Hormones and Me

Klinefelter Syndrome

Australasian Paediatric Endocrine Group

Klinefelter Syndrome

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About this Book

This booklet, *Klinefelter Syndrome* introduces a genetic condition which affects some boys, and its features from infancy to adulthood. It is also a guide to available treatments for some of these problems. The booklet is written primarily for parents and carers of boys with *Klinefelter Syndrome*, but it will also be helpful for affected adolescents and men interested in knowing more about the condition.

We encourage you to discuss any additional questions or areas of concern with your doctor after reading this booklet.

Merck is proud to bring you this booklet from the *Hormones and Me* educational series. We hope that you find it a valuable and helpful resource.

This booklet was written by A/Prof Margaret Zacharin (Royal Children's Hospital, VIC, Australia) a paediatric Endocrinologist specialising in both childhood and adult endocrinology disorders and a member of the Australian Paediatric Endocrinology Group (APEG). It was revised by A/Prof Zacharin in 2011.

The information contained in *Klinefelter Syndrome* are views of the author, a recognised expert in her field, and do not necessarily represent an endorsement or recommendation on the part of Merck Serono Australia.

Paediatric endocrinologists, A/Prof Margaret Zacharin and Dr Ann Maguire (The Children's Hospital at Westmead, NSW Australia) have reviewed the *Hormones and Me* series on behalf of the Australasian Paediatric Endocrine Group (APEG).

Introduction

Boys with Klinefelter Syndrome (KS) have two (or more) “X” chromosomes in every cell, instead of the usual one. A “Y” chromosome is always present as well, so everyone with the condition is male. Nearly all boys with KS have small testes with reduced function. Other physical changes may be found, but they do not affect all boys. Many boys and men with KS have no other unusual physical features at all.

“Klinefelter Syndrome is a chromosomal condition first described by Dr Harry Klinefelter of Boston, Massachusetts in 1942.”

Klinefelter Syndrome may be diagnosed in infancy or early childhood but diagnosis may be delayed until adulthood, at the time of a couple seeking assistance for infertility. There are a number of problems occurring throughout life that might cause this diagnosis to be considered.

This will be discussed in the booklet.

What is Klinefelter Syndrome?

Klinefelter Syndrome is extremely common. One in every 580 males has it.

It is usually characterised by some degree of hypogonadism (reduced function of the testes). Most men with KS are infertile. Only some have a lack of sex hormone and slow sexual development. Although the testes have reduced function, almost all boys with KS are male in appearance.

Boys with KS are often taller than average. Some may have some learning difficulties, particularly in the area of communication and language. The help of a professional psychologist may be needed to assess the degree of learning difficulty and to advise on strategies for dealing with this. As the boys reach teenage years, they tend to have relatively long legs in relation to the trunk, rather slender muscles and relatively wide hips, although a completely normal appearance is also common. The testes are small from birth and grow relatively little during puberty, even if other development is normal.

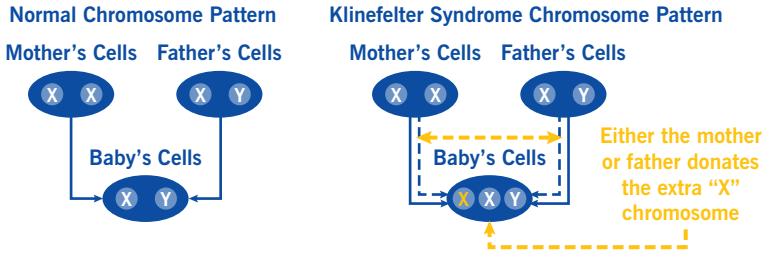
During the pubertal years, progress to a normal adult genital appearance may be slow or incomplete compared to other boys. Facial and body hair may be sparse with infrequent need for shaving. Some breast development is common during the teenage years and may be persistent. The full list of medical problems that may be associated with KS can be found in the section entitled “Associated Medical Conditions.”

The chromosomal abnormality of KS is due to the presence of one or more extra “X” chromosome. Most people have 46 chromosomes per cell, which contain the genetic “blueprint” required for their individual development.

These chromosomes are paired, with one of each pair coming from the mother and one from the father. Forty-four chromosomes (22 pairs) are the same for males and females. One pair is different between males and females and these are known as sex chromosomes. Most females have two "X" chromosomes and most males have one "X" and one "Y" chromosome. Those with KS have two (or very rarely, 3 or 4) "X" chromosomes.

