Understanding chromosome disorders

Unique

Duplications of 10p

rarechromo.org

“ He is such a happy, loving child, he brightens up our day. ”
“ He is always willing to assist. His delight in the simple joyful things is infectious and very levelling. From a difficult baby, he has grown into a kind, thoughtful adult who is looking forward to some independence at residential college.”

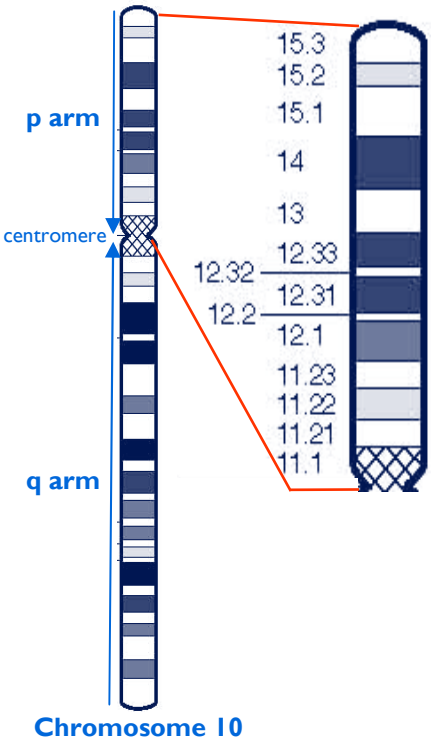
What is a 10p duplication?

A 10p duplication is a rare genetic variant in which there is an extra piece of one of the body’s 46 chromosomes. This extra piece is found in virtually all the cells in the body that are needed for growth, development and healthy functioning. For correct development, the right amount of genetic material is needed – not too little and not too much. Having an extra piece of a chromosome makes it likely that there will be some difficulties with development, health or learning.

Looking at 10p

Chromosomes are the structures inside the body’s cells that carry DNA: the genetic information that tells the body how to develop and function. They come in pairs, one from each parent, and are numbered 1 to 22 approximately from largest to smallest, as well as a pair of sex chromosomes: an X and a Y for males and two Xs for females. Each chromosome has a short (p) arm and a long (q) arm. A 10p duplication contains extra material from the short arm of chromosome 10.

Chromosome analysis



You can’t see chromosomes with the naked eye, but if you stain them and magnify them under a high-powered microscope, you can see that each one has a distinctive pattern of light and dark bands. You can see these bands in the diagram of the short arm of chromosome 10 on the left.

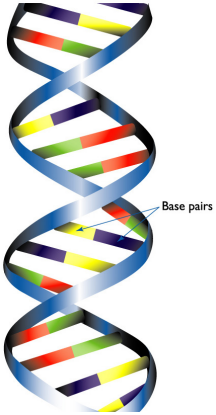
The bands are numbered outwards starting from the point at the bottom of the diagram where the short arm meets the long arm (the centromere). A low number such as p11 is close to the centromere. A high number such as p15 is very close to the end of the chromosome, at the top in the diagram.

If you magnify chromosomes to hundreds of times life size and look at them down a microscope, the extra piece of chromosome 10p may be visible. A visible extra piece is often called a duplication.

Sometimes the extra piece consists of all, or almost all, of the short arm of chromosome 10. People with an extra copy of almost all or all of 10p are sometimes said to have trisomy 10p.

Microarrays and other technologies

The extra piece of 10p can be so tiny that even when the chromosome is magnified many hundreds of times it looks normal down a microscope. The extra piece can then only be found using a combination of different techniques and, increasingly, a technique known as chromosomal microarrays, or array-CGH. Such a tiny extra piece of a chromosome is called a microduplication.



Chromosomes are made up of DNA, which has a ladder-like structure. Each 'rung' in the ladder links a pair of chemicals known as bases. The size of small duplications and microduplications is often measured in pairs of bases, called base pairs. Since each chromosome has millions of base pairs the numbers are very long. Often they are shortened, like this: one thousand base pairs can be shortened to 1 kb; one million base pairs can be shortened to 1Mb.

The genetic test results

Your geneticist or genetic counsellor will give you your child's genetic test results. If the test used chromosomal microarrays, the result is likely to look something like one of these: **arr 10p15.2p15.1(2,856,430-6,247,262)x3**

arr	The analysis used microarray technology
10p	A change was found in chromosome 10, the short (p) arm
15.2p15.1	Counting from the tip of the short arm, the change starts in band 15.2 and ends in band 15.1
(2,856,430-6,247,262)x3	The base pairs between 2,856,430 (around 2.8 Mb) and 6,247,262 (around 6.2 Mb) have been shown to be repeated. Take the first long number from the second and you get 3,390,832. This is the number of base pairs that are repeated. This can be rounded to 3.4 Mb. x3 means there are three copies of these base pairs, not two – one on each chromosome 10 – as you would expect.

arr cgh 10p14p13(RP11-278H22->RP11-462F15)x3

arr cgh	The analysis used microarray technology
10p14p13	The duplication here starts in band 10p14 and finishes in band 10p13
(RP11-278H22->RP11-462F15)x3	The test showed extra copies of two different markers whose position in bands 10p14 and 10p13 are known.

Sometimes you will receive a report like this. This report is not so helpful, because it gives you less information about how big the extra piece is.

46,XY,inv dup(10)(p15.3->p11.2)

46	The number of chromosomes in your child's cells
XY	The two sex chromosomes: XX for females; XY for males
inv dup	A duplication, or there is extra material. inv means that the extra material is inverted, running in the opposite direction to the material in the rest of the chromosome.
(10)	The duplication is from chromosome 10
(p15.3->p11.2)	The duplication is from band 10p15.3 to band 10p11.2.

