

Support and Information



Rare Chromosome Disorder Support Group

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Facebook Group for 3p26 duplications

www.facebook.com/groups/1219060931439360

Facebook Group for chromosome 3

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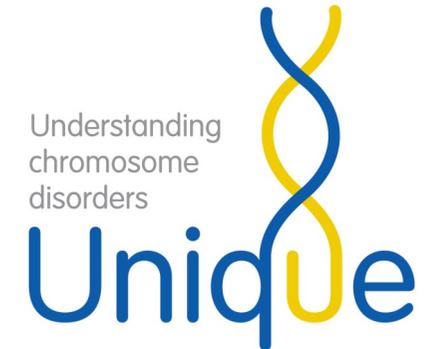


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3p duplications

rarechromo.org

Duplication of 3p

A duplication of 3p is a rare genetic condition caused by an extra part of one of the body's 46 chromosomes – chromosome 3. For a healthy development, chromosomes should contain just the right amount of genetic material – not too much and not too little. A 3p duplication can result in developmental delay and congenital (heart) malformations.

What are chromosomes?

Chromosomes are made up mostly of DNA and are the structures in each of the body's cells that carry the genetic information in the form of genes that tells the body how to develop, grow and function.

Chromosomes usually come in pairs, with one chromosome from each pair coming from the father and one from the mother.

Of the 46 chromosomes, two are a pair of sex chromosomes, XX (two X chromosomes) in females and XY (one X and one Y chromosome) in males. The remaining 44 chromosomes are grouped in 22 pairs, numbered 1 to 22 from largest to smallest.

Chromosomes have a short arm, named **p** (shown at the top in the figure), and a long arm, named **q** (shown at the bottom in the figure). The two arms of a chromosome meet at a point called the **centromere**.

Looking at chromosome 3p

You can't see chromosomes with the naked eye, but if you stain them and magnify them many hundreds of times under a microscope, you can see that each one has a distinctive pattern of light and dark bands.

Looking at chromosomes under a microscope, it may be possible to see the genetic material that is missing or extra, if the piece is large enough. However, rare chromosome disorders can be caused by subtle changes that are too small to see using a microscope. Molecular DNA technology gives a more precise understanding of the size and position of the deletion or duplication. Your geneticist will be able to tell you about the position at which the duplicated material can be found on the chromosome 3 of your child.



Notes

Duplication of 3p

The disorder was first described in the medical literature in 1972 (Rethore 1972). For this guide we included information about approximately 20 people with a 3p duplication. More than 80 people with a 3p duplication have been described in the medical literature, but in most cases these people had an additional chromosome abnormality. This makes it difficult to determine which of their signs and symptoms are related to the duplication of chromosome 3 and which are related to the additional chromosome abnormality. We have tried to make a selection of patients for whom we believe that their signs and symptoms are not influenced by the additional chromosome abnormality.

This does not mean that there are no more people with a 3p duplication. There are children registered in international databases, but often with more limited information. There are also children with a 3p duplication who have never been included in medical articles.

Main features in children with a 3p duplication

The features mentioned in this guide have been described in the medical literature in children with a 3p duplication. It is not known if all features are indeed caused by the duplication or if their occurrence in children with the duplication is coincidental. Some of the features can also occur in children without the duplication.

Because only a few people with the duplication have been described, not all the effects of the duplication are known.

The features can vary between children, but one or more of the following features can be present:

- Developmental delay and/or intellectual disability
- Congenital heart abnormalities
- Certain facial features/characteristics in their appearance

How common are 3p duplications?

It is not known exactly how common 3p duplications are. As previously stated, 80 people have been reported in the medical literature.

Sources

The information in this guide is drawn from the published medical literature. With the first-named author and publication date you can look for abstracts or original articles on the internet in PubMed (www.ncbi.nlm.nih.gov/pubmed). Articles included are: Kuller 1992; Conte 1995; Chen 1996; Kotzot 1996; Bruni 1998; Jenderny 1998; Vance 1998; Chen 1999; Kennedy 2000; McGaughran 2000; Smeets 2001; Antonini 2002; Bittel 2006; Chang 2007; Tan 2011; Guo 2012; Puvabanditsin 2013; Rodvalho 2013; Natera-de Benito 2014. When this guide was written the full text of the articles was used as far as possible, but sometimes only the abstracts were available.

Pregnancy

In some mothers of children with a 3p duplication pregnancy was normal (Bruni 1998).

