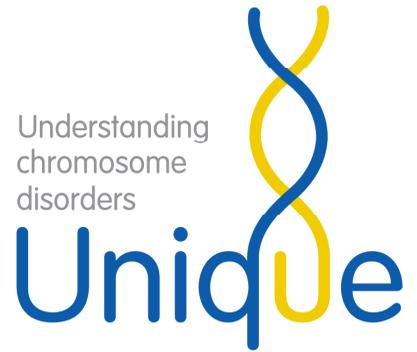


Understanding
chromosome
disorders



Duplications of 20p



Sources and references

The information in this leaflet is drawn partly from published medical research papers. We have focused on articles describing people with a 'pure' 20p duplication, involving no other chromosome material that is likely to contribute to the effects, and on articles that include a review of 20p duplications. 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*.

The leaflet also draws on *Unique's* database. When this leaflet was written, *Unique* had sixteen members with a duplication of 20p, of whom three had a pure duplication of 20p.

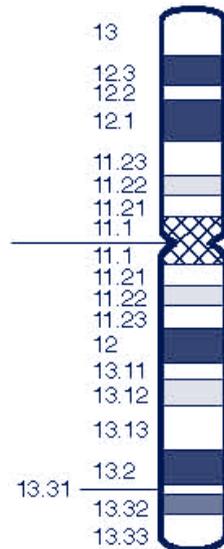
Duplications of 20p

A chromosome 20p duplication is a rare genetic condition caused by extra material on one of the body's 46 chromosomes. Chromosomes are the structures in each cell of the body that carry genetic information, telling it how to develop and function. Apart from the sex chromosomes (two Xs for a girl and an X and a Y for a boy), they come in pairs, one inherited from the mother and one from the father and are numbered 1 to 22, approximately from largest to smallest. Each chromosome has a short (p) arm and a long (q) arm.

The extra material in a 20p duplication comes from the short arm of chromosome 20 (the top part in the diagram below). People with an extra copy of all or part of 20p seem to be very rare. This may be partly because the effects can be mild and only more severely affected cases tend to be reported.

You can't see chromosomes with a naked eye, but if you stain them and magnify them to about 1000 times life size under a light microscope, you can see that each one has a distinctive pattern of light and dark bands. The bands in each arm are numbered outwards starting from the point where the short and long arms meet (the **centromere**).

Your geneticist or genetic counsellor will tell you more about how much extra chromosome material there is. You will almost certainly be given a **karyotype**, a shorthand notation for your child's chromosome make-up, which will show the points where the chromosome has broken. Comparing your child's karyotype with others, both in the medical literature and within *Unique*, will help to build up a general picture of what to expect. But there will still be differences, sometimes quite marked, between your child and others with apparently similar karyotypes. It is very important to see your child as an individual and not to make direct comparisons with others with the same karyotype. After all, each one of us is unique.



Chromosome 20 is one of the smallest chromosomes. It probably only contains 600 - 800 out of the total 20,000 - 25,000 genes.

Names

Geneticists call extra material from a specific part of a chromosome a **duplication**. It can also be called a **trisomy**, especially when most or all of a chromosome arm has been duplicated. A **partial duplication** means there is an extra copy of part of 20p.

How did the duplication happen?

Some 20p duplications occur out of the blue. The genetic term for this is **de novo** (*dn*). Others are the result of a rearrangement in one parent's chromosomes. A blood test to check the parents' chromosomes will show what the situation is.

De novo 20p duplications are caused by a mistake that occurs when the parents' sperm or egg cells are formed. When egg and sperm cells are formed, the two members of each pair of chromosomes normally line up together and then break and recombine to create new chromosomes that contain different combinations of the genes transmitted by the grandparents to the parents of the child. The recombining can occasionally take place between the wrong broken ends, and you can imagine how this could lead to a 20p duplication. However, nobody has ever seen this happen, so it is still a theory.

Recombining is part of a natural process and as a parent there is nothing you can do to change or control it. Children from all parts of the world and from all types of background have 20p duplications. No environmental, dietary or lifestyle factors are known to cause them. So there is nothing that either parent did before or during pregnancy that caused the duplication to occur and equally nothing could have been done to prevent it.

Can it happen again?

Where both parents have normal chromosomes, it is unlikely that another child will be born with a 20p duplication.

Where one parent has a rearrangement of their chromosomes, the risk of having another affected child is very much higher.

