Understanding chromosome disorders

Unique

Diploid Triploid Mosaicism

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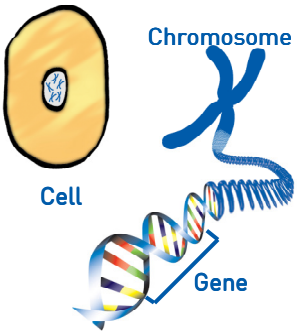
Diploid triploid mosaicism

Chromosomes, genes and diploid triploid mosaicism



Chromosomes, made up mostly of DNA, are the structures in the nucleus of the body's cells that carry the genes that tell the body how to develop, grow and function. Chromosomes usually come in pairs, one chromosome from each parent. There are usually 46 chromosomes per cell, including a pair of sex chromosomes, XX (two X chromosomes) in females and XY (one X chromosome and one Y chromosome) in males.

In people with diploid triploid mosaicism, two different populations of cells co-exist. Some cells, called diploid, have the expected number of 46 chromosomes. Other cells, called triploid, have an extra set of 23 chromosomes, making 69 in all. The extra set of 23 chromosomes can come either from the father or from the mother.

In pure triploidy, there is an extra copy of each of the 23 chromosomes in all cells. This is a more severe condition than diploid triploid mosaicism and babies with pure triploidy are not usually able to survive beyond the newborn period. Unique publishes a separate guide to Triploidy.

Triploidy is not the same as trisomy. In trisomy there is an extra copy of just one chromosome, making a total of 47. Down syndrome is an example of trisomy, with an extra copy of chromosome 21.

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

What causes diploid triploid mosaicism?

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

Diploid triploid mosaicism can arise in different ways:

- 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' also occurs when the extra chromosome set comes from the mother.
- Where the extra chromosome set comes from the mother, it is possible that a spare cell, a so-called 'polar body' (which includes an extra chromosome set and is produced in the ovaries at the same time as the egg cell but is normally discarded), is included in the cells that will become the baby. This is known as

second polar body incorporation and is the most frequently reported cause of diploid triploid mosaicism (Niebuhr 1974; Phelan 2001; Brems 2003; Flori 2003; Golubovsky 2003; Giurgea 2005; Rittinger 2008).

- Another possibility is that a normal fertilised egg with 46 chromosomes fuses with a fertilised egg with 69 chromosomes to form a diploid triploid embryo (Daniel 2001; Quigley 2005; Rittinger 2008).

A case of diploid triploid mosaicism has been reported in a girl who was conceived following *in vitro* fertilisation (IVF) with an intracytoplasmic sperm injection (ICSI) procedure. Unlike standard IVF, where an egg is mixed with many sperm, ICSI involves a single sperm being injected directly into an egg which is later transferred into the uterus (womb) of the mother. In this case, more than one sperm or a diploid sperm cell was injected into the egg during the ICSI part of the procedure (Oktem 2007).

Sources & references

The information in this guide is drawn from the published medical literature where around 45 people with diploid triploid mosaicism have been reported. 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 [http://www.ncbi.nlm.nih.gov/pubmed]. The guide also draws on Unique's database. At the time of writing, Unique had 36 members with diploid triploid mosaicism, men and women, the oldest in their forties.

(Böök 1960; Ellis 1963; Ferrier 1964; Lejeune 1967; Sacrez 1967; Van den Berghe 1970; Jenkins 1971; Niebuhr 1974; David 1975; Dewald 1975; Fulton 1977; Fryns 1980; Graham 1981; Tharapel 1983; Tantravahi 1986; Pettenati 1986; Meinecke 1986; Bendon 1988; Donnai 1988; Wulfsberg 1991; Daubeney 1993; Järvelä 1993; Müller 1993; Carakushansky 1994; Lin 1998; Daniel 2001; Phelan 2001; van de Laar 2002; Brems 2003; Flori 2003; Golubovsky 2003; Vatish 2004; Wright 2004; Giurgea 2005; Quigley 2005; Oktem 2007; Shafi 2007; Rittinger 2008; Ludwig 2009; Boonen 2011; Jewell 2014; Natera-de Benito 2014; Lalani 2015)

Diagnosis

Diagnosis almost always follows a period of knowing that something is wrong, but not knowing why. In pregnancy the most common concern is slow growth, but occasionally amounts of amniotic fluid are too low or too high, and anomalies have been found on early and mid-pregnancy scans.

Many babies are small for dates at birth or they may be unwell, or have obvious hand, foot or in some cases genital anomalies. Among children, the most common concerns are around growth and development, and around puberty for some adolescents. Other more common diagnoses are often considered first, particularly Silver-Russell syndrome in babies who are very small; Prader-Willi syndrome after the onset of truncal obesity (see **Overweight**, pages 10-11); and diabetes (see **Low blood sugar levels, diabetes & insulin resistance**, page 16). Less common diagnoses considered first include Klinefelter syndrome; maternal uniparental disomy 14; and Freeman-Sheldon syndrome.

It is rare for people to be diagnosed as adults, partly because there is little formal information on how diploid triploid mosaicism affects older people (see **Older people**, pages 25-27) (Graham 1981; Meinecke 1986; Flori 2003; Rittinger 2008; Boonen 2011; Jewell 2014; Unique).

Testing for diploid triploid mosaicism is not straightforward, because triploid cell lines are found in different tissues. This tissue-restriction differs from person to person and cells with 69 chromosomes may only be present in relatively inaccessible internal organs. Blood samples and cord blood often show only typical diploid cells with 46 chromosomes, and this can also be true for amniotic fluid. In the skin or inside the cheek (a buccal smear) a mixture with a triploid cell population with 69 chromosomes is much more likely, and some researchers have suggested also testing urine. Skin samples are usually taken from the arms, legs, abdomen, back or groin, and from normal skin or from any lighter or darker patches or streaks. Samples from internal organs such as bone marrow or the reproductive system are usually taken during a surgical intervention (Tharapel 1983; Hsu 1984; Carakushansky 1994; Flori 2003; Wright 2004; Giurgea 2006; Rittinger 2008; Boonen 2011).

Genetic imprinting disorders

An important group of disorders where symptoms overlap with diploid triploid mosaicism are called **genetic imprinting disorders**. These include Silver-Russell syndrome, Prader-Willi syndrome, Beckwith-Wiedemann syndrome and uniparental disomy 14.

In a typical person with 23 pairs of chromosomes, one chromosome in each pair is inherited from the father and the other from the mother. For most genes, it does not matter which parent the copy of a chromosome has come from, as both copies of the genes are expressed during development. However, for a small number of so-called **imprinted genes** either the copy of the gene inherited from the mother or the copy of the gene inherited from the father is turned off so only

one copy is expressed. This is essential for normal development. If genes expressed in the normal way are over-expressed because there is an additional copy of the chromosome in triploid cells, or if imprinted genes in the triploid cells are expressed incorrectly, this can result in a variety of symptoms. Symptoms overlapping with genetic imprinting disorders have been reported in several people with diploid triploid mosaicism (van de Laar 2002; Giurgea 2005; Boonen 2011; Rittinger 2008; Unique).

> “ You may notice that she has speech difficulties and some physical challenges. You will also notice that she has a tremendous enthusiasm for life and a great spirit that captivates everyone.”

