

# XYYY syndrome



## References

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

References to information from the *Unique* database and a questionnaire completed by *Unique* families with a son with XYYY syndrome are marked U.

## XYYY syndrome

XYYY syndrome, also called **Triple Y syndrome** or **48,XYYY syndrome**, is a chromosome condition that only affects boys and men. It is extremely rare and there is little information available, partly because there may be boys and men with XYYY syndrome who have developed without significant difficulties or who have not been diagnosed by medical professionals.

From the information that is available, it seems that most boys and men with this condition do not have major birth defects or major handicaps and their long term outlook is fairly good. Nonetheless, many boys and men who have been diagnosed with XYYY syndrome do experience behaviour, educational and medical problems.

## Sources

The information in this leaflet is drawn partly from the published medical literature. However, only nine people have been described in the medical literature since the first boy was diagnosed in 1965, seven of them adults. All were diagnosed because something unusual brought them to medical attention, so they are likely to represent more severely affected individuals and are unlikely to be an average group of boys and men with XYYY.

When so few people have been described with a particular chromosome condition it is not always possible to be sure whether certain features are caused by the disorder or unrelated to it. It is possible that there are young men who have XYYY syndrome who develop normally or with minimal problems and never come to the attention of the medical profession. This is believed to be the case for as many as 85 per cent of young men with XYY syndrome, who have a single extra Y chromosome.

This leaflet also draws on *Unique*'s database. All of *Unique*'s eight members aged between 11 and 24, three with mosaicism, were diagnosed during childhood. This means that they too are unlikely to represent an average group for XYYY. Their information, however, helps to give the most complete picture of XYYY available today. Four families completed a detailed questionnaire about their son's development in 2005.

## What is a chromosome?

Chromosomes are the microscopic structures in the nucleus of the body's cells that carry genetic information. In addition to 22 pairs of ordinary non-sex chromosomes (called autosomes) numbered 1 to 22, boys and men usually have one X chromosome and one Y chromosome, making a total of 46 chromosomes. The Y chromosome is distinctive for males and is always inherited from their father.

Instead of a single Y chromosome, boys and men with XYYY syndrome have three Y chromosomes. They have 48 chromosomes in a cell: 22 pairs of non-sex chromosomes, making 44, plus four sex chromosomes (XYYY), making a total of 48 chromosomes.

Boys and men with XYYY may have three Y chromosomes in all the cells of their body. Sometimes, though, a person may have some cells with XYYY, and some other cells with different numbers of X and Y chromosomes. This condition is called mosaicism and is fairly common in XYYY syndrome. Mosaicism makes it harder to predict the effects of having an XYYY chromosome make up.

### Common features

A 48,XYYY chromosome make-up does not appear to cause any major medical problems, but has been associated with some common medical and dental problems as described below.

- Behavior can be difficult, characterised by impulsivity and a low frustration tolerance. Occasional aggressive outbursts and low emotional stability seem to be common.
- Generally, boys have been somewhat delayed in starting to walk and to talk and there has been some effect on learning, so that most boys have needed some support at school. Academic skills have been quite variable but in terms of a measured IQ, the range found so far has been from 65 to 86, which would put most boys into the low normal category. Performance IQ is typically higher than verbal IQ.

### Other features

Among the other features described in the medical literature or to *Unique* are radioulnar synostosis (fusion of the two long bones of the forearm near the elbow, limiting some movements); flat feet or bony foot deformities; minor kidney anomalies; acne; a high rate of respiratory infections in early childhood and continuing asthma in later childhood; and large or irregular teeth or teeth with poor enamel formation and a high rate of dental caries (cavities). The genitalia in XYYY males usually look normal, but five out of six adult men had small testicles or impaired testicular function and no sperm. One married adult male with XYYY was diagnosed due to sexual dysfunction in adulthood (Hori 1988; Linden 1995).