Occasionally some cells in the body are found to have a normal number of sex chromosomes (46XY) while others have the extra "X" chromosome. This is known as a chromosome mosaic pattern.

Diagram 1 : CHROMOSOME PATTERNS



The cause of the extra "X" chromosome in KS is not known.

How is Klinefelter Syndrome Diagnosed?

Surveys of the newborn have shown that KS is extremely common, affecting 1 in 580 live male births. Doctors only detect a small fraction of these boys and men using conventional methods of diagnosis.

Infancy

The diagnosis of KS is made on the basis of a blood test showing the different chromosome constitution i.e. 47 "XXY". There is usually nothing to distinguish a newborn baby with KS from any other baby boy. The testes are sometimes not descended into the scrotum at birth in boys with KS but this problem also occurs in other boys, so it is not a specific feature that will help the diagnosis.

Childhood

During childhood some boys with KS may be found to have somewhat delayed general development, particularly in areas of physical activity and language accumulation. Certain learning difficulties in the early years at school are common, with problems such as reduced short-term memory span and delayed speech development. Parents might visit their child's paediatrician for consultation for this type of problem. The condition can be picked up if a chromosome analysis is performed.

Most boys, but by no means all those with KS, tend to be somewhat taller than average and a little taller than other males in their families.

If a boy also has some developmental or learning problems and is unusually tall in the family, this may lead the doctor to suspect the problem and to undertake a chromosome analysis.

Puberty

Sometimes the testes are very under-developed and cannot produce male hormones. A diagnosis of KS may be made if a boy fails to enter puberty at a normal time or when puberty development starts at a normal time but does not continue to full adult virilisation and normal adult male genital appearance. Usually boys with this type of problem will come to see a paediatrician or hormone specialist (Endocrinologist).

Adulthood

Although KS may be diagnosed at any time from infancy onwards, the most common way in which this problem is found is usually at the time when a man and his partner go to the doctor for fertility counselling. During investigations the man will be found to have no sperm and chromosome analysis will confirm the diagnosis.

> "For some, the diagnosis may be made only by chance at the time of a chromosome analysis for very specific and unrelated reasons, such as when any boy or man might offer one of his organs for transplantation to a relative or unrelated recipient."

During work-up procedures, before transplantation of any human tissue, a chromosome analysis is always performed. Another way in which the diagnosis may be made by accident is if a boy or man with KS happens to have a most unusual tumour or cancer known to be associated with KS. Chromosome tests may need to be performed at this time.

Incidental diagnosis

Sometimes a boy with KS may grow and develop in an apparently perfectly normal fashion with normal progress through puberty and normal physical development but behaviour problems can become very significant in later adolescence. If a boy and his parents seek help for problems of mood and behaviour and the doctor finds a normal boy with smaller than usual testes, chromosome analysis may lead to a diagnosis of this condition.

Problems with Physical Co-ordination and School Performance

During adolescence, as the need for accumulating increasing amounts of information in the later years of school becomes more important, a boy with KS, who may have always had some minor problems of slow learning in primary school, can suddenly find an increasing difficulty with accumulating knowledge. This can either lead to behaviour problems, increased aggression and irritability, or a tendency to be socially withdrawn and isolated. Medical attention may be sought for these issues and a diagnosis made.

Problems that May be Experienced from Infancy to Adulthood

Problems during infancy

Boys with KS are physically normal but some may have undescended testes. As this is a common problem for any infant or young child, the diagnosis may be picked up if a paediatrician is considering the possibility of KS and undertakes a chromosome analysis. However, this test is usually not performed at the time of surgery for undescended testes.

Many boys and men with KS will give a history of having had a repair for undescended testes in early life but no chromosome test was performed at that time.

Some babies and young children with KS may be more quiet and passive than other babies and later have some delay in developing physical activities such as walking. Language accumulation can be slow to mature and parents may notice a reduced participation in group activities in the early years of kindergarten and primary school.

Problems in Childhood

When a person has even a mild reduction in learning capacity or difficulties with self-expression, this can reduce the ability to form friendships and can result in social isolation. This often happens with KS. Behaviour difficulties during childhood, with poor attention span at school, a tendency to be teased and occasionally displaying 'acting-out' behaviour with aggression are commonly reported. Once a diagnosis has been made, early intervention is very important to assist with socialisation and to ensure a proper learning environment for the child's needs. Support for a boy to participate in sporting and group activities and co-operation between parents and staff are very important.