In future pregnancies, higher-risk families will be offered prenatal testing by chorionic villus sampling, amniocentesis or both, as well as high-level ultrasound screening. In a family where one member has already been diagnosed with a 20p duplication, these tests will show whether the pregnancy is affected or not.



When one family member has been diagnosed with a 20p duplication, prenatal tests can show if the next pregnancy is affected.

Most common features

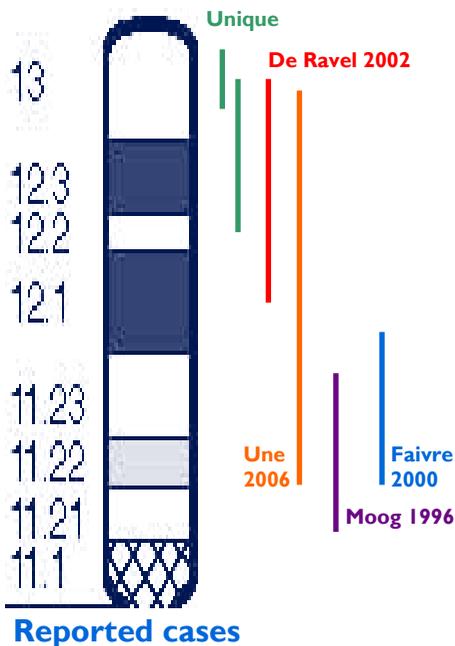
- found in more than 2/3 people with duplication of all or most of 20p

- Some developmental delay
- A variable degree of learning difficulty
- Usually no major medical problems
- Difficulty coordinating movement
- Delay in speaking
- Typical facial appearance that may include a round face with prominent cheeks, coarse and usually straight hair and eyes that slant somewhat upwards
- Dental anomalies
- Unusually formed or fused bones in the spine
- Normal pattern of growth and normal height

Other features

- found in one to two thirds of people with a 20p duplication

- Other typical facial features such as a short nose with large nostrils, widely spaced eyes, a flattened back of the head (although this may also be caused by sleeping position) and tiny skinfolds across the inner corner of the eye (epicanthic folds)
- Squint (strabismus)
- Heart problems
- Unusually positioned fingers or toes (Oppenheimer 2000; Schinzel 1980)



Are the effects different if all or only part of 20p is duplicated?

People with a duplication of only part of 20p are likely to show fewer of these features than people with an extra copy of the entire arm. Duplications of 20p are still very rarely described, and it is too early to know whether particular regions of the chromosome are linked with particular features. The diagram to the left shows the specific smaller segments of 20p that have been identified in published cases or *Unique* members. Always remember that a karyotype match (that is, the same breakpoints in the chromosome) does not mean that two children will be the same. Individuals can be different from each other despite apparently having the same chromosome rearrangement.

Growth

Growth is usually unaffected, so babies are born a normal weight and length and grow at the same rate as other children. However, two babies with a duplication of part of 20q as well as the whole of 20p were very small: they were small-for-dates at birth and grew into very short children with small heads. By contrast, five children between the ages of three and 12 years were extremely tall for their age and had a proportionately large head as well. Two of these children had only a partial 20p duplication and in one child it was in mosaic form. A mosaic form means that some cells have the 20p duplication, while others do not (de Ravel 2002; Hunter 2002; Della-Rosa 2000; Fairve 2000; Balestrazzi 1984; *Unique*).

“ She’s an average weight and height but plump around her face and stomach due in part to her low muscle tone. ”

Appearance



Although there may be little sign in the facial appearance of a baby, child or adult of the underlying disorder, doctors may notice what are known as ‘dysmorphic features’. These facial features can mean that a child looks more like others with a 20p duplication than like his parents, brothers or sisters.

Some typical facial features are: a short, upturned nose, although a few children have a beaked or rather prominent nose and the nostrils can be wide; eyes that slant slightly upwards; a flat but round face, with typically chubby cheeks and a slightly receding chin. Often, the head is rather flat from front to back so it looks wide from ear to ear. Ears can be large and set low on the side of the head and can be unusually formed. Some children have a narrowed forehead. Some have high arched eyebrows. A distinctive feature in many (but not all) children is their thick, coarse and usually straight hair (Oppenheimer 2000; Sidwell 2000; Schinzel 1980).



Children and adults with a deletion from another chromosome as well as a 20p duplication may have facial and other features more typical of the deletion.

(l) simultaneous deletion from 21q22 after successful removal of an encephalocele (tissue protruding through a gap in the skull, see page 11).

(r) simultaneous deletion from 4p causing Wolf-Hirschhorn syndrome.



