

# Klinefelter's syndrome

## AN ORIENTATION

PUBLISHED BY THE NATIONAL SOCIETY OF TURNER CONTACT GROUPS IN DENMARK

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## Introduction

This booklet was written and published in the light of a tremendous need for further information on Klinefelter's syndrome.

It is in no way an attempt of giving a complete description of all aspects of Klinefelter's syndrome.

The booklet was written in order to give a better information to Klinefelter-boys and their parents as well as to adult males with Klinefelter's syndrome, but it is also our hope that it will be read by genetic counsellors, physicians, teachers and others who come into contact with boys and adult males with Klinefelter's syndrome. More information on all levels will, however, first and foremost be valuable to Klinefelter-males and their relatives.

Publication by the Danish National Society of Turner Contact Groups should be seen as an expression of this society's wish to participate in the spreading of knowledge of Klinefelter's syndrome and create the possibility of establishing Klinefelter contact groups. Furthermore, to make an information, counselling and research center for people with Turner's syndrome and other sex chromosome abnormalities such as Klinefelter's syndrome, triple-X and XYY syndrome.

Johannes Nielsen

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## The name Klinefelter's syndrome

Klinefelter's syndrome is named after an American physician, Harry Klinefelter. In 1942, Harry Klinefelter and associates described the syndrome in males who were characterised according to their description by a tendency to breast development, considerably decreased production of sperm cells and increased excretion of pituitary hormones, the so-called follicle stimulating

and luteinising hormones.

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### **How frequent is Klinefelter's syndrome?**

Klinefelter's syndrome is found in approximately 1 per 1,000 males. That is to say that in Denmark with a population of 5 million there are approximately 3,000 males with Klinefelter's syndrome.

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### **What is the cause of Klinefelter's syndrome?**

Males usually have one X and one Y chromosome, i.e. the chromosome constitution 46,XY. Males with Klinefelter's syndrome have two X chromosomes (47,XXY), in rare cases three (48,XXXY) or four (49,XXXXY) X-chromosomes. The X-chromosomes carry genes in terms of development of testicles, sex hormone production and physical sex development in general as well as to a certain extent also height growth.

The chromosome constitution 47,XXY is found in approximately 80 %. In 6 % there is normal chromosome constitution, 46, XY, in part of the cells and 47,XXY in the rest, i.e. a so-called chromosome mosaic. In 5 % there are two X chromosomes and no Y chromosome (46,XX). In the rest there are three or four X-chromosomes or other forms of extra X-chromosome material.

Further information on the chromosome aberrations in Klinefelter's syndrome as well as other conditions in this syndrome may be found in the books mentioned in the list of literature on the last page of this booklet.

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### **What is the cause of the chromosome aberration in Klinefelter's syndrome?**

Certain chromosome aberrations appear more frequently in children of elderly mothers and, to a certain extent, also elderly fathers, but this is not the case of Klinefelter's syndrome, and today nothing definite is known about causes leading to an increase in the number of X-chromosomes as found in Klinefelter's syndrome.

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### **Does a new-born boy with Klinefelter's syndrome present any signs of**

## **this syndrome?**

No! Boys with Klinefelter's syndrome are usually quite normally developed at birth.

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## **How is the development of these boys during childhood?**

Boys with Klinefelter's syndrome are often slightly more quiet and passive as babies, and usually they have a less pronounced assertive age than their siblings. It is, however, conditions that do not play any great role for their development if there is awareness of the fact that it is important to take as much care of the baby who is quiet and passive, as of the baby who is active and demanding. It is also important not to suppress the Klinefelter-boys in their relatively weak independence period. More often than other boys Klinefelter-boys have a somewhat delayed motor and linguistic development as well as a delayed maturing period, which, however, in no way make them patients or in need of special treatment. This tendency to a somewhat delayed development in the above-mentioned areas can and should, however, to a great extent be counteracted or prevented by increased psychological, social and motor stimulation at home as well as in the day institution - the kindergarten.

It is important that quite early during childhood these boys attend a good day institution, and that there is a close co-operation between the parents and the staff in the institution - the kindergarten. If there is a retardation in language development it is important to have speech pedagogue assistance during a period. With regard to the motor development, participation in parent/child sport activities and group activities of any kind is of great value. The same is the case with regard to stimulation of the slightly retarded maturity development. In this connection it might be mentioned that it is important to stimulate these boys to independence and in no way to overprotect them.

If Klinefelter-boys are not treated with testosterone during puberty, they will usually have more difficulties than other boys. It is important that testosterone treatment is given from the age of 11. If this is the case and the conditions at home are good and stable, these boys will have a puberty development, which is somewhat late, but otherwise within the normal range.

