



Support and Information



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Tetrasomy & Pentasomy X Syndrome
Information and Support
www.pentasomy.com

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Pentasomy X



What is Pentasomy X?

Pentasomy X only affects girls. In the body's cells, there are usually 46 chromosomes, 22 pairs from 1 to 22 plus two sex chromosomes which are called X or Y. Girls usually have two X chromosomes and their chromosome make-up, known as a karyotype, is 46,XX.

Girls with pentasomy X have five X chromosomes, giving the chromosome make-up 49,XXXXX.

Common features

As babies and in early childhood, the most obvious feature of girls with pentasomy X is their petite stature. Most babies are born small and grow slowly and their hands and feet are often particularly small. Girls look and may behave like children younger than themselves. Other common features include:

- Low tone of the skeletal muscles. Babies are typically floppy and slow to gain muscular control, for example, of their head.
- Delayed development.
- Unusual dental development, with teeth late to emerge or late to fall out and some deficiencies of dentine and enamel.
- Heart conditions at birth, including a heart murmur.
- Unusually lax joints.
- Normal genital area.
- Urinary tract anomaly.
- Partial fusion of the two long bones in the forearm.

How rare is pentasomy X?

No one knows exactly, but it is very rare. Medical researchers have suggested that it is as rare as the male equivalent - 49,XXXXY Syndrome, making one baby in 85,000 a girl with pentasomy X. But it appears to be much rarer. In all, the worldwide community of girls and women with pentasomy X is truly tiny: 23 girls have been described in the medical literature, *Unique* has 10-15 member families and some more families belong to the email support group that you can find through www.pentasomy.com (Fragoso 1982; Kassai 1991; U).



6 years old

References

The text contains references to articles in the medical press. The first-named author and publication date are given to allow you to search for the abstracts or original articles on the internet in PubMed. If you wish, you can obtain abstracts and articles from *Unique*. References to information from *Unique* is marked U.

How is it possible to have so many chromosomes?

Babies with three extra non-sex chromosomes (those that are numbered from 1 to 22, called 'autosomes') would not develop and thrive so well as girls with 49,XXXXX or boys with 49,XXXXY.

Girls can cope with so many X chromosomes because only one X chromosome in any cell is fully active. All the extra X chromosomes are mostly switched off and play little or no role in development. Two small regions at the ends of the X chromosomes as well as 15 per cent of the genes on the chromosome are *not*, however, switched off and remain active and these are likely to be responsible for most of the effects of pentasomy X.

Either the additional X chromosomes cause the effects before they are switched off or the amount or timing of the genes still expressed on the X chromosome is altered.

How did this happen?

It is most likely that your daughter has four X chromosomes from her mother and one from her father. When a mother's eggs form, chromosome pairs separate to leave each egg with a single X chromosome. When a mistake occurs in cell division, two X chromosomes can be left. If a similar mistake is repeated with both the X chromosomes at the next cell division, the egg can end up with four X chromosomes. Fertilised by a single X-carrying sperm, this egg will then develop into a baby with five X chromosomes or pentasomy X.

The technical name for this type of mistake is non-disjunction and it happens much more often than you would imagine. It is believed that at conception, one baby in three is affected by non-disjunction. However, while non-disjunction of chromosomes 1-22 is more common in older mothers, this does not seem to be true for the sex chromosomes.

Could it happen again?

Sex chromosome disorders usually occur out of the blue and if they are tested, the parents themselves have normal chromosomes.

Very occasionally, a mother who has never suspected any problems before turns out to have a single extra X chromosome in some of her cells, and then her chances of having another affected daughter will be higher. This is called mosaicism and it means that the mother has some normal cells with 46,XX chromosomes alongside others with a 47,XXX make-up. This makes it more likely that an egg may develop with extra X chromosomes.

Even though the likelihood of having another baby with the same chromosome disorder is very low, you may wish to discuss prenatal testing with your genetics service before another pregnancy.



5 years old

Can pentasomy X affect behaviour?



