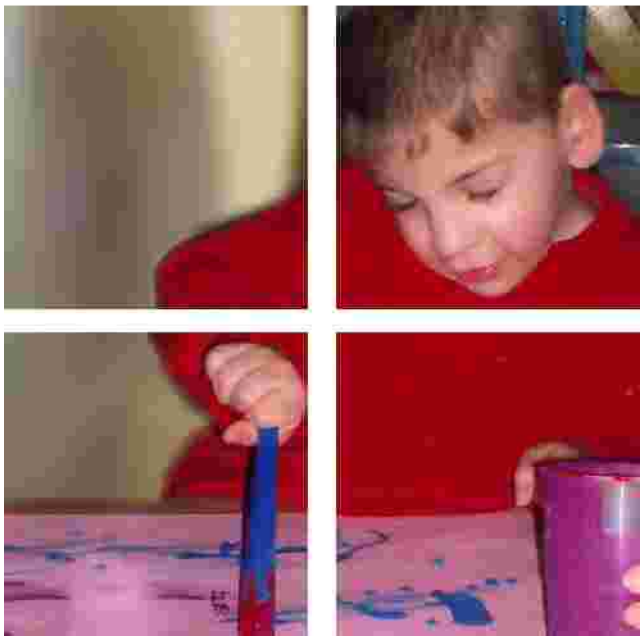
Unique

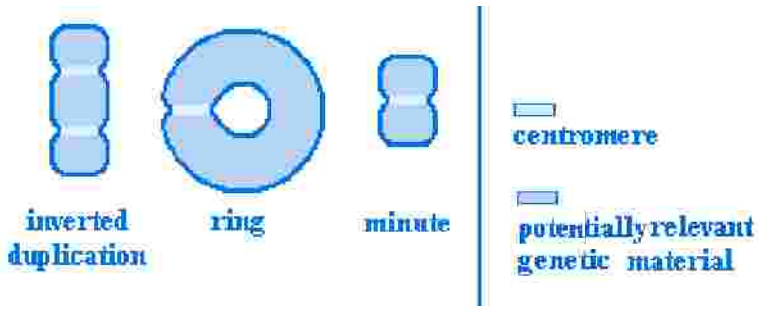
Supernumerary Chromosome 8



Supernumerary chromosome 8

Supernumerary chromosome 8 means that there is a tiny extra part of a chromosome in all or some of the cells of the body. In addition to the 46 chromosomes that everyone has, people with a supernumerary chromosome 8 have a small extra chromosome made from chromosome 8 material.

The small extra chromosome can have different possible shapes.



It can also have different names. The most common names are:

small supernumerary marker chromosome (sSMC)

supernumerary ring chromosome (SRC), if it's in the form of a ring

Other names you might find in the medical literature include:

small accessory chromosome (SAC)

extra structurally abnormal chromosome (ESAC).

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 which 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.

Sources & references

The information in this leaflet is drawn partly from published medical research where there are reports of around 40 cases. The first-named author and publication date are given to allow you to look for the abstracts or original articles on the internet in PubMed (at www.ncbi.nlm.nih.gov/pubmed). If you wish, you can obtain abstracts and articles from *Unique*. The leaflet also draws on *Unique*'s database. When this leaflet was written, *Unique* had twelve members with a supernumerary chromosome 8.

Up-to-date information on extra chromosome 8s is also to be found on the following website: http://www.med.uni-jena.de/fish/sSMC/08.htm. It is rather technical, and if you have difficulty with any of the information there, please contact us at info@rarechromo.org.

