**XXYY Syndrome**

XXYY Syndrome (also known as 48,XXYY Syndrome) is a sex chromosome abnormality that affects approximately 1:17,000 males. In the normal individual, there are 22 pairs of autosomes (numbered chromosomes) and 1 pair of sex chromosomes. A normal male has 22 pairs of autosomes (44 total autosomes) and a single X and single Y chromosome, making his chromosomal makeup (called his karyotype) 46,XY. A normal female has the 22 pairs of autosomes and two X chromosomes, making her karyotype 46,XX. In 48,XXYY Syndrome, there is an extra X chromosome and an extra Y chromosome. In addition to the 22 pairs of autosomes (44 total autosomes), males with XXYY Syndrome have 4 sex chromosomes, making their karyotype 48,XXYY. Usually, XXYY Syndrome boys have the extra chromosomes in every cell in their body, but a few have only a percentage of their cells with the extra chromosomes. This is known as mosaicism and may lessen the features of the XXYY Syndrome.

Boys and men with XXYY Syndrome show many features that are similar to males with a 47,XXY make-up (called Klinefelter’s Syndrome) as well as some similarities to males with 47,XYY Syndrome. Until recently XXYY Syndrome was considered a variant of Klinefelter’s Syndrome, but families and doctors have become aware that it has many distinctive features.

**Common features**

Boys and men with 48,XXYY share certain characteristics. However, the features are not obvious in everyone and do not affect everyone to the same extent.

- Tall stature, even when compared to family members, with long limbs.
- Minor anomalies of the skeleton are common including: fusion of the two bones in the forearm (called radioulnar synostosis), prominent elbows, a curved little finger (called clinodactyly), and flat feet.
- General developmental delay. This ranges from mild to severe delays in both the motor and speech areas. Speech and language delay is very common. Some boys are more delayed in their fine motor skills while others have more difficulty learning gross motor skills such as walking and running. Many boys have low muscle tone (hypotonia).
- Cognitive problems ranging from mild learning disabilities to mild-moderate mental retardation.
- Vulnerability to social and behavior difficulties. It varies between individuals, but some boys may be shy or lack social skills. Others have problems with impulsivity, attentional problems, mood instability, and temper tantrums. Some boys also have problems with anxiety.
- Incomplete sexual development. This may be apparent at birth in boys born with small genitalia and/or undescended testes. It may become noticeable at puberty when signs of sexual maturation fail to develop fully. Most boys have a low testosterone level, but there is not enough information to know if all XXYY boys have low testosterone.
- Large teeth (taurodontism) and other dental problems, including frequent cavities, the need for braces or other dental work.
- Poor endurance and lack of energy.
**Diagnosis**

XXYY Syndrome is diagnosed either by prenatal testing during pregnancy or by a blood test which examines the chromosomes (karyotype) of the patient. XXYY syndrome can be diagnosed during pregnancy by examining the chromosomes from the chorionic villi or amniotic fluid. Most babies identified in pregnancy are found by chance when an older mother has an amniocentesis. Occasionally a pregnancy serum screening test may show a raised level of alpha fetoprotein, an early ultrasound may show increased nuchal translucency (an increase in thickness and transparency of the skin over the neck) or a mid-pregnancy ultrasound scan may reveal a structural disorder which triggers testing.

Some boys are diagnosed immediately after birth by blood testing due to physical anomalies such as clinodactyly, small penis, undescended testicles, or a structural heart abnormality. Others are tested later in life for developmental delays, learning disabilities, behavioral problems, delayed or incomplete puberty, or tall stature. Many males may have XXYY Syndrome and remain undiagnosed because some doctors are unaware of the condition and do not do genetic testing for the developmental delays, behavioral difficulties, or physical features seen in this syndrome.

**Physical Growth and Appearance**

At birth, boys with XXYY syndrome usually have normal birthweight and length. However, from an early age boys grow noticeably tall and the extra height is most obvious in their long limbs. Boys with shorter than average parents may not be obviously tall but will still exceed their family norm. They have a tendency to be slightly taller than average in early childhood, and can grow very tall in adolescence, especially if they are testosterone deficient. Most boys reach at least six feet and a few even exceed seven feet.

Also, if testosterone deficiency develops around puberty their body shape may take on feminine proportions, with narrow shoulders and increased weight around the hips and thighs. Testosterone treatment can improve muscle bulk and masculine body habitus if patients are testosterone deficient. The hormone testosterone (either naturally around puberty or given as treatment) helps the closure of the growing ends of the bones (epiphyses) to prevent extreme tallness. The additional height can cause difficulties for boys who have hypotonia (low muscle tone) as it intensifies the apparent floppiness of movement. It also creates difficulties when buying clothes, beds & bedding, and shoes.