Pentasomy X does not appear to affect girls' behaviour in a specific way. Frustration at being unable to communicate expresses itself in tantrums and anger and one older girl is receiving counselling. A few girls are either over friendly or extremely reserved. In other ways, girls with pentasomy X are just like other girls and the same parenting techniques succeed with them (Linden 1995; U).

Families say ...

"R went through a stage of banging her head on the floor when she could not get her own way. As long as she was in no danger I just ignored her. This seemed to work and she has now stopped - R, 3.

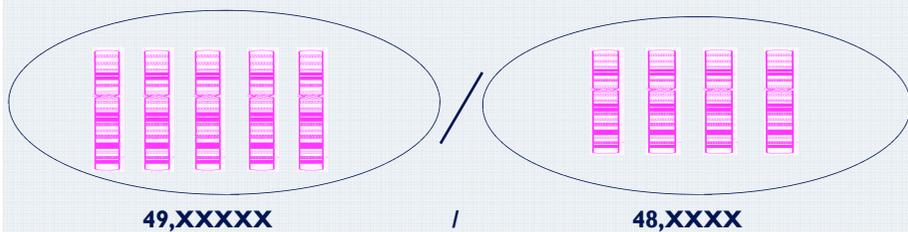
"C is a very happy child, thoughtful and considerate, with lots of friends at school, but does occasionally become frustrated - C, 12.

What about puberty?

The medical literature suggests that at least some girls will be delayed in going through puberty and that is *Unique's* experience as well. There are five reports in the medical literature of girls with either a very small uterus or underdeveloped or missing ovaries or both. Among girls with four X chromosomes (tetrasomy X), around half do not complete their sexual development without oestrogen supplementation and it is very likely that this will be true for girls with pentasomy X. Oestrogen supplementation from around the age of 10 to 12 is also likely to be helpful in preventing premature bone loss and guarding against osteoporosis (Toussi 1980; Kassai 1991; Linden 1995; U).

Most girls with pentasomy X have five X chromosomes per cell.

Some girls have some cells with four Xs (tetrasomy X). This is mosaicism and generally lessens the effects.



What can I expect in pregnancy?

Many mothers have noted unusual features during pregnancy. In the medical literature, there is one report of decreased fetal activity and this has been noted in *Unique* families as well. The most common finding you would expect is that an ultrasound scan will reveal that your baby is unusually small. An accumulation of fluid within the baby (hydrops fetalis) and an unusually large fluid pad at the back of the neck (nuchal translucency) have also been observed.

Will the birth be normal?

It seems from the medical literature and from *Unique's* experience that most girls will be born vaginally around term. A review of births in a research report showed that out of 22 babies, 12 were born at or just before term, eight were born after 40 weeks and two were premature. In *Unique's* experience, two out of 11 babies were induced, one at 35 weeks after an ultrasound scan showed that she had hydrops fetalis (a dangerous accumulation of fluid) and one at 41 weeks. One baby was born by Caesarean section because she was in the breech position; another by emergency Caesarean after an induction caused fetal distress (Kassai 1991; U).

What about the neonatal period?

The medical literature shows that some babies had a difficult time neonatally. Four babies in a series of 12 needed resuscitation after experiencing distress, although all went on to thrive afterwards. By contrast, *Unique's* experience suggests that many babies (five out of the six who gave detailed information) had an uncomplicated, easy vaginal delivery and their only postnatal concern was feeding. (Kassai 1991; U).



9 months old

Information on pentasomy X

It is many years since a formal study of girls with pentasomy X was carried out but a new study was launched in 2004. For more details, please contact *Unique*.

This leaflet was compiled from the information available in 2004, collected informally from members of *Unique* and from the medical literature. Inevitably, the information may be biased as it represents responses from families who have joined a pentasomy X community. This is also true of information in the medical literature. The tiny number of girls ascertained also means that the information cannot be complete.

Unique is extremely grateful to the families who took part in its survey.

Can pentasomy X affect growth?