Genetic Report

Your geneticist, genetic counsellor or paediatrician will be able to tell you about the results of your child’s genetic test. With diploid triploid mosaicism, the results (the karyotype) are likely to read something like the following examples:

69,XXX/46,XX This is a girl or a woman. The triploid cell line with the 23 extra chromosomes is stated first. In these cells there are 69 chromosomes, including an extra X chromosome. The / symbol means that there is more than one cell line – mosaicism. 46,XX is the chromosome count of the normal diploid cells, including 2 X chromosomes.

69,XXY/46,XY This is most likely to be a boy or man. The triploid cell line with the 23 extra chromosomes is stated first. In these cells there are 69 chromosomes, including two X chromosomes and a Y chromosome which confers maleness. The / symbol means that there is more than one cell line – mosaicism. 46,XY is the chromosome count of the normal diploid cells, with one X and one Y chromosome.

69,XXY/46,XX The baby may appear male, female or the sex may be unclear at birth. The triploid cell line with the 23 extra chromosomes is stated first. In these cells there are 69 chromosomes, including two X chromosomes and a Y chromosome which typically confers maleness. The / symbol means that there is more than one cell line – mosaicism. 46,XX is the chromosome count of the normal diploid cells, including two X chromosomes, typical for a female.
See also **Genital anomalies**, pages 13-14.

Sometimes the results are written the other way round, but it makes no difference. For example 46,XX /69,XXY is just the same as 69,XXY/46,XX . Sometimes the ratio of triploid to diploid cells is shown in numbers in square brackets, like this example:

69,XXX[21]/46,XX[9]. This means that 30 cells were tested and 21 showed the triploid 69,XXX while 9 showed a diploid 46,XX. Although you may be given this information, it is not helpful in predicting how severely a person will be affected, in particular in terms of the degree of any developmental delay or learning difficulty (van de Laar 2002; Oktem 2007; Unique).

Most likely features of people with diploid triploid mosaicism

These are:

- Growth delay before and after birth
- Delay in development
- Learning difficulties: some degree of learning support is usually needed but the amount is extremely variable
- Low muscle tone, making the body feel floppy (hypotonia)
- Asymmetrical body and/or face. The asymmetry may be very subtle
- Unusual features of the hands and feet often including webbed (syndactyly) or bent (camptodactyly) fingers or toes
- Truncal obesity: in children and adults it is common for fat to be stored around the abdomen. Arms and legs may be comparatively thin
- Typical facial features can include a small chin or lower jaw, a broad, prominent forehead, a small mouth and low set ears
- Boys may have small or ambiguous genitals depending on the sex chromosomes in the diploid and triploid cell lines. Very occasionally the genital area in girls is also affected
- Patches or streaks of darker or lighter skin

(Tharapel 1983; Carakushansky 1994; van de Laar 2002; Quigley 2005; Shafi 2007; Rittinger 2008; Boonen 2011; Jewell 2014; Rucker 2015; Unique)
These features are explained in more detail in later sections.

Pregnancy and birth

In general pregnancy appears to run uneventfully. Occasionally a blood test may suggest a concern about the baby or much more commonly a scan may show that the baby is growing slowly (intrauterine growth retardation – IUGR affects three babies in four with diploid triploid mosaicism). The baby may not kick or move as much as expected. Both too little and too much amniotic fluid have been reported, but this is not common. If concerns have been raised about the baby, an amniocentesis to examine cells shed by the baby in the amniotic fluid may be offered, and this may give the diagnosis, but because of the mosaicism results can also be normal. Once IUGR has been detected, the pregnancy will be closely monitored, and the safest way of giving birth planned. Birth may be induced or a Caesarean section planned, in some cases before term.

Preterm birth is common, with 10/24 babies in the medical literature born before 37 weeks, the earliest at 26 weeks of pregnancy. Delivery can be easy because of the baby's small size, and many babies have reasonable or high Apgar scores (a measure of the baby's condition at birth on a scale of 0-10). However, after birth some babies have breathing difficulties and need resuscitation. Admission to special care is common, usually because of the baby's size and initial feeding difficulties. Important health issues needing early surgery have been seen in a small minority, including a blocked bowel; a malformed trachea (windpipe); and a collapsed lung (Tharapel 1983; Pettenati

1986; Donnai 1988; Wulfsberg 1991; Järvelä 1993; Müller 1993; Carucashansky 1994; van de Laar 2002; Flori 2003; Vatish 2004; Wright 2004; Giurgea 2005; Oktem 2007; Jewell 2014; Lalani 2015; Unique).

“ Everything was normal in pregnancy. I knew the minute she was born she was different. Knew this was a forever child.**”**

Feeding

Some new babies feed well, usually in small or very small amounts, and often slowly. However, many have difficulty feeding. They frequently have low muscle tone around the mouth and throat which makes effective sucking both difficult and tiring. Their mouths may be too small to latch on properly to the breast. The throat may be soft and liable to collapse inwards, making it hard to breathe and feed at the same time. They may lack the coordination needed to breathe and suck simultaneously. One mother manipulated her baby’s jaw and chin for six months to teach him to suck. Babies who overcome these challenges may still not be strong enough to meet their own nutritional needs, attracting the diagnosis of ‘failure to thrive’.

Babies who are not thriving can be given a high energy formula to take alongside breast milk or instead of regular formula. If they are able to suck, they can take feeds from an adapted or standard baby bottle. Otherwise, feeds can be given through a soft plastic nasogastric (NG) tube passed up the nose and down to the stomach. The tube can stay in place for as long as the baby needs it – just a few days or a year or two.

A few babies – just 3/36 reported at Unique and 3/36 in the medical literature - bring their feeds back frequently and forcefully (gastrooesophageal reflux), and need careful positioning, and possibly medication or even surgery to help the feeds stay down. In a small number of babies these measures are not enough for them to put on weight and grow, and they are fed through a tube direct into the stomach (gastrostomy, G-tube, button). How long they need the gastrostomy varies a lot, but feeding problems do get better.

For some children the turning point comes with solids. In others the change is more gradual as they get stronger, their low muscle tone improves and their stomach grows. Solid food may

need to be mashed or chopped for much longer than for a typically developing child, and even adapted cutlery can be hard for a child with very tiny hands to hold. The good news is that the great majority of older children and adults are good, healthy eaters. Some develop an insatiable appetite, and this occurs at the same time as they accumulate fat around their waist and buttocks (see **Overweight**, pages 10-11) (Järvelä 1993; Carakushansky 1994; van de Laar 2002; Jewell 2014; Lalani 2015; Unique).

“ While she was slow to put on weight as a baby, by 8 she was eating too well, so food has to be locked away.”

“ She only gained weight slowly for the first few months, only ever drinking the exact amount for her weight. As soon as she started on solids she really started gaining weight, and at 10 years she still eats very well today.”

“ She fed well in spite of her oral motor hypotonia. At 17 years, she eats very well! She loves food and tries everything. We actually watch what she eats so that she does not gain too much weight, as she loves to eat and tends to gain weight very easily around the stomach and buttocks area. She can feed herself, but can have trouble cutting certain food items.”

Growth

Usually, babies with diploid triploid mosaicism are born small and light for dates. An average typical baby is 51cm (20”) long at birth, while the average baby with diploid triploid mosaicism is 45cm (18”). Family inheritance also plays a role however, and some babies are born a normal length.

