

The Importance of Early Diagnosis of Klinefelter's Syndrome

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The experience we have acquired at our laboratory from examining approximately 200 individuals with Klinefelter's syndrome clearly indicates that early diagnosis is of great value if subsequently a qualified team of experts provide full information, counseling, and treatment (if the latter proves necessary). The data presented here are taken from three of our studies of Klinefelter's syndrome, concerning (a) adults, (b) adolescents, and (c) newborn boys.

Adults with Klinefelter's Syndrome

This study comprises 34 adult males with 47, XXY and a control group of 16 severely hypogonadal males with 46, XY seen at the same hypogonadal clinic in Copenhagen over the same period. At the first psychological-psychiatric examination in 1965-66, they had a mean age of 26 years (Nielsen et al. 1969; Theilgaard et al. 1971). At the second examination they had a mean age of 36 years (Nielsen et al. 1980).

Occupational Rank

Table 1 shows some of the results concerning occupational rank at the follow-up study at the mean age of 36. The difference that had been found between the Klinefelter males and the controls at the first investigation had now increased, with more of the Klinefelter males going down the occupational scale as compared with the controls.

Working Capacity

Table 2 shows some of the results concerning social and occupational adjustment. These findings reveal that instability at work and lack of social adjustment in general were significantly more pronounced in the Klinefelter group than in the hypogonadal males with a normal chromosome constitution.

Table 1. Occupational rank at a mean age of 36 years

Occupational rank	Klinefelter's syndrome (%; n = 34)	Controls (%; n = 16)	Difference
Independent business or demanding job	12	38	NS
Unskilled labourer	44	13	<i>P</i> (Fisher) = 0.0528
Lower occupational rank than father	59	19	<i>P</i>(Fisher) = 0.0167
Higher occupational rank than father	9	38	<i>P</i> (Fisher) = 0.0437

Table 2. Social and occupational adjustment

Social and occupational adjustment	Klinefelter's syndrome (%; n = 34)	Controls (%; n = 16)	Difference
Well adjusted	48	93	<i>P</i> (Fisher) = 0.008
Poorly adjusted	28	7	NS

Table 3. Mental illness

	Klinefelter's syndrome (%; n = 34)	Controls (%; n = 16)	Difference
Previous mental illness	41	0	<i>P</i>(Fisher) = 0.002
Present mental illness	32	6	NS

Mental Illness

Table 3 shows some of the results concerning mental illness. It is quite evident from the follow-up study that many of the Klinefelter males (even if fewer than the controls) were living a normal and quite happy life and worked as hard as anybody else. Klinefelter boys, adolescents, and adults are, however, more susceptible to stress of any kind and thus to reactive mental disorders. Nevertheless, there were many indications that the increased frequency of mental illness among the adults could have been avoided altogether or at least reduced if **Klinefelter's syndrome** had been diagnosed during childhood; parents could then have been given professional information and counseling, and the boys could have received hormone treatment from an appropriate age, as well as informa-

tion and counseling as they grew up. Klinefelter males have no increased risk of schizophrenia or manic depressive disorders.

Criminality

The frequency of criminality with violation of the penal code was 29% for the Klinefelter group, compared with 13% for the control group. The difference is not statistically significant. A significantly higher frequency of major criminality has not been found in any of the few and small studies of unselected Klinefelter males. The increased frequency of Klinefelter males in certain institutions does not necessarily mean that such males are more likely to commit criminal acts. Rather the increase might very well be due to a greater likelihood of them being apprehended, which again might be explained on the basis of their personality development (passivity, timidity, feelings of insecurity, etc.).

Hormone Treatment

There has been no double-blind study of testosterone treatment, but in several of the 34 Klinefelter males investigated testosterone treatment had a beneficial effect. In one case a 27-year-old developed difficulties at work after testosterone treatment was terminated in his early twenties. He subsequently gave up his training as a mechanic, and although he had several jobs of short duration, his working capacity diminished. He began to use hash and LSD, committed several criminal acts (mostly burglaries), and was imprisoned for a while. After his release he was referred to a youth centre, where the psychiatrist described him as shy, insecure, and childish with a lack of self-confidence and feelings of inferiority. He was unstable and left the youth centre several times when problems arose. Treatment with testosterone was begun again, and after a few months of treatment at the age of 29 he changed completely. He now feels accepted, has confidence in himself, appears more mature, and has met a girl with whom he has satisfactory sexual relations. He has worked satisfactory since hormone treatment was reinstated and has embarked upon an apprenticeship as a blacksmith. There are several other similar examples in this study.