There are other chromosome rearrangements that can result in a duplication of chromosome 10p. One rearrangement that is fairly common is an exchange of material between two chromosomes. The short arm of chromosome 10 is attached to the long arm of chromosome 13, 14, 15, 21 or 22. In this arrangement, one short arm of chromosome 13 (or 14, 15, 21 or 22) is missing but as these short arms contain no indispensable material, the fact that they are missing shouldn't matter. *See also page 18.*

46,XX,der(13)t(10;13)(p11;p11)

In this case there has been an exchange of material between chromosomes 10 and 13, and the net result is that the short arm of one chromosome 13 is missing and its long arm is attached to a short arm of chromosome 10. As a result, there is an extra copy of 10p.

46	The number of chromosomes in your child's cells
XX	The two sex chromosomes: XX for females; XY for males
der(13)	One chromosome 13 has been changed and is known as a derivative (der) chromosome
t(10;13)	Material has been moved between chromosomes 10 and 13. t stands for translocation
(p11;p11)	Each chromosome has broken in band p11.

Sometimes the duplication is contained within a separate extra chromosome, like this.

47,XY,+mar(10)(cent->pter)

47	The number of chromosomes in your child's cells. There is an extra chromosome, so 47 instead of the usual 46
XY	The two sex chromosomes: XX for females; XY for males
+mar	The extra chromosome is what is known as a 'marker' or small chromosome
(10)	The marker chromosome is made up of material from chromosome 10
(cent->pter)	The material in the marker consists of material between the centromere and the tip of the short arm, known as the 'ter', for terminus, or end.

The report may show the letters dn. This is the short form of de novo, Latin for 'from the beginning'. This means that the parents have had a blood test and their chromosomes checked and no change was found in 10p. The duplication is then very unlikely to be inherited and has occurred for the first time in this family with this child. If the letters pat are given, then the duplication is inherited from a chromosome change in the father. The letters mat mean that it's inherited from the mother. *See also page 17.*

Sources and references

The information in this guide is drawn from what is known about a small number of people - just 47 - with a pure duplication of 10p. Twenty-six people have been described in the medical literature. Some of the cases from the medical literature were published more than 30 years ago when equipment for examining chromosomes was relatively crude. In these cases the given breakpoints may not be as precise as they would be today. 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 (www.ncbi.nlm.nih.gov/pubmed). There is a literature list on page 19. You can get articles marked **Free access** yourself on the internet. If you wish, you can obtain other articles from *Unique*. *Continued on page 5.*

Is there a 10p duplication syndrome?

Genetics experts do not agree on whether there is a clearly recognisable 10p duplication syndrome. Many older reports in the medical literature (before around the year 2000) relied on evidence from people with another chromosome change as well as the 10p duplication - usually a loss of genes from a different chromosome. Losing genes from a different chromosome tends to confuse the overall picture, so this guide and more recent reports in the medical literature rely only on people with a 'pure' or almost pure 10p duplication, without any other known chromosome change (Clement 1996; Fechtrup 2000).

There are also big differences between individuals. You can explain some of the differences by the amount of 10p that is duplicated. It can be anything from the entire chromosome arm to just a tiny fragment.

Overall, it's probably fair to say that people with an extra copy of all or almost all of 10p who have no other extra genes or lost genes do share some features.

Are duplications of specific parts of chromosome 10p associated with particular features or problems?

There have been a number of attempts to assign specific features of a 10p duplication to specific regions of the chromosome. For example, Mégarbané 2001 suggested that people with a duplication involving p11.2 to 12.2 might be susceptible to having a high or cleft palate. But numbers of people with duplications of particular parts of 10p are small and this makes it hard to be certain. Also, some features, such as a cleft palate, are generally more common among those with a chromosome disorder than those without.

Are there people with a 10p duplication who have developed normally and have no health, learning or behaviour difficulties?

So far, everyone who has been reported in the medical literature or is known to *Unique* has experienced at least some degree of delayed development and needed support with their learning. But there are still big differences between people in whom the whole short arm of chromosome 10 is duplicated and those who have a duplication of only a small part. On the Decipher database there are six people who have inherited between them seven tiny microduplications from one of their parents, who themselves seem entirely unaffected by it. These microduplications are very tiny indeed, ranging in size from 0.05Mb (just 52,828 base pairs) to 0.72Mb (715,457 base pairs). They have been found all along the short arm, in bands p15, p13, p12 and p11 (Decipher).

From page 4. Ten cases are recorded on the Decipher database at http://decipher.sanger.ac.uk. Most of these are very small microduplications, usually contained within a single band of the short arm of chromosome 10. Features associated with the microduplication or duplication are recorded in note form on the database. Other cases come from *Unique*'s own database which in some cases contains a regularly updated natural history of the condition. When this guide was written, *Unique* had 11 members with a pure duplication of part or all of 10p.

