Frequently Asked Questions About 47,XXY

**[What is the Usual Phenotype (expressed physical traits) of 47,XXY?](javascript://)**

From the NIH Genetic and Rare Diseases Information Center:

“47, XXY refers to the presence of an additional X chromosome in a person's body cells. Some individuals with a 47, XXY chromosome finding do not appear different from other individuals, and they may have mild symptoms or no apparent symptoms. During the first few years of life, most 47, XXY individuals do not show any obvious differences from typical male infants and young boys. Children may have slightly weaker muscles, delayed development of motor skills, and learning and/or language problems. In later adolescence and adulthood, 47, XXY individuals can have features of Klinefelter syndrome, which can include primary hypogonadism (decreased testosterone production), small testes, enlarged breast tissue (gynecomastia), tall stature, and/or other features. Although the vast majority of individuals with 47, XXY identify as males, some develop atypical gender identities. There have been reports of individuals with 47, XXY having a female physical appearance, but in most cases this was attributed to changes in specific genes related to sexual development. Most 47, XXY males are infertile, but many produce sperm and may be able to conceive with assisted reproduction. Treatment varies among individuals and may include testosterone therapy; however, this therapy may not be appropriate for all individuals.”

[**http://rarediseases.info.nih.gov/gard/11920/47-xxy/resources/1**](http://rarediseases.info.nih.gov/gard/11920/47-xxy/resources/1)  
  
(See FAQ Item: "A Brief Note on Gender and Identity")

**[[http://www.genetic.org/images/action.gif](javascript://)What about disclosure to relatives, schools, employers and romantic partners?](javascript://)**

Before disclosing a diagnosis to relatives, such as grandparents, determine whether they are likely to be supportive and tolerant of a range of learning disabilities and other possible health and behavior problems.  It is reasonable to wait with a prenatal diagnosis until some developmental delay presents, and an explanation to grandparents or to siblings is necessary.

A significant factor in disclosure is the need for social benefits and supports.  Most accommodations of any type have their basis in the American’s with Disabilities Act.  The XXY individual may not be disabled and yet still qualify for services and accommodations.  For example, an XXY may benefit from the protections and supports afforded by an IEP or 504 plan in school.  In the case of a child with language, physical, learning or behavioral difficulties, disclosing the chromosomal condition to relatives is often reasonable and reassuring to them.  It is important to know as much information as possible so that you can address concerns, particularly where the relative has heard one of the myths about 47,XXY.  Some of the myths about 47,XXY are that XXY causes intellectual and developmental disabilities (previously called mental retardation), increased criminal behavior, or that individuals with 47,XXY are actually women.

It is important to emphasize that most XXYs have IQ’s between 85 and 120 although some individuals with more than two additional chromosomes may have intellectual and developmental disabilities.  In addition, XXYs as a group actually have lower than expected rates of criminal convictions, when compared with the general population of males.  And, while respecting those XXYs who identify as a different gender, the presence of a Y chromosome almost always determines that a human develops as a male, although there are some syndromes (not related to 47,XXY) where a human with a Y chromosome may develop as a female, rather than as a male.  As mentioned previously, a minority of XXYs identify as another gender or intersex.

Disclosure to an employer is rarely necessary unless the employee is seeking employment through a supported work program or is seeking some other special accommodations under the ADA.  Genetic information should remain private because disclosing such information may make obtaining health or life insurance difficult.  Employers or others may make unjustified assumptions that certain myths (cited above) are true for persons with 47,XXY.  In some cases, however, it may be necessary in order to obtain Federally-mandated Family and Medical Leave, or some other benefit such as disability coverage or an accommodation under the Americans with Disabilities Act (ADA).

