Klinefelter Syndrome - An Overview

by Dr Shirley Ratcliffe

Historical Background
The collection of symptoms known as Klinefelter syndrome was first put together in 1942 by a young doctor in Philadelphia called Harry Klinefelter(1). He described 9 men who had breast development, small testicles with no sperm in their semen, and a blood test revealed raised levels of the factors (gonadotrophins) which try to stimulate the testicles to produce more of the male hormone (testosterone) and greater numbers of sperm.

What causes these problems?
In 1959 it was shown that these changes resulted from the presence of an extra X chromosome in each of the cells of the body in males with Klinefelter syndrome(2).

What are chromosomes?
Chromosomes are minute structures shaped rather like matchsticks and are found in the centre (nucleus) of each cell in our bodies, and they carry the messages which allow us to inherit characteristics from our parents. In humans each cell has 46 chromosomes, 23 from each parent. The chromosomes are made up of thousands of genes which determine many factors in our development, e.g. height, colour of hair and eyes, the shape of our faces, our intelligence to a considerable extent, as well as the risks of getting certain diseases. Two special chromosomes, the X and the Y determine whether a person will be male (XY) or female (XX).

The chromosomes in Klinefelter syndrome
As in all human activity, mistakes occur and at times an egg cell or a sperm is formed which carries an extra chromosome. In boys with Klinefelter syndrome this is an extra X chromosome (47,XXY). An extra X can also be found in some girls, this results in the child having three X chromosomes instead of two, and is known as triple X.

The frequency with which Klinefelter syndrome occurs has been shown from surveys of the population to be 1 in 750 male births(3), so that in Britain around 400 baby boys will be born with the condition each year, although in many this will not be recognised until they are adults.

Using modern techniques it has been shown that in approximately half of these cases the mistake has occurred in the mother's egg cell, and in the other half in the father's sperm. Once the mistake has happened it cannot be altered but the effect it will have on the person's health and development can be modified by appropriate treatment.

Why does it happen?
The vast majority of mothers and fathers who have a child with Klinefelter syndrome have normal chromosomes themselves. Despite careful searching for the reasons why the mistake occurred in only a few cases can we find any explanation; in these cases the older age of the mother contributes probably through a longer exposure to factors, which can damage the egg before it ripens.

Will it happen again?
This is extremely unlikely, but if you are worried then the chromosomes of the next child can always be checked early in the pregnancy.

What effect will it have on the child?
Baby boys with Klinefelter syndrome tend to be rather smaller at birth than average in

respect of weight, length and the circumference of the head. The genitals are those of an ordinary male baby and the penis is usually of normal size. Occasionally one or both of the testicles will not have come down in the scrotum, if so this may need correction by a minor operation before the boy is two years old.

As the baby grows into a toddler you may find that learning to talk tends to take a little longer than average for a boy, pronouncing words correctly may be difficult; in such cases speech therapy will be helpful and usually can be started when the child is between 3 and 4 years of age(4).

What about intelligence?
When groups of boys with Klinefelter syndrome from population surveys have been studied it has been shown that there is a small lowering of the IQ scores that would have been expected in that particular family. The average IQ score was 98 compared with our expected value of 112, with a wide range from 70 to 130. It is still possible to have above average intelligence and men with Klinefelter syndrome have been found in all walks of life. There is a tendency for these boys to do less well at school than their brothers and sisters, and it is important, therefore, to avoid emphasising differences within the family in order not to discourage the boy.

Progress at school
Around three-quarters of boys with Klinefelter syndrome have difficulty in learning to read, and will require special help on a one-to-one basis.

The problem is caused by a number of factors, poor memory, short attention span, and difficulty in keeping things in the right order.

More repetition than usual is required in order to remember what has been learned, together with much patience on the part of teachers, and parents.

It is helpful for parents to continue to read to the boy beyond the usual age, to help develop a pleasure in storytelling and to counteract the difficulties the boy himself experiences in retaining the thread of a story in the face of the continual stumbling with the process of reading.

In addition the social side of school can present problems, as the majority of boys with Klinefelter syndrome do not like fighting, and may find it hard to stand up to any bullying. They tend to be sensitive children who are easily moved to tears and this can make them the targets of more aggressive boys.

Physical growth
During childhood many boys with Klinefelter syndrome grow faster than usual especially in the length of their legs. There may be a tendency to be thin with poor muscle development, which can be counteracted by encouraging sports such as swimming. Competitive sports and those involving rough body contact are often disliked.

While muscle development may be poor, there is a tendency in about 75% of the boys to start to put on extra fat from around age 7. Careful avoidance of the intake of unnecessary sweets and fattening food such as chips and crisps is very important to prevent the development of an unattractive obesity, which can increase a boy's difficulties at school.

Sexual Development in Adolescence
The age of starting to change from a boy to a man usually occurs at the expected time and progresses normally at first, with growth of the penis, and development of pubic hair, and

hair under the arms. The voice breaks and becomes deeper. However the testicles do not enlarge fully and the level of the male hormone (testosterone), though rising at the beginning of adolescence, tends to falter and may need supplementing around age 15 to 16 years. In a minority of boys the penis does not enlarge as much as usual - the boy will seldom complain of this but may react by refusing to undress in public for school sports or swimming. Should such problems arise then extra testosterone using tablets or injections can be prescribed by the doctor and will gradually correct the problem(5).

In a small number of boys with Klinefelter syndrome excessive tallness may become a problem and again can be treated by the doctor using injections which need to be started in good time.

The original description of the condition by Dr Klinefelter included breast development in all 9 cases - when larger numbers have been examined the frequency with which this occurs is around 60% often starting around 13 to 14 years of age. In the majority it goes away on its own (and indeed occurs in about one third of all boys) but should be carefully watched by a doctor experienced in the problem. Should the breast development not subside itself then the boy should be referred to a plastic surgeon who will remove the breast tissue without leaving any scars(6,7).

Psychological adjustment
As can be seen from the description so far of what it means to have Klinefelter syndrome, there are a number of possible problems. Some boys will experience very few but others may have a harder time and may feel overwhelmed. It is important to acknowledge that this is legitimate and to seek specialised help when it is needed. Some boys react by "bad behaviour", rudeness to parents, defiance of the rules of their homes, truanting from school, stealing. Should this happen it is important to seek help from your GP, the guidance teacher at school, and from a specialist. Much can be done to prevent these behaviours from leading the boy into serious conflict with society to his own disadvantage.

Homosexuality is not more common in Klinefelter syndrome than in men with normal chromosomes.

Fertility
99.9% of men with Klinefelter syndrome will not be able to father children due to failure to produce sperm. In a few cases sperm may be produced for a brief period. It is always necessary to check the sperm count before making a definitive statement about future fertility. This requires the young man to produce a specimen by masturbation at the laboratory so that it can be examined immediately.

When should a boy with Klinefelter syndrome be told about his condition? Our practice is to start to explain in simple terms that the boy can understand at around age 10 to 11. We say that the blood test showed a variation in the cells that can make him grow too tall and put on weight easily, this explains why he is attending hospital and having tests done.

Should he need testosterone supplementation we explain this in terms of helping muscle development or growth of the genitals.

When we come to discuss fertility around age 18 we explain that while he is unlikely to have children, he will be able to have sexual intercourse like any other man. Many men with Klinefelter syndrome marry and their wives achieve pregnancy with the help of anonymously donated sperm from the infertility clinic when they want a family.

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