Testosterone in adequate doses from the age of 11-14 years, preferably at the time of increase in FSH and LH concentrations, is probably of preventive value in the majority of Klinefelter boys as far as the risk of adverse alterations in behavior, concentration, and learning abilities is concerned. Testosterone may also increase feelings of wellbeing, as well as sexual libido and potency. It usually increases muscular development and strength and may prevent gynecomastia.

There is, however, a lack of sufficiently well controlled, long-term studies of the effect of testosterone treatment in males with Klinefelter's syndrome, especially in Klinefelter boys from around the age of 11 to 14. Such studies should be encouraged, especially in order to establish whether all males with

Klinefelter's syndrome actually need testosterone treatment, or whether there are some who do not, e.g., those who have a normal testosterone level.

From the present study, as well as from a number of others, there are, however, strong indications that testosterone treatment is valuable in Klinefelter males, even if given after puberty. Anne11 et al. (1970), Caldwell and Smith (1972), and Johnson (1975) obtained good results with testosterone treatment in boys with Klinefelter's syndrome in early puberty, and a number of authors have reported good results with testosterone treatment in young males with Klinefelter's syndrome (Bablok and Janczewski 1969; Myhre et al. 1970; Beu-mont et al. 1972; Becker 1972; Fromantin et al. 1974).

Adolescents with Klinefelter's Syndrome

The following data are from a study of 15 schoolboys with Klinefelter's syndrome; comparisons are with ten controls (i.e., boys with normal karyotypes and small testes) from the same schools (Sorensen et al. 1981).

Early Development

Table 4 shows that the Klinefelter boys suffered from delays in speech and language development and speech disorders which mainly comprised stuttering and expressive difficulties.

Table 5 shows that defiance reactions in early childhood were extremely rare in the Klinefelter boys, who were considered shy, timid, and reticent by

Table 4. Speech and language development

	Klinefetter's syndrome (%; n = 15)	Controls (%; n = 10)	Difference
Delayed speech and language development	73	0	<i>P</i> (Fisher) = 0.0006
Speech disorder at preschool age	47	0	<i>P</i> (Fisher) = 0.02

Table 5. Defiance reactions, shyness, and timidity

	Klinefetter's syndrome (%; n = 15)	Controls (%; n = 10)	Difference
Defiance reaction	7	60	<i>P</i> (Fisher) = 0.01
Shy, timid, and reticent	100	10	<i>P</i> (Fisher) = 0.0001

their parents. Most of the boys with Klinefelter's syndrome were described as quiet and stolid in early childhood, and the majority preferred quiet games. This pattern was significantly different from that found among the controls [$P(\text{Fisher}) = 0.0211$].

The development of the Klinefelter boys had been deviating from that of the controls from early childhood. Delayed speech and language development was found to the same degree as in the longitudinal studies of unselected newborn Klinefelter boys described in the last part of this paper. Furthermore, speech difficulties remained prominent in several Klinefelter boys even when they were of school age.

These difficulties were often phonological, but expressive difficulties were also common. It is likely that auditory discrimination difficulties, which seem quite common in Klinefelter boys during childhood, are a contributory cause of the delayed speech development.

As mentioned above, one of the most striking features during early childhood was the almost total lack of defiance reaction. Defiance is one of the ways in which the child manifests independence; however, Klinefelter males seem to have little need for independence during childhood and adolescence, displaying as they do passivity and strong dependence on parents.

These findings might indicate an increased risk of mental illness during childhood, and a number of studies have also revealed an increased frequency of Klinefelter's syndrome among child psychiatric patients. We have studied 11 child psychiatric patients with Klinefelter's syndrome (Nielsen et al. 1970). Most of the boys were extremely quiet and easy to take care of during early childhood and expressed no defiance reactions. In spite of normal intelligence in most cases, difficulties with schoolwork were prominent features. The boys were weak, passive, and lacked initiative. They gave up easily and had difficulties in concentrating. All except two had neurasthenic symptoms. The same traits were found by Anell et al. (1970), who studied ten child psychiatric patients.

It is interesting that the Klinefelter boys in this study, although they were unselected as far as mental state was concerned, resembled in many ways the boys in the above-mentioned studies in psychiatric hospitals.

School Age

The teachers filled in questionnaires for the Klinefelter boys and the controls without knowing who had Klinefelter's syndrome. Some of the results are shown in Figs. 1 and 2. Intellect, attention, interest, and level of activity were all significantly lower in the Klinefelter boys than in the controls. Difficulties in concentrating were also more pronounced in the Klinefelter boys ($P < 0.01$), as were speech difficulties ($P < 0.05$) and dependence on parents ($P < 0.025$).