Sitting, moving: gross motor skills



Two and a half years old

Some delay in reaching childhood developmental milestones is common and although the amount of delay is very variable, it is generally only moderate. Children with a large duplication that includes part of 20q as well as the whole of 20p may experience a more severe degree of delay. Many children also show relatively poor coordination and their gait is shaky. They may have difficulties with balance both when still and when moving.

Unique's experience is that supported walking has been possible before the second birthday in children with a small duplication of part of 20p, but walking alone may not be possible until a year or so later.

Underlying the difficulty with mobility is a low muscle tone that is usually apparent from birth, so a baby will feel unusually floppy. Some joints may

be unusually loose while others may be contracted, making it difficult to control purposeful movement (Della-Rosa 2000; Schinzel 1980).

Early assessment and intervention with physiotherapy and occupational therapy will help children to achieve their full potential.



Three years old

“ She sits to watch television or use the computer but when playing with toys often gives up and lies on the floor. She tends to run instead of walking, often with her eyes shut! She has a very clumsy, rapid and uneven gait, often tripping over her own feet, falling and bumping into things. Her elbow joints are extremely contracted, while her wrists and fingers bend easily back ” – age 5

Fine motor skills

A delay in hand use and coordination is to be expected. The joints of the arms and hands may not move freely or may be too loose, grip may be loose and children may show decreased strength.

“ She finds fine motor skills such as threading beads hard and has difficulty finding correct or comfortable holding positions. At the age of 5, no hand dominance had been established. But she can undress and put her socks on and is learning to cope with buttons. ”

Learning

Children with a 20p duplication will usually need support with their learning, but the extent varies, even between children within the same family. The range of learning difficulty is from mild to severe, with most children with a duplication of the entire 20p arm having moderate difficulties. In general, children with a larger duplication extending into 20q are more severely affected and those with smaller duplications appear to be relatively spared. The evidence from *Unique* suggests that underlying cognitive skills may be more severely affected than language (Della-Rosa 2000; *Unique*).

“ She is moderately mentally retarded although you would never know it by looking at her or by listening to her talk or interact with others ” – age 8

“ She has a very good memory and enjoys using the computer at school. She started to use a keyboard at 4 and her skills are improving. Her pre-school assessment showed that her underlying cognitive skills were in the low average range for her age. She has clear difficulties with concentration and when left to her own devices her play and approach to tasks is not purposeful. There is a marked difference in her ability to engage with learning when supported by an adult who can mediate the experience. She is unable to maintain concentration on a task without adult support. I read her a new short story one night. The next night she retold it to me nearly word for word from memory. Her more able areas of learning are visual and practical, using visual cue cards and taking part. She needs to feel interested or she will not listen. She cannot read yet but enjoys being read to, her pictures are starting to take on more form and she is attempting to write her name ” – age 5

Speech and communication

Children with a 20p duplication can be expected to experience some delay in speech and language development. It appears that children with a duplication of the entire arm are more severely affected than children with smaller duplications. While children with smaller duplications appear consistently to develop effective communicative language, this has not always been possible for children with larger duplications.

Regardless of duplication size, understanding is usually more advanced than expression.

Researchers have drawn attention to specific difficulties of articulation, particularly with *ch*, *th* and *sh* sounds and raised the possibility of a common pattern (Sidwell 2000; Centerwall 1977).

“ Her language and communication have improved vastly over the past year. She understands far more than she can express but still has difficulty in understanding a task of more than two parts, such as *Pick up your shoes, take them to the living room and put them under the table*. She is able to form sentences but they are not always correct or understandable, and she occasionally babbles when excited. She still has trouble pronouncing the beginnings of words, so repeats other parts of words, such as *gog* for *dog* and *kake* for *snake* ” – age 5



Three years old

Behaviour and attention

There is no systematically collected information on behaviour patterns. The information at *Unique* suggests that behaviour difficulties that are common in children with a learning difficulty are common in this group of children. A report of the behaviour of one child with a small duplication within band 20p13 follows.

“ Sensory processing difficulties affect her ability to self regulate. This means that she will have difficulty coping with a number of sensory inputs at the same time, possibly leading to being unable to maintain a coherent understanding of cause and effect as well as the overall meaning of situations. She is quite passive in her relationships with others, rarely initiating social contact with other children. Although sociable, she is emotionally immature and can misinterpret other children’s actions. She very easily gets upset and can quickly become angry or violent when tired, misunderstood or teased. She can also be very excitable and unaware of dangers and others around her. If she refuses to do something, it is nearly impossible to get her to do it. Time out helps her to calm down ” – age 5



Three and a half years old, with younger sister, not affected

Hearing and eyesight

Both hearing and eyesight appear to be normal, although some children have a squint (strabismus) and in three children an astigmatism has been found (Della-Rosa 2000; Sidwell 2000; LeChien 1994; *Unique*).

