Klinefelter syndrome (XXY)

This leaflet explains what Klinefelter Syndrome is, the symptoms and treatment options. If you have any further questions or concerns, please speak to the doctor or nurse caring for you.

What is Klinefelter Syndrome and why do I have it?

Klinefelter syndrome (sometimes called Klinefelter's, KS or XXY) is where boys and men are born with an extra X chromosome.

Chromosomes are packages of genes found in every cell in the body. Two types of chromosome, called the sex chromosomes, determine the genetic sex of a baby. These are named either X or Y. Usually, a female baby has 2 X chromosomes (XX) and a male has one X and one Y (XY). But in Klinefelter syndrome, a boy is born with an extra copy of the X chromosome (XXY).

The X chromosome is not a "female" chromosome and is present in everyone. The presence of a Y chromosome denotes male sex. Boys and men with Klinefelter syndrome are still genetically male, and often will not realise they have this extra chromosome, but occasionally it can cause problems that may require treatment. Klinefelter syndrome affects around 1 in every 660 males.

Some men with features of KS may only carry the extra X chromosome in some of their cells, with the remaining cells being XY. These individuals have mosaic Klinefelter Syndrome (46,XY/47,XXY). Those with mosaic KS may have milder signs and symptoms, depending on how many of their cells carry the extra X chromosome. Some KS patients may also carry additional X chromosomes such as (48,XXXY) and (49,XXXY), and generally experience more severe signs and symptoms of the syndrome.

The exact cause of the condition is not known, although there is a slightly increased risk in babies born to older mothers. KS is not an inherited (from your parents) condition, but is the result of an error during the fusion of reproductive cells (eggs and sperm) from the patient's parents when forming the embryo.

What are the signs and symptoms?

These can be very mild and so it is estimated only 1 in 4 (25%) of men with KS are ever diagnosed. In men with KS, the testes do not develop and are usually small and firm. This leads to reduced testosterone production which can lead to a series of differences in development: delayed or incomplete puberty, enlargement of breast tissue (gynaecomastia) and reduced facial and body hair.

One of the most common symptoms in adulthood is infertility. This is due to a gradual loss of the cells in the testes which are responsible for the production of sperm, and results in semen containing little or no sperm. Spermatic function generally fades over time. Many men are diagnosed as adults with KS because of their difficulties conceiving. Boys and men who are

showing we care

diagnosed earlier in life should be aware of what this could mean for their fertility in case they want to start a family later in their lives.

Physical and intellectual development can also be affected by KS. Physical changes include tall stature, muscle weakness, flat feet and curved little fingers (clinodactyly) Affected people may experience delays in speech and language development, and in particular expression of emotion. The majority of patients have normal intellect.

Compared with unaffected men, adults with KS have an increased risk of developing Type 2 diabetes, osteoporosis (fragile bones), blood clots, and autoimmune (when your immune system mistakenly “attacks” your body) disorders such as rheumatoid arthritis and systemic lupus erythematosus. Life expectancy is usually normal, and many patients live normal lives.

In addition to problems mentioned above, low testosterone can give a series of symptoms: low energy levels, increased daytime sleepiness, low libido (sex drive), and difficulty concentrating, which can be treated with testosterone supplementation.

People with KS have a small increased risk of breast cancer (note that all men have small amounts of breast tissue) and testicular cancer. Men should check their testicles and chest regularly for the development of any new lumps, and speak to their GP if they are concerned.

Do I need any tests to confirm the diagnosis?

The combination of small firm testes and low sperm count (or absence of sperm in semen) indicates KS.

The key investigation is a blood test (chromosome analysis) and other blood tests looking at hormone function. This forms part of a range of genetic tests which also look for other causes of low sperm counts. One of the hormone tests is for testosterone, which is at its highest in the morning, and it is therefore important to have this blood test before 10am. Other important blood tests are follicle stimulating hormone (FSH) and luteinising hormone (LH). High levels of FSH and LH and low levels of testosterone indicate the testes are producing little or no testosterone or sperm.

Currently there is no screening program for KS, although it may be picked up prenatally (before birth) as part of screening for other chromosome abnormalities.

What treatments are available?

There is no cure for KS, although there are treatments available for the problems associated with the condition.

Testosterone replacement therapy (TRT)

TRT involves testosterone administered as gels, skin patches or injections. Gel preparations are popular as they work well and are easy to use, avoiding the need for injections, particularly in children. Testosterone replacement may be considered once puberty begins, to support development of male characteristics, such as facial and body hair, increased muscle mass, deepening voice and reduced body fat. It may also help to improve energy levels. TRT is also an option in adulthood and may help to prevent osteoporosis and improve low mood, concentration levels, energy levels, libido and self-esteem.