### **What were the first signs?**

Most likely, the first signs of XYYY will be developmental delays, especially in speech development. ‘With hindsight, it would have been early on, he didn’t smile very often, slept very little and as he got older his speech did not develop,’ one family recalled.

### **Might the pregnancy be different?**

There is no evidence that pregnancy with an XYYY baby will be abnormal. Three out of four *Unique* babies were born after their due date and one boy described in the medical literature was born one month early (Sele 1975; U).

### **How might it affect my newborn baby?**

*Unique* families have reported a normal newborn period with no cause for concern. One baby with 48,XYYY mosaicism was persistently cold, so his family had to dress him warmly when asleep (U). A few babies reported in the medical literature had respiratory infections in infancy and some choking or other feeding difficulties.

### **What about growth?**

Birth weight is typically in the normal range. Stature is usually tall normal with average height around six foot (180-185 cm), and also depends upon family height. Some boys have a very slender build; others have a fat distribution around the tummy, thighs and bottom, but there is no consistent pattern (Schoepflin 1972; Ridler 1973; Sele 1975; U).

### **What about food and eating?**

In *Unique*’s experience, babies have no particular feeding difficulties. A few babies reported in the medical literature had choking with feeds or other feeding difficulties. Some families have reported a reluctance to eat chewy foods and others have reported an unusually small appetite, but neither pattern is consistent and most boys eat a wide range of healthy foods (U).

## How can XYYY syndrome affect a child's ability to learn?

Boys are likely to need some support with their learning. Their typically mild to moderate learning difficulties mean that parental support, careful school choice and sometimes educational interventions are important to enable them to realise their potential. While they can access the curriculum, they generally work more slowly through it at the level of a younger child.

Many boys will do better at manual, structural and conceptual work, such as computing, art, design and practical activities than at tasks that require high verbal fluency. However, many boys are delayed in their hand control and use which undermines their practical skills.

Reading and especially writing may be somewhat delayed and while reading skills usually catch up, *Unique* families suggest that writing remains immature because of poor fine motor skills.

Typically, boys can be easily distracted, so working in a large group is difficult and they tend to thrive better when taught 1:1 or in a small group. Attention span is often short and boys usually need their learning packaged into small units.

Some boys attend a mainstream school but in *Unique*'s experience most attend a special school at least for their secondary education.

While not all boys will have a statement of special education need or its equivalent, entitling them to extra educational support, most *Unique* boys do have a statement, granted around school entry or before transfer to secondary school.

## Speech and communication

In young boys, speech delay is often the most obvious first sign of XYYY syndrome and in *Unique*'s experience, it is the most consistent. Speech and language difficulties are associated with other X and Y chromosome variations as well.

Typically, first words emerge rather late between two and four years. Many boys will need additional speech and language input before and at school and some may benefit from attending a speech and language centre or having 1:1 language support.

With sufficient input, boys may put their speech delay behind

## Families say...

*“ His reading is excellent, but his writing is pretty bad, mainly because he can't concentrate long enough to try – age 11.*

*“ His writing is improving and he loves to read newspapers and sports pages in magazines – age 17.*

## Families say...

*“C knows all his letter sounds except c and y, and can say the names of h, i, j, k, p and z. He finds it hard to blend sounds together to read a consonant-vowel-consonant word such as **bag**. He also experiences problems hearing the middle sound in these words, and does confuse the middle sounds **eli** and **olu**, and beginning sounds **b/d/p** - teacher's report, age 11.*

*“Speech is still his worst ability. Strangers would find it difficult to understand him without help. He has difficulty with certain consonants and speaks with restricted sounds - age 14.*

*“He cannot walk far, as he gets pains in his legs. One leg is longer than the other, his feet roll in and over when walks, and he seems to walk from his knees – age 15.*

them before starting secondary school but in *Unique's* experience, stumbling over words, immature patterns, grammar and structures and difficulties with making specific speech sounds may persist. Despite these difficulties, as adults they speak in full sentences and can express their ideas and carry on conversations.