Five babies (of 4 mothers) have been described in the medical literature in whom the diagnosis was established during pregnancy, because of abnormalities noted during ultrasound examination (Chen 1996; Chen 1999; Kennedy 2000). These children all had holoprosencephaly. In holoprosencephaly the left and right sides of the brain do not separate properly (for more information, see page 6). In addition, they had facial abnormalities. For instance, one child had only one eye socket. In 4 of the 5 pregnancies, the parents chose to terminate the pregnancy. The fifth child was born after a pregnancy of 33 weeks after premature rupture of the membranes. The child died shortly after birth. One of the mothers had previously lost a child one week after birth as a result of multiple congenital abnormalities including the heart and brain.

One girl was born after premature labour at 28 weeks of pregnancy. She was part of a twin pregnancy. Both girls had congenital heart abnormalities. They died shortly after birth (Puvabanditsin 2013).

In one boy, several abnormalities were seen on the ultrasound examination during pregnancy. The diagnosis was made after birth. He had several abnormalities including a cleft lip and palate, brain abnormalities and heart abnormalities. He died 5 weeks after birth as a result of a severe bowel infection (necrotising enterocolitis) (Kuller 1992).

One girl was born after a pregnancy of 35 weeks. She had respiratory problems and seizures shortly after birth. Further examinations revealed a complex heart problem (tetralogy of Fallot, see page 6) (Chang 2007).

Newborn babies

In 8 babies reported in the medical literature and born after a pregnancy of at least 37 weeks, a birth weight is reported (Kotzot 1996; Bruni 1998; McGaughran 2000; Antonini 2002; Bittel 2006; Tan 2011; Rodovalho 2013; Natera-de Benito 2014). Mean birth weight was 3.421 kg (range 2.750-4.100 kg).

Two babies (in addition to the children described under 'Pregnancy') were reported as having problems after birth. One girl was born after a caesarian section because of breech position. She was blue after birth as a result of a shortage of oxygen, but resuscitation was not needed. The girl was shown to have a congenital heart anomaly (atrial septal defect). She had frequent respiratory infections. She died 19 months after birth (Rodovalho 2013).

One boy was born after a normal pregnancy. He had a slow heartbeat during labour. He did not start breathing spontaneously and he needed respiratory support (Tan 2012).

Can it happen again?

The risk of having another child affected by a rare chromosome disorder depends on the genetic code of the parents. If the chromosomes in both parents are normal, the chance of having another affected child is very low. Nonetheless, there is a small chance that some of the egg cells of the mother or some of the sperm cells of the father carry the change ([germline mosaicism](#)). This means that parents who are not found to carry the change still have a very small chance of having another affected child.

The chance of recurrence is much higher if one of the parents is found to carry the duplication or a chromosomal rearrangement that involves the short arm of chromosome 3. Each family situation is different and a clinical geneticist can give you specific advice on the chance of recurrence in your family as well as options for prenatal diagnosis and preimplantation genetic diagnosis. PGD requires the use of in vitro fertilisation and embryo biopsy, and only healthy embryos are transferred to the mother's uterus. If the parents choose to conceive naturally, prenatal diagnosis options include chorionic villus sampling (CVS) and amniocentesis to test the baby's chromosomes.

Appendix

Results of the chromosome test

In a 3p duplication, the result may read something like this:

46,XY,dup(3)(p24.1p26.2)

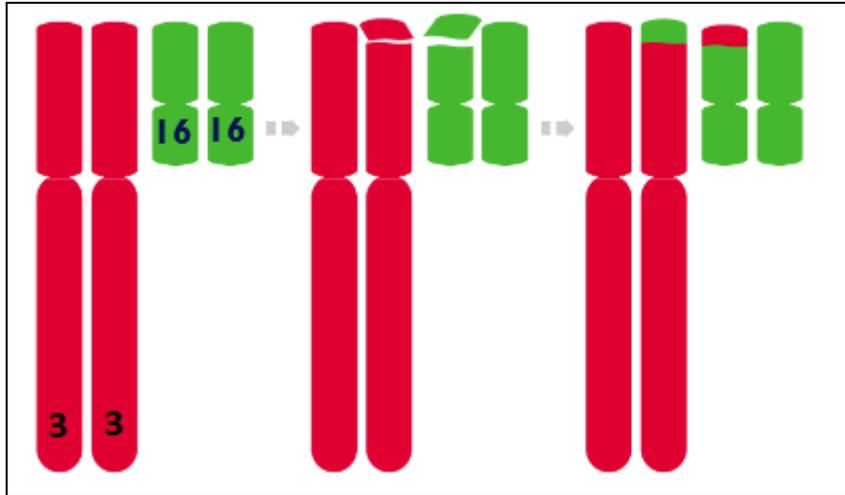
46	The total number of chromosomes in your child's cells
XY	The two sex chromosomes, XY in men, XX in women
dup(3)	A duplication, or extra material of chromosome 3
(p24.1p26.2)	The part of chromosome 3 that is extra is from the short arm (p) and involves bands 24.1 to 26.2