(Cantu 1975; Nakagome 1975; Yunis 1976; De Chieri 1978; Aller 1979; Fryns 1979; Gonzalez 1983; Delaroche 1984; Schwartz 1984; Snyder 1984; Harris 1985; Blennow 1996; Clement 1996; Stone 1996; Benzacken 1998; Berend 1999; Fechtrup 2000; Voullaire 2000; Chen 2001; Mégarbané 2001; Dabir 2006; Daniel 2008; Decipher; *Unique*)

What I know now that I wish I had known at the start

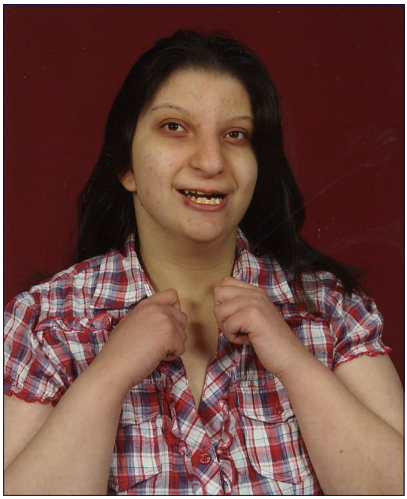
“ That our lives would be full of challenges with lots of upheavals. ”

“ Actually nothing. I had to learn to trust my gut feelings. ”

Can people with a 10p duplication have children and if so, will they also be affected by the 10p duplication?

There aren't any reports at the moment of people with a complete or almost complete duplication of 10p having children. But there are reports of people with smaller duplications having children and in some families a small 10p duplication has gone down more than two generations. For a parent with a 10p duplication, in each pregnancy there is theoretically a 50% chance of the baby also having the 10p duplication and a 50% chance of having a baby without the duplication. The Decipher database shows six families where the duplication has apparently affected the child but not the parent (Stone 1996; Voullaire 2000; Decipher).

Duplication of all or almost all of the short arm of chromosome 10: main features



19 years old

- **Developmental delay**
- **Motor delay**
- **Hypotonia** – low muscle tone
- **Abnormal foot positioning**, such as clubfoot
- **Cleft** lip and/ or palate
- Some **unusual facial features**, including a prominent forehead, widely spaced eyes, a broad nasal root and low set ears
- **Growth delay** and short stature

■ Developmental delay

A delay in the expected rate of development is usually obvious from a baby's early months and confirmed by 5-6 months of age. The delay typically affects all areas of development, including moving, learning and communicating. It is important to introduce early learning interventions and therapies to give a baby the best chance possible. Nonetheless, evidence from *Unique* suggests that development will continue to be slow and the gap with typically developing babies and children will widen. There is individual variation in the degree and severity of the delay, but evidence from *Unique* again suggests that it is likely to be quite significant, with young adults developmentally at toddler level and dependent on their caregivers for their personal needs.

In terms of learning support, children are likely to thrive best in a school where their special needs can be appropriately met. Complex academic skills such as reading and writing may not be attainable, but children are nonetheless quite capable of learning and remembering important information such as familiar faces and routes (Fechtrup 2000; *Unique*).

“ He has compensated over the years and is well able to hold and grab whatever he wants. The TV remote he even manages with one finger ” - *almost 19 years*

“ She has a good memory for routes to familiar places ” - *19 years*

“ He remembers people’s faces; nevertheless looks very puzzled when he meets them out of their or his usual environment ” - *almost 19 years*

■ Motor delay

Babies are very late to gain control of their bodies - first by holding their head steady, then by sitting before becoming mobile. Physiotherapy (physical therapy) introduced very early will maximise their capacities, but it is likely that in the long term mobility will need to be supported with aids such as a wheelchair.

Evidence from *Unique* shows that rolling over is a skill that toddlers acquire around 2-3 years. Some children are able to stay seated earlier than this, in the earliest instance at 15 months, while others achieve this skill around 3 years or even later. Early mobility may well take the form of scooting or shuffling rather than crawling. Progression to walking has been achieved between the ages of 5 and 8 years but even when this is not possible, there are exciting mobility opportunities, as the first account below shows (Fechtrup 2000; *Unique*).

“ He loves swimming and also goes horseback riding every fortnight. He floats around in the pool with armbands and doggy paddles to wherever he wants to get to. We went bi-skiing also, which he very much enjoyed. He loved the speed and being on the chairlift up the mountain. We bought an outdoor wheelchair which is brilliant: it has twin wheels at the back like mountain bike wheels and a big balloon wheel at the front so it is easy to push over gravel, soil and sand. It can even be brought into the water - it floats ” - *almost 19 years*

“ She walks short distances, then collapses to the floor, and needs a wheelchair as she gets very tired. Her favourite physical activity is swimming ” - *19 years*

■ Hypotonia – low muscle tone

One factor underlying the motor skill delay is a low muscle tone, making the body feel floppy and making it hard to move purposefully. By contrast, one baby was born with contracted joints. Physiotherapy is very helpful and should be an essential component of the care package for all children (Decipher; *Unique*).

■ Abnormal foot positioning, such as clubfoot. Hands may also be held in an odd position

The great majority of babies with trisomy 10p are born either with clubfoot, usually affecting both feet, or with a lesser degree of abnormal foot positioning. In some cases, this is the first sign that anything is wrong. Abnormal foot positions include metatarsus adductus (the front half of the foot turns inwards, the arch is high and the big toe is separated from the second toe by a ‘sandal gap’) and pes varus, where the foot points

18 years old

towards its inside edge. In addition, the big toes are often flexed upwards. Less common anomalies include fused toes and rocker bottom feet, where the sole of the foot is curved outwards so that it resembles the base of a rocking chair.

Treatment of clubfoot is individually tailored and aims to straighten the foot so that it can grow and develop normally, offering the best chance of walking. While first-line treatment is often non-surgical and may include manipulation, casting, taping, physiotherapy and splinting, followed by bracing to prevent relapse, *Unique*'s experience is that surgical correction is often necessary.

The hands are also often held in an odd position, with all or most of the fingers clenched or abnormally flexed (Nakagome 1975; de Chieri 1978; Gonzalez 1983; Schwartz 1984; Snyder 1984; Clement 1996; Fechtrup 2000; Daniel 2008; *Unique*).