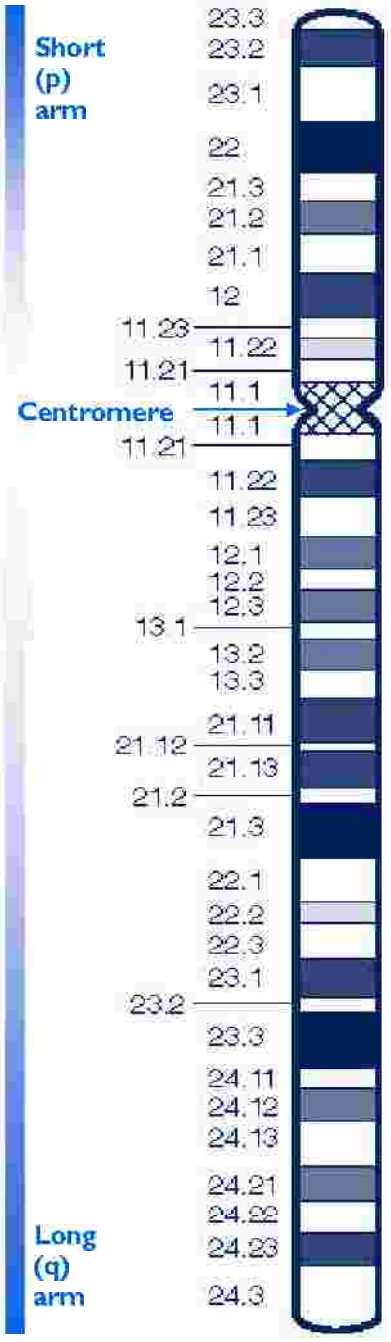
People with an extra chromosome 8 usually have some cells with 46 chromosomes and others with 47 chromosomes (46 plus the extra chromosome). When cells with a different chromosome make-up exist alongside each other, the condition is known as mosaic. People with a small extra chromosome 8 are almost always mosaic. The degree of mosaicism can be different in every body tissue. So it can be different in the blood, the skin, the lungs, heart, brain and so on.

Chromosome 8 is a medium-sized chromosome and contains 700-1,100 genes out of the total of 20,000 to 25,000 genes in the human genome. The extra chromosome usually only contains a few of these genes but it's generally believed that these extra genes cause any clinical difficulties that someone with a supernumerary chromosome 8 may face.

You can't see chromosomes with the naked eye, but if you stain them and magnify them under a microscope, you can see that each one has a distinctive pattern of light and dark bands. The diagram on this page shows the bands of a normal chromosome 8. These bands are numbered outwards starting from the point where the short and long arms meet (the centromere). A number starting with a 'p' is in the short - petit - arm (at the top in the diagram) and a number starting with 'q' is in the long arm (at the bottom).

Some chromosome bands contain no important genes and only irrelevant genetic material (called heterochromatin). Having extra material from bands containing heterochromatin does not generally affect development. Other bands contain relevant genetic material (called euchromatin). Having extra euchromatin is more likely to affect development but does not always do so.

Some people with an extra chromosome 8 have a single extra copy of the genes in the euchromatin. Other people have two extra copies. People with an inverted duplication (*see image on page 2*) have two extra copies.



Chromosome 8

Your child's karyotype or molecular results

Your geneticist or genetic counsellor will tell you more about what chromosome material your child's extra chromosome consists of. You will almost certainly be given a karyotype, a shorthand code for the image of your child's chromosomes. This may show the points where the chromosome has broken. A karyotype for a boy with supernumerary chromosome 8 might look like this:

mos 47,XY,+r(8)(p12q21.3)[28]/46,XY[22]

mos	= mosaic or cells with a different chromosome make-up exist alongside each other
47	= total number of cells in the first cell line is 47. There is one extra chromosome
XY	= the two sex chromosomes, XY for males; XX for females
+r(8)	= the extra chromosome consists of material from chromosome 8 and is in the form of a ring
(p12q21.3)	= the chromosome has broken in the short arm at band p12 and in the long arm at band q21.3, so the extra chromosome consists of the material between these two points, including the centromere
/	= information after this sign is about a different cell line
46,XY	= the chromosomes in the second cell line are those of a normal male
[28] [22]	= these figures tell you that 50 cells were analysed, of which 28 contained the extra chromosome and 22 normal chromosomes.

Comparing your child's karyotype with others, both from the medical literature and within *Unique*, can 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 small extra chromosomes. It is very important to see your child as an individual and not to make direct comparisons with others with the same karyotype.

Diagnosis

The extra chromosome cannot usually be identified accurately under a microscope. It may be so tiny that it is even hard to know which chromosome it comes from. The origin and amount of extra material can usually only be identified using new, sensitive molecular techniques such as FISH (using specific DNA probes that show up in fluorescent colour) and array-CGH (also known as microarrays), a way of analysing thousands of different DNA sequences at the same time. In terms of predicting the outcome for any individual child or pregnancy, it is important to be as precise as possible about the breakpoint in each arm of the chromosome.

