48,XXYY syndrome

Description

48,XXYY syndrome is a chromosomal condition that affects development in people who are assigned male at birth. There is a lot of variability in symptoms between people with 48,XXYY syndrome. Almost all affected individuals have developmental delays in infancy and develop decreased testosterone levels (hypogonadism) during adolescence. People with 48,XXYY syndrome are also at risk for other health problems.

Adolescents and adults with this condition usually have small testes that do not produce enough testosterone, which is the hormone that directs male sexual development. Without treatment, a shortage of testosterone during puberty can lead to reduced facial and body hair, poor muscle development, low energy levels, and an increased risk of breast enlargement (gynecomastia). Because their testes do not function normally, individuals with 48,XXYY syndrome have difficulty having biological children (a condition called infertility), but they may be able to have children using assisted reproductive technologies.

48,XXYY syndrome can affect other parts of the body as well. Affected individuals are often taller than their peers, with an average adult height of 6 feet, 4 inches (193 cm). They may develop a mild to moderate hand tremor that typically starts in adolescence and may increase with age. Dental problems are frequently seen in people with this condition, including delayed appearance of the primary (baby) or secondary (adult) teeth, thin tooth enamel, crowded or misaligned teeth, and multiple cavities.

Additionally, individuals with 48,XXYY syndrome may have flat feet (pes planus), elbow abnormalities, abnormal fusion of certain bones in the forearm (radioulnar synostosis), allergies, asthma, type 2 diabetes, seizures, congenital heart defects, and an inflammatory condition in the throat (esophagus) called eosinophilic esophagitis. As people with 48,XXYY get older, they may develop a narrowing of the blood vessels in the legs called peripheral vascular disease. Peripheral vascular disease can cause skin ulcers to form. Affected individuals are also at risk of developing a type of clot called a deep vein thrombosis that occurs in the deep veins of the legs.

Most individuals with 48,XXYY syndrome have an IQ score that ranges from 60 to 80 and have some degree of difficulty with speech and language development. The development of motor skills such as sitting, standing, and walking may be delayed in some children with 48,XXYY syndrome. They may also have poor coordination. Learning disabilities are very common in people with this disorder, especially in the

areas of reading and written expression. People with 48,XXYY typically perform better at tasks focused on math, visual-spatial skills such as puzzles, and memorization of locations or directions. Affected individuals have higher-than-average rates of other neurodevelopmental and behavioral disorders, such as attention-deficit/hyperactivity disorder (ADHD); mood disorders, including anxiety and depression; and autism spectrum disorder, which affects communication and social interaction.

Frequency

48,XXYY syndrome is estimated to affect 1 in 18,000 to 40,000 newborns who were assigned male at birth.

Causes

48,XXYY syndrome is a condition related to the the sex chromosomes. People normally have 46 chromosomes in each cell. Two of the 46 chromosomes, known as X and Y, are called sex chromosomes because they help determine whether a person will develop male or female sex characteristics. Females typically have two X chromosomes (46,XX), and males have one X chromosome and one Y chromosome (46,XY). 48, XXYY syndrome results from the presence of an extra copy of both sex chromosomes in each of a male's cells (48,XXYY). Extra copies of genes on the X chromosome interfere with sexual development, preventing the testes from functioning normally and reducing the levels of testosterone.

Many genes are found only on the X or Y chromosome, but genes in areas known as the pseudoautosomal regions are present on both sex chromosomes. Extra copies of genes from the pseudoautosomal regions of the extra X and Y chromosome contribute to the signs and symptoms of 48,XXYY syndrome; however, the specific genes have not been identified. The presence of extra sex chromosomes can also lead to changes in activity of other genes in other chromosomes.

Learn more about the chromosomes associated with 48,XXYY syndrome

- x chromosome
- y chromosome

Inheritance

48,XXYY is not inherited; it usually occurs as a random event during the formation of reproductive cells (eggs and sperm). An error in cell division called nondisjunction results in a reproductive cell with an abnormal number of chromosomes. In 48,XXYY syndrome, the extra sex chromosomes almost always come from a sperm cell. Nondisjunction may cause a sperm cell to gain two extra sex chromosomes, resulting in a sperm cell with three sex chromosomes (one X and two Y chromosomes). If that sperm cell fertilizes a normal egg cell with one X chromosome, the resulting child will have two X chromosomes and two Y chromosomes in each of the body's cells.

In a small percentage of cases, a normal sperm cell with one Y chromosome can fertilize a normal egg cell with one X chromosome, but right after fertilization, nondisjunction of the sex chromosomes causes the embryo to gain two extra sex chromosomes. This produces a 48,XXYY embryo.

Other Names for This Condition

- XXYY syndrome

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Anomaly of sex chromosome (https://www.ncbi.nlm.nih.gov/gtr/conditions/C0036868/)

Genetic and Rare Diseases Information Center

- 48,XXYY syndrome (https://rarediseases.info.nih.gov/diseases/5677/index)

Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD) (https://rarediseases.org/)

Clinical Trials

- ClinicalTrials.gov (https://clinicaltrials.gov/search?cond=%2248,XXYY syndrome%22)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%2848,+XXYY%5BTIAB%5D%29+OR+%28XXYY%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D)

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