Overall intelligence for boys with KS is reported as being only slightly below average and many boys have great skills and ability in certain areas. However, when any person has difficulties with language and social skills, this can interfere with school learning and may cause an overall lower achievement than is expected for other boys. It is unusual for boys with KS to achieve tertiary education but almost all boys with "XXY" manage to finish a normal 12 year secondary school education. For boys with rare variations of KS, which include a number of extra "X" chromosomes (XXXY and XXXXY), learning problems can be greater and intellectual difficulties can be quite severe.

Problems during adolescence

Puberty commences in normal boys somewhere between 11 and 14 years of age, the most common age being around 13. Progress through puberty generally takes about 3 years to complete, with growth of the penis and pubic hair and testes occurring first. A growth spurt occurs towards the end of puberty, (unlike girls, whose growth spurt is in the early stages of puberty).

Some boys with KS enter puberty at a normal time but progress may be extremely slow and incomplete. Others will fail to enter puberty altogether and advice will be sought from a doctor because of this problem. Other boys will progress, with apparent normality, through the virilisation and growth process but will present to a doctor for other associated problems such as breast development or learning or behaviour difficulties.

It may be discovered at that time the testes are small and the male hormone levels are lower than expected for age. These features may lead the doctor to perform a chromosome test.

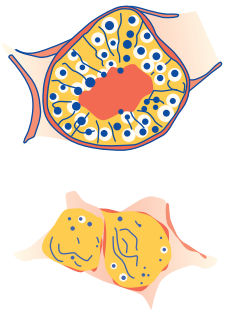
Sexual Development

Apart from learning and behaviour difficulties that may occur during childhood, the most common way in which boys with KS present to the doctor is due to a failure of the testes to function properly and therefore failure of sexual development.

Normally the testes have two separate functions, firstly production of testosterone for normal male genital development, growth and adult sexual function and secondly, for production of sperm in the adult male, for fertility. Testosterone is also necessary to build and maintain normal bone strength and to provide a healthy profile of cholesterol and other fats in the blood.

Diagram 2 : CHROMOSOME PATTERNS

Normal seminiferous tubule producing sperm



Abnormal seminiferous tubule that doesn't produce sperm, as in KS (XXY)

Boys with KS have normal sized testes during childhood, but they may be unusually firm to feel. The size of the testes is mainly related to production of sperm. A small adult testes size in this condition reflects the failure of sperm formation.

Testis size can occasionally increase to about half of a normal adult size during puberty, but unusually the testicular size remains that of a child despite normal growth of the penis and pubic hair at that time.

If puberty is absent or has stopped its normal progress and the diagnosis of KS is made, replacement hormone treatment may be necessary.

If testosterone production is poor or hormone replacement treatment is inadequate, growth of body hair and beard is sparse. Treatment with testosterone returns this to normal completely (see section entitled "Medical Management in Childhood and Adolescence").

Sexual interest (libido) and potency are normal for many young men with KS even if they have low levels of testosterone, however, low levels of testosterone are more commonly associated with low libido as a man gets older. In teenage years there is a surprising lack of correlation between the level of testosterone and normal sexual function. Even with very low levels of testosterone sexual function can be completely normal. Potency is therefore not a good guide to adequacy of levels of normal adult male hormones in a young man. On the other hand, if hormone replacement treatment is required long term, provided the level of testosterone is satisfactorily maintained, sexual potency will be completely normal.

For an adult male with KS, ejaculation occurs normally even in the absence of sperm production. Many men believe that the presence of an ejaculate means that sperm production is normal. Most of the volume of the ejaculate comes from the prostate gland and other accessory glands and not from sperm production. The volume of ejaculate for a man who does not have sperm production, is slightly reduced but the difference from normal may not be obvious to either the person with KS or to his partner.

"Spontaneous sperm production in boys and men with KS is usually zero."

Within the testis itself a few sperm can be formed but these are not sufficient for normal fertility in most boys with this condition. If the chromosome appearance is mosaic (a mixture of 46XY and 47XXY), fertility may be possible, although sperm numbers are reduced (see section entitled "Adulthood and Fertility")

Breast development occurs in 60% of all boys during puberty and usually shrinks or disappears within two years of onset. For boys with KS, the problem is very common and the breast tissue frequently does not disappear. It usually reflects a general lack of testosterone.