" His feet were put into casts until 4 months. He now has special orthoses to let him stand and lift his body upright as a therapeutic treatment for short periods. His hands were also twisted and folded up against his arms. Even now he usually holds them closed, but is able to hold things or grab for things " - *almost 19 years*

" Her hands were clenched at birth; today her fingers point upwards like a pianist's " - *19 years*

■ Cleft lip and/ or palate

Half of babies with trisomy 10p have been born with a cleft palate (split in the roof of the mouth), and 6/20 were born with a split in the upper lip as well. Cleft lip and palate is caused by an error in fusion when the fetus is forming. The lip and palate fuse from pieces that start on opposite sides of the head. The lip fuses around weeks 6-7 and the palate at around 12 weeks. A cleft occurs when the pieces come round but do not join. Defects in the roof of the mouth are common in children with and without a chromosome disorder. The hard palate at the front of the mouth may be split or the split may be found further back in the soft, fleshy tissue at the back of the top of the mouth. Occasionally the split is only seen in the tissue that hangs down above the tongue at the very back of the mouth (uvula, known as a bifid uvula when it is split). A cleft palate causes difficulties both in feeding and in speech production. Surgical repair of the palate eases these difficulties and may eliminate them altogether (Cantu 1975; Nakagome 1975; Yunis 1976; de Chieri 1978; Blennow 1996; Berend 1999; Fechtrup 2000; Daniel 2008; *Unique*).

Some unusual facial features

Your baby will have features in common with the rest of your family, while at the same time it's likely that she or he will also in some ways resemble other people with a duplication involving 10p. Among the facial features commonly seen in people with a duplication of 10p are unusually shaped ears, frequently set low on the sides of the head; a tall, bulky or prominent forehead; a relatively small chin and/or lower jaw; widely-spaced eyes; a broad base to the nose; and an unusually-shaped mouth with downturned corners and sometimes a thin, inverted upper lip.

Growth

Everyone reported in the medical literature or known to *Unique* either has growth delay or is in the bottom ten per cent of the population for height and usually for weight as well. Some children are very tiny and this is seen at all ages from newborn babies to young adults. Heights of two teenagers are 149 cm (4' 11") at 17 years and 153 cm (5') at 15 years. A girl who was treated with growth hormone from 9 to 16 years reached an adult height of 157 cm (5' 2"). When she started treatment she was severely underweight, but by the time she finished she weighed 74 kg (more than 11½ stone) (Cantu 1975; de Chieri 1978; Aller 1979; Gonzalez 1983; Delaroche 1984; Snyder 1984; Blennow 1996; Fechtrup 2000; Chen 2001; *Unique*).

What else?

Seizures

It has been suggested that babies and children with trisomy 10p are more likely than typically developing children to have seizures. This does seem to be the case, although only around one third of babies or young children had any seizures by the time their clinical history was reported in the medical literature. What's more, none of *Unique*'s members with a duplication of 10p has had seizures, up to 19 years of age.

Seizures started in the first year of life in all the reported cases. Treatment details are not always given, but two children were treated with ACTH – adrenocorticotrophic hormone: a type of steroid medication sometimes used to control seizures that occur many times a day, such as infantile spasms (de Chieri 1978; Schwartz 1984; Fechtrup 2000; *Unique*).

Heart

Although heart conditions are not usually considered to be part of any 10p duplication syndrome, a number of babies are born with a structural anomaly or a heart condition. Out of 16 babies born with a full 10p duplication, six had a heart condition. Two had a hole between the upper or lower chambers of the heart (VSD, ventriculoseptal defect, or ASD, atrial septal defect); one had a mild narrowing of the blood vessel that takes blood from the heart to the lungs (pulmonary stenosis); three had an enlarged heart (cardiomegaly); one had dextrocardia, where the heart is situated on the right rather than the left side of the body; and one had unspecified anomalies. Some babies had more than one heart problem. Two of these babies died of their heart condition but it's important to say that generally speaking the outlook for babies born with a heart condition is very much better today than a generation or two ago (Cantu 1975; Delaroche 1984; Schwartz 1984; Snyder 1984; Berend 1999; *Unique*).

Kidneys

Out of 16 people reported in the medical literature or at *Unique*, five have a significant kidney anomaly. A baby who was sadly stillborn had multiple fluid-filled cysts in the kidneys (polycystic kidneys) and underdevelopment of the tubes that lead from the kidneys to the bladder; two other babies were born with a missing right kidney. Two *Unique* members have relatively poor function in at least one kidney and one has repeated kidney and urinary infections and has had a large stone removed from one kidney. He takes a drug (tamsulosin) to help ensure that urine drains fully from his bladder in order to protect him from kidney infections. The other *Unique* member with one malfunctioning kidney does not have repeated urinary or kidney infections (Cantu 1975; Yunis 1976; Snyder 1984; *Unique*).

Minor genital anomalies

Minor genital anomalies are somewhat more common among babies born with a chromosome disorder than among typically developing babies. Among those with a 10p duplication, 6/16 are reported as having some genital anomaly, although no *Unique* members are known to be affected. Three baby boys were born with undescended testicles. If the testicles do not descend naturally in time, they can be brought down in a short operation under general anaesthetic called an orchidopexy. One of these boys also had hypospadias, where the hole normally at the end of the penis is on the underside instead, as well as a hooked penis (chordee). One boy was born with a very tiny penis (microphallus). One girl had a slightly enlarged clitoris while another had a channel (fistula) linking the rectum with the vagina (Cantu 1975; Nakagome 1975; Yunis 1976; de Chieri 1978; Delaroche 1984; Schwartz 1984).