Girls are usually born small and generally follow a growth curve that falls near or below the lowest curves on growth charts. According to the medical literature, birth weights range between 3lb 15oz and 6lb 6oz (1786g - 2891g). As well as being light, most girls are short and many also have an unusually small head, so they are in proportion. However, parental height modulates this, so girls with tall parents are more likely to reach an average height (Dryer 1979; Monheit 1980; Kassai 1991; U).

Slow weight gain can be worrying for parents but may be normal for a girl with pentasomy X. A group of four girls who weighed between 4lb 7oz and 6lb 5oz (2012g - 2863g) at birth reached weights between 12lb and 14lb 12oz by their first birthday (5442g to 6689g). Some girls put on weight faster than this (13lb - 5896g at six months) and some girls, probably the minority, gained weight at a normal rate (Dryer 1979; U).

“ The best advice I was given is that as long as she is gaining steadily that is all right.

Should I give extra milk or calories?

It is not known why girls with pentasomy X put on weight so slowly but they certainly have small appetites. Breast milk is best for all babies and if your baby is gaining weight and growing steadily, however slowly, you may feel confident enough to resist pressure to give her high calorie supplements. However, this is an individual decision and some mothers feel reassured to see even an ounce of milk go down.

Weight gain tends to slow in babies when they start solids and at this point you may think again about using a high calorie milk. However, anecdotal evidence from *Unique* shows that girls adjust their intake of solids to match the greater calorie intake from the enriched milk. Most families do use high calorie milks – and most doubt with hindsight that they made much difference.

“ C’s weight started on the 3rd centile and stayed just below it until 20 weeks. Then it followed its own path - below the 3rd centile. We tried numerous calorie additives to her feeds but it didn’t help much.

Feet and hands

Girls typically have particularly tiny feet, so that they wear first shoes for a long time. Their toes may overlap, requiring straightening or making shoe choice more difficult. Perhaps one girl in four is born with a positional anomaly of one or both feet, such as a club foot or the intoeing position known as metatarsus varus.

One family reported that their daughter had particularly cold hands and feet, perhaps because of poor circulation. On the hands, the little finger typically curves inwards and is sometimes short. Some girls also have a single crease across the palm on one hand or both (Kassai 1991; U).



girls should be fully immunised and parents should anticipate a longer recovery time from illness and operations for their daughters.

A high arched palate may also cause dysfunction of the Eustachian tube (the connection between the throat and the middle ear) resulting in more frequent ear infections.

■ Seizure activity

Seizures do not appear to be a frequent feature of pentasomy X. The medical literature shows that while in some girls an EEG recording may be on the borderline between normality and abnormality, seizures have not been noted. One *Unique* member experienced seizures between the age of 3 and 11 but is currently off medication and seizure-free.

■ Hearing

A hearing impairment has been noted in two children in the medical literature, one of whom also had external abnormalities of the ears. However, this has not been a concern for *Unique* families: out of 11 families, one child is reviewed regularly and another has tiny external ear canals but no structural problems of the inner ear. However, frequent ear infections may increase the likelihood of glue ear (conductive deafness) so regular hearing screening is recommended.

■ Eyesight

Impaired eyesight has been noted once in the medical literature and one child was described with ptosis, an inability to fully open the upper eyelid. One *Unique* member also has ptosis, but not so severely that the pupil is covered. Another child is markedly short-sighted. No other vision concerns have been recorded.

■ Teeth

Dental abnormalities have been noted to be very common both in research reports, affecting 10 out of eleven girls studied, and in the *Unique* series. Some girls cut both baby and adult teeth late and when they emerged they had thin enamel or other deficiencies. First teeth emerged among *Unique* members between 10 months and two years and tooth development was still not complete in one girl at the age of 17. Baby teeth were frequently late to fall out and in many girls had to be removed. The enamel deficiencies mean that girls need regular dental care and fluoride protection may be helpful.

■ Constipation

Three *Unique* families specifically mentioned constipation as a major problem, requiring treatment with stimulant laxatives. Constipation is common in children with chromosome disorders who are not very active, but that is not generally true of girls with pentasomy X. However, it may be exacerbated by a low fluid intake and girls' generally small appetites.