Boys with KS who produce enough testosterone of their own do not usually develop breast tissue. For boys with this condition who do need hormone replacement treatment, use of adequate levels of testosterone replacement may cause breast tissue to decrease and disappear over 6-12 months. The subcutaneous (under the skin) method of delivery of testosterone or the use of recently available long acting, flat profile testosterone injections seems to be more effective in reducing this problem than the older short acting intramuscular injections, which only lasted 2 weeks.

Adulthood

Although the testes of a man with KS may have enough testosterone for normal pubertal progress and virilisation, they are not normal. Ability to produce testosterone may reduce with time. Hormone replacement treatment with testosterone may be needed, to maintain adult levels of male hormone, normal libido and potency in future and to build a strong skeleton.

This is also very important in older men, to maintain normal bone quality and to reduce future fracture risk.

Fertility is severely reduced with this condition but modern management has allowed a number of men with KS to father their own children using a specialised technique (see section entitled “Adulthood and Fertility”). This is now a realistic possibility to consider.

Both parents and boys or men with KS sometimes have a concern that an extra “X” chromosome may in some way make them more female or even possibly change their sexual orientation to a homosexual preference. The extra “X” chromosome, although it causes problems with testis development, does not have anything to do with extra female appearance or thought processes and has absolutely no effect whatsoever on the development of a tendency towards homosexuality. Sexual orientation in men with KS is no different from the rest of the community and is determined by other factors than the chromosomal makeup.

Psychological Behaviour Problems in Adolescence and Adulthood

Mild problems of disturbed behaviour and aggression are very common in boys during adolescence and particularly common where there is also some form of medical condition making a boy different from his peers. Although a particular pattern of behaviour has been reported for young men with KS, this has yet to be conclusively shown. This pattern includes difficulties with generally increased aggression, together with a tendency for poor decision making and impaired judgement.

Young people with KS are sometimes particularly vulnerable to problems of lack of insight or judgement and a poor ability to learn from adverse or bad experiences. This can lead to repeated patterns of behaviour that may even lead to conflict with the law.

When a person has an aggressive tendency, it is commonly thought that the use of testosterone would increase or aggravate that tendency. In fact, for boys and men with KS who have reduced testosterone production, this makes them feel inadequate, with lowered mood and self esteem as well as lowered motivation, learning and memory capacity.

Adequate and balanced testosterone replacement treatment frequently lessens and improves all of these problems.

Psychological problems stemming from difficulties with achieving goals, a feeling of being different, issues arising from poor planning, decision making and judgement all need to be recognised and addressed as early as possible, to provide the best outcome for the person. Psychological or psychiatric counselling and treatment, particularly to assist with decision making processes, may be extremely helpful for young men to help them avoid escalating or recurring problems.

Associated Medical Conditions

KS can be associated with an increased risk for a number of different medical conditions throughout life. Although the risk for developing any of these problems is quite small, it is higher than for the average member of the community.

Boys and men with KS should have regular medical check ups and where necessary have screening tests every 1-2 years for possible problems. Adult onset diabetes and an under active thyroid gland (known as Hashimoto's thyroiditis) may occur.

There is a small increase in lifetime risk for men with KS to develop leukaemia or lymphoma (cancers of blood cells). Tumours or cancers of the testis known as seminoma and teratoma are also more common than in the general population.

If an unusual lump occurs in the testis, medical assistance should be sought to make an early diagnosis. It is usually best not to wait many months before asking the doctor about an unusual lump.

Yolk sac tumour is a rare cancer, found in the midline of the body, which can occur during childhood or adolescence in boys with KS.

Bone quality in adulthood is partly determined by having normal amounts of appropriate sex hormones. If a man does not have enough testosterone on a regular basis over many years, this may cause a lowering of bone density or bone quality and eventually osteoporosis. It is therefore very important for all men who have KS to have regular checks of their testosterone levels if they are not using hormone replacement treatment, and to have a bone density test performed every 2-5 years, depending on the advice of their doctor. This may help prevent osteoporosis as the man gets older.

Development of a normal bone structure through childhood is not dependent on male hormone levels and is not a problem for boys with KS.