The facial appearance of most boys with XXYY syndrome looks very normal. Some boys have small, flattened cheekbones (midface hypoplasia), or wide-set eyes, but this is not usually noticeable to most people. Most people will not be able to tell there are any abnormalities by physical appearance.

**Medical and Dental Problems In XXYY Syndrome**

Boys and young men with XXYY are generally healthy, but associated medical problems have been reported. Description and recommendations are included below.

1) **Asthma and allergies**

Asthma and environmental allergies are common in XXYY Syndrome. Asthma in babies and young children may persist into adolescence. The severity of
asthma varies, and can usually be controlled by standard asthma therapies such as inhaled bronchodilators and inhaled corticosteroids if necessary. Some boys appear to be prone to chest infections in the winter and these can be severe and need hospital treatment. All boys should be fully immunized against pneumococcal infection, pertussis (DTaP), and influenza, as well as all other recommended vaccinations.

2) Orthopedic and Bone Problems
Among boys the most frequent problem is flat feet, sometimes called pes planus. This can cause inversion at the ankles and knock knees (genu valgum) in some patients. The severity varies and while some boys outgrow their flat feet, some need orthopedic insoles. All boys should have a physical therapy or medical assessment to evaluate the need for braces, orthotics, and ongoing physical therapy.

Elbow abnormalities are also common. Many boys have prominent or hyperextensible elbows. In some boys, the prominent elbows are due to radioulnar synostosis (a fusion of the two bones in the forearm near the elbow). This bony abnormality makes it impossible for some boys to rotate the lower arm at the elbow and may also limit the ability to fully straighten the arm at the elbow. This abnormality can create a narrowed “carrying angle”, called cubitus varus. A variety of other orthopedic problems have been observed in men with XXYY, including joint dislocations and spinal curvature (scoliosis).

Low bone density and osteoporosis can develop from testosterone deficiency, as well as from nutritional vitamin and mineral deficiencies. This can predispose to fractures and severe problems as the men age. Most importantly, XXYY males should be followed by an endocrinologist to ensure they are getting appropriate testosterone treatment to prevent osteoporosis. Good nutrition and exercise is also important for healthy bones for XXYY children and adults. To maintain bone density, boys should perform weight-bearing exercise such as running three times a week for 30-60 minutes at a time starting in adolescence. They should also eat a healthy diet that provides the FDA recommendations for calcium, vitamin D and phosphorus.

3. Neurologic Problems
Neurologic problems can also be present in XXYY Syndrome. The most common is a fine hand tremor, which usually develops in grade-school or adolescence. Usually, the tremor is an intention tremor (their hands tremble when they try to perform a purposeful task); but sometimes it is present at rest. The tremor can often make handwriting difficult, contributing to their challenges in the school setting.

Seizures are not universal among boys with XXYY, but they are more common than in the general population. Some boys outgrow their seizures, and others need to remain on anticonvulsant medications for their lifetime. All XXYY families should be taught seizure first aid. If seizures are present, an EEG and MRI are recommended to evaluate brain structure. Neurologic motor tics may also be present. Tics can be treated with medications if they are severe.
In some individuals, neuroimaging has revealed different structural abnormalities in the brain or in the fluid surrounding the brain. One example is agenesis of the corpus callosum (failure of development of the tract of nervous tissue that connects the two hemispheres of the brain). Other patients with areas of cortical atrophy or abnormal cerebrospinal fluid collections have also been described.

4. Heart and circulation
Eight to ten percent of boys with XXYY have a structural heart abnormality. Some examples include septal defects (small holes in the septum of the heart), pulmonary stenosis (narrowing of the artery that takes blood to the lungs), tetralogy of Fallot, and mitral valve prolapse (a weak heart valve on the left side of the heart). All boys with XXYY should have a careful heart exam by their pediatricians, and a cardiology evaluation and echocardiogram (ultrasound of the heart) if a heart murmur or abnormal heart sounds are heard. Also, antibiotic prophylaxis is needed for XXYY boys with certain heart conditions prior to dental visits.

Circulatory disorders are seen in many older boys and men with XXYY Syndrome and worsen with age. Most commonly, circulation to the legs and feet is poor. One study revealed a marked restriction and limitation of the blood vessel network in the lower limbs. Feet with poor circulation also tend to get cold and discolor easily. In older men, this may contribute to ulcers, and careful foot care is imperative. Testosterone treatment may improve the peripheral circulation.