(Dryer 1979; Monheit 1980; Toussi 1980; Funderburk 1981; Kassai 1991; U)

“ We have tried everything - lactulose, picosulphate, enemas and glycerine suppositories - but the most effective thing has been shredded wheat cereal!

Medical concerns

■ Heart conditions

Reports in the medical literature and the experience of *Unique* agree that around 50 per cent of girls are born with a heart condition. However, the medical literature includes girls with an innocent heart murmur. Although a heart condition sounds alarming and babies do need to be monitored and sometimes to take medicines to improve the flow of blood through the heart, the problems are often fairly simple and some resolve without surgery. The most common defects are holes between the lower chambers of the heart and a condition called persistent ductus arteriosus (PDA) that is a left-over from the way the circulation operates during fetal life. A minority of girls are born with a more complex heart condition and will need a surgical operation.

■ Orthopaedic problems

Many girls have joints that are unusually loose, extensible, stiff or clicky. The elbows are commonly affected and about half of the girls will have radioulnar synostosis where the two bones that link the elbow with the wrist are fused, making it impossible to rotate the arm fully and limiting elbow movements. The shoulders, hips, knees and ankles may be affected and some girls are born with shallow hip sockets and joints that need stabilising with a splint or plaster. The loose joints and low muscle tone can give girls with pentasomy X a typical stance: standing up straight, their feet tend to be flat and slope inwards and their knees appear to bend inwards and backwards. Some girls will need good ankle support before they can walk. Five out of 19 girls are reported in the medical literature with the unusually angled foot of talipes (club foot), but this has not been reported in *Unique* members.

■ Kidneys and urinary tract

Kidney and urinary tract conditions are unusually common according to the medical literature where they are reported to affect four out of five girls. That is not the experience of *Unique*, where only four out of eleven girls are reported to have a renal or urinary condition. However, girls should be thoroughly screened. Two girls have kidneys with multiple cysts caused by an error during the development of the kidneys and in two girls one or both kidneys is small.

■ Infections

Children with chromosome conditions appear to take longer to get over the normal upper respiratory infections of childhood than other children. This is a marked feature in girls with pentasomy X and has been noted by researchers and parents. Five families out of six who gave detailed information reported that their daughter had had repeated serious respiratory infections in early childhood. Serious respiratory infections are also common in girls with tetrasomy X (four X chromosomes), suggesting a common cause. One parent noticed that her daughter took in general twice as long to heal as other children. At the very least this apparent vulnerability to infection means that

How might pentasomy X affect a girl's ability to learn?

Girls with pentasomy X learn somewhat more slowly than other children. Most start their education in a mainstream nursery or school and some stay in mainstream education throughout their school life. Other families find that their daughters' slower pace of learning is better catered for in a school where special help is available. In some girls the level of learning difficulty is hard to characterise, but the general picture within *Unique*'s membership is of a moderate learning difficulty.



These snapshots give an idea of what girls achieved at different ages.

- “ *M stayed in mainstream school until she was 21 with a part-time support teacher, following a similar curriculum but at a simpler level - M, age 28.*
- “ *K has a great memory and is currently learning living skills in high school - K, age 17.*
- “ *C attends a school for children with moderate to severe learning difficulties. She is achieving at the preparatory levels of the curriculum and her areas of highest achievement are number, shape and space, music and English speaking and listening. She started reading since she was 8 and writing since 9 - C, age 12.*
- “ *M can count by rote reliably to 6, identify and name colours and sort by colour and kind. She is at nursery full time with 100% learning support. We are hoping to place her in a special school to maintain her progress - M, age 5.*
- “ *R was assessed to be eight months behind at two and a half years old. She is coping extremely well with playgroup and interacts very well with other children. I found that early intervention has helped a great deal - R, age 3.*

How serious can pentasomy X be?

Unique's oldest member is 29 years old and our experience is that pentasomy X does not generally affect the major organs (heart, lungs, liver, brain) severely.

However, about half of the girls have a heart condition and a minority experience distress at birth and need resuscitation.