Does the proportion of cells with the extra chromosome matter?

This question refers to the numbers in square brackets in the karyotype. It tells you more about the mosaicism – the cell line with the extra chromosome and the cell line with normal chromosomes. Although you will often be given this information, in fact it probably doesn't help in understanding the effects. The cells tested are usually only from blood or sometimes from scrapings inside the cheek - but this doesn't tell you about the proportion of cells with the extra chromosome in other tissues of the body, such as the heart, or liver, or lungs or brain.

Can someone with a supernumerary chromosome 8 have similarly affected children?

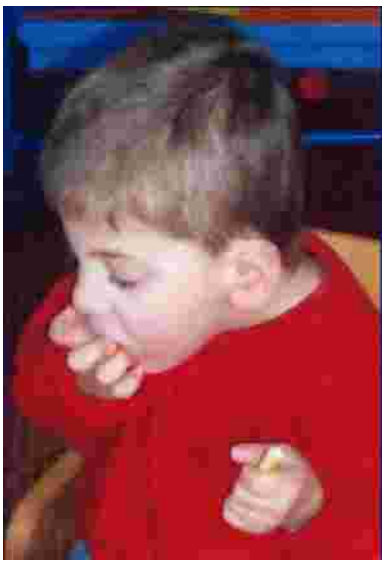
In adults, especially men, with a small extra chromosome 8, fertility can be affected but some people will be able to have children. The children can inherit the extra chromosome. The chance of inheriting a small supernumerary chromosome from one's mother is twice as high as from one's father (Liehr 2006).

A small extra chromosome containing no genetically relevant material can run in some families from generation to generation without causing any problems. But when a parent passes on a small extra chromosome that contains genetically relevant material, the baby can have more or fewer affected cells than the parent - and this of course can change its effects (Rothenmund 1997).

How will the extra chromosome affect my child?

The effects of the extra chromosome depend mostly on whether it contains genetically relevant or irrelevant material, how much material it contains and from which bands of chromosome 8. Your geneticist or genetic counsellor will be able to tell you whether the extra chromosome contains genetically relevant material or not and which part of the chromosome it comes from.

To discover about the possible effects, one good way is to contact info@rarechromo.org and ask for help in selecting relevant cases from the website at http://www.med.uni-jena.de/fish/sSMC/08.htm. You can then take a list of these cases to your genetic specialist. You can also look in this leaflet for the relevant page/s (6-15). The information in these pages was correct when we wrote this leaflet in early 2009, but the picture can change as new babies and children are diagnosed and reported in the medical literature.



Four years old

Are there people with a supernumerary chromosome 8 who are healthy and whose development has not been affected?

Yes, there are. When the extra chromosome only contains genetically irrelevant material, development isn't affected. And there are one or two children with an extra chromosome made up of material from very close to the tip of the short arm (8p) who appear to be developing quite normally (Herry 2004; de Pater 2005). There are around 15 other reports in the medical literature of people with normal development where the size of the extra chromosome 8 hasn't been established. These include: a 31-year-old woman with apparently completely normal development, a normally developing seven-year-old girl and a normally developing two-year-old (Gravholt 1995; Tonk 2000; Daniel 2003).

Extra chromosomes containing only genetically irrelevant material from around the centromere between 8p11.21 and 8q11.21

Chromosomes that contain no genetically relevant material are probably harmless and do not affect development.

The chief effect of these otherwise harmless extra chromosomes is that they may affect fertility.

Chromosomes containing only genetically irrelevant material do not generally extend beyond band 8p11.21 in the short arm or beyond band 8q11.21 in the long arm (Starke 1999; Gole 2005).

Extra chromosomes consisting of small amounts of material including the centromere and as far as 8p11.21~22 in the short arm or 8q11.22 in the long arm

Only a small number of cases have been characterised in detail. From these, the most likely features in the affected child appear to be:

- Some degree of developmental delay
- Delay in acquiring language
- Some difficulties with social skills
- Some behaviour difficulties including problems with attention and activity levels or autistic-like behaviour (Daniel 2003; Loeffler 2003; Liehr 2006; Bettio 2008; *Unique*).