Male breast cancer is a rare condition, however in the past it was reported to occur more commonly in men with KS than in other men. This may have been due to a tendency for less medical management in the past, with low levels of testosterone for many years and ongoing breast tissue development. These days the breast tissue is either treated with adequate testosterone replacement, where is tends to disappear quite rapidly or, if necessary the unwanted breast tissue is removed surgically. This risk is therefore considerably lower than it was in the past.

Medical Management in Childhood and Adolescence

Undescended testes

For any boy whose testes fail to descend into the scrotum after birth, by age one year, it may be necessary for them to be brought down to their proper position surgically. This should preferably be done in the second year of life and must be performed before the age of 6 to maximise any possible function.

There are several reasons why testes should be brought down, even if they do not have perfect function, such as for boys with KS. Firstly, there may be an increased risk of cancer of the testes whenever the testis is not normally formed. They should be in a position where they can be observed. It is only possible to check for any unusual lump within the testes if they are outside of the abdomen in their correct position. Secondly, even though the chance of fertility for a man with KS is minimal, treatments to allow some sperm formation are now possible and therefore the testes should be in a position where they have the best chance of function.

Behaviour problems during childhood should be addressed with a psychologist, psychiatrist or paediatrician at an early stage for the best outcomes and for help with decision making and social skills. If specific learning difficulties are found, planned assistance with extra school help can be organised and coordinated at a time when it will produce the most benefit.

Adolescence and Hormone replacement Treatment with Testosterone

Provided the testes of a boy with KS are able to produce testosterone, the likelihood of such a boy entering puberty at the expected normal time (between 11 and 14 years) is the same as for the rest of the population.

If puberty is delayed and has not occurred by age 14-15 years, it is very likely that hormone replacement treatment with testosterone will be required.

Measurement of the boy, comparison with the expected heights for his family and a blood test can together help make a decision as to whether treatment should be recommended.

If a boy needs to be taken completely through puberty with the aid of a testosterone supplement, it is usually commenced as a daily tablet or capsule. The dose is slowly increased over 1½–2 years until development has reached a stage where a stronger preparation is required.

For long-term treatment and for the higher doses of testosterone needed for the later stages of puberty, there is a choice of treatment. Most boys nowadays use a long acting, flat profile, intramuscular testosterone injection. Each injection lasts approximately 12 weeks. Provided it is administered slowly over about 1-2 minutes it is only mildly uncomfortable and is well tolerated by most boys and men.

This type of testosterone has largely replaced the older type of injections that only lasted 2 weeks. At around 7-10 days following one of these injections, there was quite a sharp peak in the blood level of testosterone. The hormone level lasted in the normal adult range for two weeks and then another injection was required.

For adolescents, fluctuations of mood every few weeks related to the rising and falling levels of testosterone can be quite a problem. Visits to the doctor also need to be fairly frequent when injections are chosen.

Some boys still prefer an under the skin preparation of testosterone. This formulation is in pellet form, and is inserted by the doctor under the skin of the hip or abdomen. The pellets provide an adult level of testosterone with no variations or fluctuations over approximately 24 weeks. Fresh pellets are inserted at the end of that time. They act by the body dissolving the wax pellet very slowly at body temperature and releasing the testosterone at a constant rate. The advantages of this type of preparation relate to the steady profile of male hormone release and the freedom from the need for medical assistance between six-monthly visits.

Testosterone patches are available for older men who have a need for hormone replacement. They are quite large and at least two patches need to be worn simultaneously to provide enough testosterone for young men.

They also need to be changed every day. There is a moderate incidence of skin allergy and many young men do not like the idea of having a visible preparation on their skin.

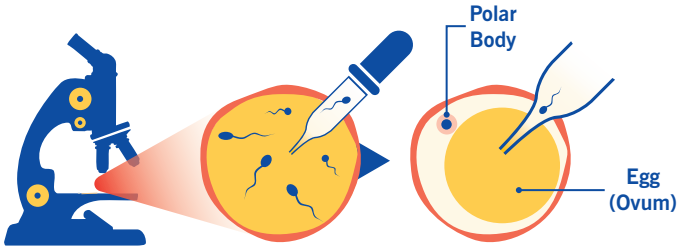
Testosterone gels, which are rubbed into the skin, provide normal pubertal progress and adult male hormone levels. Testosterone gels are accepted by older men. However, the gel needs to be applied daily and is a little messy. Most young men either refuse this type of treatment or do not use regularly, resulting in poor management of testosterone levels.

