"His health is excellent, he is a very happy and balanced little boy, has a superb nature and a terrific sense of humour – a pleasure to have and the love of my life! - age 11.

"He is very dependent and needs to know he is loved. He also needs a routine and clear limits otherwise he can feel confused and uncertain and finally lose his temper - age 12.

"He is a people person who enjoys interacting. He is very sensitive to the tone of conversation around him and loves music, music and more music - age 19.

" She has a delightful manner and is very loving, gentle and kind - age 19.

Support and Information

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Tel/Fax: +44(0)1883 723356
info@rarechromo.org | www.rarechromo.org

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Diploid Triploid Mosaic Syndrome Texas Family Conference
https://www.facebook.com/groups/724989094223159

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.

This information guide is not a substitute for personal medical advice. Families should consult a medically qualified clinician in all matters relating to genetic diagnosis, management and health. Information on genetic changes is a very fast-moving field and while the information in this guide is believed to be the best available at the time of publication, some facts may later change. Unique does its best to keep abreast of changing information and to review its published guides as needed. It was compiled by Unique and reviewed by Dr Jacques Giltay, clinical geneticist, University Medical Center, Utrecht, Netherlands, and by Professor Maj Hultén BSc, PhD, MD, FRCPath, Professor of Medical Genetics, University of Warwick, UK. 2004. (PM)

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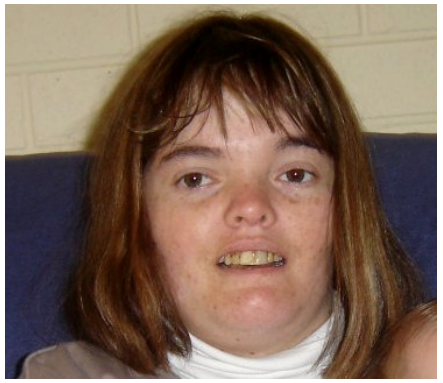
Understanding chromosome disorders Unique

Diploidy Triploidy



rarechromo.org

Sources

The information in this leaflet is drawn from the published medical literature, where by 2005 around 30 people have been described. 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. At the time of writing, *Unique* had 15 members with diploidy triploidy, the oldest in their twenties.

Diploidy triploidy

People usually have 46 chromosomes in the cells in the body. Chromosomes are the microscopically small structures in the nucleus of the body's cells that carry genetic information. In people with diploid triploid mosaicism, two populations of cells co-exist. Some cells, called **diploid**, have 46 chromosomes. Other cells, called **triploid**, have an extra set of 23 chromosomes, making 69 in all.

Other names for diploidy triploidy are diploid triploid mosaicism, 2n/3n mixoploidy or triploidy mosaicism.

Triploidy is not the same as trisomy. In trisomy there is an extra copy of just one chromosome, making a total of 47. Down's syndrome is an example of trisomy, with an extra copy of chromosome 21. In triploidy, there is an extra copy of each of the 23 chromosomes, making a total of 69. *Unique* publishes a separate leaflet on **Triploidy**.

Does it help to know the ratio of diploid to triploid cells?

The geneticist or paediatrician may tell you the proportion of diploid to triploid cells. Usually almost all or all of the cells in the blood have 46 chromosomes. In the skin a mixture of cells is more likely. However, knowing the ratio does not seem very helpful, in particular in terms of the level of any learning difficulty (van de Laar 2002; U).

What causes diploid triploid mosaicism?

There is no reason to believe that your lifestyle or anything that you did in pregnancy caused the diploidy triploidy. There is also no evidence that older mothers are more likely to have babies with diploid triploid mosaicism.

Diploid triploid mosaicism can arise in various ways, such as:

- Where the extra chromosome set comes from the father, the most likely explanation is that two sperm or a single sperm with a double set of chromosomes fertilised a single egg, creating a fertilised egg with triploidy. In the very early stages of cell division after fertilisation, a parallel cell line developed with the normal (diploid) number of chromosomes. This 'triploidy correction' may also occur when the extra chromosome set comes from the mother.
- Where the extra chromosome set comes from the mother, it is possible for a spare cell (including an extra chromosome set) that is normally discarded to be included in cells that will become the baby. This is known as second polar body incorporation.