Treatment of strabismus depends on the cause but can include patching the stronger eye, exercises, glasses to correct a refractive error such as long sight and surgery to realign the muscles that hold the eye in place.

Astigmatism is when the cornea (the clear cover over the iris and pupil) is abnormally curved. The effect on vision is to make objects appear blurred. Sometimes the brain can compensate for astigmatism although it may be too strong for this to happen without the aid of glasses.

Teeth

Dental problems are often mentioned in the medical literature although there is less evidence of this from *Unique*. The types of problem are quite varied, including irregular teeth, frequent decay and a delay in the permanent teeth coming through. The likelihood of dental problems means that all children should have access to expert special needs dentistry (Une 2006; Centerwall 1977).

Medical and other concerns

■ Bones and spine: abnormalities of the vertebrae

X-rays of the spine have frequently shown abnormalities in reported cases. Some vertebrae may be fused together or have an irregular shape or there may be less than the usual space between them. In many children, these findings will not affect movement, although the part of the spine where any vertebrae are fused will be less flexible than usual. Other children develop a spinal curve, most typically a forward curve (kyphosis), but this may be related to their muscle tone and strength as much as to any spinal abnormality (Sidwell 2000; Balestrazzi 1984; Centerwall 1977; Subrt 1974).

One child had a marked demineralisation of the bones (osteopenia), as a baby, although this improved when he reached puberty. In other children, reduced density and increased fragility of the bones (osteoporosis) has been seen, making accidental fractures more likely (Sidwell 2000; Schinzel 1980).

■ Hands and feet

Minor differences in the way the hands look are quite common in children and adults with a chromosome disorder. Children with a 20p duplication have been seen to have broad or stubby hands, short plump fingers (especially the fingertips) and broad thumb ends as well as incurved little fingers.

The big toes may also be broad at the end and some children have toes that overlap each other (especially the second and third toes). Some children have flat feet and some have a rather prominent heel or a 'rocker bottom' foot, where the sole curves outwards (Della-Rosa 2000; Schinzel 1980; Rudd 1979).

“ She had special PVC shoes made to straighten her feet so she didn't walk on the insides and didn't walk with her toes pointed inwards. Her toes do now point out but she still rolls onto the instep of her feet. She does not need special shoes any more, just ones that support her feet ” – age 8

■ Genitals and reproductive system

Minor anomalies of the genitals are relatively common among children with a chromosome disorder, especially boys. Among those with a 20p duplication, three out of 21 babies had a minor genital anomaly. In one case, the hole usually at the end of the penis was situated on the underside instead (hypospadias) and one testicle did not descend into the scrotum and was brought down surgically. More unusually, a 9-year-old boy had very large testicles. A girl has been described in whom the clitoris and anus



Two views of left foot, age 4, showing uneven toe length and overlapping toe

were sited unusually far forward and in another there was a bridge of skin joining the upper part of the buttocks (Sidwell 2000; Balestrazzi 1984; Schinzel 1980; *Unique*).

■ Heart conditions

Most babies with a 20p duplication are born with a normal, healthy heart. However, as a significant heart condition has been found in one-third to a half of affected babies, a careful cardiac examination should be carried out.

Among the heart defects described are holes between the upper or lower chambers (atrial septal defect/ ASD or ventricular septal defect/ VSD) and failure of the ductus arteriosus to close (persistent ductus arteriosus/ PDA). The ductus arteriosus is a channel between the vessels leading from either side of the heart that is open during fetal life but usually closes shortly after birth. Other conditions include problems with heart valves. In all these heart conditions, treatment will depend on severity and the effects on the baby but if necessary surgery can correct the problems. A more complex defect known as tetralogy of Fallot has been seen, but not in babies with a pure 20p duplication (Une 2006; Wieczorek 2003; Voullaire 1999; Schinzel 1980).

■ Less common clinical problems

One boy with a large duplication extending into band q11 of the long arm of chromosome 20 and a few babies and children with involvement of another chromosome had **kidney anomalies**. No kidney anomalies have been seen in babies or children with a pure 20p duplication (Wieczorek 2003; Sidwell 2000).