Adulthood and Fertility

As well as adequate testosterone replacement where needed, men with KS frequently seek advice with regard to fertility. In the past they were told that they would not be able to father children at any time. The only exception to this rule was the occasional man with a mixed (mosaic) chromosome pattern, where reduced sperm numbers could still allow fertility.

Intra-Cytoplasmic Sperm Injection (ICSI) technology has changed the outcome for men with KS. Firstly, sperm is retrieved using one of several techniques. Using a very tiny tube with the aid of a microscope, a single sperm, if found, can be removed and put together by the technique of In Vitro Fertilisation (IVF) with an egg (ovum).

Diagram 3 : INTRA-CYTOPLASMIC SPERM INJECTION (ICSI)



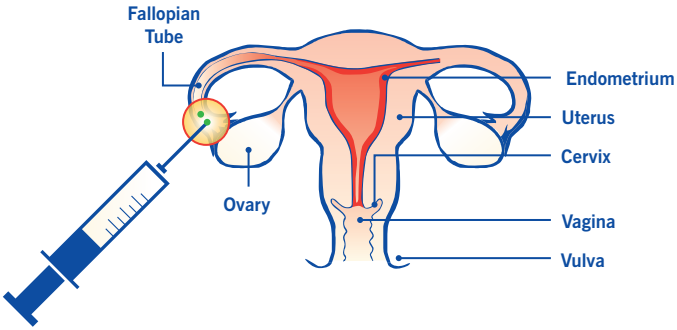
Under a microscope, one sperm is collected

Under a microscope one sperm is injected, with a small instrument, directly into the egg (ovum)

A slightly different method of assisted conception uses transfer of sperm into the female partner's fallopian tube, to allow fertilisation to take place naturally within the fallopian tube (this is called Gamete Intra-Fallopian transfer (GIFT)).

Several successful pregnancies resulting in live births have taken place using this technique. So far almost all children born after sperm salvage and transfer have had a normal set of chromosomes (46XX for girls and 46XY for boys). The risk for abnormal chromosomes seems to be less than that for other infertile couples having similar treatment.

Diagram 4 : GAMETE INTRA-FALLOPIAN TRANSFER (GIFT) IN THE FEMALE REPRODUCTIVE SYSTEM



As far as the technology is concerned, it is early days and with time there may be the likelihood that fertility chances may improve. This is however, a technique that is at present available for consideration for all young men with KS who wish to achieve fertility.

"The chance of a man being able to produce enough sperm for the technique to be successful is still quite limited."

Other Medical Problems

Most of the medical problems discussed in the previous chapter such as autoimmune diseases, osteoporosis or possible cancer risk, may only occur infrequently. It is important for the doctor attending a boy or man with KS to be aware of these conditions. A screening test for blood glucose levels, thyroid function, full blood count and cancer markers is usually taken every two years. This is in addition to a normal physical examination every year.

When a boy with KS transfers care from a paediatrician to an adult physician it is most important for him to provide the new doctor with information concerning his condition and with explanation of past treatment and future needs. Not all adult doctors may be aware of the details of a problem that causes more difficulties in youth than in adulthood.

Questions and Answers

Is a boy with Klinefelter Syndrome a "proper" boy?
Yes. The extra "X" chromosome does not cause any female appearance and boys with KS are almost always born looking exactly like other boys even though they may sometimes have undescended testes. The penis is normal and from physical appearances it is not possible to tell these boys apart from any other boy.

Does the extra X chromosome cause a female appearance?
No. The extra "X" chromosome's main function is to cause damage to the normal function of the testis. However a lack of testosterone at puberty can cause a boy with KS to have less well-developed muscles in the upper body and a relatively narrow shoulder girdle with somewhat wider hips and the deposition of fat on the abdomen. A lack of testosterone is also associated with the development of breast tissue in adolescence. The use of adequate testosterone replacement at and after puberty usually improves body shape and reduces breast tissue.

Do boys with Klinefelter Syndrome have normal intelligence?
There is a range of intelligence for all of the population. Boys with KS often do not achieve marks at school that are high enough to allow them to pursue a tertiary education. This is frequently due to specific learning problems in some areas and may be made worse by unrecognised behaviour or mood problems. If these issues are addressed early and with continued treatment and support, the chance of a boy with this condition achieving a much better outcome in terms of learning is higher.

