Fact sheet **39**

KLINEFELTER SYNDROME

This fact sheet talks about the chromosome condition Klinefelter syndrome and includes the symptoms, cause, treatment or available testing.

IN SUMMARY

- Klinefelter syndrome is also called XXY syndrome and affects males
- The condition comes about because instead of the usual one copy of the X chromosome, males have two or more copies
- Klinefelter syndrome is thought to occur in 1 in every 500 or 1 in every 1,000 males born in Australia each year.

WHAT IS KLINEFELTER SYNDROME?

Klinefelter syndrome (also called XXY syndrome), was first described in 1942 by Dr Harry Klinefelter and is one of the more common chromosome conditions in males. An additional X chromosome is found in the cells of the body, giving them two X chromosomes instead of the usual one (see later).

Some people with this condition will have more features of the condition than others and there may be a difference in the degree of severity of the symptoms. In some, a diagnosis of Klinefelter syndrome is not made until puberty and some may never be diagnosed with the condition.

Features include:

- Learning difficulties which may be the greatest developmental challenge. IQ however, is usually in the normal range, although it may be 10-15 points lower than that of their siblings
- People with Klinefelter syndrome may be slower to develop language and speech, motor (movement) skills and emotional maturity than others. Poor attention, limited problem solving skills and autism spectrum disorder may be a feature. They may benefit from extra help or intervention at school and with therapists.
- As people with Klinefelter syndrome grow older, shyness and relative immaturity may continue
- There is a tendency to grow at a slightly quicker rate than others so that their final height may be a little more than expected
- In around 50% (1 in 2) of people with the condition there is some growth of breast tissue at puberty (*gynaecomastia*). Sometimes, plastic surgery may be considered to reduce breast tissue
- Differences of genitalia include undescended testes (*cryptorchidism*), the opening of the urethra is unusually placed on the underside of the penis (*hypospadias*), or the penis may be smaller (*micropenis*). Body hair, beard growth and size of testicles may be reduced in males with Klinefelter syndrome. The use of the male hormone testosterone has been effective in increasing strength and developing a more masculine appearance. Treatment usually begins around the age of 11-12 years. Early consultation with an endocrinologist (a hormone specialist) is advised to support testosterone treatment
- There may be differences in ability to break down sugars in the usual way (type 2 diabetes) or differences in processing fats that need to be watched and/or treated. High blood pressure may also be a feature
- Sexuality is as expected, although people with Klinefelter syndrome are usually infertile.

WHAT CAUSES KLINEFELTER SYNDROME?

Klinefelter syndrome is caused by the presence of an extra copy of the X chromosome.

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In each cell of the body, except the egg and sperm cells, there are 46 chromosomes. Chromosomes come in pairs and each pair varies in size.

There are therefore 23 pairs of chromosomes, one of each pair being inherited from each parent.

- There are 22 numbered chromosomes from roughly the largest to the smallest: i.e. 1-22. These are called autosomes
- There are also two sex chromosomes, called X and Y.

In females, cells in the body typically have 46 chromosomes (44 autosomes plus two copies of the X chromosome). They are said to have a 46,XX karyotype. Eggs (female reproductive cells) are different as they only contain half of the chromosomes (23 made up of 22 numbered chromosomes and an X chromosome).

In males, cells in the body typically have 46 chromosomes (44 autosomes plus an X and a Y chromosome). They are said to have a 46,XY karyotype. Sperm (male reproductive cells) are different as they only contain half of the chromosomes (23 made up of 22 numbered chromosomes and an X chromosome or a Y chromosome). *Figure 39.1* shows a chromosome picture (karyotype) set from a typical male (46,XY). The usual way a sperm and egg combine at conception is shown in *Figure 39.2.*

Sometimes, when the egg and sperm are forming, the chromosome pairs do not separate in the usual way. The result is an egg or sperm cell that has only 22 chromosomes while others have 24 chromosomes.

If an egg or sperm carrying 24 chromosomes combines with an egg or sperm carrying the usual 23 chromosomes, the result would be a person with 47 chromosomes instead of the usual 46. (See *Figure 39.3*).

Figure 39.1:
Chromosome picture (karyotype) from a male (46,XY).