TRT does not improve sperm production and, if fertility is important, TRT should be delayed until after fertility issues have been addressed. Testosterone in excess can lead to health issues such as liver problems, increased red cell blood count (which can cause stroke or heart problems), and in the long term urinary problems. TRT requires careful monitoring, however many men safely receive this treatment under supervision of their doctor.

Increased aggression and mood swings can also be seen and it can take some time to find the right dose for each individual patient.

Fertility therapies
For some men with KS who have no sperm in their semen, it is possible to take sperm directly from the testes with surgery called microTESE (microscopic testicular sperm extraction). The sperm can then be frozen or used immediately for in vitro fertilisation (IVF) with intra-cytoplasmic sperm injection (ICSI) into an egg. In patients receiving TRT, it has been suggested that testosterone should be stopped for 6-9 months before undergoing microTESE, to improve sperm retrieval rates. For some men, hormonal manipulation with stimulatory drugs is sometimes tried before this procedure.

Not all patients will have sperm retrieved, but evidence suggests that younger patients have a greater chance of success. An alternative is to consider donor sperm for fertility treatment, or adoption.

The lack of sperm does not affect the ability to have sexual intercourse, and the physical sex life of men with KS is usually normal.

Funding for fertility therapy will depend on your Care Commissioning Group (CCG). Details on how to find your local CCG are at the end of this leaflet.

Endocrine management
Endocrinology is the management of problems with hormones. For KS patients, with an increased risk of diabetes and osteoporosis (weak bones), input from an endocrinologist is sometimes needed to make sure the patient remains healthy. Endocrinologists and urologists both manage testosterone replacement therapy for the patient.

Cognitive and physical therapies
Speech and language therapy can be offered during childhood to aid speech development, as well as educational and behavioural support at school for children with learning and behavioural difficulties. Physiotherapy can help to improve muscle mass and strength, and occupational therapy for co-ordination difficulties associated with the condition. Psychological support is also available for KS patients affected by mental health issues. For those with excess breast tissue, breast reduction surgery may be offered.

Genetic counselling
When you are told that your genetic makeup is abnormal, it can create a lot of anxiety. It is a very complicated subject and other conditions may be found by accident. A counsellor can help you understand this better.

What happens if I do not receive treatment?

Many men with KS who do not receive treatment live normal, healthy lives. As men with KS are at slightly higher risk of other conditions, long-term follow-up can help to prevent these. The

condition cannot be inherited by children of men with KS, even if assisted fertility techniques have been used.

Is there anything I can do to help myself?

KS is to do with your genes so lifestyle changes cannot cause or cure it. However, leading an active and healthy lifestyle may improve symptoms of low testosterone, and may reduce the risk of developing conditions such as Type 2 diabetes, osteoporosis, cardiovascular disease, blood clots, mental health conditions, and breast cancer that KS is associated with.

Healthy lifestyle changes such as stopping smoking, keeping alcohol intake within recommended limits, maintaining a well-balanced diet, maintaining a healthy weight, and taking part in regular exercise can improve symptoms of low testosterone and reduce the risk of developing KS-associated conditions. Smoking, low calcium intake, and lack of exercise are particularly associated with an increased risk of developing osteoporosis, and it is recommended that men with KS attend DEXA scans (a scan that measures bone density) to check for any changes to their bones.

Useful sources of information

Klinefelter's Syndrome Associaton, **w:** www.ksa-uk.net
Patient.co.uk, **w:** www.patient.info/health/klinefelters-syndrome-leaflet

Contact us

If you have any questions or concerns about the Klinefelter Syndrome Multi-Specialty Clinic, please contact the andrology specialist nurse, **t:** 07717 346821, Monday to Friday, 9am-5pm.

Your local CCG can be found here: **w:** www.england.nhs.uk/ccg-directory/

For more information leaflets on conditions, procedures, treatments and services offered at our hospitals, please visit **w:** www.guysandstthomas.nhs.uk/leaflets

Pharmacy Medicines Helpline
If you have any questions or concerns about your medicines, please speak to the staff caring for you or call our helpline. **t:** 020 7188 8748, Monday to Friday, 9am-5pm

Your comments and concerns
For advice, support or to raise a concern, contact our Patient Advice and Liaison Service (PALS). To make a complaint, contact the complaints department.
t: 020 7188 8801 (PALS) **e:** pals@gstt.nhs.uk
t: 020 7188 3514 (complaints) **e:** complaints2@gstt.nhs.uk

Language and accessible support services
If you need an interpreter or information about your care in a different language or format, please get in touch. **t:** 020 7188 8815 **e:** languagesupport@gstt.nhs.uk

Leaflet number: 4680/VER1
Date published: January 2019
Review date: January 2022
© 2019 Guy's and St Thomas' NHS Foundation Trust
A list of sources is available on request