Disclosure to the school is only necessary if there are significant learning or behavior problems that require special education classification, such as an IEP or Section 504 accommodation.  Schools will often be unaware of the condition, and staff will need to be educated about XXY, usually by the parent.  Bring a selection of website printouts explaining the condition and its impact on learning.  Some parents have found that special education services are more likely to be appropriate when the pediatrician provides a diagnosis under the classification of “other health impaired” such as Pervasive Developmental Disorder-NOS (PDD), rather than 47,XXY.  Schools understand autistic-like behavioral and language difficulties when they occur in high-functioning children and many schools have programs in place to address these problems.  In addition, these programs are mandated in many states for children with autism spectrum disorders of which PDD is one.  The schools may not realize that XXY children often have the same deficits and are also eligible for these services.

To access these accommodations, parents are well advised to learn the glossary of key terminology that “pushes all the right buttons” that qualify the student for these supports.  It also may be helpful to recruit local disabilities advocates, such as the ARC, to assist with the qualification process.

Individuals with 47,XXY fall in love and the condition, as any other medical condition, should be discussed at the right time.  It certainly is not necessary in early dating, but at the point at which the relationship becomes “serious”, disclosure as well as a thorough education about the disorder should take place.  Support groups and list-serves can introduce couples to others who have been through building a relationship and a family; this is one occasion on which support from others in the same situation can be very helpful.

**[[http://www.genetic.org/images/action.gif](javascript://)What is 47,XXY?](javascript://)**

47,XXY, also commonly referred to as Klinefelter Syndrome, is estimated to occur in 1 out of 600 males, making it the most common chromosomal disorder.  Rather than the usual pattern of 46 chromosomes, with one X chromosome and one Y chromosome, there is an additional X chromosome, resulting in a genetic signature of 47,XXY.  This happens when paired chromosomes fail to separate at the first or second stage of meiosis.  The exact cause is unknown.  The extra chromosome can come from either parent; there is little relation to either maternal or paternal age.  An extra chromosome in a pair (ie the X and Y chromosomes) is called a *trisomy*.  47,XXY, unlike most trisomy conditions, is highly survivable for the fetus and causes symptoms that vary greatly from one person to another.    An extra or missing sex chromosome yields a syndrome called *sex chromosome aneuploidy.*  A syndrome is a collection of symptoms and physical signs.  In some individuals, the manifestations of 47,XXY are mild and barely noticeable while in others, there is more severe symptomatology.

**[[http://www.genetic.org/images/action.gif](javascript://)A brief note on Gender and Identity](javascript://)**

**AXYS celebrates the diversity of the human family; including sex and gender, skin color, ethnicity, religion, sexual orientation, gender identity, age, socioeconomic status, physical characteristics, and mental abilities.  While the majority of 47,XXY individuals we serve identify as male, a minority identifies as “intersex” or another gender.  Many also consider themselves as “being XXY” rather than “having XXY.”  Out of respect for these individuals, we have attempted to minimize gender references, and, where practical, we have called individuals XXYs and stated that they “are XXY.”**

**[[http://www.genetic.org/images/action.gif](javascript://)What are the symptoms of XXY?](javascript://)**

It should be emphasized that most XXYs have some, but not all, of the symptoms of 47,XXY, and that symptoms vary greatly from one individual to another.  Klinefelter Syndrome is a term to describe a bundle of symptoms often associated with 47,XXY.  Not all XXYs have Klinefelter Syndrome, and Klinefelter Syndrome is sometimes used to describe the symptoms associated with other conditions.  They are not interchangeable terms despite the fact they are often used interchangeably.

One of the most fundamental and prevalent symptoms of 47,XXY is hypogonadism.  In XXYs, hypogonadism manifests as small, firm testes, near infertility and inadequate levels of testosterone.  Hypogonadism can also lead to delayed or incomplete puberty, sparse facial and body hair, female pattern body-fat distribution, gynecomastia (breast development, long limbs and poor coordination.  A small number of individuals may have micro-penis, which can be partially corrected with testosterone therapy at “mini-puberty” as a toddler.  Untreated, hypogonadism can also contribute to problems with concentration, mood swings and other emotional and behavioral difficulties.  It can also lead to a number of comorbid conditions, such as osteoporosis, that can be prevented with testosterone hormone replacement therapy (HRT).