Seventy-five per cent of the boys with Klinefelter's syndrome had been referred to the school psychologist for an examination, compared with 33% of the control boys [$P(\text{Fisher}) = 0.0231$]. The boys referred to the school psychologist all had remedial teaching for a varying length of time.

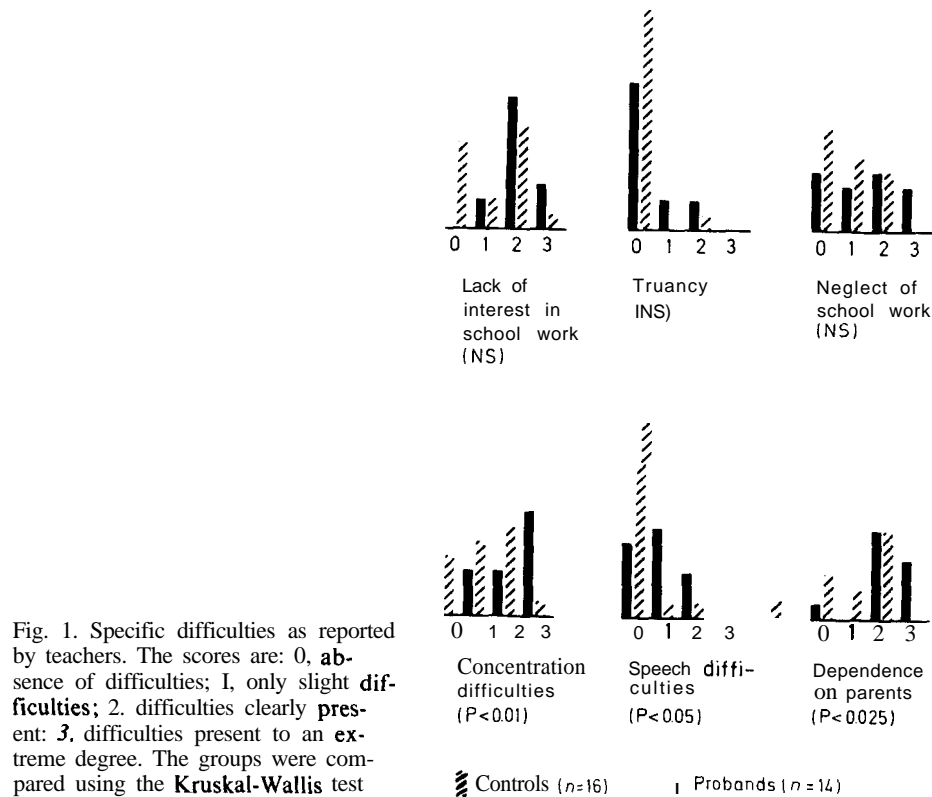


Fig. 1. Specific difficulties as reported by teachers. The scores are: 0, absence of difficulties; 1, only slight difficulties; 2, difficulties clearly present; 3, difficulties present to an extreme degree. The groups were compared using the Kruskal-Wallis test

Table 6 shows the results of intelligence testing with the WAIS test. Although the Klinefelter boys had lower IQs, with a mean verbal IQ of 91 compared with 109 in the controls, most of them had intelligence within the normal range, and their intellectual level and poor school attainment were disproportionate. Closer analysis of the intellectual functions revealed that the Klinefelter boys had the most pronounced difficulties in those WAIS subtests which required understanding of social and human causality. In the projective tests, the most remarkable feature in both the Klinefelter boys and the control group was the rather poor adaptation to the male gender role. If it is assumed that re-

Table 6. Intelligence, testing with WAIS

	Klinefelter's syndrome (%; n = 15)	Controls (%; n = 10)	Difference
Mean verbal IQ	91	109	P < 0.001
Mean performance IQ	101	111	P < 0.05

