tissue; extra fingers; club hand and foot; broad thumbs; small final finger joints; and fingers that are bent and cannot be straightened, even by someone else.

Among *Unique* members, one child with a 10p14 deletion and three out of 10 with a 10p13 deletion had webbed toes (joined by skin and tissue), especially toes 2 and 3; this affected one out of four children with a 10p12 deletion. The family of one child with a 10p12 deletion reported that he had large thumbs. From the medical literature, one child with a 10p14 deletion had short arms and another had small hands and feet with shortened final finger and toe joints (Fryns 1981; Suci 1983; *Unique*).

#### ■ Genital anomalies

Among baby boys, minor genital anomalies are fairly common, regardless of the breakpoint in 10p. At birth one or both testicles (testes) may not have descended from the abdomen, where they develop during fetal life, into the scrotum (cryptorchidism). Regardless of whether they have a chromosome disorder or not, cryptorchidism is found in about three in 100 baby boys born at term but by the age of one year, 80 per cent of undescended testes have come down naturally. Treatment for undescended testicles depends on the suspected cause but whatever the cause, treatment is usually needed if the testicles do not descend naturally in time. If a hormone problem is suspected to be the cause, a short course of hormone treatment may be suggested. Otherwise, or if hormone treatment does not work, the testicles can be brought down in a short operation under general anaesthetic called an orchidopexy.

Hypospadias may also occur, where the hole through which urine passes is not at the end of the penis. In addition, all the foreskin may be at the back of the penis with none at the front and the penis may curve when it is stiff. This can be corrected surgically.

Among girls, one with a deletion between 10p13 and 10p14 was found to have a duplicated Fallopian tube; a girl with a 10p14 deletion had a developmental defect of the uterus.

#### ■ Intestines and bottom

A girl with a 10p14 deletion was born with a malpositioned anus; this was surgically corrected. Meanwhile for six months she had a colostomy, a surgical operation in which part of the colon (large intestine) is opened through the wall of the abdomen, functioning as a substitute anus.

Two *Unique* members with a 10p13 deletion experienced pyloric stenosis as young babies. In this condition the opening between the stomach and the beginning of the intestines narrows so that milk cannot get through. It affects young babies usually between two and eight weeks old and causes forceful vomiting. After first treating any dehydration and mineral imbalances caused by the vomiting, the tight pyloric muscle is repaired surgically. There are usually no long term effects and the problem is unlikely to recur.

#### ■ Seizures

Seizures may occur in children with 10p deletions. One cause is a low level of blood calcium and vitamin D/calcium replacement prevents this type of seizure from occurring. Among three children with a 'pure' 10p15 deletion and normal calcium levels, two have experienced seizures, controlled with medication.

#### ■ Eyesight

There are two typical vision problems associated with untreated 10p deletions but both are generally avoidable. Ptosis (hooded eyelids) can cause vision problems when they obscure the pupil and it may be helpful to operate surgically to raise the eyelid. Untreated hypocalcaemia can also cause cataracts to develop over the lens of the eye but these do not progress once the low calcium levels are corrected.

Otherwise, no typical vision problems are associated with 10p deletions. However, individual youngsters have experienced a range of eye conditions. These have not been reported in children with 10p15 deletions, but among 10 children with 10p14 deletions two children had blocked tear ducts and three had strabismus (squint). One out of 21 children with a 10p13 deletion was described with strabismus. If strabismus does not respond to glasses or patching or if these are not possible, it can be corrected surgically if necessary. Other eyesight problems described in the medical literature but not among *Unique's* membership include abnormally small eyes, Rieger eye malformation (a collection of abnormalities including a small cornea, an underdeveloped iris and abnormally joined surfaces at the front of the eye) and degeneration of the retina, the light-sensitive film at the back of the eye.

#### ■ Teeth, mouth and jaw

Many children with a 10p deletion have a high palate and a relatively small, receding lower jaw. In one adult the small size of the jaw became less noticeable with age. Apart from the difficulties that the small jaw can cause with latching on as a small baby and later with eating solid foods, it can make the teeth overcrowded so that some need to be removed and others straightened. Some families have noticed that teeth emerge with a thinned enamel.