The range of normal birth weights in babies without chromosome anomalies is 2.5 kg (5lb 8oz) to 5 kg (11lb). Average birth weight in babies without a chromosome anomaly is 3.4 kg (7lb 8oz). The average birth weight of a baby with diploid triploid mosaicism is 2.15 kg (4lb 12oz)– that is, 1.25kg (2lb 12oz) less.

The known and reported range of weights at birth at term for babies with diploid triploid mosaicism is from 1.27kg (2lb 13oz) to 3.37kg (7lb 7oz).

Usually, growth remains slow and children are short. This is not, however, true for all. Some children are average height, and one or two are tall for their age.

To treat short stature, three children are known to have been prescribed growth hormone. Individual families found it helpful both in terms gaining extra height and improving muscle tone, but the effects in diploid triploid mosaicism have not been fully evaluated. One adult woman with a delayed bone age who took growth hormone as a child from the age of 6 achieved an adult height of just 145.3 cm (4 9”).

Final adult heights known to Unique and reported in the medical literature range from 145cm (4’ 9”) to 173cm (5’ 8”) for women. The height of two men is 134.6cm (4’ 5”) and 165cm (5’ 5”).

Children taking growth hormone should have their spines checked regularly during treatment to ensure that any spinal curvature is not progressing (Fryns 1980; Boonen 2011; Jewell 2014; Unique).

❝ Extraordinary with her reliance, strength, determination, and infectious laugh and personality. She reminds us, and hopefully those she meets, that life is fragile, precious and full of opportunities and moments of unexpected gratitude for our challenges.❞ 10 years

❝ At 10 years, she is 4' 9"(145cm). She has been on growth hormone for 6 years. We believe it was helpful with both growth and muscle tone. Her body was/is actually making enough growth hormone, but it was not being used effectively.❞
❝ She was born with very low weight, but has always been a good eater, so she gained weight and height quickly. At 17 years, she is tall - 5' 4" (162.5cm). ❞
❝ He is 31, and top heavy due to his large trunk, a 6' 2" (188cm) upper body squashed into a 4'5" (134.6cm) frame. ❞

Appearance

Facial features


30 years

Doctors may look for facial features that might suggest a chromosome syndrome, but in diploid triploid mosaicism these are usually subtle, and in some ways children resemble other members of their family. Every child is different, but typical facial features can include a slight asymmetry, a prominent forehead, a short, upturned nose with a broad, flat bridge, a small mouth, perhaps with downturned corners, a small chin and lower jaw, and unusually shaped ears that are set below the line of the eyes. The feature that parents comment on most often at birth is the small chin that can give the baby a pixie-like appearance.

Children are mostly unaffected by their facial features, but the small mouth and lower jaw can make feeding difficult in tiny babies (see **Feeding**, pages 7-8). One Unique member also noted that her son's short neck makes anaesthesia difficult when he needs dental surgery. In two Unique children the bone plates of the skull fused too early, not allowing enough room for the brain to grow, and they needed surgery to reshape the skull. An adult member has hair growth on her face and shoulders, needing monthly waxing.
❝ Having his teeth out can be difficult as his neck is so short that it is very hard to get a clear airway.❞

Asymmetry

The face, body or both are often asymmetrical. This can 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 most it persists and can increase. The hips can be misaligned and one arm, leg or both can be slightly

shorter than the other, but the difference is usually no more than a centimetre or two even in adults and does not normally affect hand or arm use. If needed, an insole or built up footwear can be provided for the shorter leg, and shoes of different sizes may also be needed. When the discrepancy is troublesome, leg length can be evened out surgically. Asymmetry of the trunk and legs can lead to a Curved spine (see page 14) (Jewell 2014; Unique).

" One side of her face seems more developed than the other."

" The asymmetry is clear when you look at him in the mirror."

Streaks or patches of irregular skin colour

Between one third and one half of children develop streaks, whorls or patches of irregular skin colour, a feature typical of chromosomal mosaicism. The darker or lighter skin patches often follow the Blaschko lines – the lines along which skin cells move while the embryo is developing. We all have these lines but they are usually invisible. In children with diploid triploid mosaicism, the darker or lighter skin can be visible at birth, or only years later, although some babies are born without skin discoloration and never develop it. The darker/ lighter skin can develop anywhere on the body – the chest, back, buttocks, arms and legs and even the teeth - but it seems to be rarely seen on the face. It can be more obvious in the summer, and can fade or become clearer with age. To protect the skin from sunlight, a high factor sun block is recommended (van de Laar 2002; Flori 2003; Rittinger 2008; Ludwig 2009; Boonen 2011; Jewell 2014; Natera-De Benito 2014; Unique).

" A gentle nature."
25 years

Very overweight, particularly around the waist and buttocks

Babies and children most typically grow and put on weight slowly (see **Growth**, pages 8-9). But at some point they start to put on weight in a characteristic pattern around their belly, torso, chest, abdomen, waist, bottom and the tops of their thighs (truncal obesity). Just when truncal obesity becomes obvious is variable: it was first noted at the age of 11 months in one baby and at 18 months in another, but not until 11 years in another child. Most typically, it is obvious from around 5 or 6 years, and may be accompanied by being generally overweight, or be specific to the waist and buttocks area. In some children the weight gain is very sudden and can go hand in hand with a ferocious appetite (food has to be locked away) that is reminiscent of children with Prader-Willi syndrome, but this is not always so. Weight gain can also be exacerbated by medication for some conditions, particularly epilepsy. It may be especially obvious in a short child or adult with slim forearms and lower legs.

Families need expert guidance and realistic expectations to achieve the best weight control in a difficult situation.

Unique families ensure their child follows a well balanced low fat, low calorie diet, without snacks, limited sugar and with lots of fruit and vegetables. An active day programme is important, especially for children who tire quickly and

for adults who can otherwise gain so much weight that standing for long periods is painful and walking is difficult.

The scale of the problem is clear if the Body Mass Index [BMI] of adults is calculated. For seven adults, it ranges between 29 and 52, with one adult classified as overweight, one as obese, three as severely obese and two as very severely obese. Although interpreting BMI in the context of diploid triploid mosaicism is not straightforward, these levels do put individuals at a worryingly high risk of ill health (Donnai 1998; Flori 2003; Rittinger 2008; Boonen 2011; Jewell 2014; Unique).

“ Truncal obesity, along with a desire to always be eating and easy fatigue has been difficult to control. We keep a very healthy diet and limit sugar.” 10 years

“ She is very short and obese despite having a very good diet.” 20 years

“ Weight is a huge problem. Obesity makes walking difficult at times and she sometimes has to use a wheelchair. She can walk but not far. I worry about her as she has a lot of pain.” 26 years

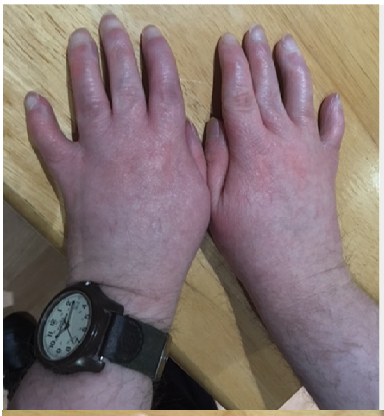
“ He has an insatiable appetite and will try to eat everything. He is completely obsessed with food and this is the main reason for his behavioural issues. We have put a lock on the kitchen door. ” 31 years