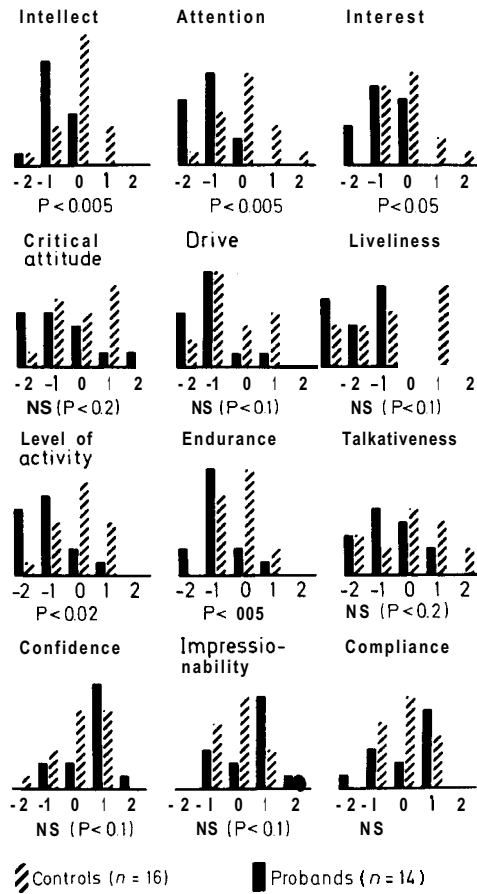


Fig. 2. The degree of some characteristics of the 14 Klinefelter boys and the 16 controls as reported by their teachers. Explanation of scores in Fig.

jection of tables in TAT or rejection of drawing a self-portrait are indications of difficulties in this area, the Klinefelter boys had significantly more male gender role problems than the controls. They also had significantly lower masculinity scores than the controls. This should not, however, be interpreted as feminization of the Klinefelter boys but rather as demasculinization.

The findings support the view that gender role is not entirely socially determined: Biological factors such as sex chromosome constitution and pre- and postnatal sex hormone levels are also involved.

Sexual Activity

Sexual activity and sexual libido as judged by the frequency of masturbation were significantly lower in the Klinefelter boys, compared with a large, unselected group of young Danish males ($P < 0.01$) examined at the compulsory draft examination (Hertoft 1968). Neither the Klinefelter boys who had re-

ceived testosterone for more than a year nor the control group differed from the expected frequency. This is one good reason for early diagnosis and treatment with testosterone from the age of puberty.

Hormone Treatment

All Klinefelter boys were offered testosterone treatment. The results of the hormone treatment were considered favorable when the boys, as well as the parents, reported a clear improvement in psychic functions. It was taken as further confirmation of the beneficial effect of testosterone if the school reported a similar improvement in behavior, learning, and concentration, or if cessation of treatment, perhaps only transitory, resulted in relapses. Judged by these criteria, 10 of 11 Klinefelter boys who had received testosterone for more than a year were considered to be clearly improved. The improvement was most often described as increased vitality, increased zeal and capacity for work, and improved ability to concentrate.

With regard to sexual activity, there was no doubt that testosterone treatment resulted in increased sexual libido, but the treatment did not eliminate the poor adaptation to the male sexual role.

Summary

Table 7 shows that the Klinefelter boys differed significantly from the controls in a number of ways. The above-mentioned personality traits could be ex-

Table 7. Significant differences between adolescents with Klinefelter's syndrome and controls

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1. Later speech development
 2. More frequent speech disorders
 3. More frequent nail biting
 4. Preference for quiet games
 5. No or only weak defiance reactions
 6. More frequently shy and reticent
 7. Poorer school attainment
 8. More difficulties in concentrating
 9. More dependent on parents
 10. Poorer attention
 11. Less interest in surroundings
 12. Lower level of activity
 13. Lower degree of endurance
 14. Lower intelligence level, especially for verbal intelligence
 15. Fewer hobbies
 16. More gender role problems
 17. Lower degree of self-esteem
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pected to result in a greater susceptibility to social stress and in a number of difficulties in adult life with regard to emotional and human relations as well as work (cf. our findings in the study of adult males with Klinefelter's syndrome). However, in the light of the considerable level of unemployment among young people in Denmark it was remarkable how well the Klinefelter males managed with regard to work; we believe that the testosterone treatment played a considerable role in this as well as in other previously mentioned respects.

This study, like the study of adults with Klinefelter's syndrome, clearly revealed the great need for early diagnosis of Klinefelter's syndrome, preferably at birth and definitely no later than puberty. Data from the Danish National Cytogenetic Register reveal that at present not even 10% of males with Klinefelter's syndrome are diagnosed at the age of puberty, and less than 20% of all males with Klinefelter's syndrome are diagnosed in areas with no special screening program. Such programs should be encouraged at birth or in school. Physicians in general should be encouraged to perform a simple **testis** examination using Prader's orchimeter, and all males with small testes should undergo chromosome investigation or at least a sex **chromatin** examination.