In a translocation the result may look like this:

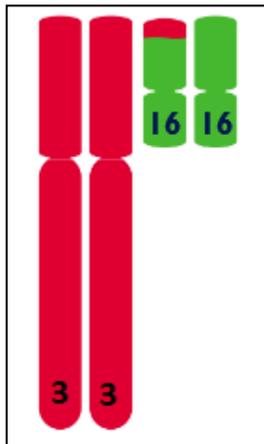
46,XX,der(7)t(3;7)(p24.2;q35)

46	The total number of chromosomes in your child's cells
XX	The two sex chromosomes, XY in men, XX in women
der(7)	An abnormal (derivative) chromosome 7 was found
t(3;7)	The abnormal chromosome is derived from a translocation (t) between chromosome 3 and 7
(p24.2;q35)	The translocation resulted from a break in band 24.2 on chromosome 3 and band 35 on the long (q) arm of chromosome 7. The derivative chromosome 7 is missing the material from band 35 to the tip of the chromosome. In exchange, it contains material from the short arm of chromosome 3: from band 24.2 to the tip of the chromosome

In a substantial number of children the 3p duplication is the result of a change in the chromosomal pattern of one of the parents: a so-called balanced reciprocal translocation. In a balanced reciprocal translocation the material of 2 chromosomes has switched places, but no material has been lost or gained, which is why we use the term balanced. People with a truly balanced translocation are themselves usually symptomless, although they may have difficulties with fertility and do have an increased risk of having a pregnancy affected by an unbalanced translocation.



Someone with an unbalanced translocation has an extra part of one chromosome and a deletion from another chromosome, e.g. a 3p duplication and a deletion from another chromosome. It is therefore important that both parents of a child with the duplication have their own chromosomes tested. In both situations there is nothing you could have done to have stopped this. No one is to blame and nobody is at fault.



Feeding and growth

One girl had difficulties swallowing (dysphagia) (Rodvalho 2013). A boy had gastro-oesophageal reflux (McGaughran 2000). One girl was a poor feeder (Smeets 2001). Another girl suffered from diarrhoea during her first year. This improved after a change in her diet. She was small. Her bone age was behind as compared to her actual age (Bruni 1998). Another boy had a mild growth delay (Kotzot 1996). Short stature is mentioned as one of the features of a 3p duplication (Natera-de Benito 2014).

Appearance

A number of facial features have been reported to occur more commonly in children with a 3p duplication (Puvabanditsin 2013; Rodvalho 2013; Natera-de Benito 2014). Some children have a small head (microcephaly). The eyes may be wide apart (hypertelorism). The face may be square shaped with prominent cheeks. The ears may be abnormally shaped and low set. The philtrum (groove between nose and upper lip) is often prominent. The lower jaw may be small and set back (microretrognathia). The neck is often short. Some children have a cleft palate and/or lip.

Skeletal features

A number of children have skeletal abnormalities. Two children have scoliosis (Antonini 2002; Rodvalho 2013). In addition, several abnormalities of the hands, wrists and feet have been described in 3p duplication, such as bowing of the fingers and wrists, syndactyly (joined fingers/ toes), hyperlaxity or limited mobility of the joints and flat feet (Antonini 2002; Bittel 2006; Rodvalho 2013; Natera-de Benito 2014). One girl had extensive skeletal abnormalities (McGaughran 2000).

Learning and psychomotor development

Most children with a 3p duplication have developmental delay and/or intellectual disability. The delay is usually mild to moderate.

Six children for whom information is reported learned to sit at a mean age of 10 months (range 4-18 months) (Kotzot 1996; Antonini 2002; Bittel 2006; Guo 2012; Natera-de Benito 2014). Four children were able to crawl by a mean age of 12½ months (range 6 – 20 months) and six children who learned to walk independently could do this by a mean age of 22 months (range 12-30 months) (Kotzot 1996; Antonini 2002; Bittel 2006; Tan 2011; Guo 2012).

Speech and language development can be delayed. Information on 5 children is available. They spoke their first words at a mean age of 21 months (range 12-36 months) (Kotzot 1996; McGaughran 2000; Bittel 2006; Tan 2011; Guo 2012).

A 7 year old girl was reported to have a normal (age appropriate) development (Bruni 1998).