Speech and language problems can cause frustration and behaviour difficulties in the pre-school years and undermine a boy's confidence at school age. Timely, effective support will help to prevent these unnecessary extra problems.

## Mobility and activity

A slight delay in sitting, crawling and walking is common but not true of all boys. Boys typically first sit between the age of nine and 14 months, become mobile between eight and 12 months and walk independently between 15 months and two years.

In some boys, muscle tone may be low (making the body feel floppy) and joints may be unusually mobile and loose. Occasionally these boys may need to wear a supporting splint or brace on the lower leg or ankle or supporting boots. Other XYYY males have tight joints, and sometimes bone abnormalities limit the range of motion at joints.

Some boys with XYYY are active and enjoy sports and this helps them to improve their mobility skills naturally. One boy has been described in the medical literature as having specific sports prowess. Finding the right sport is partly trial and error - sports that *Unique* families say their school age sons particularly enjoy include swimming, hockey and hurling, while older boys keep fit by playing football, basketball, hockey, badminton and cycling. Other XYYY males with poor coordination or other orthopaedic problems such as flat feet may find team sports or running difficult (Hunter 1973; U).

## Using their hands and arms

*Unique* families suggest that boys with XYYY syndrome may be more than usually clumsy and delayed in learning tasks that call for fine manual attention and coordination. This fine motor difficulty delays their ability to feed themselves, particularly the move to a knife and fork and makes dressing difficult when it involves zips and buttons.

Slip-on clothes and shoes with Velcro fastenings can make life much easier. At school, this difficulty can make writing more difficult and lead to a wide gap between reading and handwriting abilities. It is very likely that boys with XYYY syndrome will make faster progress with writing when using a keyboard.

Some boys with XYYY syndrome have short fifth fingers with a wedge-shaped middle joint that makes the finger curve inwards. This feature (known as clinodactyly) is harmless.

## **Elbows and forearms**

In people with sex chromosome variations including XYYY syndrome, the two bones in the forearm are occasionally found to be fused together at some point along their length. This may have no effect or it may limit some turning and twisting movements of the elbows or make it impossible to fully straighten the arms. The condition is called radioulnar synostosis. It can be identified by X-ray, but treatment is not usually necessary.

Occasionally, the elbows may be affected in other ways, with the joints oddly shaped or allowing the arm to bend at more than 180 degrees. Treatment for these unusual features is also not usually needed (Hori 1988; Mazauroic-Stuker 1992; James 1995; U).

## **Puberty, sexual development and fertility**

It appears that most baby boys are born with a normal sized penis and testicles that are already descended into the scrotum. One boy, however, was born with an undescended testicle; in another boy, both the testes and the penis were small (Townes 1965; U).

Sexual development usually proceeds normally and puberty is usually unaffected by the extra Y chromosomes. In some boys with XYYY chromosomes, however, incomplete sexual development becomes noticeable at puberty when signs of sexual maturation fail to develop fully. These boys may have a low testosterone level and may show little or no sexual interest. Sperm may be absent from seminal fluid, in which case infertility will be inevitable. It is not yet known how often this happens in men with XYYY syndrome, but due to reports of low testosterone levels, boys with XYYY syndrome should be evaluated by an endocrinologist at puberty to determine if monitoring or treatment is needed.

## **Acne**

Acne has been reported to be pronounced in adolescence in some XYYY males. Acne treatment may require more than over-the-counter preparations, and medical evaluation by your doctor or a dermatologist should be sought to determine if prescription medications are needed (Townes 1965; Poszonyi 1970; Hunter 1973; Ridler 1973; Hori 1988; U).

## Fertility

In five out of six adult men, infertility was present. Men with XYYY should be evaluated for fertility prior to attempting to have children as they are highly likely to have a low sperm count or absent sperm (Hori 1988; Linden 1995).