Eyesight

Most people with a 10p duplication appear to have normal eyesight. Abnormalities have been identified in a minority, including use of only one eye; atrophy of the nerve linking the eyes with the brain; and a squint (strabismus). Two babies were identified as having multiple vision defects, both by the same researcher in the 1970s; defects included developmental abnormalities of various parts of the eye in both babies. One baby also had abnormally small eyes with small corneas (the front, transparent part of the eye) as well as swelling and irritation of the uvea, the middle layer of the eye (Cantu 1975; Aller 1979; Schwartz 1984; Berend 1999).

Hearing

Since many babies' hearing has not been reported, it is impossible to know how common hearing problems are among people with a 10p duplication. The reports include hearing impairment requiring tubes to be inserted and the need for hearing aids; an unspecified hearing impairment as a newborn; and growth of a recurrent cholesteatoma (skin growth or cyst full of old skin cells and other debris that develops inside the eardrum within the middle ear, usually after repeated ear infections), requiring repeated surgery and ongoing ear, nose and throat follow-up (Schwartz 1984; Fechtrup 2000; *Unique*).

Lungs

Babies born with a 10p duplication usually seem to have healthy, normally formed lungs. Some, but not all, have repeated respiratory infections but there is no evidence of this

among *Unique* members. Among four babies diagnosed with a 10p duplication during pregnancy where the pregnancy was terminated or the baby was stillborn, three had unusually formed lungs. Lungs are typically divided into three segments, but in two of these babies the right lung had only two segments. In a third baby the diaphragm that separates the contents of the chest from those of the stomach was only a thin membrane and the lungs were underdeveloped (Nakagome 1975; Yunis 1976; Clement 1996).

■ Other

Individual babies and children have been born with particular clinical features and concerns. Since only one person was affected, it is unknown whether the 10p duplication is the cause or not. These features are: missing gall bladder (Clement 1996); umbilical hernia (de Chieri 1978; Delaroche 1984); narrowing or blockage of the anus (Nakagome 1975); spina bifida (Aller 1979); incomplete development of one side of some vertebrae (Clement 1996); dislocated hips (Schwartz 1984); asymmetry with one breast much larger than the other (*Unique*); Raynaud's syndrome, where the tiny blood vessels in the fingertips and toes go into spasm, turning the fingers and toes white or blue (*Unique*); and missing toes (Decipher).

■ Communication and speech

Although there are nine reports covering social communication or speech, the great majority of the information comes from *Unique*. *Unique* babies generally started to smile around the appropriate age or a little later, in marked contrast to babies reported in the medical literature from 30 or 40 years ago, who showed no social communication or recognition of their parents in their second or third year. Babbling emerged as early as eight months in one baby, who progressed slowly to using single words by the age of 13 as well as signing, vocal noises and a communication device. In other babies babbling emerged later or not at all, but even in the absence of speech, youngsters were well able to communicate their feelings and to some extent their wishes. There appears to be no link between hearing impairment and the development of speech, with the one youngster who uses words also having the most severe hearing problems. Overall, these findings agree with the conclusion that among older people, some may be able to say single words, others syllables, while others have no speech at all. (Cantu 1975; de Chieri 1978; Aller 1979; Berend 1999; Fechtrup 2000; *Unique*).

" She cries when she is in pain and uses single words and signs. We strongly recommend using a communication device and speech therapy " - *almost 19 years*

" He has no expressive speech. He knows his own name but if his brothers are referred to by name he doesn't know who we are talking about. However, when he hears them over the phone, he knows who they are. He has phases of making multiple sounds, from giggles and deep laughter to growls when he is angry " - *19 years*

■ Behaviour

We can only offer snapshots of information on behaviour, apart from one report in the medical literature of a child with a mosaic form of the 10p duplication (so affecting some but not all cells in the body), who is described as 'immature but pleasant' (Blennow 1996). Reports from *Unique* follow on the next page.

❝ He is a happy young man, loves music and is very interested in what is going on around him, though like any teenager he can be stubborn. He loves going out to the cinema, opera, swimming and lately bi-skiing. He knows which movies he likes and remembers characters and tunes. He understands some cause and effect: for example, that the remote control affects the TV. When he is well, he smiles most of the time and enjoys life. When in pain, he cries silent tears: he cannot cry aloud.

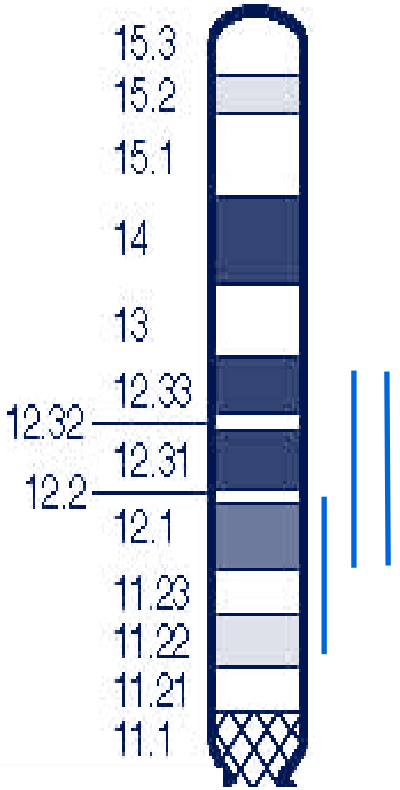
❝ I have gotten so used to his ways that nothing seems too difficult to cope with. If he gets angry, I try to find out why and if I can't find out, I leave him to his anger, talk to him and try to comfort him. When I take him shopping, I allow enough time and space for him to explore so that we never get into inappropriate situations.