A tendency to an increased need of sleep and tiredness, to a great extent can be counteracted or totally eliminated by testosterone treatment. With regard to muscle development and development of motor abilities from the earliest childhood, participation in different types of sport during childhood is of great importance.

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## **Are Klinefelter-boys of average intelligence?**

If Klinefelter-boys grow up in a good, stable and stimulating environment their intelligence will usually be within the normal range, even if the 10 distribution is somewhat skewed, so that there are slightly fewer boys than expected with an intelligence level above 110, but there is no increased frequency of boys with an intelligence level below 90. In a group of adult Danish males with Klinefelter's syndrome we found an average intelligence level of 108 compared to 115 in a control group.

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## **How do they manage at school?**

Boys with Klinefelter's syndrome manage within the normal range, but with a tendency to certain learning difficulties, especially during the first years at school. This can, however, be remedied by an increased pedagogical effort in relation to need. Learning difficulties are most pronounced during the first years at school, and they are not present in nearly all Klinefelter-boys, but it is, however, important to know that if such difficulties are present, they need to be investigated and dealt with accordingly, both at home and at school. Learning difficulties such as a short memory span can be overcome by careful analysis and appropriate measures. It is of great importance for both parents and educators to know this and to act accordingly. If there are problems in relation to speech development it is also important that speech therapy is given.

If conditions at home are good, stable and stimulating, and if there have been good conditions in the day institution, where the Klinefelter-boy has been, learning problems rarely have any consequences.

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## **Do they have special diseases during childhood or later in life?**

Boys with Klinefelter's syndrome have no increased risk of special disorders. They have, however, an increased risk of developing mamma tissue in late puberty. This appears in approximately half of these boys. The mamma tissue can be removed if it is cosmetically disturbing. This operation should always be made by a plastic surgeon so that the scars can be as small and invisible as possible. Otherwise the scars may be as psychologically straining as the mamma tissue was before the operation.

With testosterone treatment from the age of 11 it is possible that development of mamma tissue can be reduced or prevented.

There are indications that varicose veins and ulceration on the legs are more frequent than expected in elderly males with Klinefelter's syndrome. It is, however, possible that continuous testosterone treatment from the age of 11 can prevent such development.

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### **How is the height growth?**

Boys with Klinefelter's syndrome have a somewhat greater height growth acceleration than other boys from about 4-5 years of age. This is especially due to an increased growth of the legs, but also to a certain extent of the body. The average final height is a few cm above the expected height, but Klinefelter-males are within the normal range as far as height is concerned, and the increased height does not present any problems. Testosterone treatment from the age of 11 tends to reduce the increased height.

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### **How is the physical sexual development?**

Klinefelter-boys have testicles of normal size at birth, but whereas the testicles in boys with normal chromosomes rapidly increase in size around the age of 11-12 from the average size of 2 to 12 ml, the testicles of the Klinefelterboys usually stay around 2 ml or below that all through life.

The Klinefelter-boys develop a normal scrotum, and penis is usually of normal size. In the few cases where penis is quite small, this can be treated with testosterone ointment with a good result.

Body hair and beard growth is usually somewhat sparse and below that of normal males, but also in this case testosterone treatment from the year of 11 has a normalising effect.

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### **How is the development of sexual libido and potency?**

Sexual libido and potency develop normally, especially if testosterone treatment is given from the age of puberty. In connection with information to parents of boys with Klinefelter's syndrome it is important to stress this information, and the same is true when information is given to Klinefeltermales in connection with counselling testosterone treatment.

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## **Are Klinefelter males able to have children?**

As a rule only a few sperms are present in the testes, usually only a few thousand sperms per ejaculation compared with 200 mill. sperms per ejaculation in males with normal chromosomes.

In spite of this condition a few males with Klinefelter's syndrome (6 cases) have got children with paternity well documented on account of blood typing.

However, it is possible that some Klinefelter-males with chromosome mosaics, i.e. normal chromosomes in part of the cells (46,XY14/,XXY), actually are fertile. There is a description of a Klinefelter-male with a chromosome mosaic, 46,XY/47,XXY, who was the father of 3 sons. When fertility counselling, advice should, however, always be given to consider adoption or in vitro fertilisation with semen from donor.

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## **Are Klinefelter-males more often homosexuals than expected?**

Several parents of a Klinefelter-boy are afraid that their son with two X-chromosomes and one Y-chromosome may become homosexual. The chromosome constitution has, however, nothing to do with homosexuality, and Klinefeltermales have no increased tendency to homosexuality.