Numerous other symptoms can be associated with 47, XXY and its related variations.  Many individuals exhibit several of these, but each person is different.  Other symptoms may include:

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| **Pre Puberty** | | **Post Puberty** |
| Speech/Language Difficulties | Low muscle tone (hypotonia) | Gender identity issues |
| Autism Spectrum Disorders or Asperger’s Syndrome | Pervasive Developmental Disorders | Low testosterone levels |
| ADD/ADHD | Sensory Integration Problems | Stalled Puberty |
| Learning Disabilities | Impulse Control Difficulties | Higher risk for autoimmune disorders |
| Obsessive Compulsive Disorder | Poor Social Skills and Delayed Social Development | Near infertility that advances with age and HRT (see section below) |
| Anxiety | Low Self Esteem | Osteoporosis |
| Depression | Immaturity | Ineffective coping strategies |
| Shyness | Taurodontism | Depression |
| Clinodactyly | Pectus excavatum | Greater risk for developing diabetes |
| Radio-Ulnar Synostosis | Hypospadias | Difficulty with interpreting or reacting to social cues |
| Micro-Penis (Rare) | Torticolis | Difficulty with expressing emotions |
| Cryptorchidism | Low energy | Challenges with employment |

**[[http://www.genetic.org/images/action.gif](javascript://)How is 47,XXY diagnosed?](javascript://)**

Because the condition is characterized by an extra chromosome, cells must be obtained, prepared and observed to count the extra chromosome.  Generally, a specialized blood test, called *karyotyping (a karyotype)*, a new buccal swab test called XCAT, or in some cases, *FISH* (fluorescence in situ hybridization), or microarray analysis is performed to look for chromosomal abnormalities.  Any physicians, including family physicians and geneticists, can order genetic testing when a chromosomal or genetic condition is suspected or needs to be ruled out.

Some pregnant women who have specific risk factors or have other concerns regarding possible genetic conditions have invasive prenatal testing during pregnancy.  The two invasive prenatal tests available are *amniocentesis* or *chorionic villus sampling*.  These tests provide cells from the fetus that can be studied to detect extra chromosomes.  A new, noninvasive prenatal test is also available.  Because most pregnant women do not have invasive prenatal testing during pregnancy, only about 10 percent of cases of 47,XXY are detected prenatally.

**[[http://www.genetic.org/images/action.gif](javascript://)What is the prevalence of 47,XXY?](javascript://)**

There is some debate about the prevalence of 47,XXY.  Studies have demonstrated between 1 in 500 and 1 in 800.  A large-scale genetic screening of over 40,000 newborns in Denver demonstrated a rate of approximately 1 per 600 male births.  Longitudinal population studies in the Netherlands have confirmed these estimates.  47,XXY is more common than Down Syndrome.  It is estimated that only 35 percent of all XXY individuals are ever diagnosed, due in part to the subtle and varying physical and psychological symptoms, and in part to a lack of training in medical schools about sex chromosome aneuploidies and their diagnosis and treatment.

**[[http://www.genetic.org/images/action.gif](javascript://)What are variant karyotypes of 47,XXY?](javascript://)**

Approximately 80 percent of those with 47,XXY have the 47,XXY genetic signature.  In the other 20 percent, there may be more X and Y chromosomes, with genetic signatures of 48,XXXY, 48,XXYY, and 49,XXXXY.  Or, individuals may have a mix of cells within the body, some XY and others XXY, which is called *mosaicism*.  Some individuals have a genetic signature of 46,XX, but have a tiny piece of the Y chromosome appended to one of the X chromosomes, giving them male genitalia and secondary sex characteristics, such as facial hair and male muscle development.

47,XYY is incorrectly associated as a variant of 47,XXY, but it is actually a distinctly different sex chromosome aneuploidy.  The most obvious difference is that 47, XYY males have none of the medical and infertility issues that individuals with 47,XXY may have, although there can be behavioral difficulties and learning disabilities associated with XYY.