❝ He has definite preferences for certain people and gives huge hugs which are difficult to break! He knows in an instant if he likes somebody or not. He stares at them and if he likes them he'll wheel up to them, touch and hug them, if he's allowed. If not, in the best case he ignores them; in the worst case, he grunts aloud and we or they have to leave ❞ - *19 years*

❝ She has severe behaviour problems: for example, when the car slows down or stops in traffic, she screams, attacks you, takes her clothes off. At school she is great, just has a tantrum now and again. She either likes you or doesn't, just by looking in your eyes. If you pay her attention she likes it, but if you ignore her, she hates it ❞ - *almost 19 years*

14 years old

Partial duplications: p11 and p12



There are three reports in the medical literature: Mégarbané 2001; Harris 1985; and Fryns 1979. Fryns and Harris report duplications of the p12 band only, while in Mégarbané the duplication extends from p12.2 into the p11.2 band. The ages of the people with the 10p duplications are 4, 21 and 30 years, allowing some information on a longer term outlook. In addition, there are three reports on the Decipher database, with duplications in the p12.1 or 11.23 bands.

The common features are developmental delay with late emergence of speech and language, some unusual facial features, a lack of any serious birth defects or medical problems, and somewhat short height as adults: for example, an adult woman was 152 cm (4' 11") and an adult man 160cm (5' 3") tall.

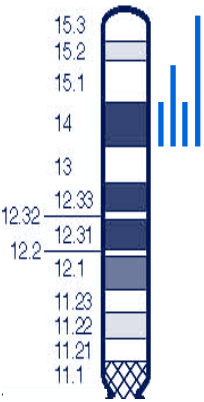
However, within the small group of three reports in the medical literature, there is quite wide variation in development. While one was walking at 19 months and another at 2 years, the third needed support to walk at the age of three. Two of the three Decipher reports mentioned hypotonia (a low muscle tone). A child of 4 was using single words to communicate, while one of the adults had spoken his first words at 2½ years and was talking in sentences at the age of 3; this adult was judged to have an IQ of 45. As regards behaviour, one of the adults was described as 'very sociable and interactive', while another displayed autistic behaviour and had shown aggression and made suicide attempts from the age of 7.

In the absence of birth defects, the babies were considered normal at birth, although at diagnosis a variety of unusual facial features were noticed. The Fryns and Mégarbané reports include photographs that *Unique* can send to families on request. One baby also had a small head that was short from front to back; one Decipher report also shows a very small head (microcephaly).

Investigations of the heart and brain in the individual with a duplication of p11.2 to p12.2 were normal and the only clinical concerns were a conductive hearing loss in the four-year-old (which is common in the general population and is typically temporary) and a mild squint (strabismus) in one of the adults.

One Decipher report records an enlargement of the fluid-filled ventricles within the brain. Another shows abnormal development of the kidneys and recurrent infections. The fingers are long and thin (arachnodactyly) in the report of a p11.23 duplication.

Partial duplications: p13 to p15



There are 5 reports covering a total of 11 people, including one report from *Unique* and four in the medical literature: Stone 1996; Benzacken 1998; Voullaire 2000; and Dabir 2006. Stone reports a duplication from band p14 in two sisters and their father; Dabir reports a child of 2 years old with a p14 to p15 duplication, while Voullaire reports on 5 members of a family with 8 affected relatives with a duplication of the p14 band; the *Unique* member has a duplication that extends from p14 to p15.3. Reports range from newborn to adult, allowing some information on possible outcomes.

There are six reports from the Decipher database, including one individual with four separate duplications in the p13 band, one with a microduplication in band p15.1, one in p15.2 and three in p15.3.

Medical concerns

Overall, birth defects and medical concerns are unusual: 4/4 babies were born with a normal birth weight and none of the 11 individuals has a known heart problem. One baby was born without an external ear and with two ear tags. One child with duplications in p13 has multiple anomalies of the kidneys and urinary system, with multiple cysts, double drainage tubes from the kidneys to the bladder and swelling of the kidneys, often associated with blockage. This child also has a low calcium level (Decipher). Apart from a very small head (microcephaly), which affects three babies, clinical concerns have been reported in only one individual, raising uncertainty whether they can be clearly attributed to the 10p duplication. One boy has small testes and one adult has a somewhat humped back.

Brain

One child was born with the band of nerve fibres linking the two sides of the brain missing (agenesis of the corpus callosum: ACC); the effects of ACC range from mild to severe and depend on associated brain abnormalities: mildly affected children can have normal intelligence and only subtle difficulty in matching visual patterns, while children with severe effects can have intellectual disabilities and seizures.

Another child was shown on MRI imaging to have a number of slight brain anomalies, including unusual folding patterns on both temporal lobes (at the side of the brain); slight irregularity in the shape of the main fluid-filled spaces (ventricles) within the brain; and slightly less of the white matter in the brain that is responsible for transmitting messages. Neither child with a brain irregularity had seizures and one had a normal electroencephalogram (EEG: a recording of the electrical activity in the brain), although another child with no brain anomalies did have seizures.

General health

As far as is known, people with this duplication of 10p are generally healthy, although two sisters have reduced resistance to infection and receive regular infusions of immunoglobulins to boost their resistance.

Vision and hearing

The father reported in Stone 1996 has some eye anomalies, including abnormalities of the nerves carrying information to and from the eye to the brain, but these have no

effect on his vision. However one of his daughters, also with the 10p duplication, has a severe development defect of both eyes and is registered as blind. The other sister with the same 10p duplication has normal eyesight. One of the adults reported in Voullaire 2000 is deaf, but her son who has the same duplication has normal hearing.