Newborn Boys with Klinefelter's Syndrome

This final group comprises 13 unselected boys with Klinefelter's syndrome found **among** 17363 newborn children during the years 1969-1974 and 1980-1982 in the Arhus area (Nielsen et al. 1982, to be published). The present study involves just those 8 of the 13 boys who were between 8 and 11 years of age at the last examination; the other **five** boys were only between 1 and 2 years old at that time. The controls comprise siblings and in some aspects unselected groups of children from the same area as the Klinefelter boys.

Motor Coordination

We found poor gross motor coordination to a significantly higher degree in **Klinefelter** boys than in siblings and controls. Studies on 63 unselected boys in Århus, Denver, New Haven, Toronto, Winnipeg, Tokyo, and Edinburgh revealed motor coordination to be poor in 14 of 51 boys with XXY (**27%**), compared with 4 of 64 sibs and controls (**6%**) ($P < 0.004$) (Nielsen and Sorensen 1979). Such a delay in gross motor coordination may lead to a tendency for the boys to isolate themselves, be clumsy, and have difficulties in playing with others: this calls for special attention from parents and educators, and it is desirable to make a particular effort to stimulate such children to achieve better gross motor function by means of gymnastics and other sports. This will also tend to counteract the tendency to passivity. In some cases there is also a delay in fine motor coordination which may **give** rise to writing **difficulties**: again, teachers should devote special attention to this problem.

Intelligence

When examining Klinefelter boys we found a significantly lower verbal intelligence (as compared with siblings and controls) up to the examination between the age of 4 and 8 years, but at the next examination between the ages of 8 and 11 this decrease in verbal intelligence level had disappeared.

In a study of 63 unselected boys with Klinefelter's syndrome from Scotland, Denmark, Canada, the United States, and Japan (Nielsen and Sorensen 1979), the mean verbal IQ was significantly lower than in controls and siblings ($P < 0.001$), and in a later follow-up study of the same group intelligence analysis of 61 boys with Klinefelter's syndrome revealed a higher than expected incidence of impairment of verbal IQ, with 48% below IQ 90 in contrast to 20% of controls. In this connection it is interesting that in the boys (mean age, 17) and adults (mean age, 26) we studied who had received no special attention during childhood owing to the diagnosis not being made, we found both a significantly lower verbal IQ and a significantly lower performance IQ as compared with controls. This was also the case in the collected groups of unselected boys with Klinefelter's syndrome from Canada, the United States, Japan, Scotland, and Denmark.

We believe that the group of Klinefelter boys we have followed up from childhood may have a higher intelligence level due to the information and counseling given to parents and teachers on the importance of early and pronounced stimulation and remedial teaching, with special efforts being devoted to reading, writing, language in general, learning as such, and behavioral problems. These findings indicate the importance of diagnosing Klinefelter's syndrome, as well as other sex chromosome abnormalities with similar effects, at a very early age, and preferably at birth.

Speech and Language Development

Delay in speech and language was found to a greater extent in the Klinefelter boys than in the controls. These results correspond well with the findings in a study of 63 unselected boys with Klinefelter's syndrome from Århus, Denver, New Haven, Toronto, Winnipeg, Tokyo, and Edinburgh (Nielsen and Sorensen 1979), which showed delayed speech development in 38 of 55 boys (50%), compared with 2 of 60 sibs (3%) ($P < 0.001$).

Walzer et al. (1982) studied 13 unselected boys with 47, XXY. These boys had various problems in expressive language skills. Deficits in syntax were evident, and they demonstrated word-finding problems (dysnomias) as well as problems in creating a coherent, organized, and developed narrative. They had decreased auditory memory, and more difficulty than the controls in phonemic discrimination of similar words. The parents reported delays in sentence-building skills, difficulties with speech sound production (articulation), problems with intonation and accent, and difficulties in finding specific words with which to express thoughts clearly. Of particular interest is the observation that the word-finding difficulties persisted into later age.

The delay in speech and language development, especially expressive function with auditory discrimination, dysnomias, word-finding difficulties, etc. implies that these children, especially in school situations, have difficulties in verbalizing experiences, as well as in reading and writing. We have found a strong tendency towards timidity, passivity, and withdrawal from group activities in boys with Klinefelter's syndrome; to a certain extent this is probably due to the delay in speech and language development referred to above as well as to the delay in motor coordination.

School Achievement

Evaluation of the Klinefelter boys by teachers showed that the Klinefelter boys had a significantly lower general school achievement than controls. However, only one had a poor school achievement, and slightly more than half had a satisfactory school achievement. Achievement in the Danish language, both orally and written, was significantly lower than in the controls, whereas there was no significant difference in mathematics. The teachers also reported significantly lower levels of attention, activity, endurance, self-confidence, and drive.