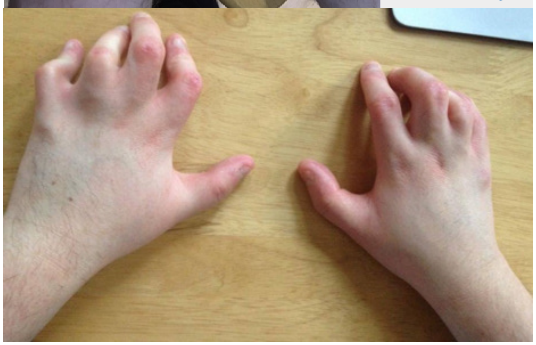
“ She would eat until she got sick if you let her.” 42 years

Hands

Most babies are born with something unusual about their hands. These features can vary a lot from child to child, and can affect one hand or both. Sometimes they only affect appearance (such as a single unbroken crease across the palm), and sometimes they affect function (such as fused fingers). Many children have had surgery to improve the function of their hands, some successfully, others not. The hand features seen in diploid triploid mosaicism include:

- Small hands. One adult has ‘hands the size of a 2 year old child’. The hands may be so tiny and the fingers so short that children need to use baby cutlery.
- Hands may also be slender. Very occasionally, the hands are long.
- Fingers may be joined with skin





Two men’s hands. Left, toddler size. Below, several surgeries around 11 years to release the skin gave no more flexibility.

or tissue (syndactyly). The middle and ring (3rd and 4th) fingers are most often joined, but webbing or fusion can affect all four fingers. Rarely, even the nails are fused. The entire length of the fingers may be joined, or webbing may only be partial. If the webbing or fusion is affecting the child's functioning, the fingers can be separated and if necessary straightened surgically. Success rates vary.

- Fingers may curve inwards in a fixed position (clinodactyly). The little (5th) finger is most often affected, but any of the other fingers may also curve inwards. One or more fingers may also be bent in a cup-like position which can become more marked with age (camptodactyly). Surgical straightening is usually possible, and carried out when fused fingers are released, but success rates vary.
- One or more fingers may overlap the others. Occasionally the fingers are unusually long and thin (arachnodactyly).
- Single unbroken crease on the palm of the hand.

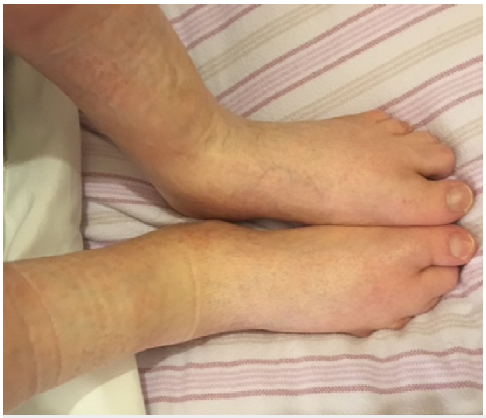
Less common features are effaced finger creases; absent knuckle joints; very small thumbs; an extra joint in the thumbs; and thick fingertips.
(Fryns 1980; Graham 1981; Tharapel 1983; Meinecke 1986; Donnai 1988; Wulfsberg 1991; Järvelä 1993; Müller 1993; Carakushansky 1994; Lin 1998; van de Laar 2002; Flori 2003; Oktem 2007; Shafi 2007; Rittinger 2008; Boonen 2011; Jewell 2014; Natera-DeBenito 2014; Lalani 2015; Unique)

"Her hands are small and her curved little fingers affect the strength and function of her hands. An operation to correct the curved little fingers was unsuccessful." 8 years

"He underwent several surgeries to his hands at about 11 to release skin and try to obtain more flexibility but it really didn't give him any more movement." 31 years

"The third and fourth fingers on her right hand are fully webbed and those of her left hand partially webbed, but this does not cause problems. The webbing on her hands was separated surgically when she was 18 months old but by nearly 10 years she had a lot of scar tissue so her fingers were not flexible. Her fused fingers were surgically separated when she was 6 years old." 30 years

"She has very small hands, and her fingers are all bent. She uses her hands OK for their small size, although she is not all that coordinated, but she can do jigsaw puzzles. She often picks up a single hair and fools with it. We had the fingers on her left hand straightened years ago but it did not make enough difference to do her right hand." 42 years



An adult's small, short feet

Feet

Most typically, babies, children and adults with diploid triploid mosaicism have very small, short feet. One Unique adult man wears size 2 shoes (US 2/3; European 33; Australian 2). There is a suggestion from Unique that feet may stop growing earlier than in other children. The feet may not be the same size, and older children may need a shoe one size larger for their bigger foot. Tiny feet present a problem to adults who are overweight, making walking difficult or impossible.

The toes on one or both feet are also quite commonly joined with skin or tissue (syndactyly). The 2nd and 3rd toes are the most commonly joined, and sometimes the 4th toe as well. There is not usually any need to separate the toes.

Less common features are a twisted position of the whole foot, part of it, or of individual toes; talipes (club foot) usually needing straightening; a relatively short big toe; a large 'sandal gap' between the big and second toes; rocker bottom feet where the sole of the foot is curved like the rocker on a rocking chair; an excessively high arch (pes cavus); irregular positioning of the toes; very small toes and/ or nails; and bent toes. Surgical correction is not usually needed, but features like a hammer toe can be corrected so that normal shoes can be worn.

Differences in leg length (see Asymmetry, pages 9-10) mean that some people need to wear shoe inserts, and others need special support footwear or splints to steady their ankles and feet while walking.

(David 1975; Dewald 1975; Fryns 1980; Graham 1981; Tharapel 1983; Meinecke 1986; Donnai 1988; Wulfsberg 1991; Järvelä 1993; Müller 1993; Carakushansky 1994; Lin 1998; van de Laar 2002; Flori 2003; Oktem 2007; Shafi 2007; Rittinger 2008; Boonen 2011; Jewell 2014; Lalani 2015; Unique).

Genital anomalies

See also **Genetic Report** (page 5).

Baby girls with diploid triploid mosaicism are typically born with normal internal and external reproductive systems. This is because in the great majority of cases they only have X sex chromosomes. Their karyotype is most often

69,XXX/46,XX and so they have female characteristics and the genital area is usually normal. Minor differences in the genital area have been occasionally noted, and in one girl no ovaries were found on ultrasound scan (Pettenati 1986; Järvelä 1993; Carakushansky 1994; van de Laar 2002; Lalani 2015; Unique).

Very occasionally, a baby who appears female at birth turns out to have a Y chromosome in one or both cell lines. There is one report of a girl with normal external genitalia and a small uterus (womb) with 69,XXY/46,XY chromosomes (Sacrez 1967). There is another report of a child with a fully female reproductive system with a 69,XXY/46,XX karyotype. This occurred despite the Y chromosome being expressed in the reproductive organs (Oktem 2007).

Babies with a 69,XXY/46,XY karyotype, giving them a Y chromosome in both cell lines, are most typically male, with small genitals (but see above, Sacrez 1967). In one adult man, the genitals were described as 'the size of a toddler's'. The penis is frequently small with the urethral opening which normally opens at the end of the penis being on the underside instead (hypospadias) or even buried in the folds of the scrotum (the sac behind the penis). The scrotum may be divided (bifid). The testes may not be descended into the scrotum at birth. The anomalies may need no treatment, or they may be corrected with surgery, and undescended testes brought down and anchored in the scrotum (Böök 1960; Ferrier 1964; Sacrez 1967; Tharapel 1983; van de Laar 2002; Unique).