5. Gastrointestinal Problems
Many boys and men will have significant constipation. This can often be helped with a diet that includes drinking plenty of water and high-fiber containing foods. Some boys will need medication to soften their stools and to stimulate bowel activity.

6. Dental Problems
Dental problems can be significant in XXYY Syndrome with many patterns of atypical dental eruption, missing or extra teeth (especially adult molars), severely decayed teeth, or taurodontism (a condition in which the teeth have very large pulp chambers and long roots and where the teeth appear very large). Boys with XXYY should have dental visits every 6 months starting from tooth eruption. They are very likely to need dental surgery and orthodontia.

Sex hormones, Puberty, and Testosterone Treatment
The extra X chromosome in XXYY Syndrome is responsible for the pubertal problems and testosterone deficiency. In boys with an extra X chromosome, the testicles are normal at birth but usually undergo fibrosis as they grow. It is unknown why this occurs. The testicular cells called Leydig cells that usually make testosterone are destroyed as the boy grows.

The amount of testosterone in the body is measured from a blood test. In normal 46,XY males, testosterone is usually produced in response to rising levels of two
pituitary hormones released from the brain called luteinizing hormone (LH) and follicle stimulating hormone (FSH). In males with 48,XXYY levels of these hormones may be high as the pituitary gland tries to stimulate the testicles to make testosterone, but levels of testosterone remain low (this state is called hypergonadotrophic hypogonadism).

Before puberty, testosterone levels in boys with XXYY are usually normal. It is assumed that boys with a small penis or undescended testes at birth may have experienced testosterone deficiency before birth, but even this is not certain. Some endocrinologists will treat XXYY males with a short penis with small doses of testosterone in infancy to increase penile length.

During childhood or puberty, other signs of testosterone deficiency may emerge: boys may grow some breast tissue (gynecomastia), the long bones in their arms and legs may grow disproportionately long, their muscles may be less developed compared with other boys, and they may have severe fatigue and mood instability.

The timing and degree of changes at puberty varies in XXYY Syndrome. Most commonly puberty starts at a normal age or slightly late but it remains incomplete because not enough testosterone is produced. In some boys, puberty develops at the normal time and at a normal pace. Occasionally, it starts early (called precocious puberty). If secondary sex characteristics (growth in penis size, male hair distribution) do not develop or if puberty remains incomplete, testosterone replacement therapy can be given by injection, patch, or gel. It is very important to know that testosterone treatment in XXYY Syndrome has NOT been shown to lead to any increase in aggressive behavior.

Boys with XXYY Syndrome should be seen by an endocrinologist at approximately 9-10 years old, and followed through puberty for the high possibility of testosterone deficiency. There is no established protocol for when to start testosterone treatment in boys with XXYY Syndrome. Some endocrinologists start all XXYY boys on testosterone replacement at a certain age, others base their treatment on symptoms, and others treat boys according to the levels of testosterone, FSH, and LH found in their blood.

Testosterone can be given by injections (every 2-4 weeks), by patch, or by gel. Different endocrinologists use different types of testosterone. There used to be testosterone pills available, but these were found to cause liver damage and are no longer recommended. Testosterone replacement also prevents some consequences of deficiency, such as osteoporosis and muscle wasting. Treatment has also led to improved activity levels and less fatigue in some adolescents. Many boys have also had improvement in mood instability and behavioral problems after starting testosterone.

Normal boys with 46,XY chromosomes typically experience a ‘mini-puberty’ with a small surge in testosterone at around 3 months of age. Some endocrinologists treat all babies with an extra X chromosome with 3 low-dose injections of testosterone in infancy to reproduce this “mini-puberty”. This practice is controversial because the positive effects are unclear, and the importance of this “mini-puberty” is also unclear. The benefits and harmful effects of extra testosterone in infancy are also unclear.
**Feeding Problems and Eating in XXYY Syndrome**

Feeding problems may occur in XXYY Syndrome but they do not affect all boys. Some babies are slow to latch on and suck and those with hypotonia may also be affected by gastroesophageal reflux (spitting up). Occasionally boys have difficulty co-ordinating breathing, sucking and swallowing and a small number of boys require feeding by nasogastric tube for a short time after birth. Some boys and men are reluctant to chew or find it very difficult and prefer to be fed soft foods. Reluctance to chew sometimes results from a sensory integration problem. Sensory integration disorders - where children over- or under-respond to sensory stimuli - have been diagnosed in many individuals with XXYY Syndrome. Some occupational therapists have specific techniques which address sensory integration issues and this should be encouraged for XXYY children with sensory and feeding issues. This diagnosis is still slightly controversial and trials on the effectiveness of sensory integration therapies are still in progress. Conventional approaches such as speech therapy and traditional occupational therapy should be used in addition to sensory integration therapies.