**[[http://www.genetic.org/images/action.gif](javascript://)Are all XXYs infertile?](javascript://)**

In general, yes, but with notable exceptions:

* Individuals with XXY/XY mosaicism may produce enough viable sperm to be biological fathers without requiring infertility treatment.
* In the last decade, with the use of reproductive technology advances, a number of XXYs have achieved biological fatherhood.  This can be an expensive process, ranging from $20,000 per attempt (2011 dollars).  Typically three techniques are required:

**a.** TESE:  *testicular sperm extraction* typically involves harvesting sperm directly from the testes;

**b.** ICSI:  *intracytoplasmic sperm injection* is an in vitro technique in which individual sperm are injected into ova in a Petri dish to create embryos

**c.** IVF:  *in vitro fertilization* then implants the fertilized egg into the womb

Time is of the essence for XXYs considering reproductive therapies.  Hormone replacement therapy must be managed very carefully to avoid total suppression of sperm production and the availability of viable sperm declines rapidly with age.  Parents of adolescents are advised to explore fertility questions with a qualified fertility clinic soon after puberty.

It’s also important to note that most XYYs are capable of having a normal, satisfying sex life despite their infertility.  Many XXYs are parents via adoption, donor sperm and other techniques commonly employed by other families facing fertility issues.

**[[http://www.genetic.org/images/action.gif](javascript://)Will an XXY child look any different from one with 46 chromosomes?](javascript://)**

Babies who are 47,XXY rarely have any obvious physical differences, which is the reason that so few children are diagnosed soon after birth.  However, a baby may have very low muscle tone *(hypotonia),* or (rarely) an extremely small penis *(micropenis)* that may cause a pediatrician to suspect a genetic problem.  A condition known as *torticolis,* in which the baby’s head and neck are slightly twisted to one side, may be present.In children with 48 and 49 chromosome variations, there may be more pronounced physical signs including facial abnormalities or ambiguous genitalia that indicate a possible chromosomal or genetic condition.

**[[http://www.genetic.org/images/action.gif](javascript://)How does XXY affect children and adolescents?](javascript://)**

Children with 47,XXY may be language delayed, and have poor muscle tone, leading to poor fine and gross motor skills.  They may be shy and very hesitant about any new experiences, such as pre-school or new foods.  Children who are 47,XXY can seem immature by comparison with other children their age, and their limited verbal skills may contribute to difficulty in play situations.  Many XXY children have poor impulse control and attention deficits, which may be diagnosed as *attention deficit disorder* or *attention deficit hyperactivity disorder* (ADD or ADHD).  There is much anecdotal evidence that because XXY children may have social skill deficits, poor verbal abilities, shyness to the point of avoiding eye contact, and rigidity and inflexibility in their play patterns (ie insisting on lining up all car and truck toys, and becoming upset when the toys are disturbed) as well as interactions with other children and adults, an initial diagnosis of an *autism spectrum disorder*, such as Asperger Syndrome or Pervasive Developmental Disorder, is made.  47,XXY is not an autism spectrum disorder, even though there appears to be significant overlap of symptoms.  Children who are XXY may need special supports in school, including the protections of an IEP or 504 Plan.  They may also benefit from a teaching aide, protection from bullying and special accommodations such as  “self-imposed time outs.”

A developmental pediatrician or geneticist will often recognize the subtle physical signs of 47,XXY in a child initially diagnosed with learning disabilities, ADHD, and/or an autism spectrum disorder, leading to genetic testing and a more complete diagnosis.   Small testes, a smaller-than-average penis, *hypospadius* (urethra located on the shaft of the penis) or *chryptorchidism*(undescended testicle) are included in these physical signs.  Other signs include an arm span measure that is greater than the child’s height, and a significant acceleration in height percentile around the age of 6 or 7 years.  Another body disproportion that may be present is leg length (foot to waist) that exceeds head to seat measurement.  Some XXYs may have *clinodactyly* (slightly curved fifth finger), *pectus excavatum* (a depression in the chest over the sternum), *radio-ulnar synostosis* (inability to completely straighten the elbow joint), or *taurodontism* (relatively thin enamel on the tooth with a large, pulpy root area).  For adolescents ages 13 or over, failure to begin puberty or to progress through puberty completely may alert the pediatrician to consider and test for 47,XXY.