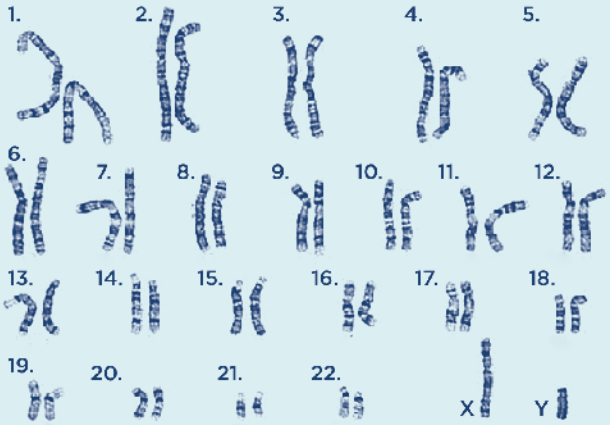


Figure 39.2:
At conception the sperm and egg combine

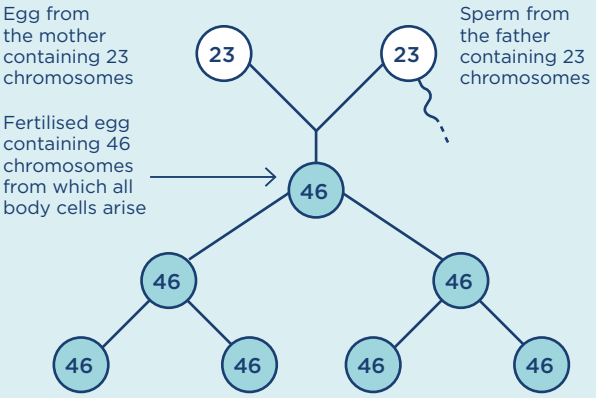
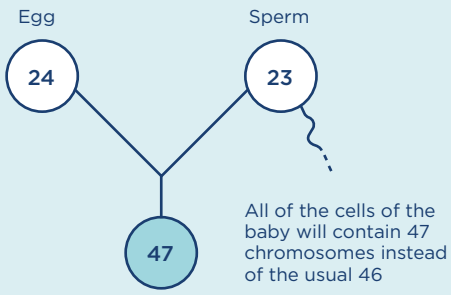


Figure 39.3:
When the egg has 24 chromosomes, and the sperm has the usual 23, the baby's cells will contain 47 chromosomes instead of 46 (47,XXY).



The chromosome pattern in people with Klinefelter syndrome usually includes a whole extra copy of the X chromosome (47,XXY). This extra chromosome causes an imbalance and is the reason why there are differences in those with this condition.

Figure 39.4 is a picture (karyotype) of the chromosomes from a person with Klinefelter syndrome (47,XXY). If there are 3 copies of the X chromosome with the Y (48 chromosomes) or 4 copies of the X chromosome with the Y (49 chromosomes), signs and symptoms may be more severe.

Some people have Klinefelter syndrome as a result of a mosaicism

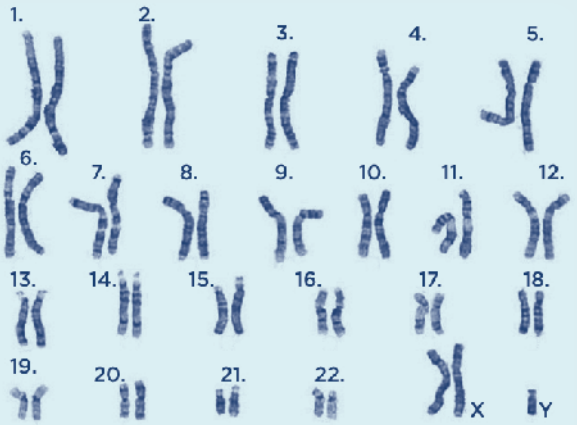
Most people have the same chromosome makeup in all the cells in their body. People with Klinefelter syndrome as a result of mosaicism have some cells in the body with a typical sex chromosome makeup e.g. one X chromosome and one Y chromosome, and other cells may have two X chromosomes and one Y chromosome. Someone who is mosaic for a chromosome change therefore has a mixture of cells in their body. Although signs and symptoms may be milder when compared with people with chromosome differences in all body cells, it may be difficult to predict how signs and symptoms will show up, just from a blood test.

HOW IS KLINEFELTER SYNDROME INHERITED?

In most cases, a person with Klinefelter syndrome will be the first and only person with the condition in that family.

It is usually assumed that if the parents of a person with Klinefelter syndrome (e.g. 47,XXY) have the usual two sex chromosomes, then the extra X chromosome in their child was a result of an egg or sperm with 24 instead of 23 chromosomes.

Figure 39.4:
Chromosome picture (karyotype) from a male with Klinefelter syndrome. In this cell, there are 47 chromosomes including two copies of the X chromosome instead of one.



IS THERE ANY TESTING AVAILABLE FOR KLINEFELTER SYNDROME?

Chromosome testing can be done using a blood sample. A doctor may suspect Klinefelter syndrome in a person based on characteristic features or symptoms associated with the syndrome.

Testing for pregnancy

Chromosome testing may be offered during pregnancy to check for Klinefelter syndrome.

Prenatal tests can happen in a number of different ways and at certain stages of the pregnancy. In general, there are two main types of prenatal test – a screening test and a diagnostic test.

Screening tests give a risk or estimate of the chance that a baby has a health condition. These tests do not generally look directly at a sample from the developing baby and are therefore very safe. Included in the group of screening tests are ultrasounds, non-invasive prenatal testing, first trimester screening and second trimester screening.

Diagnostic tests provide a more accurate result since they are generally directly testing the baby. Because of this, in a very small number of cases, a test may also cause a miscarriage. Examples of diagnostic tests are chorionic villus sampling (CVS) and amniocentesis.

Testing during pregnancy is optional and should be talked about in full with your doctor, midwife or genetic counsellor. Making a decision to have a test or not is always up to you.

It may also be possible to have pre-implantation genetic diagnosis (PGD) to look for chromosome conditions in an embryo made using in vitro fertilisation (IVF). When planning a family, options for testing are best talked about and considered before pregnancy.

More support and information is available for individuals and families through support organisations including Genetic Alliance Australia.