**Speech and Language Development**

Boys with both 47,XXY and 47,XYY have a specific speech delay and this is also evident in boys with 48,XXYY. Speech development is usually delayed but usually begins at 2-3 years of age. It may be much later in some XXYY boys. Speech therapy should be aggressive in all XXYY boys with speech delay, and should be available through government early-intervention programs and/or the school system. Many boys will benefit from learning sign language until their speech becomes fluent enough for them to communicate their needs and wishes. Speech therapists and other professionals should investigate the use of assistive technology for language and communication in XXYY children.

Most boys have better language comprehension skills than language expression, but both areas are affected. Specific difficulties have been recorded in word retrieval, short term memory, sentence structure, volume, articulation, dysarthria (unclear pronunciation), dysphasia (failure to arrange words in proper order) and dyslexia. It is important that concepts and instructions be delivered singly and sometimes reinforced by visual prompts, allowing time to process the information they have heard.

As adults, most XXYY men are able to express themselves but they may prefer to use shorter phrases, choose from a limited vocabulary, stumble over words and continue to have difficulties with understanding.

**School and Learning**

The spectrum of effects of sex chromosome variations on children’s ability to learn is extremely broad. There is a rule of thumb that with each extra chromosome, overall IQ falls by 10-15 points – a difference that is often noticeable from their brothers and sisters with no chromosome abnormality. Many boys with both XXY and XYY chromosomes have no discernible learning disability. Others encounter specific problems particularly in the early years of education and while acquiring the language-based skills of reading and writing. Other boys find it hard to meet the behavioral expectations of a school setting.
Boys with 48,XXYY have features of boys with both 47,XXY and 47,XYY and as a group show more difficulties with learning. Overall, around 10 per cent of boys have an IQ within the normal to above-average range, while most have a mild learning difficulty. Psychological testing shows that performance IQ is typically higher than verbal IQ, although this is not universally true. Because of problems with verbal comprehension, many boys with 48,XXYY boys are visual learners who frequently have difficulties processing auditory information. Particularly where boys have problems with expressive or receptive language, it is important that visual aids and other non-verbal strategies are chosen.

In general boys achieve more if tasks are broken down into manageable components. Many boys are prone to sensory overload and respond well to a clear learning structure with small group and individual teaching. Most boys are sociable and their wish to please is helpful in an educational setting as is their characteristic determination and strong will. Memory skills are highly variable but some boys have strong visual memories for skills like route-finding and puzzles.

Although many boys have social difficulties that suggest an autistic spectrum disorder, only a small percentage are diagnosed with autism. Those boys diagnosed with autism in addition to XXYY also need specific treatment for autism. The social development and rates of autism in males with XXYY Syndrome is currently being studied.

If young boys have the hand tremor and poor coordination commonly seen with XXYY Syndrome, handwriting can be difficult and very messy. These boys need access to a keyboard from an early age and other alternatives to writing.

The best schooling for boys with XXYY Syndrome depends on his abilities and what is offered locally. Many boys start their education in mainstream (regular) schools, and profit from one-on-one support being available when needed. They may need to be withdrawn for language activities or other special classes. As the curriculum becomes more demanding, most boys transfer to a special education setting where their individual needs can be met better. For more severely affected individuals, intensive treatment and special classrooms may be needed, especially if autism is present. There is not yet a model IEP for XXYY Syndrome.

**Motor Skills**

Muscle tone, balance and coordination are often affected and may delay the average age at which boys reach their motor skill milestones. In addition, lack of muscle mass can lessen strength and stamina. Hypotonia (low muscle tone) is most significant in infancy and childhood and may improve with exercise and maturity, but it also may persist into adulthood. Occupational and Physical therapy help to improve muscle tone and to advance skills in movement.

Many boys can develop into agile movers, but coordination problems can affect activities such as football and other ball games. In general, many adolescents and adults with XXYY prefer to stay fit with activities such as walking, cycling, and swimming.
Exercise is important to XXYY boys who share with 47,XXY boys a tendency to put on weight around the midriff and potentially to develop type II (non insulin dependent) diabetes. Regular exercise also helps to build up muscle mass and to preserve bone density which can be compromised by the low testosterone levels. A common problem is that boys tend to tire quickly and may need frequent rests.