**[[http://www.genetic.org/images/action.gif](javascript://)Is early intervention effective in reducing developmental delay in XXY children?](javascript://)**

Early intervention appears to be very effective in reducing delays in development of both motor skills and language.  Children who are diagnosed prenatally or in infancy may begin receiving services within the first year if they show early delays in motor skill acquisition.  For children who have not been diagnosed, families may be wrongly reassured that “He will catch up-boys are slower”.  Children who are not meeting speech, motor and social developmental milestones on pediatric screening instruments need to be evaluated further by a developmental pediatrician or a child development center.  Parents are encouraged to insist on evaluation where development is progressing slowly because these children rarely “catch-up” without intervention services.

**[[http://www.genetic.org/images/action.gif](javascript://)What treatments are available for 47,XXY?](javascript://)**

Adolescents who have reached the age of puberty and adults often require supplemental testosterone because their bodies make insufficient hormone to help them develop male secondary sex characteristics such as facial hair, a deep voice, and male pattern muscle and fat distribution.  Those who identify as another gender are encouraged to seek the guidance of an endocrinologist to mitigate the risks of low testosterone.  Testosterone, however, does not correct infertility.  Testosterone may also be needed to help to increase and maintain bone density at normal levels, to create sexual desire and capacity for erections, and to build muscle mass.  Individuals whose testosterone levels are low may feel fatigued, anxious and depressed.  Testosterone treatment is a very individualized therapy and should be overseen by an endocrinologist who can use blood levels and the patient’s reports of well-being to adjust the dosage properly.  Children who are reaching adolescence should be evaluated by a pediatric endocrinologist who can determine when hormone therapy should begin, generally between the ages of 9 and 13, depending on bone development and blood tests.

Testosterone can be injected every 10 days to 3 weeks.  It is also available as a gel applied daily to the shoulders or abdomen, or as an adhesive patch worn daily.  Oral testosterone tablets are not recommended because they can cause liver problems.  There are on-going clinical trials of a buccal dissolving tablet, placed between the gum and cheek.  Implanted pellets that slowly deliver testosterone over several months have recently been approved for use in the US.  Recently, an underarm roll on testosterone applicator was introduced in the US.

In infancy, the only treatments that may be indicated are several injections of testosterone within the first 3 to 4 months, especially if the child has a very small penis.  In 46,XY infants, there is an initial spike of testosterone production, called mini puberty, during this period that babies with 47,XXY may not produce.  After this spike in testosterone production, virtually no testosterone is produced again until the start of puberty at the age of 9 to 11.

The symptoms of 47,XXY can be treated and managed in childhood with occupational, physical and speech therapy as well as counseling and social skills training.  Special education accommodations and teaching methods can help achieve academic success despite learning disabilities.  An increasing number of colleges and vocational schools have instituted programs to help those with learning disabilities to obtain degrees and credentials necessary for careers.  Parents are encouraged to explore the benefits and protections afforded by an IEP or 504 plan, covered elsewhere in AXYS’s library.

**[[http://www.genetic.org/images/action.gif](javascript://)Are there special issues that should be considered with adolescents and young adults regarding maturity and decision making?](javascript://)**

There is current research that indicates some 47,XXY individuals may experience delayed maturation relative to brain development associated with executive decision-making. This may be more prevalent with individuals that are not diagnosed at an early age and do not receive testosterone hormone replacement therapy. Anecdotal reports indicate there may be a 5+ year delay between chronological age and maturational age for many of these individuals which can be very difficult to diagnose or measure objectively. It is a well-known fact that teenagers in general can demonstrate very poor decision making relative to risk-taking behavior and some XXYs may benefit from stronger guidance and careful parenting for longer periods (ie, into their late teens and twenty’s) to prevent serious legal and social problems.  For those XXYs with tall stature, society may be slow to recognize this immaturity and fail to make needed accommodations.