## Medical and dental concerns

### ■ Chest infections, asthma, coughs and colds

Two researchers have noted an unusual frequency of upper respiratory tract infections in XYYY syndrome, and this is common in *Unique* families as well. Coughs and chest infections are more common in children with chromosome disorders and in children with sex chromosome variations, so it is likely the increased infections are related to problems caused by the additional chromosomes (Townes 1965; Hori 1988; U).

Among *Unique* families, three out of four older boys have asthma and another boy is allergic to a wide range of foods, including dairy, nuts and citrus fruits.

### ■ Teeth

Dental development is often imperfect in children with chromosome disorders and specifically sex chromosome variations. In boys with XYYY syndrome, poor enamel formation and discoloration have been reported frequently in the medical literature and among *Unique* members, there are reports of irregular teeth, very large teeth and teeth that have had to be removed because they did not fall out naturally (Townes 1965; Ridler 1973; Hori 1988; U).

Boys with XYYY syndrome should practise excellent dental hygiene with regular brushing and flossing, and have regular dental check-ups. Boys should qualify for community dentistry and given the rate of difficulties it is important to find a child-friendly dentist to care for your child's teeth.

### ■ Hearing and eyesight

Hearing and eyesight are usually normal in XYYY syndrome.

## What therapies are boys likely to need?

All boys should have a full evaluation including speech therapy, occupational therapy, physiotherapy (physical therapy) and psychology when first diagnosed to determine their specific need for therapies. Many boys will need speech and language therapy as a pre-school intervention and during their primary school years. Occupational therapy is often also necessary to improve hand use and to develop coordination. Physiotherapy (physical therapy) may be needed if there are motor delays or orthopaedic problems.



## Behaviour

Typically, boys are vulnerable to social, emotional and behavioural difficulties. This is the most consistent effect of XYYY syndrome reported by families within *Unique*. The exact expression of the behavioural difficulties varies between individuals, but boys may be immature, shy, easily embarrassed or lack emotional judgment. These traits can make them vulnerable. They may be prone to outbursts of temper, and have a low frustration tolerance, showing a marked switch from their normally quiet behaviour. These highly typical behavioural difficulties mean that families should be offered anticipatory behaviour management and access to parenting support. Boys with behavioural difficulties should be evaluated by a psychologist, psychiatrist, and/or developmental paediatrician, who can help provide guidance to the family, behavioural intervention strategies and medications if necessary. Medications can help treat significant problems with inattention, impulsivity, mood instability and aggression.

*One 11-year-old boy – family says ...*

“His behaviour difficulties were first obvious around the age of 3. He reacts badly if he isn't the first or the winner, and can be tearful, shout or have an angry outburst. If he does not get his way, he has a temper tantrum. He constantly pushes the boundaries, has run off several times and is unaware of danger. On a number of occasions he has had to be brought back, sometimes by the police. He finds noisy, packed places hardest to handle and will not go in a lift, does not like water on his face and does not like having his hair washed. His peers find it hard to cope with him. He often says the wrong thing and this can cause problems.

“He is erratic and some days are better than others. His behaviour is better at school than at home. If he's had a good day at school, he can behave and he can behave in respite care.

*One 11-year-old boy – school says ...*

“If he is praised often for good behaviour or helpfulness his behaviour will rarely change for the worse. When he behaves well, he will behave in a responsible and mature manner. He is keen to help members of staff (when not participating in another activity). He reacts well to receiving responsibility. He also likes to help other younger or less able children. He does not like to be told what to do, but if he is given options, he will react positively.

“There are many things that can trigger his bad behaviour, such as being told what to do, things not going how he planned, people not doing as he tells them to and sometimes being woken up. When he does become aggravated he will shout and call people names. He also tends to take his aggression out on everybody in sight. Instead of telling a carer that somebody has annoyed him, he leaves it until he is so annoyed that he can't control it. To calm down, he needs to be given space, and not make a big deal out of what has happened. Telling him to calm down does not work. Joking with him can work, but only if he is not too aggravated.