Development

In terms of development, any learning difficulties are described as mild or borderline. One child of 13 has learning difficulties but a normal IQ of 104 (Stone 1996); a child of 3 years has a good memory and learned numbers, colours, shapes and letters quickly (*Unique*). One adult who had special schooling and worked at first in a sheltered workshop moved on to working as a forklift truck driver.

Only 4 reports contain information on speech and communication development. They show delay in expressive speech (talking) in 3/3 children but normal speech in an adult.

" He knows about 10 signs and vocalises, pushes, pulls or uses gestures to attract attention. He understands at a 2-2½ year level; expresses himself at a 10-month level " *- 3 years*

Behaviour

Out of 4 reports on behaviour, three from the same family and concerning individuals ranging in age from 2 years to adult, one child is described as hyperactive and aggressive, one as boisterous, and an adult as prone to anger. One child was diagnosed with autism at 2 years, 10 months.

" Generally very passive and placid so long as his needs are being met. He can be restless, self-stimulating (tapping, pulling hair, faecal smearing). He fails to acknowledge his sibling and peers. He acknowledges and seeks out adult company but makes no distinction between friends and strangers " - *3 years*

Development: sitting, moving, walking

As regards learning to sit and walk (motor development, gross motor skills), 2/4 reports show normal development or only mild delay in early childhood, while one child first rolled over at 13 months, sat alone at 10 months, did not crawl but bottom-shuffled at 15 months and started walking at 2 years 4 months. At the age of 3 years, he walks stably but tires and falls easily and has a normal, if slouching posture. Muscle tone is low when reported, contributing to the difficulties with movement. Two children are reported to have excessively mobile joints: in one case, specifically the ankles. One baby was born with dislocated hips and spent most of his first 6 months in a harness.

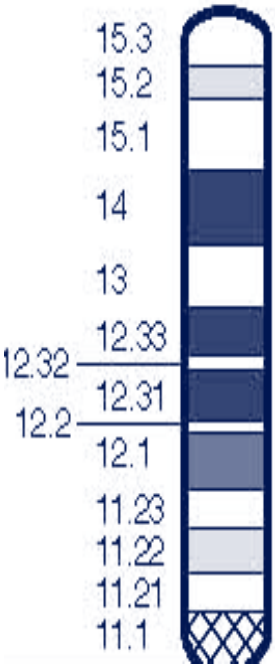
Feeding

There is information on feeding for only 2 children. One baby had difficulty feeding as a newborn, caused by a narrowing of the larynx at the level of the vocal cords (glottic stenosis). Another breastfed exclusively for 6 months but was slow to wean onto solid food and at 3 years still required food to be mashed or puréed, unless it was dry and crunchy. This child also had multiple food intolerances leading to constipation and diarrhoea.

Growth

Out of 6 people with information on growth and height, five are shorter than average and three are in the lowest 5 per cent of the population for height. One child of 3 years is average both in height and weight.

Partial duplications: p15 to the end of 10p



Although we know of no cases of pure duplication of 10p from band p15 to the end of the short arm, there are at least three cases where this duplication is combined with a loss of the very tip of the long arm of chromosome 4 from band 4q35. In addition, there are five reports of tiny microduplications within band p15 on the Decipher database; in one case a double microduplication in bands p15.1 and p12.33-2 (Cingoz 2006; Decipher; *Unique*). With the loss of the tip of the long arm of chromosome 4 there may be no known problems, minor behaviour issues or developmental delay, and other concerns more typical of a larger loss from chromosome 4q. So some people at least with this particular unbalanced translocation may show pure effects of the 10p duplication.

Birth weight, feeding & growth

Birth weight is only known for one baby and was normal. Two babies had difficulty sucking and feeding in the newborn period and in one case these difficulties continued into early childhood. Growth in two cases was normal and one adult woman of 39 years reached a height of 168 cm (5' 6").

Medical concerns

Two babies were born with a small hole between the upper filling chambers of the heart (atrial septal defect: ASD), which healed naturally in one baby.

One baby was born with a split (cleft) in the area at the back of the roof of the mouth, known as the submucous palate. One baby had a single clubfoot. One baby was born with enlarged kidneys and underwent surgical repair at 6 years. In one baby the diaphragm that separates the contents of the chest from the contents of the abdomen was raised abnormally high.

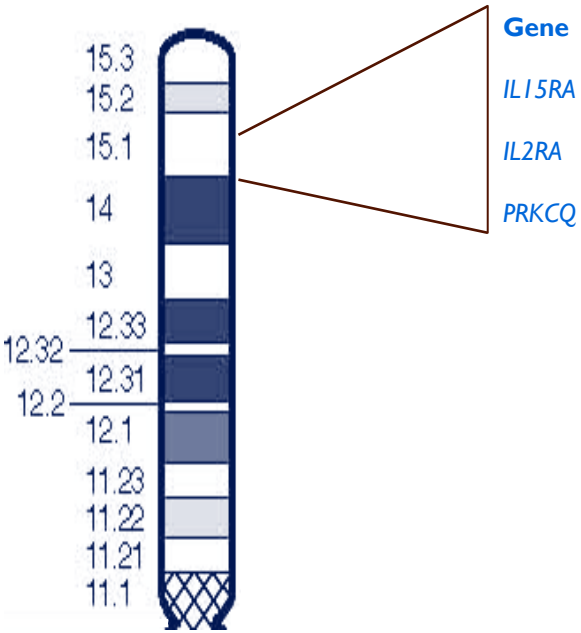
A baby with a p15.3 microduplication was born with an unusually small head and went on to have seizures. Another, also with a p15.3 microduplication, had unusually elastic skin, while another child with a p15.3 microduplication has eczema.