**[[http://www.genetic.org/images/action.gif](javascript://)Are there health risks associated with 47,XXY?](javascript://)**

Hypogonadism associated with 47,XXY can lead to a host of comorbid conditions.  None appear at alarmingly high rates, but some are three to five times more prevalent among XXYs that among XY men. Among the more common medical complications are *osteoporosis,* a thinning of the bones making fractures more likely, and *autoimmune disorders* such as rheumatoid arthritis, lupus, and Type 1 diabetes.  XXYs, particularly those who have not had testosterone supplementation, may suffer from *venous ulcers*.  Thyroid disorders are also more common than usual.  XXYs are more likely to suffer from seizures.  Mood disorders, including *depression and bipolar disorder*, appear to be much more common among XXY individuals than in the population as a whole, although this has not yet been studied rigorously enough to quantify.  Studies are underway to determine the impact of testosterone therapy on reducing the risks of these complications.

AXYS is developing a comprehensive summary of comorbid conditions associated with all X and Y chromosome variations.

**[[http://www.genetic.org/images/action.gif](javascript://)What is gynecomastia?](javascript://)**

Gynecomastia is the development of breast tissue.  In XXYs, this is related to hypogonadism.  Most males develop some gynecomastia in adolescence that resolves in the mid-teens.  In some XXYs, the breast development is pronounced and becomes both embarrassing and uncomfortable.  Approximately one-third continue to suffer from significant gynecomastia after adolescence.  Many opt for surgery to remove the excess breast tissue and create a normal male chest profile.  Gynecomastia slightly increases the risk of breast cancer from less than 1 % for the male population overall to 3.7%.  All XXYs should perform regular breast exams for any nodules.  Mammograms are not medically indicated for XXY individuals unless a physician orders one to check an unusual finding in a breast exam.

**[[http://www.genetic.org/images/action.gif](javascript://)Do individuals with 47,XXY have any special talents?](javascript://)**

There are no current systematic studies of unusual talents and skills in XXY individuals.  Anecdotal information from conferences and websites suggests that math, computers, chess, music and art tend to be interests of XXYs, and that many excel in these areas professionally.  There is *Magnetic Resonance Imaging* (MRI) evidence that may support this.  Research at the National Institutes of Health by Dr. Jay Giedd, a child psychiatrist who is conducting a large multi-year study of over 40 XXY children, demonstrates that the volume of gray matter on the right side of the brain, the part of the brain controlling spatial abilities and computational skills, is actually larger than for control subjects.  XXYs may use this strength to compensate for the slightly smaller than average volumes of the left half of their brains, which control language functions and social skills, and may explain deficits in these areas.

**[[http://www.genetic.org/images/action.gif](javascript://)When and how should I discuss XXY with my child?](javascript://)**

With children who are diagnosed prenatally or as young children, it is best to begin short, simple explanations at about age 5 or 6.  You can explain that every cell in the body has “messages” to tell the body how to grow, and that the extra X sends some extra messages, which may help to explain the need for extra help in the resource room at school.  If medication, such as Ritalin for ADD, is required, you can point out that the extra chromosome may help explain why the medication is needed to improve attention at school.  Later, during visits to an endocrinologist, you can provide more detailed explanations about the need to take testosterone supplementation.  47,XXY should never be kept a secret; the child will sense that there is something that the parent is withholding.  When it’s time to learn about sexuality and reproduction, you can introduce the issue of lowered fertility and the need for infertility treatment, donated sperm or adoption to create a family later in life.  Reassure your child that the condition is common and that learning disabilities do not make your child “disabled”.

<http://www.genetic.org/Knowledge/FAQ.aspx>