Additional details from a description of a *Unique* member at 15 years: normal birth weight; early feeding difficulties and breast refusal; no underlying health problems or physical abnormalities; motor development just within normal limits and normal mobility – sitting, walking, running etc; late acquisition of fine motor skills but no limitation; need for specific support with learning. Particular difficulties with mathematics and abstract subjects including history and geography. Attended mainstream (regular) primary school with a 1:1 teaching aide. At 15 years, attends a special education school where the curriculum is styled to his level and he is taught in small groups without an aide. He reads comics, teen magazines, TV guides, the weather and movie sections of the newspaper. His expressive language is delayed, so he can only express himself in a limited way and it is not always clear how much he understands. He spoke his first words at two and by five a few more words, but at 6-7 had a great leap in vocabulary. At 15, he speaks in somewhat simplified and repetitive sentences.

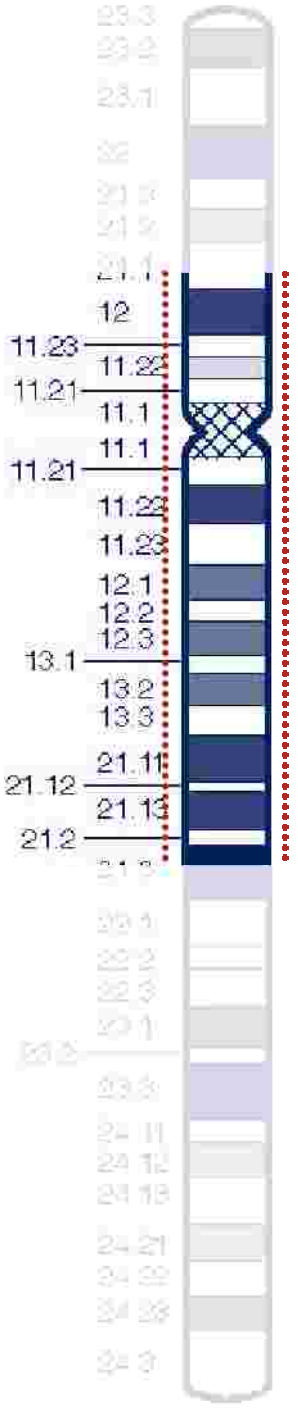
He has had a diagnosis of atypical autism (pervasive developmental disorder) since he was five. He also has some obsessive-compulsive behaviour. He responded immediately to Applied Behavioral Analysis therapy (ABA) at 5-7 years and made great strides in all major skill areas. At 15, he is shy with children of his own age, doesn't always understand what they say or mean and is worried he will act inappropriately. As a child between 1.5-7 years he had big sleep problems, waking for hours every night. A gluten/casein-free diet helped his sleep, as did melatonin before bedtime.

Extra chromosomes containing material from beyond band 8p11.22 in the short arm and band 8q11.22 in the long arm

Two young children within *Unique* each have a ring chromosome made up of material from the short and the long arms of chromosome 8. In one child the breakpoints are assessed to be at 8p12 and 8q11.21 and in the other child with a slightly larger ring they are at 8p21 and 8q21.3 (*Unique*).

The child with the larger ring was born slightly early at 37 weeks but at 3.2kg (7lb 1oz) was a healthy weight. The main complication in pregnancy was very marked excess amniotic fluid. He spent the first two weeks of his life in special care and was tube fed, partly because he had difficulty coordinating breathing with feeding. He also tended to bring milk back during and after feeds (reflux) and this persisted until he stopped milk feeds. As a newborn baby his most obvious feature - apart from some subtly different facial features and a sacral dimple at the base of the spine - was talipes (club foot), requiring casting to realign the feet ready for walking. This has been completely successful and having started to walk at 3, he is now trying to run. He is generally healthy but has had repeated respiratory infections as a young child. The only regular medicine he takes is slow-release melatonin to help him stay asleep.

Developmentally, he is starting to toilet train at four years old, he says occasional words, is trying to talk, understands when asked to do something and is learning some sign language at his speech therapy sessions. He's sociable, plays well with other children and is in a mainstream nursery with 1:1 support and will hopefully attend a mainstream school one day a week. He loves CBeebies, singing, mobile phones, the touch screen computer and the family dog!



" Above all, we have tried to treat him like other children