Support Services
Once diagnosed all XXYY males should have a full evaluation by a developmental pediatrician. Early intervention programs are necessary, and should include evaluations to determine if speech therapy, occupational therapy, physical therapy, behavior management therapy and early preschool programs are necessary. Many boys with XXYY will not need the full range of therapies, but it is important to have a detailed evaluation of their needs. Early intervention is known to improve the speech and language problems of boys with XXYY and may also help with any social and behavioral concerns. In general, the most affected individuals will need all of the services above, which can take an extreme amount of dedication and organization by the caretakers.

Behavior in XXYY Syndrome
All boys with XXYY chromosomes are vulnerable to behavior difficulties although not all of them will develop problems. Even allowing for ascertainment bias – the families that doctors see and report on tend to cluster at the severe end of the spectrum – the effect of the extra chromosomes on behavior does appear to be very common. The behavior difficulties are attributed either to the additional Y chromosome (because they are not seen typically in boys and men with XXY chromosomes) or to the fact that there are two extra chromosomes (gene dosage effect).

Our experience and evidence from the medical literature suggests that typically, as babies, the boys are relaxed, easy-going and even sometimes passive. Passivity can develop into a problem if it continues into childhood and adolescence so that boys need to be persuaded or coerced to perform tasks like washing, cleaning their teeth, making new friends, etc. As toddlers, boys seem often eager to please, but are easily frustrated, especially when they cannot communicate their needs and wishes, when they face problems they cannot deal with, or when they do not have their needs met. They can sometimes have self-injurious behaviors such as head-slapping or head-banging as young children.

By early to mid-childhood a personality unfolds that is typically sweet and loving and among older boys and men a disposition that is happy, friendly, and helpful. Easily frustrated and impulsive, however, boys are prone to mood swings and temper outbursts that can be extreme. They can challenge authority and when swept up in an outburst or when reacting to a stressful situation, boys may be aggressive, destructive, verbally offensive or unmanageable within a conventional educational or social setting. In this context, they may self-harm. Among adults with XXY, the extreme tantrums may persist in a milder and more manageable form as men gain greater understanding of their own behavior and acquire greater verbal fluency.

Parents should be prepared for this by learning behavior management techniques when their son is still young. Parents and their pediatricians should seek out parenting classes, behavior therapy, etc to establish strong skills early before
problems emerge. Behavior management therapists are often available through the community or the school setting and should be utilized as soon as behavioral problems arise.

A number of boys show features of Asperger’s syndrome or an autistic spectrum disorder. In these cases, their behavior includes a need for routine and inflexibility in adaptation. These boys also may have repetitive behaviors, interests unusual in their intensity, and obsessions with objects or parts of objects. Specific treatment for autism is very important if it is present.

Some boys have a short attention span although hyperactivity is not universal. Many boys also have a diagnosis of Attention Deficit Hyperactivity Disorder. Some boys also have tics or repetitive behaviors and many have a tendency to chew their nails, their clothes, or other objects.

Some boys have repeatedly run away and need close supervision, as they may not understand the full impact of dangers around them. Others can tell “tall tales” to try to fit in with others or to get out of trouble, but often tell the truth when questioned appropriately or when a stressful situation calms down. It is important to know that not all XXYY boys have the behavioral problems above. Each XXYY boy is different with their own behavioral strengths and weaknesses, just like typical XY boys have differences in their behavior.

It is important that caretakers understand the common behavioral problems in XXYY Syndrome and provide a stable home environment and consistent parenting and guidance. There are longitudinal medical studies that show that a stable and supportive home environment can prevent poor social outcomes and severe behavioral problems in children with sex chromosome abnormalities.

Outcomes are very dependent on the intervention received and the timing of the intervention. Boys who receive early intervention and appropriate medical treatment do better in their language development and their social development. Boys who have a late diagnosis or who do not receive the appropriate hormonal and psychopharmacologic treatments have a much harder time.