Occasionally the baby's sex may not be clear at birth. This is most common where the chromosomes show a 69,XXY/46,XX karyotype. In this situation a decision needs to be made whether to bring up the baby as a boy or girl. The decision rests on the results of hormone tests and tests on the tissue that the gonads are made of, as well as discussions between doctors and parents, and with people in appropriate support groups (Lejeune 1967; David 1975; Dewald 1975; Tantravahi 1986; Unique).

The gonads (ovaries or testes) are sometimes removed (gonadectomy) because the Y chromosome in 69,XXY/46,XX raises the risk of developing a tumour (gonadoblastoma) in one or both of the gonads.

> "An engaging and charming young lady. She is a delight to talk to and makes friends easily in new circumstances. I'm proud to be her mom."
>
> 10 years

Medical concerns

Curved spine

A curved spine is common in diploid triploid mosaicism. The curve is usually S-shaped (scoliosis), but it can be forwards hunching (kyphosis) or backwards (lordosis). Low muscle tone and body asymmetry both play a role in the development and progression of the curvature. Some babies are born with it; in some it progresses slowly; in others it gets rapidly worse. It can be so mild that it only needs regular monitoring or improved seating, or so marked that it appears to weaken the back and affects breathing. There are various

treatments, including corsets, braces and rods inserted along the spine to guide growth. Children taking growth hormone should have their spines checked regularly during treatment (Fryns 1980; Tharapel 1983; Bendon 1988; van de Laar 2002; Shafi 2007; Rittinger 2008; Jewell 2014; Lalani 2015; Unique).

Seizures

Seizures are fairly common. Reports in the medical literature and Unique's experience shows that about half of all children have seizures which often start in babyhood or early childhood. The types of seizure vary and include absence seizures (a brief 'switching off'), myoclonic seizures (a sudden, jerk-like movement), and generalised tonic–clonic epilepsy (two-stage seizures in which you pass out, first stiffening, then twitching). One child had an abnormal brainwave pattern (hypsarrhythmia), suggesting infantile spasms (brief head nods). In many children, seizure activity is completely controlled with medication. In others seizures resolve with age. Seizures may come back after a seizure-free period.

Parents have noticed an effect of untreated or long seizures on their child's development, awareness and understanding, and also the effect of medication on their child's level of awareness and weight gain. Seizure control improved some children's learning capacity (David 1975; Tharapel 1983; Donnai 1988; Järvelä 1993; Müller 1993; van de Laar 2002; Flori 2003; Rittinger 2008; Boonen 2011; Jewell 2014; Unique).

"She has had 2 bad ones. The last 2 years ago she almost did not make it. I do not think she has fully come back from it. She is unstable and weaker, more withdrawn. She has always had imaginary friends and now has more." 42 years


8 years

Muscular disorders

Muscle wasting has been reported in approximately one third of people including 3/10 Unique members. This particularly affects the lower legs and arms, and contributes to balance and mobility problems, especially in the presence of truncal obesity.

One woman was diagnosed at the age of 25 with central core disease, a neuromuscular condition which causes muscle weakness and hypotonia in babies, delayed motor development, and reduced muscle bulk. Central core disease was diagnosed from a muscle biopsy primarily as the result of back pain and rapid onset of thoracolumbar kyphosis (excessive curvature of the upper back).

The diagnosis is important because it is strongly associated with malignant hyperthermia, a potentially life threatening complication of general anaesthesia. However, this woman had never had problems with general anaesthetics. Despite the frequency of the hallmark signs of central core disease among people with diploid triploid mosaicism, no Unique members have reported problems with general anaesthesia (Fryns 1980; Tharapel 1983; Wulfsberg 1991; van de Laar 2002; Shafi 2007; Unique).

Breathing

Some babies have breathing problems in the newborn period, and some need respiratory support. Respiratory infections also appear to be common in early childhood. Some of the reasons for the high rates of infection include: severe spinal curvature or hollowed chest (pectus excavatum) can restrict organ growth so that lungs are small; low tone in the muscles of the lungs can lead to shallow breathing and ineffective coughing; babies who have swallowing difficulties or reflux are at risk of inhaling part of their feeds, setting up a focus for infection.

Generally, respiratory problems ease with age and many children diagnosed with year-round or winter asthma outgrow it in later childhood. However a progressive spinal curve can exacerbate an existing breathing problem (see Curved spine page 14) (Donnai 1988; Järvelä 1993; van de Laar 2002; Lalani 2015; Unique).

Low blood sugar, diabetes and insulin resistance

While most people with diploid triploid mosaicism have normal levels of sugar in the blood, some have a disorder that causes the blood sugar to drop too low (hypoglycaemia) or to rise too high (hyperglycaemia). Excessive production of insulin by the pancreas (hyperinsulinism), causing a low blood sugar, has been reported. The opposite condition (insulin resistance), causing a high blood sugar, has also been seen at Unique. So have both type 1 diabetes (insulin-dependent) and type 2 diabetes (treated with diet and/ or medication). It is not yet clear whether these disorders are the result of an imprinting disorder caused by the diploid triploid mosaicism (see **Genetic imprinting disorders**, pages 4-5) but this is likely. Both types of diabetes could also be caused by family history, and type 2 diabetes could result from the overweight that is characteristic in diploid triploid mosaicism. Although there are only two cases of diabetes in the medical literature, 6/36 Unique members are affected. The insulin disorder has emerged at birth, in adolescence (12, 13 years in four Unique members) and in adulthood (28, 39 years)(Giurgea 2005;Jewell 2014; Unique).

“ The large doses of insulin that he takes are not reducing his blood sugars but are having an impact on his obesity**.”** 31 years

“ She had problems with hypoglycemia, but does not have diabetes. She has been hospitalised for low blood sugar three times and is now hypoglycemic and eats six small meals a day to control her blood sugar. Her blood sugar is usually very low but can swing very high.**”** 42 years

Lipid disorders

A Unique child was diagnosed with hyperlipidaemia at the age of 13. Adults have been diagnosed with hypercholesterolaemia (a high cholesterol) between the ages of 18 and 28. It may be of interest that a Unique adult was diagnosed with gallstones, which commonly form when the liver excretes too much cholesterol.

There is a possibility that the high cholesterol levels are caused by an imprinting disorder (see **Genetic imprinting disorders**, pages 4-5), since this is a feature of maternal uniparental disomy 14. The high cholesterol could also be linked with being overweight (Jewell 2014; Unique).

Early puberty

Most adolescents with diploid triploid mosaicism go through puberty at the normal time in the normal way. In some, it comes late (Donnai 1988; van de Laar 2002; Rittinger 2008; Jewell 2014; Unique). A small number of babies and children, particularly girls, show very early signs of puberty. One baby showed characteristics (bleeding, enlarged breasts, but no pubic hair) at the age of 5 months, and another at 6 months. The signs subsided without treatment in the first baby. A Unique baby developed bleeding at 9 months, and a little breast tissue at 16 months. Precocious puberty also affected one Unique boy who went into puberty at the age of 4; another boy started showing signs at eight years (Daubeney 1993; Järvelä 1993; Müller 1993; Unique).

The timing of puberty matters, because it affects growth. If puberty comes too early, there will be less time for growth. For this reason, medication may be given to postpone it, and allow a short child longer to reach his or her adult height (Jewell 2014; Unique).

“ She began puberty at 11, did not alter in any way and remained a pleasant, sociable and loving little girl.”