(Niebuhr 1974; Phelan 2001; Brems 2003; Golubovsky 2003; Giurgea 2005)

Medical concerns

Breathing

Some babies will have **breathing problems** in the newborn period, and may need respiratory support. Respiratory and ear infections may also be common in early childhood (van de Laar 2002).

Seizures

Seizures are fairly common. Reports in the medical literature show that almost half of all children are affected and in many the seizures develop in babyhood or early childhood. The pattern of seizures varies from child to child and in many children, seizure activity is completely controlled with medication.

The experience of *Unique* members echoes the information from the medical literature. Seven out of 15 members have diagnosed epilepsy and in another, abnormal brainwave patterns were detected at three months. In some children the seizures were very infrequent. Children exhibited a variety of types of seizure activity.

Parents have noticed an effect of untreated seizures on their child's ability to learn. In one child, short term memory was affected. Seizure control improved the learning capacity of a four-year-old (Tharapel 1983; van de Laar 2002; U).

Early puberty

The medical literature shows that around half of all girls with diploid triploid mosaicism start puberty very early. One baby born with severe hypothyroidism developed precocious puberty (bleeding, enlarged breasts, but no pubic hair) at the age of 5 months, another at 6 months, another at 11 months. Precocious puberty also affected one *Unique* member who went into puberty at the age of 4. A boy started showing signs of puberty at nine.

By contrast, a 15-year-old passed through puberty at 11 without any problems; a boy developed first signs of puberty (mild acne, pubic hair growth) at 12 and a 21-year-old girl developed normal, age appropriate secondary sexual characteristics (Fryns 1980; Jarvela 1993; Mueller 1993; van de Laar 2002; U).

> *"She began puberty at 11, did not alter in any way and remained a pleasant, sociable and loving little girl.*
>
> *"Behaviour wise, he has become a little moody and bad tempered in the last 12 months - age 11.*

Behaviour

Children with diploid triploid mosaicism generally appear to have a calm and loving disposition. One mention in the medical literature notes that the child has good social contact and plays well alone. *Unique* members said that their children were placid and contented, enjoying playing on the computer and listening to music. One child was described as 'very loving and affectionate' and sociability appeared to be a strength in the group as a whole. Puberty may naturally bring mood changes as with any adolescent and knowing that they are different can cause some children real frustration (van de Laar 2002; U).

Families say …

“ *His best mobility is in water where he confidently bobs around, stands up and lies on his back with the aid of arm bands. Now he is quite some size, he finds it harder to bum shuffle and roll* – age 11.

“ *She does not like walking or taking part in any physical exercise. She can walk short distances for a reward, such as food. Her mobility is governed by her weight and bulk* – age 15.

Sitting, moving, walking

In general, babies are delayed in reaching their mobility milestones but there is a great discrepancy between individuals. Reports in the medical literature reveal fast developers sitting at 6 to 10 months, standing at 10 to 15 months and walking at 19 to 22 months. A slow developer by contrast sat at 16 months and stood with support at 4 years. A number of children never walked independently.

Among *Unique* members, there is a similar discrepancy. Rolling may occur at 5 months or not until two years; sitting between 7 months and 3 years; crawling between 13 months and 2 years or not at all; and walking between 19 months and four years. The pattern appears to be predicted by the earliest movements: babies who rolled early were the most likely to stand and walk early. Late rollers and sitters may always rely on a wheelchair for mobility.

One of the underlying causes of a child’s delayed physical development is **low muscle tone** (hypotonia) which makes movements floppy. Hypotonia generally improves with age and activity and in some children may disappear altogether. However in diploid triploid mosaicism this seems to be uncommon.