Many boys and men with KS have different talents in a variety of arenas and occasionally most unusual expertise and flair in one particular area, whilst they may have quite major learning problems in another area.

It is very important to define talents at an early stage so that they can be nurtured and helped for the best possible outcome.

Do boys with Klinefelter Syndrome develop normally through puberty?
This varies a lot, from complete lack of puberty requiring medical attention to a very slow progress or a stopping of pubertal progress, which needs medical care. However many men with KS have had a perfectly normal growth and development process and the problem is only picked in adulthood at the time of a couple seeking fertility assistance.

Is sexual function normal with Klinefelter Syndrome?
Sexual function in young men is not correlated very well with testosterone levels and is frequently normal even though the testosterone levels may be quite low. In older men a normal level of testosterone is necessary to maintain normal sexual function. If sexual function has been poor due to lower male hormone levels, it returns to normal when appropriate replacement takes place. Boys and men frequently mix up different functions of the testis. Infertility simply means that sperm are not produced. Provided male hormone (testosterone) levels are adequate, sexual function is completely separate from issues of fertility and is completely normal.

Are boys with Klinefelter Syndrome tall?
Yes. Most boys with this condition are taller than average but height depends also on the height of the family. Boys with KS are not abnormally tall.

When should a boy with Klinefelter Syndrome be told about his condition?

Children only ever take in information at a level they can understand. A parent should not be frightened to talk to a boy with KS about his condition. It could be discussed as soon as the child is able to understand that he may have to visit a doctor periodically for check-ups, or that he may need to have extra help with learning at school or to see a psychologist.

As a boy becomes older he can ask questions suitable for his age and stage of development. Parents may find it difficult to discuss the subject. This can be started through simple explanations as to why he is receiving medication or attending a doctor. Any secrecy about the problem can lead to anxiety and distrust for a child and parents. Where information is lacking, imagination tries to fill the gaps and frequently the imagined problems are far worse than the real situation. Information from unreliable sources can also cause problems.

Many problems experienced by boys and men with KS can be assisted or corrected with appropriate treatment. Awareness of potential risks for lifetime conditions helps a person to take a healthy preventative attitude to his own management.

Most people and many doctors are still not aware of the possibility for fertility for boys with KS. Understanding this potential option for the future can be extremely helpful in relieving anxiety and concern about one's future.

Who should be told about a diagnosis with Klinefelter syndrome?
Parents and a boy with this condition should know about it and any doctor treating a boy with KS should be made aware of the diagnosis. Decisions about whether other relatives or friends should know about the condition may best be made in consultation with a paediatrician or adolescent doctor.

It may be hard for some people to understand the implications or variations of differences in sex chromosomes and they may have varying (usually incorrect) ideas about what they mean. Information of this sort is a private matter for most individuals and does not need to be divulged in public.

However, it may be necessary for certain members of school staff to have some understanding about very specific learning difficulties at school in the context of the underlying condition and occasionally it may be appropriate for this information to be divulged. Problems of fertility need to be discussed with a long-term sexual partner. It is not necessary to divulge these details to a casual partner.

Why does Klinefelter Syndrome increase the risk of osteoporosis?
Testosterone in the adult male is necessary to maintain bone quality, to increase the thickness of the outside part of the bone and keep mineral levels constant on the inner bone structure. Provided testosterone levels remain adequate throughout adolescence and adulthood, osteoporosis should not occur. However if the testosterone replacement is not maintained and if the levels are low, bone will be lost and osteoporosis may result with a long term risk of fractures, particularly in the back bones (vertebrae). This can cause chronic pain and disability. Monitoring to assess bone density should be obtained by consultation with a specialist.

Is life-span normal for a man with Klinefelter Syndrome?
There is no evidence to suggest that men with KS have a reduced life-span although they can have an increased risk of developing life threatening conditions such as diabetes mellitus, leukaemia and lymphoma.

How is a specialist selected for adults with Klinefelter Syndrome?
When the time comes for a boy with KS to be transferred to adult care, he should take with him a letter from his paediatrician, detailing all of the possible problems that have been outlined in this booklet that may possibly occur during adulthood. Although KS is a common condition, the difficult parts of management are often seen by a paediatrician and therefore doctors dealing with adults with this condition may not have a full knowledge of the problems that occur.

Does Klinefelter Syndrome occur due to the age of the boy's parents?
No association has been seen with age of either parent.