“ She had 4 or 5 pubic hairs at 5 months but nothing else developed. She then got pubic hair at 12 years and has had menstruation inhibited by taking the contraceptive pill because she is not able to take care of her own personal hygiene because her arms are too short to reach. She has no breast development at all.” 30 years

Heart

The great majority of babies with diploid triploid mosaicism are born with a healthy, structurally normal heart. The problems reported in the medical literature and at Unique are holes between the upper or lower chambers of the heart (septal defects, atrial for the upper chambers and ventricular for the lower chambers) or persistent ductus arteriosus (PDA, a feature remaining from fetal circulation). In most children, these problems resolved naturally with time, or were corrected with medication. Of the 8 babies reported with a heart problem (4/46 in the medical literature and 4/36 at Unique), only 2 needed surgery, and it was successful in both (Pettenati 1986; Järvelä 1993; van de Laar 2002; Unique).

Low thyroid levels

Low levels of natural thyroid hormone have been seen in 6/82 Unique members or people reported in the medical literature (Järvelä 1993; van de Laar 2002; Unique). Replacement therapy is with thyroxine.

Profuse sweating

Unique has five reports of babies, children and adults sweating profusely. This appears to be unrelated to obesity. In two cases this only occurred in infancy and was limited to the head and trunk. In the three other cases it has persisted. One adult was diagnosed with an inability to sweat normally, associated with not having enough skin pores (Unique).

“ She does sweat more than other family members in the same situation, so we limit outside time when possible if it is extremely hot or humid. ” 10 years

Urinary tract and kidneys

The great majority of babies are born with well-functioning, healthy kidneys. In the medical literature and at Unique there are 5 /82 reports of kidney problems. One child had one multicystic kidney (a non-functioning kidney full of cysts and scar tissue), and two had unspecified anomalies. Three Unique members have had repeated urinary infections, in one case leading to kidney scarring. In two adult men, the infections were troublesome. One man needs daily washing to limit infection as his small hands and limited dexterity mean he cannot clean himself; another has had urinary catheterisation twice for up to 8 months (David 1975; Meinecke 1986; Unique).

Low bone density

Unique has three reports of members who had frequent (5-12) fractures in childhood after only minor trips and falls. On investigation, bone density was low and two were diagnosed with osteoporosis (Unique).

Hearing

Hearing loss can limit speech and language development. Children with speech delay will usually have their hearing checked. A temporary form of hearing loss (glue ear) is very common among all babies and young children and treated by inserting aeration tubes into the eardrum (grommets) in a minor surgical procedure. Some children also wear hearing aids (Boonen 2011; Unique).

Permanent (sensorineural) hearing loss is less common. Hearing aids help, but some find them uncomfortable to wear (Müller 1993; van de Laar 2002; Unique).

“ His hearing has been moderately reduced since childhood and the loss is now approximately 70%. ” 31 years

“ She lights up the darkest room, and makes it a point to include everyone. She has to hug or shake hands with everyone in the room. She is determined and faces every hurdle with great pride in herself and the biggest smile on her face.” Almost 8 years

Development

Learning


6 years

Some 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. Some children are on target or above average in selected areas of learning, particularly reading. Others are unable to read. One child apparently had no intellectual or developmental delay in his first year of life. A child of 6 years had no learning difficulty. Another girl had borderline learning difficulties at the age of nine. In other children the degree of delay varied from severe to mild. One adult has the cognitive abilities of a toddler, but others have been reported with milder learning difficulties (Fryns 1980; van de Laar 2002; Ellis 1963; Graham 1981; Wulfsberg 1991; Giurgea 2005; Oktem 2007; Shafi 2007; Unique).

Generally speaking, children find practical and computer-based activities easier than academic ones. One child of 10 was given an award for being helpful. One adult has a special talent for mending electrical equipment and computers, and is a talented actor. Some families have commented on their child's determination to learn.

Where a child is educated depends on local policy and parental preference as much as on the child's abilities. Among Unique members, children are in mainstream (public) school usually with part inclusion in some non-academic activities, and with a varying amount of support to allow them to access the curriculum; some are in special education, particularly for secondary schooling, or for academic subjects; or they are home schooled, particularly in the US.

Observations of Unique members show the variation:

❝ She has significant learning difficulties, but is a great reader and really enjoys reading. She finds math concepts very difficult and is on about a 1st grade level. She attended a Montessori preschool, but has been homeschooled since she was 7. We are able to go at her level. She would be in a special education class if in public school. She has difficulty with concentration and attention, so we keep lessons very short and have short days.❞ 10 years

❝ She is best at practical tasks, like cooking, gardening, cycling, or helping younger children in the lower classes with anything sensory. She finds academic tasks, written maths or questions most difficult. She was awarded the 'Community Shield' for being helpful last year.❞ 10 years

❝ She is hyperlexic, that is, she decodes accurately and quickly, and has amazing spelling. However, her reading comprehension is very delayed, and she has difficulty with inferences, connections, and generalisations. She also has trouble writing detailed, coherent essays. Her work ethic is amazing: she is focused, persistent and dedicated. She is on track to graduate with a High School Diploma. It has been a lot of work, but she is up to the task! She has an aide to help her go from class to class, and to navigate unstructured times like lunch, which is tough for her given her delayed social skills. ❞ 17 years

❝ He can read, but doesn't write. His understanding of numbers is very limited. Initially he attended a mainstream school until he was 9 years old, then he went to a special school. He is strongest at reading, and weaker at money and counting skills. He graduated with his Higher School Certificate - equivalent to year 12.❞ 31 years

Speech and communication

Speech delay is typical, but the great majority of children and almost all the adults we know about do talk. There are only three reports of people unable to talk: two children of almost 5 and 6 years, and an adult. First words may be heard on time or very late: the known range is from one to 8 years. Some children only use a single word or a handful, while in others vocabulary expands quickly: a child of 3½ years had a 100-word vocabulary. Grammar may be childish or fluent. The most consistent feature is that both children and adults have difficulty speaking clearly: words can sound anything from slurred to incomprehensible. Even close family members may struggle to understand. One adult was reported to have dysarthria (unclear speech that is otherwise normal). It is likely that the typical low muscle tone in the face plays a role, and children will benefit from early speech and language interventions to help them communicate and form sounds consistently, correctly and clearly.

Children usually understand much more than they can express. Signing and using picture exchange systems can be difficult for children with significant low muscle tone in the hands and arms, but one of Unique's most severely intellectually delayed members is able to communicate with signs and some speech, although '99 per cent is not understandable' (Carakushansky 1994; van de Laar 2002; Shafi 2007; Rittinger 2008; Boonen 2011; Unique).

❝ She has difficulty expressing all that she wants to say with a picture exchange system or vocal output device due to fine motor weakness. However, she is able to select from a field of multiple pictures to answer comprehension questions and to communicate wants and needs. She is also quite adept at getting her needs met non-verbally but she can become frustrated when there are things she wants to say and simply cannot. She has learned to say a couple of full complete sentences to include "I need help" and "I did it".❞ 8 years

❝ Fluent speech with an occasional stammer.❞ 8 years
❝ She is great at understanding and signing. At 7 years she called her mother 'mama' for the first time and she now has a few words, and more have come together in the past year.❞ Almost 8 years
❝ Her receptive language is great, but she has great difficulty with expressive language. She takes a long time to come up with responses. I would estimate that non-immediate family can understand about 60% of what she says.❞ 10 years
❝ Since her processing is slow, she needs time to remember vocabulary and articulate phrases.❞ 17 years
❝ His speech is OK, but it was clearer when he had speech therapy.❞ 31 years
❝ She is very verbal although her speech is hard to understand and her words are limited. She has trouble with certain letters but can certainly get her point across.❞ 42 years

Sitting, moving, walking

In general, babies are delayed in reaching their mobility (gross motor) milestones but there are big differences between individuals. Most children do learn to walk, but their walking style may be unusual, and walking may remain an effort if their low muscle tone persists and particularly if they put on too much weight.