(10p14 deletions: Verri 2004; Yatsenko 2004; Skrypnik 2002; Van Esch 1999; Kinoshita 1992; Suci 1983; Bourouillou 1981; Fryns 1981)

(10p13 deletions: Faivre 1999; Schuffenhauer 1998; Sunada 1998; Dasouki 1997; Hasegawa 1997; Shapira 1994; Greenberg 1993; Kiss & Osztovcics 1993; Elstner 1984; Klep-de Pater 1981)

(10p12 deletions: Schuffenhauer 1998; Hon 1995)

## Interstitial proximal 10p deletions



**Two children with an interstitial proximal deletion. Above, at 3 years. Right, at 12 years.**



A loss of material from within a chromosome means that there are two breakpoints and is known as an **interstitial deletion**. Loss of chromosome material from bands 10p11 and 10p12 is known as a **proximal deletion**. By 2011, 8 children had been described in the medical literature with a loss of a segment in this area; *Unique* has eight further members, making a total of 16 affected people.

The points where the chromosome has broken vary widely as does the amount of lost chromosomal material. Microarray diagnoses show losses ranging in size from 1 Mb (one million base pairs or DNA building blocks) to more than 10 times larger. There is no obvious link between the size of the deletion and the extent and severity of effects.

The most common features are a delay in development, with a need for learning support, and some speech delay. However, the extent of delay varies a lot and while some children are significantly delayed, others are more mildly affected. Many youngsters learn to sign and the great majority talk, with first words emerging usually in the third or fourth year. Some go on to speak fluently. A similar range is seen in mobility skills: children learned to sit between 8 months and 3 years; to crawl around 16-18 months; and to walk between 15 months and 3½ years. Children gradually learned to climb stairs and to run, albeit in some cases with a clumsy style, their legs apart, or with a poor sense of balance. One child was not able to walk at 4 years. Some children but not all had low muscle tone, making them feel floppy to hold as babies and making it harder and more tiring for them to learn to crawl and walk. Some children needed leg supports or insoles while walking. A few children had evolving abnormalities of muscle tone, or showed a mixture of high and low muscle tone in different parts of the body.

Nine of the children have had episodes of difficult behaviour, most commonly hyperactivity, autistic-type behaviours and outbursts of aggression. They have generally responded well to medication for their difficult behaviours. Three children have also had very disturbed sleep and needed medication such as melatonin.

Feeding presented difficulties for 5 newborn babies but apart from one, who had a split in the soft palate at the back of the mouth and reflux (bringing feeds back) and had a feeding tube placed direct into the stomach, feeding was normal once past early babyhood. Three of these 5 babies and 1 other also had significant constipation, treated with stool softeners.

Before birth, babies generally grew normally, although birth weights at term ranged from 1.92 kg (4lb 4oz), well down in the lowest 3 per cent of newborn babies, to 3.645 kg (8lb 1oz), in the top 60 per cent. Growth in babies and children varied quite widely, with some children significantly short for their age, some short, some of a normal height and one at the upper limit of normal.

As far as their health was concerned, the most common difficulty for more than half the babies was a heart problem. Five babies had holes between the lower, pumping chambers of the heart (ventricular septal defects/ VSDs), sometimes as the only problem, sometimes linked with other heart problems. At least one baby needed open heart surgery to close the VSDs, but thrived well afterwards. Four babies were born with a persistent ductus arteriosus. This occurs when a normal short cut in the circulation of an unborn baby fails to close naturally soon after birth. In 2 babies it closed on its own; the other two needed surgery. Two babies had a significant narrowing of the aorta, the blood vessel that leads from the heart to the rest of the body, requiring surgery to widen it. Two babies had a problem with one of the valves in the heart, in one case the pulmonary valve through which blood passes on its way to the lungs, in the other case the aortic valve which regulates blood flow into the aorta.

Ten children have some kind of vision defect. Four have a squint (strabismus), 3 have an astigmatism (an abnormal curvature of the cornea at the front of the eye); 2 have amblyopia (a 'lazy eye', where the brain prefers one eye to the other); 2 are short sighted, 1 is long sighted and one child has long sight in one eye and short sight in the other; 1 child has a developmental defect of structures at the back of the eye and underdevelopment of the front part of both eyes; and 2 children are visually impaired in one eye.

Six children have some hearing loss. In 2 children the hearing impairment is caused by glue ear, so is temporary, in a third child, glue ear contributes, but in 4 children, there is a degree of permanent sensorineural impairment. In one teenager, hearing got progressively worse until she had a profound impairment.