Notes

Notes

Glossary

Adolescence
The period in development between the onset of puberty and adulthood.

Autoimmune disease
An illness caused, or associated with, the development of an immune response to normal body tissues.

Chromosome
A thread like structure that carries genetic information in the form of genes composed of DNA. Normally, each human cell contains 23 pairs of chromosomes of DNA. Normally, each human cell contains 23 pairs of chromosomes, one pair of these are the sex chromosomes. Genes and chromosomes are like blueprints for the body's development, and so play a large part in determining a person's characteristics.

Chromosome mosaic pattern
Some cells in the body have the normal number of chromosomes (46) with normal male sex chromosomes present (XY) and some have an extra "X" chromosome.

Chronic
A term used to describe a disease or condition persisting for a long period of time, often for the remainder of the person's lifetime.

Diabetes
Any disorder of metabolism causing excessive thirst and the production of large volumes of urine.

Ejaculate
The fluids ejected (e.g. semen) from the urethra.

Endocrinologist
A doctor who specialises in the disorders of the endocrine glands (hormone specialist).

Gamete Intra-Fallopian Transfer (GIFT)
A technique where the egg and sperm are transferred into one of the fallopian tubes to allow fertilisation to take place naturally within the fallopian tube.

Sugar
Normally circulating in the blood of all people, but sometimes found at higher levels than normal.

Hormones
Blood chemicals that stimulate growth and sexual development and help to regulate the body's metabolism. Normally the body carefully controls the release of hormones as too much or too little may disrupt the body's delicate balance. They are produced by endocrine glands and carry messages from one cell to another via the bloodstream.

Hormone replacement treatment
Treatment of diseases with substances that stimulate hormonal effects.

Hypogonadism
Reduced function of the sex hormone producing glands as a result of either poor structure of those glands or a lack of message to them from the brain.

Infertility
Inability to reproduce offspring (male or female).

Intra-Cytoplasmic Sperm Injection (ICSI)
The method of fertilisation by injection of sperm into the cytoplasm of an egg.

Intramuscular
Injected directly into the muscle tissue.

In Vitro Fertilisation (IVF)
The process of fertilising a woman's egg outside her body, allowing it to grow and inserting it back into her body.

Leukaemia
Malignant disease where there is an excess of white blood cells.

Lymphoma
Any malignant tumour of lymph nodes.

Osteoporosis
A condition that is characterised by thin, brittle bones.

Paediatrician
A specialist in children's diseases.

Prostate Gland
A small conical gland at the base of the male bladder and surrounding the first part of the urethra.

Puberty
The process of physical changes when a child's body becomes an adult body and becomes physically capable of reproduction.

Subcutaneous
Under the skin.

Seminoma
Malignant tumour of the testis.

Teratoma
Tumour (usually malignant) of embryonic origin most commonly found in the testes and ovaries.

Testes
The male reproductive glands, which produce sperm, the male reproductive cells.

Testosterone
Most potent male sex hormone, which is produced in the testes (testicles) and controls male sexual development.

Thyroid
The ductless gland found on both sides of the trachea that secretes the hormone thyroxine which controls the rate of metabolism.

Under active thyroid gland
Chronic inflammation of the thyroid gland.

Undescended testes
Testes that do not descend into the scrotum and remain within the abdomen or inguinal canal.

Virilisation
The process of changing from a child like to adult physical appearance under the effect of male hormone.

"X" Chromosome
The female sex chromosome.

"Y" Chromosome
The male sex chromosome.

Yolk sac tumour
A rare cancer found in the midline of the body.

Support Organisations

Andrology Australia
c/o Monash Institute of Medical Research
PO Box 5418, Clayton, VIC 3168
Australia
www.andrologyaustralia.org

Australian Klinefelter Syndrome Support Groups
www.klinefeltersyndrome.org/australia.htm

The American Association for Klinefelter Syndrome
www.aaksis.org

Klinefelter's Syndrome Association UK
www.klinefelter.org.uk

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Merck is proud to bring you this booklet from the *Hormones and Me* educational series. We aim to provide readers with a better understanding of the issues relating to endocrine disorders particularly in children. We hope that you find it a valuable and helpful resource.

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Speak to an appropriate healthcare professional

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Hormones and Me

Klinefelter Syndrome

This booklet is valuable reading for boys who have Klinefelter Syndrome.

It is also recommended reading for their family and friends.