Approaches that parents have found successful in managing their son’s behavior include:

- A behavior plan developed specifically for the child by a psychologist/behavior therapist, and implemented in the home and school setting
- Medication. ADHD, anti-anxiety, and mood-stabilizing medications can be helpful in controlling extreme behaviors but these medications have side effects and should be discussed in detail with the child’s psychiatrist or pediatrician. Medications that have been used successfully for other boys include methylphenidate/Ritalin (slow-release as well as fast-acting), Adderall, sertraline (Zoloft), fluoxetine (Prozac) and risperidone.
- Seeking behavior support at the earliest signs of disturbance. Persisting until understanding and competent therapists are found.
- Clear routines, a calm and supportive environment
Social Interactions

In childhood, many boys show awkward and/or immature social skills and may interact better with people older or younger than themselves. As a group, they are generally sociable and want social contact but may have difficulties initiating and managing it with their peers. Their language delays and poor auditory processing can contribute to their social difficulties. They may show poor judgment of other people’s feelings and fail to pick up on social cues. They sometimes act as if they are a few years younger than their actual age. Some boys are shy and introverted at school, while others are more outgoing and gregarious.

Boys benefit from exposure to social opportunities with peers, both peers with developmental delays and typically-developing children. This helps them learn to interact with their peers in controlled and somewhat supervised contexts such as playgroups, after-school activities, sports teams or clubs. They should engage in activities that they are good at to build their self-esteem. For boys with moderate social difficulties, many schools and organizations have specific interventions to teach social skills to children and young adults with developmental disabilities, and these can be very helpful for XXYY boys.

Psychiatric illness in XXYY Syndrome

The most common mood problems in XXYY Syndrome include problems with anxiety, and sometimes depression. A very small percentage of adolescents and men with XXYY have been reported to have more severe psychiatric illness, specifically bipolar disorder and schizophrenia. It is most likely that the psychiatric illness is a chance association, and not caused by XXYY Syndrome itself. Overall, mild depression and anxiety are much more common in XXYY Syndrome than bipolar disorder and schizophrenia.

Sleep problems in XXYY Syndrome

Sleep disorders have not been systematically studied, but they are believed to be more common in XXYY boys. A minority of boys have severe sleep difficulties. These may develop in childhood but more typically progress in adolescence, with many families of adults with XXYY reporting that their sons stay up very late at night and then are very difficult to arouse in the morning. Other XXYY boys have been diagnosed with narcolepsy, as well as excessive sleep talking, sleep apnea, problems falling asleep or a very rapid descent into sleep (short sleep latency). Firm, consistent sleep routines from the infancy are helpful but some families will need specialist sleep training and for others medication may be helpful.

Strengths in XXYY Syndrome

With their strong visuo-spatial abilities and sometimes good memory skills, boys with XXYY are relatively good at activities such as board games, computer games and direction finding. Some have a talent for chess or art. Among the activities that they enjoy, computer games are favorites, closely followed among younger boys and adolescents by sports activities including cycling, walking, swimming, fishing, many ball games including soccer, basketball and baseball, and water sports. As a group they are also affectionate, friendly and non-judgmental and can be generous with their time, making themselves available to help others in need. They
can also be very thoughtful, caring and considerate, particularly to other people with special needs.

**Fertility in XXYY Syndrome**
The additional X chromosome impairs sperm production and the semen of men with 48,XXYY generally contains no sperm. There have been no reported fertile males with XXYY Syndrome. Treatment with testosterone does not improve fertility or increase testicular size. Although men are not fertile, they may be sexually active.

**Causes of XXYY Syndrome**
In almost all cases, the parents of boys with XXYY syndrome have a normal number of chromosomes themselves. The cause of the extra chromosomes is almost always a biological mistake that occurred during the formation of the father’s sperm. It is possible that there was a problem that occurred during the formation of the egg or very early after fertilization as well.

When sperm or egg cells are forming, the two members of each pair of chromosomes usually separate so that each sperm or egg contains 23 chromosomes. Sometimes one pair of chromosomes fails to separate. This is called non-disjunction of the chromosomes. The extra chromosomes in boys with XXYY syndrome are assumed to have come from the father and the extra X chromosome from the mother but this has never been shown to occur in boys with XXYY syndrome. Non-disjunction is more common in older mothers, but not in older fathers and the cause is not understood. There is also a very small possibility that XXYY Syndrome is transmitted from a father who himself has 47,XYY Syndrome. There is no evidence that XXYY Syndrome is caused by something the parents did before or during the pregnancy. It has not been associated with environmental or drug/alcohol exposures, illness, or medications. At this time, there is nothing we know of that parents could have done to prevent XXYY Syndrome.

Most XXYY syndrome occurs by chance so it is unlikely that it will occur in a subsequent pregnancy. However, some parents choose to have a test of the baby’s chromosomes in their next pregnancy.