In the summary of clinical findings in Klinefelter boys from Canada, Scotland, USA, Denmark, and Japan (Nielsen and Sorensen 1979), maladjustment for structured school situations was present in 20 of 45 Klinefelter boys (44%), compared with 32 of 136 sibs and controls (24%) ($P < 0.025$). Later follow-up of the same group (Stewart et al. 1982) revealed that 64% of 58 boys from all centres had disorders of educational achievement; among the controls such disorders occurred in only 26%.

These findings further indicate that it is extremely important to counsel parents, teachers, and educators on the importance of finding ways to encourage greater independence and self-confidence, to reduce feelings of inferiority, and to promote interest and engagement in schoolwork or at least in some parts of the schoolwork. The latter would hopefully lead to increased interest in schoolwork in general, to an increase in activity level, and probably also to greater endurance.

There is also a great need for speech therapy with regard to all the specific difficulties reported by Walzer et al. (1982) and others. Speech therapy should be given at an early age or whenever speech problems appear. The findings also indicate the importance of paying attention to physical activities in view of the delay in motor coordination development, the decrease in physical strength, and the low level of activities outside school as found in the present study. Children with Klinefelter's syndrome and other sex chromosome abnormalities need special stimulation, support, and teaching efforts on learning to read and write. This may be due to a number of factors such as speech difficulties, auditory discrimination problems, and short memory span. The children should be stimulated to participate in group activities both inside and outside school in order to overcome problems in relationships with other children. This

may also help to improve their low levels of self-confidence, drive, activity, and independence.

Emotional Development

Delays in emotional development were found in 47% of the Klinefelter boys, compared with 22% of siblings and controls ($P < 0.025$). For Klinefelter boys this corresponds to our findings in adult males in previously mentioned studies, as well as to the finding that almost a third of 63 unselected boys with 47,XXY (32%) from various countries (Nielsen and Sorensen 1979) had delayed emotional development, compared with 9% of the sibs ($P = 0.02$). This calls for special attention to social stimulation by parents, in day institutions, in kindergartens, and in schools.

Minor Psychological Problems

We found a significant increase in minor psychological problems up to the ages 4-8, but at the last examination between the ages of 8 and 11 there was no significantly increased frequency of psychological problems in the boys with Klinefelter's syndrome or in any of the children with sex chromosome abnormalities. This is especially interesting because our studies, as well as others, have shown that adult males with Klinefelter's syndrome have a significantly increased risk of psychological problems and mental illness. We believe, however, that this can be prevented by early diagnosis, information, stimulation, remedial teaching, counseling, etc.

Psychiatric Problems

At the last follow-up examination between 8 and 11, only 2 of 25 children with different sex chromosome abnormalities had psychiatric problems, which is no more than one would expect in the general population. One of these had Klinefelter's syndrome with 47,XXY, and one had 47,XYY. Both children were boys from broken homes and had been brought up by mothers with personality problems. These two boys had quite pronounced speech problems of an impressive as well as an expressive nature, and both had difficulties in expressing themselves. Neither of them could read at the age of 10. Verbal IQ was 78 in both, and performance IQs 98 and 104. Neither of the boys had been stimulated at home to a satisfactory degree during the upbringing, which was characterized by insecurity, lack of continuity, and lack of a stable father figure. Both boys clearly preferred to stay in the institutions where they were being treated when last examined.

There is no doubt that the main reason for their behavioral and learning problems is to be found in their environment and the way they were brought up, rather than in the presence of an extra X or Y chromosome. However, their siblings with normal chromosomes had fewer problems.

Etiology, Information, Counseling, and Stimulation

Etiology of Deviation in Mental Development

Our findings of a low serum testosterone level in blood samples taken from the umbilical cord at the time of birth in Klinefelter boys (Sorensen et al. 1981) indicate that the androgen level may be low prenatally or perinatally in these boys in spite of the fact that it seems to be within the normal range later in childhood. If this is confirmed, it might be one of the causes of personality deviation and low verbal intelligence in Klinefelter boys. Genetically determined mechanisms of a nonhormonal nature might also be one of the etiological factors involved. It is unlikely that physical stigmata are a cause, as these do not appear till around puberty. We further found that severely hypogonadal adult males with the same physical signs as Klinefelter males, but normal karyotypes, had none of the mental characteristics found in Klinefelter's syndrome (Nielsen et al. 1969).

Maternal overprotection and anxiety are often found in Klinefelter boys and may very well aggravate their mental development, resulting in the immaturity, passivity, insecurity, weakness, and lack of emotional response which we have found and described in a group of Klinefelter boys admitted to a child psychiatric hospital (Nielsen et al. 1970).