Behaviour

Two boys with a 3p duplication and autism have been described in the medical literature (Guo 2012). Another boy showed behaviour similar to autism (PDD) and suffered from anxiety (Bittel 2006). Another boy had temper tantrums and was easily frustrated. He had difficulties adapting to a new environment (Natera-de Benito 2014). Another boy was hyperactive. He bit his own hands and repeated words (Antonini 2002).

Medical concerns

■ Head and brain

Six children have been described in the medical literature with a 3p duplication and holoprosencephaly (see also Pregnancy). In holoprosencephaly the left and right sides of the brain do not separate properly (Chen 1996; Vance 1998; Chen 1999; Kennedy 2000).

One child who died shortly after birth had a enlarged brain ventricles (Chen 1996). Another boy who died when he was 5 weeks old had abnormalities on a CT scan of his brain (fused thalami, hypothalamic hamartoma; Kuller 1992).

Another boy had a cyst near one of the meninges (brain lining as shown on CT (Antonini 2002).

Three children had seizures (Conte 1995; McGaughan 2000; Chang 2007). In one of the children the seizures occurred during fever (Conte 1995). One boy had an abnormal EEG, but he had no seizures.

■ Heart

A substantial number of children with a 3p duplication have heart problems. Two children had tetralogy of Fallot, a complex heart condition (Kennedy 2000; Chang 2007). Six children had an opening between the left and right sides of the heart (atrial septal defect or ventricular septal defect) (Kuller 1992; Chen 1996; McGaughan 2000; Tan 2012; Puvabanditsin 2013; Rodvalho 2013). Two children had an open ductus Botalli. This is a short vascular structure that connects the pulmonary artery with the aorta. Normally, the structure closes after birth. One child had heart problems, but no details were given (Jenderny 1998).

■ Vision

A number of children with holoprosencephaly also had cyclopia (one eye socket instead of two). One girl had strabismus (a squint) (Rodvalho 2013). A 5 week old boy had microphthalmia (small eyes) and a coloboma (Kuller 1992). One girl had shallow eye sockets (McGaughan 2000). She was also near sighted (myopia). Additional eye examinations showed further anomalies.

■ Low muscle tone

Some children with a 3p duplication have low muscle tone (hypotonia) (Conte 1995; Kotzot 1996; Smeets 2001; Antonini 2002; Chang 2007; Tan 2011; Natera-de Benito 2014).

■ Genital area and puberty

Minor anomalies of the genitals are common in babies with chromosome disorders, most often affecting boys.

Three boys had a small penis (micropenis) (Kuller 1992; Chen 1996; Bittel 2006). Two other boys had undescended testes (cryptorchidism) (Chen 1996; Natera-de Benito 2014). One of these boys also had hypospadias. In hypospadias the urinary opening is not located at the tip of the penis, but slightly below (Natera-de Benito 2014).

Finally, one girl had prominent labia majora and undeveloped labia minora and clitoris (McGaughan 2000).

■ Kidneys

Three children with a 3p duplication and kidney abnormalities have been described (Chen 1996; Smeets 2001; Puvabanditsin 2013). One had renal cysts. In the other two the urinary flow in the kidneys was obstructed causing enlargement (hydronephrosis) (Chen 1996; Smeets 2001).

■ Other

A number of children with a 3p duplication had respiratory tract problems including hypersensitive airways or frequent respiratory tract infections (Kotzot 1992; Chang 2007; McGaughan 2000; Smeets 2001; Tan 2011; Rodvalho 2013). Two children had regular ear infections.

One girl had a malrotation of the bowel. In a malrotation, the bowel did not twist and turn correctly during development in the abdomen. This leads to an increased chance of obstruction.

In one boy the pituitary gland did not function correctly. The pituitary gland normally produces a number of hormones that in turn influence growth and thyroid function (Kuller 1992). Another child had hypothyroidism (Chang 2007). Two children had high cholesterol levels (Kotzot 1996; Bruni 1998). One girl had multiple haemangiomas (birth marks). A boy had a café-au-lait spot (Antonini 2002).

If one person in a family with the duplication 3p is mildly affected, will others in the same family also be mildly affected?

It is difficult to answer this question as there are only a few families in which multiple family members carry the duplication (Chen 1996).

Why did it happen?

When children are conceived the genetic material is copied in the egg and sperm that make a new child. The biological copying method is not perfect and occasionally random rare changes occur in the genetic code of children that are not seen in the DNA of their parents. The term doctors use for this is de novo. This happens naturally and is not due to your lifestyle or anything you did to cause a change.