Learning to control their bodies follows a sequence, and generally those who sit early or on time are those who walk early or on time. Babies with diploid triploid mosaicism learned to sit without support between 7 months and 2 years, with an average age of 18 months. Sitting alone is not possible for a small number of children who need continued support. Some babies first became mobile by rolling. Children often first mastered walking supported with a walker, and took their first independent steps between 12 months and 10 years, with an average age of around 3½ years.

For a small number of children walking is not possible or only achievable on a flat surface indoors, and they will rely on a wheelchair.

One of the underlying causes of a child's delayed physical development is low muscle tone (hypotonia) which makes the body appear floppy and makes moving effortful. Hypotonia generally improves with age and activity and in a few children may disappear altogether.

Specific features of diploid triploid mosaicism that make mobility harder include children's typically tiny


6 years

feet and short slender legs that have to bear the weight of a relatively bulky body. Orthotic shoes, support footwear and splints can be very helpful. Any marked difference in leg length adds to the problems, although this is usually more of a concern for adults when the discrepancy can reach 2cm (an inch).

Regular physiotherapy (physical therapy) is important in managing mobility, and some children do overcome any mobility problems. Many people with diploid triploid mosaicism compensate for their difficulties with balance by walking with their feet wide apart (broad-based gait). Others learn to run, jump and dance (see picture, page 13), and to walk reasonable distances at their own pace (Wulfsberg 1991; Järvelä 1993; Carakushansky 1994; van de Laar 2002; Oktem 2007; Rittinger 2008; Jewell 2014; Unique).

❝ At first she was able to roll around to get where she wanted to go, then at about 7 or 8 she started walking with the aid of a walker. Later she was able to walk by herself on flat surfaces.❞

❝ She walks, runs and jumps but her balance is poor and she falls sometimes.❞ 8 years

❝ She is able to roll around her environment with ease, pull to stand, crawl, and walk using the assistance of counters, a walker or holding someone's hands. She has limited but ever increasing mobility. Her lack of muscle tone affects her ability to walk independently the most.❞ 8 years

❝ Her mobility is good: she can run (slowly) and ride a 3-wheel bike.❞ 10 years


31 years

❝ She is walking, although much slower than most. She is mobile, but tires easily. If we are going to a museum or long day trip, she will use a wheelchair. She loves going to the park, but tires after a short time. In school, she was not able to keep up with the other children.❞ 10 years

❝ Given her low muscle tone, poor balance, and poor coordination, she is very clumsy, and the quality of her running swimming, etc. is poor. She cannot do certain activities like ride a bike. With time, she has become stronger.❞ 17 years

Fine motor skills

Children with diploid triploid mosaicism typically need specialist support and a referral to occupational therapy to help with fine motor skills. Their hands are usually small or tiny, their fingers may be curved and inflexible and they may not have a full range of movement. Typically they also have low muscle tone.

> “ She has changed our outlook on life: We know it’s hard to get things done, so we don’t take anything for granted. We appreciate every milestone she makes, and celebrate the little things.”

Families frequently comment that their child is ‘clumsy’ or ‘weak’ or ‘unco-ordinated’.

Children need practice and determination to master complex skills from feeding themselves and cutting up food, to doing up buttons, tying shoe laces, placing jigsaw pieces, cutting with scissors, and writing legibly.

“ She has just mastered her seat belt – quite an accomplishment! Small buttons, shoe tying are not mastered. Handwriting improvement is ongoing.” 10 years

Personal care

How independent someone with diploid triploid mosaicism can become in looking after themselves depends largely on their cognitive ability and their motor skills. Unique’s experience is that the great majority of people known to them need support, but how much support they need varies a lot. Important factors are the small size and impaired movement of their hands, the short length of their arms, and low muscle tone. Children usually need help for longer than typically developing children with feeding, tooth brushing, washing, hair washing and particularly dressing. By the age of 8 years, most of the children known to Unique still needed help with feeding (particularly cutting up food) and tooth brushing, and all needed help with dressing. By adolescence, some children had mastered dressing but needed help with detail such as small buttons, tying shoe laces and getting clothes on the right way round.

As for toilet training, a few children achieve it on time, most are late to be clean and dry, especially at night, and for some it is not possible. Children at Unique were successfully trained between the ages of 2½ and 8 years, with an average age of nearly 4½ years. The others were in nappies or pads day and night through most of their childhood, and some adults were as well. A frequent report is the need for help with wiping after a bowel movement because hands are too small, and arms too short.

Behaviour

Children with diploid triploid mosaicism generally appear to be affectionate, sociable and a pleasure to be with. Problems are rarely mentioned, and much more often in the medical literature than at Unique, but when they are, they usually focus on attention deficit, overactivity, sudden mood swings, inability to

> “ At 8 years, she is good natured, sociable, bright and funny. Everyone comments on her friendly character.”

cope with change, and frustration.

Unique families frequently describe their child as fun-loving, happy and enthusiastic. Some families are sensitive to the discrepancy between their child's enthusiasm and their ability to communicate with people they don't know very well. Parents of some older children comment on mood swings, and say that behaviour can switch from delightful to unpleasant in a second, perhaps in response to a change in activity. They say that adults with diploid triploid mosaicism need clear expectations, boundaries and responses to unacceptable behaviour. One family attributed behaviour difficulties to epilepsy medication; another to their son's food obsession (Fryns 1980; Tharapel 1983; van de Laar 2002; Oktem 2007; Unique).

> "She is a very loving, kind and gentle person. She endears herself to everyone she meets." 30 years

"She is good natured, sociable, bright and funny. She does overreact to correction, shouting, crying or biting herself if she is told that time is up when she is enjoying an activity eg iPad. Socially, she prefers adult company, and although her peers like her, she doesn't interact too much with them." 8 years

"She is generally very sociable and well behaved, but she does struggle to cope in loud, new environments. She suffers from drastic mood swings and at times can cry/scream uncontrollably without reason. She is under the care of a neurologist for her behavior and takes clonidine daily." 8 years

"She can be very kind and sweet but she can also be very difficult. She doesn't like changes of activity and can be argumentative and obtuse." 10 years

"She is very enthusiastic and loves to be around people, but cannot interact well given her delayed speech. We worry that she will make poor decisions as she gets older just because she wants to get attention and please others. Her open mouth posture, her lack of coordination, her rounder stomach, her different speech pattern make strangers wonder. We have been teaching her to self advocate and to say no when she is in uncomfortable situations." 17 years

"Very lovable, but would blow up in a second and be sorry as quickly. He needs clear guidelines (threat of removing his iPad) as he pushes the boundaries. Very much a people person: he enjoys laughing, and participating in laughter." 31 years