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## **Are Klinefelter-males real males?**

Klinefelter-males identify themselves as males and are as much real males as males with normal chromosomes.

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## **Can Klinefelter-males marry?**

The above-mentioned information hopefully makes it quite clear that Klinefelter-males can marry as well as other males, adopt children or get children by donor insemination. Klinefelter marriages are most probably neither better nor worse than other marriages. A prerequisite for a good sexual relationship is, however, usually regular testosterone treatment.

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## **Should male sex hormone (testosterone) be given?**

The male sex hormone, testosterone, is produced mainly in the testicles. On account of insufficient development of these, the production of testosterone is not sufficient, and it is important that testosterone is given, preferably in the form of testosterone tablets (testosterone undecanoate, Restandol) already from the age of 11. Usually this treatment ought to be continued till the fifties and then gradually scaled down. Treatment may also be given in the form of injections with so-called depot testosterone every second, third or fourth week.

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### **How about occupation and adaptation to work?**

With regard to occupation, Klinefelter-males are in the normal range, but with the main stress on the manual occupation, unskilled and skilled labourers, and relatively few with academic jobs. Investigations of a group of Danish males with Klinefelter's syndrome followed through 20 years to an average age of 47 have shown that males who grew up under good, stimulating and stable conditions and who have received testosterone treatment are well adjusted as far as work is concerned and have a degree of occupation on the level expected for their age group.

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### **Is Klinefelter's syndrome a disease?**

No! Boys with Klinefelter's syndrome should definitely not be regarded as patients. With fully detailed information to parents and themselves, and when growing up in a good and stimulating environment as well as receiving hormone treatment at the right age these boys will usually manage quite well and at any rate within the normal range. But on the other hand there is no doubt that it may be stressing to have Klinefelter's syndrome, even if one grows up in a good and stimulating environment. The fact that it is usually necessary to take hormone treatment and that there are not many chances of having children is of course unpleasant, and the same is the risk of developing breast. Breast development may, however, be operated with good result, and testosterone treatment from the age of 11 may prevent such development.

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### **Is there an increased risk of getting mentally ill?**

For boys with Klinefelter's syndrome, who grow up in a good environment and who have got the love, support and stimulation they need as well as hormone treatment and information, there will be no increased risk of mental

disorders.

For males with Klinefelter's syndrome, who grow up in poor environment without sufficient stimulation and information to their parents and to themselves, there is a slightly increased risk of having mental problems, which may lead to anxiety, loneliness and problems with social adjustment and work. These males may, however, be helped by psychological/psychiatric counselling and treatment. There are under no circumstances any increased risk of schizophrenia, manic-depressive disorders or other serious mental disorders.

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### **Should parents have fully detailed information?**

Yes! Parents of boys with Klinefelter's syndrome should always have fully detailed information. It is very important that parents get as much knowledge as possible about Klinefelter's syndrome as early as possible in the life of their son and preferably already from the date of birth. This is important for many reasons, but especially because it makes it possible for them to create the best possible conditions for their son with Klinefelter's syndrome with maximum stimulation in all aspects and with incitement to independence and maturity, trying to avoid overprotection and infantilising.

Many examples show that parents who relatively late got the information that their son had Klinefelter's syndrome have realised that they could have done much more for him if at an earlier period in life they had got the information on what Klinefelter's syndrome is, and what can be done for these boys.

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### **Should males with Klinefelter's syndrome have fully detailed information?**

Should boys with Klinefelter's syndrome have information on all conditions concerning this syndrome such as chromosome constitution, hormone conditions etc.? As in the case of information to the parents the answer according to our experiences in Risskov is definitely yes.

It is clearly wrong to try to protect a boy with Klinefelter's syndrome by avoiding to explain to him what is wrong. He will try to find out about it himself anyway, and being secretive about it can only lead to anxiety and lack of confidence in parents, physicians and adults in general.

It is our experience that boys with Klinefelter's syndrome in the same way as others with sex chromosome abnormalities often have been poorly informed and informed too late. They have often made their own impression and

imagination about what is wrong, and this is usually worse than getting the real information.

It would have saved most Klinefelter-males a lot of anxiety and worries if they have got fully detailed information at an earlier time on why they were later developed than other boys, why they have small testicles or have developed breast tissue, and why they have scanty beard and body hair growth. The above mentioned conditions may, however, as mentioned under hormone treatment most possibly be reduced or even prevented by testosterone treatment from the age of 11.