Regular physiotherapy (physical therapy) is important in the management of hypotonia. To illustrate this, one *Unique* member who received regular therapy outgrew the hypotonia that affected her as a baby, so that by the age of four she could jump and dance but not yet hop or ride a tricycle. A 12-year-old boy was fully mobile and could walk reasonable distances at his own pace. The limiting factor, apart from hypotonia, was his very small feet that quickly became painful when walking. An 11-year-old was unable to weight bear or crawl, hampered chiefly by his continuing hypotonia and his very small lower legs and feet.

Scoliosis (spinal curvature) may be marked. Two *Unique* members had strengthening rods successfully inserted into the spine (Fryns 1980; U).

The **small**, relatively weak **hands and feet** that some children with diploid triploid mosaicism have as well as their relatively slender arms and legs with low muscle bulk may affect their ability both to hold their weight and to acquire fine motor skills and they benefit from occupational therapy. By mid-childhood or adolescence, children may also need orthotic support or adapted shoes to help their feet bear their weight.

Lifespan

Generally, babies do not appear to have the severe heart, kidney or brain problems that are typical of triploidy. The oldest people known to *Unique* and described in the medical literature are in their twenties but there may well be older people who have not been diagnosed (Fryns 1980; U).

Pregnancy

In general pregnancy appears to run uneventfully. The mid pregnancy anomaly scan may reveal that the baby is growing slowly (intrauterine growth retardation - IUGR affects three babies in four) and the baby may not kick or move much (van de Laar 2002; U).

Feeding

“ *He would eat without stopping if you let him.*

Feeding difficulties seem to be common in the newborn period and may continue into early childhood. Research reports show that feeding difficulties affected four out of 14 newborn babies. In at least two children these were severe enough for a gastrostomy tube to be placed to allow direct feeding into the stomach. Both children had severe gastro oesophageal reflux (feeds and stomach contents return up the food pipe and may be vomited or inhaled, causing aspiration pneumonia). Among *Unique* members, feeding problems do not figure prominently. Four mention no problems at all, one baby had fluctuating gastro oesophageal reflux and a third had oesophageal lag, so that food had to be pre-cut into bite-sized portions and washed down with drinks between mouthfuls. A problem identified in one *Unique* adult is an ‘insatiable appetite’ (van de Laar 2002; U).

Growth

Typically, babies are born **small** for dates. Many babies weigh less then 2000g (4lb 7oz) at birth, but a few are average size and weight. Typically in childhood, growth is slow and bone age is delayed. To treat short stature, some children have been prescribed growth hormone. However, the effects in diploidy triploidy have not been fully evaluated and it has been reported to trigger the onset of overweight around the waist and middle body. Among *Unique*’s membership, growth is affected, with individuals reaching 4’ 8” (145cm) by 19 years, four feet (122cm) by 15 years, 5’ (150cm) by 12 years and 4’ 6” (137cm) by 11 years (Tharapel 1983; Pettenati 1986; Carukashansky 1994; van de Laar 2002; U).

Appearance

The child’s face or body may be **asymmetrical**. This may be immediately obvious or so subtle that only a doctor looking for particular features would notice it. It may become less apparent as the baby grows, but in some older children it persists. In some children one leg is shorter than the other.

Typically, children develop **truncal obesity** during early childhood and this may be especially apparent by contrast with the child’s slim arms and legs. Overweight is typically carried around the chest and abdomen, waist, bottom and the top of the thighs. *Unique* members suggest that the onset of obesity is around age 4 - 6.

Between one third and one half of children develop **streaks or patches of irregular skin colour**, a feature typical of chromosomal mosaicism. However, some babies are born without skin discoloration and never develop it. *Unique* members have noted that it may become more obvious in summer and can fade with age (Donnai 1988; Flannery 1990; Wulfsberg 1991; U).

Doctors may look for **facial features** that might suggest a chromosome syndrome, but in diploid triploid mosaicism these are usually subtle. Typical facial features may include a small chin and lower jaw, unusually shaped ears that are set below the line of the eyes, a flat, broad nasal bridge and a prominent forehead. One *Unique* member noted abnormal tooth development.