It has been suggested that a lack of or inhibition of lateralization in individuals with 47,XXY (and probably also in those with other sex chromosome abnormalities involving an extra X chromosome) might be the cause of the delay in emotional maturity, the poor learning ability, the low verbal IQ, and the difficulties in language development. As early as 1945 Torgersen stressed that lateralization of the brain function is of fundamental importance to psychological individuality and cognitive style. The effects of interhemispheric equality on intellectual function show some similarities to findings in, for instance, adult males with Klinefelter's syndrome. Netley and Rovet (1982) noted an increase in non-right-handedness in a sample of 33 unselected males with 47,XXY and suggested that this, in combination with a previously published visual field study, reflects failure to establish left hemisphere dominance for language in men with a supernumerary X chromosome. Bender et al. (1983) did not, however, find any increase in non-right-handedness in 14 boys with 47,XXY, and dichotic listening studies showed no significant difference between Klinefelter boys and controls.

Information Concerning Sex Chromosome Abnormalities

It is our experience in Risskov from examination of approximately 600 persons with different types of sex chromosome abnormality that they have often been given very poor or no information at crucial periods in their life. Information should be given to parents as early as possible and to the children with the chromosome abnormality when they ask for it or no later than around puberty, at which age hormone treatment should be recommended for Klinefelter boys

and Turner girls. It is preferable that information is given to children by the parents on the basis of the information and counseling they have received. It may also be given by members of a contact group.

Parents of children with Klinefelter's syndrome diagnosed late in childhood have often developed guilt feelings if the mental development of the child has deviated from that of siblings. Such guilt feelings can, in our experience, usually be prevented or eliminated when thorough information and counseling are given to the parents while the child is still young, and this in itself tends to have a stabilizing effect on the mental development of the child and on the child/parent relationship in general.

Advice to Parents on Appropriate Stimulation

All parents were advised to make use of all their own possibilities and the facilities provided by the Danish social and school services to aid the child in those ways shown to be desirable by the psychological and psychiatric follow-up examinations.

In all cases social stimulation through the use of all playing possibilities with children in the neighborhood was advised. When there were hardly any children in the neighborhood, we discussed the possibility of the family moving to a part of the city with better playing opportunities.

Attendance at kindergarten was strongly advised from the age of 2-3, and in all cases in which the advice was followed (which was the majority), the results were good. In some cases there was rapid improvement in speech, purposeful activity instead of restlessness, improved communication and association with other children, and progress in emotional maturity. The positive effect that such improvements have on parental attitude towards the child is of great importance in creating an optimal and stimulating environment for him. In some cases where there is a long waiting list for attendance at a kindergarten, or when the parents cannot afford to pay, we have held discussions with the local social services or submitted a written application in order to help to get the child into kindergarten on account of its special need.

We have experienced several examples of how a passive Klinefelter boy or a triple X girl with delays in speech, gross motor coordination, and emotional development (in some cases with behavioral disorder) improved to a remarkable degree even after only a few months of attendance at kindergarten. This was also the case for the boys with doubly Y.

Attendance at a preschool class from the age of 5-6 is not compulsory in Denmark, and such schools are not available in all areas. We have strongly advised all parents to try to get their child into a preschool class at the age of 6 before entering school, which in Denmark usually takes place at the age of 7. In some cases we have advised that the child spends 2 years in a preschool class owing to delays in speech and emotional development and difficulties in adjusting to the rules of a structural school situation.

In all families we have advised parents to develop a warm, affectionate, and stable relationship with their children with a sex chromosome abnormality,

but **first** of all we have given advice on the practical possibilities of stimulating emotional development, language, and physical activity. We have found that most parents have followed the advice, and that generally the effect on the development of the child has been very good. In a couple of cases there has, however, been a tendency to overstimulation with a short-lasting adverse reaction, such as stuttering and anxiety, which disappeared after a reduction in the intensity of stimulation.

In two of the three Klinefelter boys with full-scale IQs above the mean level of 109 for the control group, the parents had followed our advice, being very active in all types of stimulation, and had a warm, affectionate, and stable relationship with their children. These Klinefelter boys had neither a delay in emotional and language development nor any psychological problems.