Two members of *Unique* have experienced serious complications, which may, however, be coincidental: one developed hydrops (an abnormal accumulation of fluid) as a fetus; another has hydrocephalus (an increased quantity of fluid within the brain) (U).

Families say ...

"A is babbling, making sounds like mama and num num - A, 13 months.

"R uses about 15 to 20 single words and builds some phrases like 'Oh look, mum!' She also babbles and uses vocal noises. She speaks very clearly and her understanding is excellent - R, 3.

"Z talks and uses 2 to 3-word sentences, but only with people she knows well and is confident with. Her speech is still unclear and we are having to battle for speech therapy - Z, 4.

"Speech is coming along well. M constantly vocalises and says new words and phrases, some more clearly than others. She can say things like 'I want the toilet' and understands more than she can communicate - M, 5.

"C is extremely vocal and loves singing. She sometimes uses long, complex sentences although some words are difficult to recognise and she still has difficulties with s and f sounds - C, 12.

How can pentasomy X affect speech and communication?



3 and 5 years old

Language is known to be directly affected by the number of X chromosomes, so that girls with pentasomy X are at risk for language disabilities and delays and while delays are common in both speech and understanding, they are more obvious in speech.

Girls with pentasomy X are in general skilled communicators, using expression, vocal noises and gestures to get their meaning across. Parents find that their daughters understand more than they can say and in general speech is delayed and may never become fluent conversation. Some difficulties with articulation are persistent, but speech therapy helps.

The general picture that emerges from *Unique's* experience is that by their second year, girls are babbling and using 'jargon', the speech-like sounds that convey a meaning but are not actual words. First words may emerge around now or not for another few years. By the playgroup and nursery years, girls are linking words together into short phrases. During the school years, speech continues to develop and girls start to use longer and more complex sentences.

A cleft or very high arched palate can affect speech production and has been reported in 6 out of 13 girls with pentasomy X. However, only 2/7 *Unique* families mentioned this: in one girl with a high arched palate speech was unaffected, in another girl with a cleft palate it was severely affected (Dryer 1979; Toussi 1980; Kassai 1991; Linden 1995; U).

How might pentasomy X affect sitting, walking and other developmental milestones?

At birth, the tone of the skeletal muscles is typically low (hypotonia) and a continued floppiness of movement may be the first sign that anything is amiss. However, hypotonia is not universal, and at least one *Unique* member was unaffected.



Some girls also have extremely loose joints, so they either appear double-jointed or else their joints are 'clicky' or dislocate easily. This affects the elbows particularly and to a lesser extent the hips but virtually any joints may be unusually lax. A common feature in people with extra X chromosomes is partial fusion of the radius and ulna (the two long bones in the forearm) known as radioulnar synostosis, which limits twisting movements from the elbow.

A combination of these factors slows girls' development, so they reach their gross motor 'milestones' rather late but the great majority do achieve them. Rolling over is a skill that girls may find particularly tricky and while most achieve this by the second half of their first year, many are sitting by the time they can roll, scoot or bottom shuffle instead of crawling (their arms may buckle under their weight) and while many can walk with support in their second year, it may well be another year before they can walk alone. *Unique* has one member who did not walk at age 12 – but this did not hold her back (Dryer 1979; Kassai 1991; U).

Once mobile, girls may still need some support and steadying and they are less sure on their feet than other children. Some continue to need splints and others wear support boots. They may well continue to tire more quickly than other children and find walking over a distance exhausting. This does not stop them from enjoying themselves.

Families say ...

"K is very mobile, she likes to run, walk and ride her adult tricycle and has learned to swim without a life jacket - K, 17.

"C can stand with splints or a standing frame but so far has not stood alone or walked. But she enjoys many activities like swimming and dancing in her chair. She gets around brilliantly and is a real expert at manoeuvring her chair - C, 12.

"Z has just started gymnastics with a special needs coach. She loves water - this helps her stiff and clicky joints - Z, 4.

"R enjoys swimming, playing with sand and going to the park. Swimming has helped a lot with her joint problems - R, 3.