Klinefelter Syndrome

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Klinefelter syndrome is a chromosomal condition in boys and men that can affect physical and intellectual development.

genetic conditions

1. Introduction

Most commonly, affected individuals are taller than average are unable to father biological children (infertile); however the signs and symptoms of Klinefelter syndrome vary among boys and men with this condition. In some cases, the features of the condition are so mild that the condition is not diagnosed until puberty or adulthood, and researchers believe that up to 75 percent of affected men and boys are never diagnosed.

Boys and men with Klinefelter syndrome typically have small testes that produce a reduced amount of testosterone (primary testicular insufficiency). Testosterone is the hormone that directs male sexual development before birth and during puberty. Without treatment, the shortage of testosterone can lead to delayed or incomplete puberty, breast enlargement (gynecomastia), decreased muscle mass, decreased bone density, and a reduced amount of facial and body hair. As a result of the small testes and decreased hormone production, affected males are infertile but may benefit from assisted reproductive technologies. Some affected individuals also have differences in their genitalia, including undescended testes (cryptorchidism), the opening of the urethra on the underside of the penis (hypospadias), or an unusually small penis (micropenis).

Other physical changes associated with Klinefelter syndrome are usually subtle. Older children and adults with the condition tend to be somewhat taller than their peers. Other differences can include abnormal fusion of certain bones in the forearm (radioulnar synostosis), curved pinky fingers (fifth finger clinodactyly), and flat feet (pes planus).

Children with Klinefelter syndrome may have low muscle tone (hypotonia) and problems with coordination that may delay the development of motor skills, such as sitting, standing, and walking. Affected boys often have learning disabilities, resulting in mild delays in speech and language development and problems with reading. Boys and men with Klinefelter syndrome tend to have better receptive language skills (the ability to understand speech) than expressive language skills (vocabulary and the production of speech) and may have difficulty communicating and expressing themselves.

Individuals with Klinefelter syndrome tend to have anxiety, depression, impaired social skills, behavioral problems such as emotional immaturity and impulsivity, attention-deficit/hyperactivity disorder (ADHD), and limited problem-solving skills (executive functioning). About 10 percent of boys and men with Klinefelter syndrome have autism spectrum disorder.

Nearly half of all men with Klinefelter syndrome develop metabolic syndrome, which is a group of conditions that include type 2 diabetes, high blood pressure (hypertension), increased belly fat, high levels of fats (lipids) such as cholesterol and triglycerides in the blood. Compared with unaffected men, adults with Klinefelter syndrome also have an increased risk of developing involuntary trembling (tremors), breast cancer (if gynecomastia develops), thinning and weakening of the bones (osteoporosis), and autoimmune disorders such as systemic lupus erythematosus and rheumatoid arthritis. (Autoimmune disorders are a large group of conditions that occur when the immune system attacks the body's own tissues and organs.)

2. Frequency

Klinefelter syndrome affects about 1 in 650 newborn boys. It is among the most common sex chromosome disorders, which are conditions caused by changes in the number of sex chromosomes (the X chromosome and the Y chromosome).

3. Causes

Klinefelter syndrome is a sex chromosome disorder in boys and men that results from the presence of an extra X chromosome in cells. People typically have 46 chromosomes in each cell, two of which are the sex chromosomes. Females have two X chromosomes (46,XX), and males have one X and one Y chromosome (46,XY). Most often, boys and men with Klinefelter syndrome have the usual X and Y chromosomes, plus one extra X chromosome, for a total of 47 chromosomes (47,XXY).

Boys and men with Klinefelter syndrome have an extra copy of multiple genes on the X chromosome. The activity of these extra genes may disrupt many aspects of development, including sexual development before birth and at puberty, and are responsible for the common signs and symptoms of Klinefelter syndrome. Researchers are working to determine which genes contribute to the specific developmental and physical differences that can occur with Klinefelter syndrome.

Some people with features of Klinefelter syndrome have an extra X chromosome in only some of their cells; other cells typically have one X and one Y chromosome. (Rarely, other cells may have additional chromosome abnormalities.) In these individuals, the condition is described as mosaic Klinefelter syndrome (46,XY/47,XXY). It is thought that less than 10 percent of individuals with Klinefelter syndrome have the mosaic form. Boys and men with mosaic Klinefelter syndrome may have milder signs and symptoms than those with the extra X chromosome in all of their cells, depending on what proportion of cells have the additional chromosome.

Several conditions resulting from the presence of more than one extra sex chromosome in each cell are sometimes described as variants of Klinefelter syndrome. These conditions include 48,XXXY syndrome, 48,XXYY syndrome, and 49,XXXXY syndrome. Like Klinefelter syndrome, these conditions affect male sexual development and can be associated with learning disabilities and problems with speech and language development. However, the features of these disorders tend to be more severe than those of Klinefelter syndrome and affect more parts of the body. As doctors and researchers have learned more about the differences between these sex chromosome disorders, they have started to consider them as separate conditions.

3.1. The chromosome associated with Klinefelter syndrome

- x chromosome

4. Inheritance

Klinefelter syndrome is not inherited; the addition of an extra X chromosome occurs during the formation of reproductive cells (eggs or sperm) in one of an affected person's parents. During cell division, an error called nondisjunction prevents X chromosomes from being distributed normally among reproductive cells as they form. Typically, as cells divide, each egg cell gets a single X chromosome, and each sperm cell gets either an X chromosome or a Y chromosome. However, because of nondisjunction, an egg cell or a sperm cell can also end up with an extra copy of the X chromosome.

If an egg cell with an extra X chromosome (XX) is fertilized by a sperm cell with one Y chromosome, the resulting child will have Klinefelter syndrome. Similarly, if a sperm cell with both an X chromosome and a Y chromosome (XY) fertilizes an egg cell with a single X chromosome, the resulting child will have Klinefelter syndrome.

Mosaic Klinefelter syndrome (46,XY/47,XXY) is also not inherited. It occurs as a random error during cell division early in fetal development. As a result, some of the body's cells have the usual one X chromosome and one Y chromosome (46,XY), and other cells have an extra copy of the X chromosome (47,XXY).

5. Other Names for This Condition

- 47,XXY syndrome
- Klinefelter syndrome (KS)
- Klinefelter's syndrome
- XXY syndrome

- XXY trisomy

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