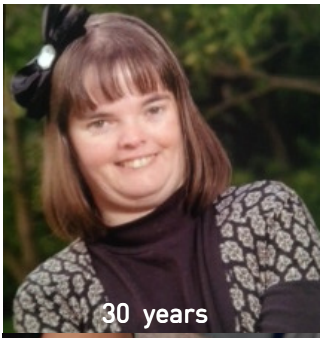
"She greets everyone with a smile and is very sociable. She loves music, dancing, computer games and puzzles. She's funny and fun at times – and then sometimes quite the opposite. Sometimes she needs a stern reminder, other times a time out." 42 years

> "Very sociable, has a very happy, positive disposition. He never complains. He has taught us all to be patient." 31 years

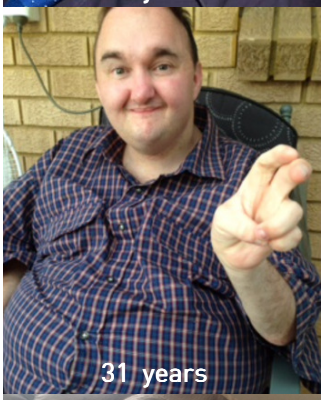
Older people with diploid triploid mosaicism

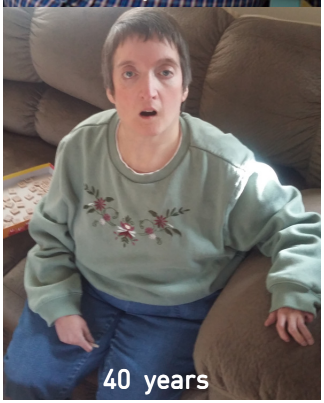
The oldest people known to Unique are in their thirties and forties and the oldest described in the medical literature are in their twenties, but there may well be older people who have not been diagnosed.

Of the three women in their twenties reported in the medical literature, the oldest is 29 years (Fryns 1980; Shafi 2007; Jewell 2014). Unique has 17 members aged over 16, the oldest 42 years. Six of their families completed a Unique survey in 2016.


30 years


30 years


31 years


40 years

Mobility

After adding strength in adolescence and early adulthood, mobility appears to become an increasing problem with age because of the marked tendency to carry excess weight combined with small lower limbs with slender muscles and small, even child-sized feet. Pre-existing low muscle tone, poor balance and co-ordination compound the difficulties so that the quality of physical activities such as walking, running and swimming is often poor. Adolescents and adults typically lack the skills for sports and need support footwear or splints, or even a walker or wheelchair.

“ She can walk but not far. ” 26 years

“ He walks unaided but is very nervous about walking on uneven surfaces. He is getting more unsteady on his feet, worried that he will fall. ” 31 years

“ After being able to walk by herself on flat surfaces, she is now is back to using a walker and is too unstable not to. She seems to be more bent over and stiff when she stands now, though some days are better than others. ” 42 years

Self care and independence

Everyone within Unique needs some help looking after themselves. Two are able to do important things for themselves like cooking and showering, but need supervision. Two cannot dress themselves, but three more can, although one of them needs help with buttons, zippers and laces. Two others need help with hairbrushing, shaving, washing, tying shoes and folding clothes. One woman has monthly waxing to remove hair from her chin and shoulders.

Two adults can use the toilet alone, but two others

still need pads, especially at night. Having very small hands means they need help wiping after a bowel movement. The family of one adult reported constipation with overflow leading to bowel accidents caused by inadequate exercise. She was under the care of an incontinence nurse and had set places each day to try to prevent accidents, as well as using a fibre supplement and lactose free dairy products.

All adults live at home or with 24/7 care and supervision. One man in his 30s works voluntarily for an hour a week in a hospital kitchen cleaning tables and filling the dishwasher.

❝ Her mood and wellbeing are good. She has left school and attends a 30-hour 5-day lifestyle program. She doesn't work, and lives at home. She is slightly incontinent at night - doesn't wet herself but has urine leakage.❞ 30 years

❝ He lets nothing stand in the way of his living a full, independent life. He works unpaid for 1 hour a week. He cannot dress himself or wipe his bottom, and sits down to urinate.❞ 31 years

❝ At 39 years she was living in a home care situation and was very happy to be somewhat independent. Now she is probably going to move into a new home in the next few weeks.❞ 42 years

■ *Learning & cognition*

All the adults have needed a high level of full time learning support, but some attended regular/ mainstream schools especially for primary education, while others made more progress in special education. A 17-year-old girl is on track to graduate with a high school diploma; one man of 31 works best with electrical equipment especially washing machines, TVs and fixing problems with computers; another man of 31 graduated with his Higher School Certificate, equivalent to year 12; one woman of 26 is 'excellent with computers'; and a woman of 42 is best at working out which buttons to press on a radio or computer.

One mother voiced concern that her daughter's mental abilities were deteriorating at the age of 17, but adulthood has seen no further deterioration.

❝ He played Fagin in Oliver. He was a great pickpocket! ❞ 31 years
❝ He can read, and this is what he is best at, but he doesn't write. His understanding of numbers and money is very limited. ❞ 31 years
❝ Some things she picks up right away other things she never gets.❞ 42 years

■ *Speech and communication*

Speech and communication are affected, but all the adults known to Unique and most of those

❝ She LOVES music. She plays the piano and knows all the pop songs. She watches The Voice, American Idol, etc. on TV.❞ 17 years

reported in the medical literature use some speech. Like many others with a learning disability, they need longer to process language and respond, although in general people understand more than they can express. Language may be simplified with a limited vocabulary and sentence structure. Speech is usually unclear, and one adult has been diagnosed with dysarthria (unclear enunciation of normal speech). Low muscle tone in the facial muscles may undermine speech clarity (Shafi 2007; Unique).

"His speech was really clear when he had speech and language therapy. Now it's OK." 31 years

"She is very verbal although her speech is hard to understand and her words are limited. She has trouble with certain letters but can certainly get her point across." 42 years

Health

Among the medical disorders first diagnosed among adults are:
recurrent kidney infections; osteopenia (low bone density); central core disease, a disorder that affects the muscles used for movement (skeletal muscles), causing a weakness that ranges from barely noticeable to very severe (see page 15); tonic–clonic seizures (once called 'grand mal'); high cholesterol levels; type 2 diabetes (non-insulin-dependent); rapid-onset spinal curvature; undiagnosed pain. One Unique member reported that surgery to remove her son's gallstones was aborted as his short neck made anaesthesia too risky (Shafi 2007; Jewell 2014; Unique).

Mental health

Families describe their children as sociable, affectionate and happy. On the whole their mental health is good.
However, anxiety, depression, and obsessive behaviour were diagnosed in a woman of 21. At Unique one adult has been diagnosed with depression, and another family described their daughter, 25, as slightly obsessional (Jewell 2014; Rucker 2015; Unique).

Can an adult with diploid triploid mosaicism have children of their own?

So far, we are not aware that this has happened. But a girl whose ovaries were removed when she was 8 years old had her eggs frozen in the hope of using them for fertility treatment as an adult (Oktem 2008). The ability of people with diploid triploid mosaicism to look after a child is likely to depend on their own cognitive ability.

"He can connect with anyone in this world. He sees people as human beings, not their religion, creed or colour. He has an abundance of love. He lets nothing stand in the way of his living a full, independent life."
31 years

Support and Information

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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 Rosalyn Jewell, Specialty Registrar in Clinical Genetics, Yorkshire Regional Genetics Service, United Kingdom.

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