Hernias are fairly common in children with or without a chromosome disorder. A hernia occurs when a section of intestine protrudes through a weakness in the abdominal muscles. A soft bulge can be seen under the skin where the hernia has occurred. Among 21 children, two babies had an umbilical hernia (near the navel/ belly button). One child had inguinal hernias (in the groin) on both sides. An inguinal hernia is usually corrected by surgery to avoid the intestine becoming trapped while a wait-and-see approach may be adopted for an umbilical hernia at first as many close naturally in time (Della-Rosa 2000; Sidwell 2000; Schinzel 1980).

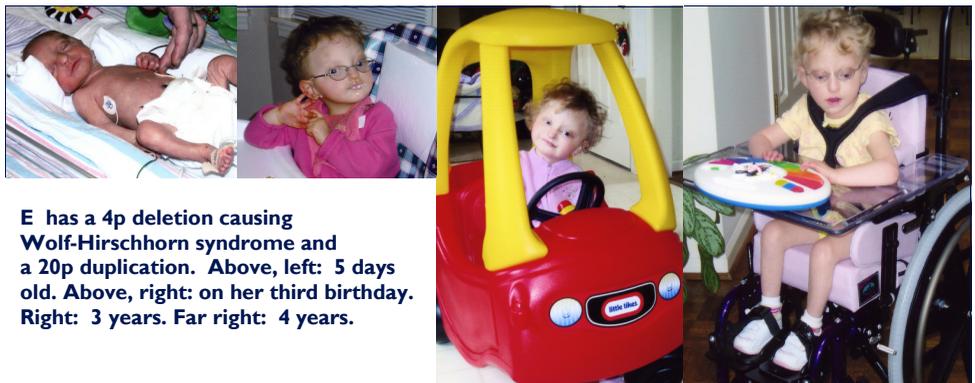
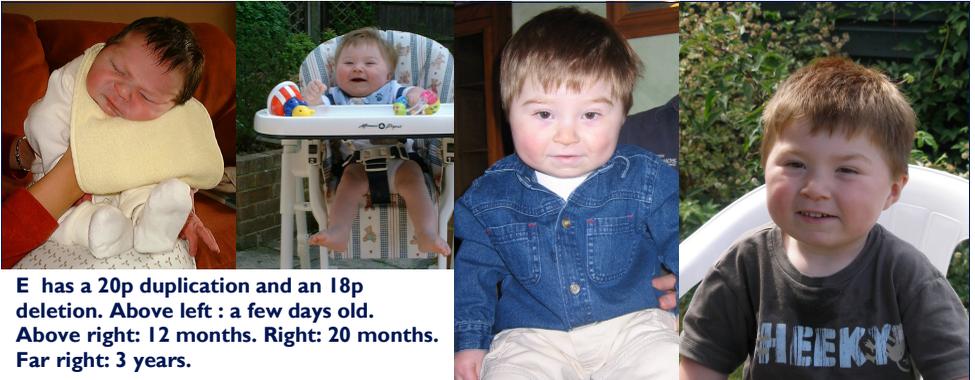
One boy with a mosaic duplication of 20p11.2 to 20p12.1 (he had a normal cell line as well as cells with the extra 20p material) had a very large **head** (and **brain**) and developed seizures at 14 months, but seizures have not been seen in others with a 20p duplication. However, slight changes in the relative size of different parts of the brain have been seen occasionally. In one child the band of nerve fibres that connects the right and left hemispheres of the brain did not develop (absence of the corpus callosum); in an unborn baby much of the brain was found not to have developed (Une 2006; de Ravel 2002; Hunter 2002; Faivre 2000; Zumel 1989).

Four members of the same family with a small duplication of 20p11.21-23 had features typical of **Alagille syndrome** but without liver problems. It is assumed that one breakpoint in the chromosome disrupted the Jagged1 (*JAG1*) gene whose deletion or disruption causes this syndrome (Moog 1996).

Outlook

The outlook depends mostly on whether vital organs such as the heart are affected. In children whose vital organs are not affected, healthy survival into adulthood and a normal lifespan seem quite possible (Oppenheimer 2000; Sidwell 2000; LeChien 1994).

Three children



Support and Information



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Chromosome 20 and beyond is a Facebook community for anyone affected by a disorder of chromosome 20

www.facebook.com/groups/507113779406575

Unique lists external message boards and websites in order to be helpful to families looking for information and support. This does not imply that we endorse their content or have any responsibility for it.

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