## Behaviour (continued)

*One 15-year-old boy – family says ...*

“He is like Jekyll and Hyde, just goes from good to wild. Wild doesn’t last long now, five minutes and then he comes down. He finds the answer ‘No’ hardest to handle. He has no sense of danger (lit a fire in the house to get the fire engine to come), and has pulled knives and forks on people, he talks to strangers, wanders off, fantasises and lies and is obsessive about masturbation. He has ongoing behaviour treatment.

*One 16-year-old boy – family says ...*

“He can go from calm to absolute outrage in minutes. His behaviour is at its best if everyone and everything around him is calm and he probably gets his own way most times to keep him calm.

## Can boys ever live independently?

Most boys take care of their personal needs from a reasonably early age. Toilet training appears to be only slightly delayed and daily activities such as dressing, eating and hygiene are reasonably well managed. However, in *Unique’s* experience, the typical behaviour difficulties mean that boys and young men need regular supervision, so that independence may be limited. *Unique’s* members may not be typical of all XYYY men, and it is clear from the medical literature that some XYYY men can live independently and marry (Hori 1988).

## Causes

Rearrangements occur in chromosomes as part of evolution. They affect children from all parts of the world and from all types of background. They also happen naturally in plants and animals. So there is no reason to suggest that your lifestyle or anything that you did would make XYYY syndrome or any other sex chromosome variation more likely.

XYYY syndrome arises from the fertilisation of a woman’s egg with a sperm containing an atypical number of Y chromosomes. Normal male sperm contain either one X or one Y chromosome, and in XYYY syndrome the sperm contains two or three Y chromosomes. Sperm containing additional Y chromosomes can arise in a number of ways. Usually, it is due to a series of mistakes in sperm development where copies of the Y chromosome fail to separate from each other. This is called nondisjunction. Another possibility is that the father has additional Y chromosomes as well, either having XYY chromosomes in all of his cells (XYY syndrome) or in just some of his cells that give rise to the sperm. Sperm containing two Y chromosomes are found in over one per cent of samples from normal adult male sperm donors, so they are fairly common. The father himself usually has normal chromosomes but a mistake has occurred when his sperm were forming. When YY sperm are involved in XYYY syndrome, the third Y chromosome is most likely to result from a mistake in the very earliest days when the embryo is developing after conception (when the baby is made). Typically when the mistake happens after conception, mosaicism is the result, so there may be cells with a single Y, no Y’s, two Ys or four Ys as well.

## Growing up with XYYY syndrome



10 months



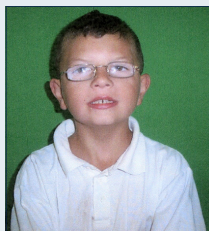
18 months



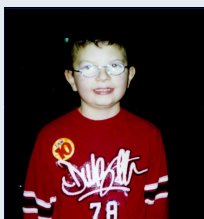
5 years old



9 years old



9 years old



10 years old

## Support and Information



### Rare Chromosome Disorder Support Group,

G1, The Stables, Station Road West, Oxted, Surrey RH8 9EE, United Kingdom

Tel/Fax: +44(0)1883 723356

info@rarechromo.org | [www.rarechromo.org](http://www.rarechromo.org)

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### AXYS - Association for X and Y chromosome variations

[www.genetic.org](http://www.genetic.org)

Unique lists external message boards and websites in order to be helpful to families looking for information and support. This does not imply that we endorse their content or have any responsibility for it.

This information guide is not a substitute for personal medical advice. Families should consult a medically qualified clinician in all matters relating to genetic diagnosis, management and health. Information on genetic changes is a very fast-moving field and while the information in this guide is believed to be the best available at the time of publication, some facts may later change. Unique does its best to keep abreast of changing information and to review its published guides as needed. The guide was compiled by Unique and reviewed by Nicole Tartaglia, MD, fellow in Developmental-Behavioural Pediatrics, UC-Davis Medical Center MIND Institute, and by Professor Maj Hultén BSc PhD MD FRCPath, Professor of Reproductive Genetics, University of Warwick, UK 2005. (PM)

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