Genetic Advice in the Case of a Fetus with Klinefelter's Syndrome

In Denmark more than 12 000 prenatal examinations were carried out between 1970 and 1981. Table 8 shows that abortion was induced in 81% of the children with sex chromosome abnormalities. This high rate is probably to a certain extent due to a lack of knowledge of the many positive aspects of the development of children with sex chromosome abnormalities among the geneticists giving information and counseling to the parents. Such information is procured from this and similar studies which compare unselected **children** who have sex chromosome abnormalities with their siblings and with controls (Robinson et al. 1982; Ratcliffe et al. 1982; Stewart et al. 1982; Walzer et al. 1982; Leonard et al. 1982; Nielsen et al. 1982).

Table 8. Induced abortion of fetuses with sex chromosome abnormalities in Denmark, 1970-1981

10 of 13 boys with Klinefelter's syndrome
All 8 boys with 47,XYY
10 of 15 girls with 47,XXX
8 of 9 girls with Turner's syndrome
2 with other chromosome abnormalities
81% of all fetuses with sex chromosome abnormalities

We believe that if parents are prepared to and able to provide a good environment, if they are willing to follow counseling, and if the school system allows for **remedial** teaching measures according to need, parents might expect their child with Klinefelter's syndrome to develop within the normal limits.

It is important for genetic advisers giving prenatal information to place equal stress on the positive and negative aspects of child development in cases of Klinefelter's syndrome – and there are many positive aspects, especially if **the genetic advisers can provide the sort of information**, counseling, and treatment that we have already mentioned.

Prenatal diagnosis and abortion of fetuses with Klinefelter's syndrome and other sex chromosome abnormalities is easy, but in most cases unsatisfactory and discriminatory against the thousands of individuals with these chromosome abnormalities who live a normal life. However, in Denmark, where there is free abortion, it is the parents who decide whether they want induced abortion or not.

Ethical Considerations

The diagnosis of sex chromosome abnormalities at birth, provision of information to the parents, and follow-up examinations of such children have all previously been considered unethical by some. During the 1970ies a wave of **geneticophobia** swept over the United States (and to a certain extent some European countries), practically stopping all chromosome studies of newborn children there. No doubt there were many reasons for this, but one of the main ones was probably the fear that when a genetic abnormality is diagnosed, there is no hope of a cure or of positive environmental effects; this, of course, is not true at all.

Geneticophobic people may also wrongly believe that counseling parents of a child with a genetic abnormality such as Klinefelter's syndrome will have a negative effect on the child, e.g., through a self-fulfilling prophecy of deviations in behavior, low intelligence, and a risk of mental illness. Alternatively they may believe that counseling will lead to parental anxiety and overprotection and thus have a negative effect on the child's mental development and behavior. This might be the case if examinations are made, for instance, every few months and constant surveillance is kept on the family, or if insufficient time and expertise are available for the examination, for providing information, and for counseling. It is, however, our experience after four follow-up examinations of children with sex chromosome abnormalities diagnosed at birth that providing parents with information, advice, guidance, and support when their child is young, repeating this at 2-3 yearly intervals, and constantly adopting an "open door" advice and information policy can to a great extent reduce or even prevent the increased risk of aberrations in mental development which has been found in individuals with sex chromosome abnormalities diagnosed later in life. Studies like the present one and close international cooperation between groups making such studies as manifested in two monographs published by the National Foundation, March of Dimes in the "Birth Defects: Original Article Series" are greatly needed so that parents of children with sex chromosome abnormalities will be provided with better information and guidance.

We are so convinced of the importance of the early diagnosis of sex chromosome abnormalities that during **the last** 3 years we have, in close cooperation with the obstetric department in Århus, offered a chromosome examination at birth to all parents in Århus, where there are approximately 3000 live births per year. More than 90% have accepted this offer as a natural and reasonable preventive measure. We are convinced that physicians in general, and

probably especially geneticists and psychiatrists, have so far been far too little engaged and interested in early diagnosis, the provision of information, counseling, and treatment (if this proves necessary). We badly need to intensify our research efforts in these respects.

Summary

The experience we have gained at the Cytogenetic Laboratory in Risskov from examining a great number of children, adolescents, and adults with Klinefelter's syndrome, as well as from conducting follow-up studies of Klinefelter boys from the time of birth, has convinced us that it is very important to diagnose Klinefelter's syndrome at birth or at a very early age during childhood so that all relevant information and counseling can be given to the parents and later to the affected individuals themselves. It is also important to give testosterone treatment from an appropriate age.

It is our experience that if the parents of boys with Klinefelter's syndrome are able to provide a good environment and are willing and able to follow relevant professional counseling, and if the school system allows for any necessary remedial teaching measures, development within the normal limits may be expected. There is thus no special need for induced abortion when Klinefelter's syndrome is diagnosed prenatally.

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