Development

In terms of development, there were considerable differences between individuals. One child was significantly delayed in reaching baby milestones, while another had no such delay. The adult had learning disabilities and the 13 year old child had problems with attention and learning and performed at the level of an 8 year old child. While he had a reduced sense of time and space, he had a remarkable memory for numbers.

Among those on Decipher, one child with a p15.3 microduplication has autism and is hyperactive, another has unspecified behaviour problems, while another is described as aggressive. Three of the five have either developmental delay or need support with their learning. These include the child with the tiniest microduplication of just 52,828 base pairs, who also has speech delay.

Genes



It has been suggested that the extra *PRKCQ* gene in band 10p15.1 and the extra *IL2RA* and *ILI5RA* genes in 10p15.1 may lead to an imbalance in immune response and predispose to recurrent infections or a vulnerability to allergies (Cingoz 2006; Stone 1996).

Identifying the gene or genes responsible for certain features is important to researchers and doing so may help to guide future studies, but this does not at the moment lead directly to immediate improved treatment. Even if there is one extra copy of a supposedly responsible gene, the associated feature(s) will not necessarily be present. Other genetic and environmental factors are often important as well.

Why did the chromosome duplication occur?

A blood test to check both parents' chromosomes will be offered to find out why the 10p duplication occurred in the child. Whatever the reason, what is certain is that as a parent there is nothing you did to cause the 10p duplication and nothing you could have done to prevent it. No environmental, dietary or lifestyle factors are known to have caused these chromosome changes. So no one is to blame when this occurs and nobody is at fault.

Some 10p duplications happen out of the blue when both parents have normal chromosomes. The term that geneticists use for this is dn, short for 'de novo' and Latin for 'from the beginning', meaning that in this family the duplication has occurred for the first time with this child. Dn 10p duplications are caused by a mistake that occurred when the parents' sperm or egg cells were formed or else very shortly after conception, when the baby was made. *See also page 4.*

Sometimes, one parent is found to have a change in their own chromosomes that makes them much more likely to have a child with this type of duplication. In some cases, the parent has a chromosome change known as a balanced translocation, where two chromosome sections have swapped places. When one parent has a balanced translocation, an affected child usually has both a 10p duplication and a loss of material from the other chromosome involved in the swap.

In other parents, the chromosome change is one known as a pericentric inversion, where chromosome 10 has broken in the short arm and the long arm and the piece between the two breaks has turned round 180 degrees and reinserted itself into the chromosome.

People with balanced translocations and pericentric inversions usually have no health or developmental problems themselves, although they may sometimes have difficulties when they want to have children. *Unique* publishes a guide to **Balanced Translocations** where you can find out more.

Chromosomes 13, 14, 15, 21 and 22

Five of the 24 different chromosomes are different to the other 19. Like the other chromosomes, they have a short and a long arm, but the short arm carries no essential genes. You can lose the short arm of one of these chromosomes without any ill effects. When the chromosomes of the parents of a child with a 10p duplication are examined, surprisingly often it is found that one of them carries a balanced translocation between one of these five chromosomes and the short arm of chromosome 10. This translocation in the parent makes it much more likely that they will have a child with an unbalanced translocation and a duplication of 10p. Losing material from the short arm of chromosome 13, 14, 15, 21 or 22 is not expected to affect the child, but having extra material from the short arm of chromosome 10 will (Clement 1996).

A duplication within chromosome 10

Sometimes the duplication is a repeat of material within the short arm of chromosome 10. The DNA in this repeated chromosome material can run in the same direction as the rest of the chromosome (a tandem duplication); or it can run in the opposite direction (inverted). The direction doesn't seem to make any difference to the effects of the duplication.

An extra chromosome

Sometimes the extra 10p material is contained within a small separate extra chromosome, called a 'marker' chromosome. Sometimes the extra chromosome consists of two copies of 10p; it is then called an isochromosome. Having the extra chromosome material as a marker or isochromosome doesn't seem to make any difference to the effects (Clement 1996; Berend 1999; Fechtrup 2000).

Could my child with a 10p duplication have similarly affected children?

When the duplication is small it is possible to pass it on from parent to child (Stone 1996; Voullaire 2000; Decipher). As advances in technology, especially the use of microarrays, uncover tiny microduplications, the possibilities increase of discovering families where a small duplication has been passed from generation to generation. Theoretically, someone with the duplication would have a 50 per cent chance of passing it on and a 50 per cent chance of having a child with normal chromosomes.

Scientific articles

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Dabir 2006: Trisomy 10p with clinical features of facio-auriculo-vertebral spectrum: a case report *Clinical Dysmorphology* Volume 15 pages 25-27

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Schwartz 1984: Duplication of Chromosome 10p: Confirmation of Regional Assignments of Platelet-Type Phosphofructokinase *American Journal of Human Genetics* Volume 36 pages 750-759 **Free access**

Snyder 1984: A de novo case of trisomy 10p: Gene dosage studies of hexokinase, inorganic pyrophosphatase and adenosine kinase *Human Genetics* Volume 67 pages 187-189

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Voullaire 2000: Chromosomal duplication of band 10p14 segregating through four generations *Journal of Medical Genetics* Volume 37 pages 233-237 **Free access**

Wiktor 1994: 10p Duplication Characterized by Fluorescence In Situ Hybridization *American Journal of Medical Genetics* Volume 52 pages 315-318

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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

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