A wide variety of unusual features affecting the **hands and feet** are typical. They are usually small and this becomes increasingly apparent when weight gain accelerates during childhood as the small feet contribute to mobility problems. Small, slender hands, joined or webbed fingers (especially the third and fourth fingers) and/or toes and incurved little fingers affect more than half of children. Many also have a single unbroken crease on the palm of at least one hand. A large 'sandal gap' between the big toe and the second toe and a short big toe have also been found in many children. Other features include unusually short or unusually long fingers, toes that may be irregularly placed and talipes (club foot) (van de Laar 2002; U).

Among boys, it is common for the **penis** to be small and the testicles not to be descended at birth. One *Unique* member noticed that her son had slight hypospadias, where the hole is on the underside of the penis instead of at the end. The genital area in girls is usually normal (Graham 1981; Tharapel 1983; U).

Older people with diploidy triploidy

There is one report in the medical literature of a woman in her twenties. *Unique* has three members in their twenties. The evidence suggests that mobility becomes an increasing problem with the onset of overweight, combined with small lower limbs and muscle wastage. A brief survey in 2005 showed that among four *Unique* members aged 11 and over, 1/3 had osteoporosis (diagnosed at age 19), 3/3 spinal curvature, 1/2 muscle wastage secondary to low muscle tone (hypotonia), 0/2 had a thyroid disorder, 1/3 had diabetes, 4/4 were overweight, 0/4 had behaviour problems and 0/4 had mental health problems. The variation in development makes it difficult to predict in babyhood or even early childhood what level of independence an individual will reach. Watching a child develop will give the clearest indication. Among *Unique* members the picture is varied. Some children acquired basic skills like toilet training at or near the normal age. Others required intensive personal support even as adults (Fryns 1980; U).

Learning

Some degree of learning difficulty is usual but the degree is extremely variable and not related to the proportion of triploid cells in a blood or skin sample. One child apparently had no intellectual or developmental delay in his first year of life. Another girl had borderline learning difficulties at the age of nine. In other children the degree of delay varied from severe to mild.

Any impairment of vision or hearing will impact directly on a child's ability to learn. Two *Unique* members have a hearing loss.

Observations of *Unique* members show the variation:

❝ *She has some developmental delay, especially in speech. Her fine motor skills are slightly delayed, her gross motor skills more so, while daily living and socialisation skills are average for her age* – age 3.

❝ *At 4, he could count to three, he knew the signs for many colours and could match but not identify a colour. Within a year his learning ability was greatly increased by seizure control. He could now count to 5 alone and to 10 with help, he could identify numbers 1 and 2 and identifies three colours* – age 5.

❝ *He is very aware, bright and able in lots of areas and a little wizard on the computer. He has a great memory* – age 11.

❝ *He grasps simple concepts easily but needs longer and more repetition than other children. He learns much better when it's fun. We are proud of his relatively good reading and practise every day* – age 12.

❝ *She works well in a 1:1 situation, loves drawing, painting, jigsaws, dancing and music* – age 15.

❝ *He has severe and profound delay and an IQ of 18. But he is continually learning new things. It is subtle but awesome. At age 19, his cognitive ability was assessed at 21 months. He can identify pictures, match colours, sort similar items, take clean clothes out of the dryer and put away cans in a low cupboard.*

Speech and communication

The medical literature suggests that speech delay is typical and is likely to reflect a child's general learning ability. This was echoed among *Unique* members. A few children started to use single words in their second year and while most relied on single words, there was one report of a child acquiring a 100-word vocabulary. This child started to use full sentences at the age of four. There were one or two reports of understanding outstripping the child's expressive ability. All children who were taught to sign found it a useful adjunct to speech.

❝ *His speech is very unclear unless you are familiar with him. Speech therapy really helps* – age 12.

❝ *David babbles like a 14-month-old. He understands about 50 signs and can sign about 20 words, mostly about his needs* – age 20.