Three children have had seizures, although one newborn baby had a single seizure shortly after birth. The brains of 8 children, including 2 who had seizures, were found to have some unusual structure: 2 children had a thin or underdeveloped corpus callosum (the band of nerve fibres linking the two sides of the brain); 2 had an underdevelopment of the cerebellum part of the brain; 3 had somewhat enlarged fluid-filled spaces within the brain; 1 had a mild degree of hydrocephalus (accumulation of fluid); 3 had cysts; 1 had abnormal slits or clefts in the cerebral hemispheres of the brain, known as schizencephaly; and one had a skull with the appearance of beaten copper.

Two/7 baby boys were born with one or both their testicles not yet descended into the scrotum. Other problems affect individual children: one baby was born with a blockage of one nasal passage and of part of the sinuses; another had had defects in the formation of the anus, with a stenosis (narrowing) and a channel linking the anus with the vagina; another with a failure of the collar bone to form properly; one has coeliac disease; another has an extra rib and hypothyroidism, treated with thyroxine; and one child has inguinal hernias.

(Yatsenko 2004; Shahdadpuri 2008; Wentzel 2011; *Unique*).

For the seven children described in the medical literature with one breakpoint in band p11 or p12 and the second in band p13, information is limited because only clinical descriptions are available. In general, clinical descriptions focus on problems rather than areas of normality or strength. From what is known, it seems that most children, if not all, would need support with their learning; one child was described as having a



moderate difficulty with learning at the age of seven. Speech and language may also emerge late; one child spoke his/her first words at the age of four. Baby milestones were also likely to be delayed; one child sat at 12 months and walked at two years.

Information on growth does not appear consistent. Two babies were born small for their gestational age, while another was an average weight at birth and continued to grow at a normal rate.

Minor anomalies of the hands and feet were common. Four children had either broad thumbs, contracted fingers, incurving fifth fingers or an underdeveloped nail on the fifth finger and two children had webbed or broad toes.

In terms of possible birth defects and general health, the most common problem was a heart defect and specifically an ASD (see page 14), found in four out of seven children. Two children had a cleft (split) in the soft palate at the back of the mouth and one also had a cleft lip. One child had a permanent hearing loss in both ears.

(Firouzabadi 2005; Yatsenko 2004; Schuffenhauer 1998; Kato 1996; Lipson 1996; Pignata 1996; Obregon 1992,1)

## Why did the 10p deletion occur?

Some 10p deletions are the result of a rearrangement in one parent's chromosomes. This is usually a **balanced translocation** in which material has changed places between chromosomes but no material has been lost or gained and the parent usually has no difficulties with health or development. Occasionally, when the deletion is very small, one parent has the same deletion as the child. A blood test to check the parents' chromosomes will show what the situation is.

Most 10p deletions occur when both parents have normal chromosomes. The term that geneticists use for this is **de novo (dn)**. De novo 10p deletions are caused by a change that has usually occurred when the parents' sperm or egg cells were formed or less commonly around the time of conception.

Children from all parts of the world and from all types of background have 10p deletions. No environmental, dietary, workplace or lifestyle factors are known to cause them.

There is nothing that either parent did before or during pregnancy that can be shown to have caused the deletion and equally nothing could have been done to prevent it. So no-one is to blame or at fault.

## Can it happen again?

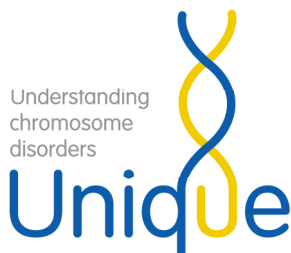
The possibility of having another pregnancy with a 10p deletion depends on the parents' chromosomes. If both parents have normal chromosomes, the 10p deletion is very unlikely to happen again.

If a blood test shows that either parent has a chromosome change involving 10p, the possibility is increased of having other pregnancies with chromosome changes. Usually one parent has a balanced translocation. Occasionally one parent has the same chromosome change as the child.

Once the family chromosome change or translocation is known, a test can be done in any future pregnancy to find out whether the baby's chromosomes are affected. Discussing the chromosome change with other family members gives them the opportunity to have a blood test to see if they too carry it.

A genetic specialist can give you more guidance for your family.

## Support and Information



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