It is also important for these males to get information on their relatively few chances of having children. At the same time they should also have information on the fact that their chances of adopting a child is as good as anybody else's, and one should also give them the information that adopting a child can give as much happiness for both parents and child as for biological parents and the same applies to donor insemination.

All the positive aspects of adoption should be stressed, and promises made to support and help if difficulties arise in relation to a permission to adopt a child. In the same way one should stress that with testosterone treatment they may have as normal a sexual life and married life as other males. A key word in the professional relation to boys with Klinefelter's syndrome is information and not only superficial information given quickly by a busy physician with relatively little experience of Klinefelter's syndrome.

Information of Klinefelter's syndrome should be given by persons with good knowledge and good experience of this syndrome and with a lot of time. I also think that such information should be given by members of Klinefelter contact groups or Klinefelter associations, if such groups are available, and if the boy or male in question is interested in talking with members of such a group.

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### **What kind of information should be given to parents, who have got a foetus with Klinefelter's syndrome diagnosed prenatally?**

Twenty-nine of 41 foetuses (71%) with Klinefelter's syndrome diagnosed by prenatal chromosome examination in Denmark were aborted until 1985. It is difficult to believe that so many parents would choose to have induced abortion of a foetus with Klinefelter's syndrome if they also had got fully detailed information about the many positive aspects of the development of Klinefelter boys as is known at present from follow-up studies of unselected groups of boys with this syndrome. It is of course up to the parents to decide whether they want to have a son with Klinefelter's syndrome or have an induced abortion after prenatal chromosome examination at least in a country with free abortion like Denmark.

Parents make their own decision whether to carry through the pregnancy in case of a foetus with Klinefelter's syndrome or interrupt it, but they make it on the background of information they are given by the counsellors, and the weight they have put on the positive contra the negative aspects as well as to some degree on the background of the counsellor's attitude to abortion of a foetus with Klinefelter's syndrome.

It is very important for prenatal counsellors to put as much weight on the information about intelligence in the normal area, even if it is slightly lower within this area as well as on the fact that these boys have approximately the same school and educational level as others.

Giving information about the risk of developing breast tissue, it is important to tell that this can be treated surgically with great success and that testosterone treatment from the age of 11 most probably will restrain or prevent breast development. When giving information on sterility and the very few chances of becoming father of a child, it should at the same time be told that the possibilities of adopting children are as great for Klinefelter-males as for others. Donor insemination should also be mentioned. It is also important to tell the fact that the relationship between adoptive parents and their children is as good as between biological parents and their children, and one should stress that males with Klinefelter's syndrome have as normal sexual and marital relations as others.

To hint at or to have the attitude that foetuses with Klinefelter's syndrome should be aborted is in my opinion a clear discrimination against males with Klinefelter's syndrome who usually are healthy physically and mentally, well adjusted and with an intelligence within the normal range.

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### **Should the public have information on Klinefelter's syndrome?**

Information to the public about Klinefelter's syndrome should be given by professionals with a good knowledge of Klinefelter's syndrome. Information should be given in close co-operation with Klinefelter contact groups where such groups are found.

We physicians have got and still get poor education with regard to giving fully detailed information to the public about disorders and deviations in general. It is my experience that the value of good understanding of any chromosome aberration and easily available information cannot be overestimated, and this is also the case of Klinefelter's syndrome.

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## **Klinefelter contact groups**

In the same way as there are Turner contact groups all over Denmark and a national society of Turner contact groups, there ought to be established Klinefelter contact groups. The first attempt with contact between 3-4 couples of parents of Klinefelter-boys was made in Aarhus in 1985. In this connection it might be mentioned that Turner contact groups are made up of girls and adult women with Turner's syndrome as well as parents of babies and girls with Turner's syndrome. Members of the contact group meet at varying intervals 4-8 times per year. There are now Turner contact groups in Copenhagen, Odense, Haderslev, Aarhus and Aalborg and as previously mentioned a national society. They talk about common pleasures and problems. They get to know each other. They get into contact with each other. They have a cosy time together or invite physicians and others to talk about Turner's syndrome or answer questions. If one is interested in further information on the Turner contact groups, such information can be procured from the chairman of the national society, Bente Konradsen, (same address as below), one can get the book about Turner's syndrome and Turner contact groups by Johannes Nielsen and members of Turner contact groups in Denmark published by the National Society of Turner Contact Groups in 1985 by writing to or calling Bente Konradsen.

If you are interested in Klinefelter contact groups you may call Johannes Nielsen, Cytogenetic Laboratory, Aarhus Psychiatric Hospital, DK-8240 Risskov, tel. +45 86 - 17 77 77, ext. 3680.

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## **Literature about Klinefelter's syndrome**

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