

The Department of Internal Medicine B,
Rigshospitalet, Copenhagen

A FERTILE PATIENT WITH KLINEFELTER'S SYNDROME

BY

Erik Warburg

ABSTRACT

Investigations have shown a marked likelihood that a patient with Klinefelter's syndrome is the father of a son, and it is not unlikely that he is also the father of another, now deceased, son. Owing to the relatively common finding of positive sex chromatin in male infants and the striking paucity of cases showing Klinefelter's syndrome, the present case is presumably not excessively rare.

A case of Klinefelter's syndrome with positive sex chromatin and with a typical karyotype is described. The patient is married and has had two sons one of whom died of poliomyelitis at the age of 6 years. A study of the blood groups and the anthropological study of the patient, his wife and surviving son ruled out any suspicion of an extramatrimonial relation, showing that there was a ten to one chance that the patient was the boy's father.

To my knowledge no fertile case of Klinefelter's syndrome with positive sex chromatin and of a karyotype with preponderant XXY chromosomes has so far been reported.

CASE REPORT

A. A. S., born 1. 5. 1916, admitted to Department B, Rigshospitalet, Copenhagen: 26. 3.-7. 5. 1956, 30. 10.-13. 12. 1957, 3. 3.-7. 4. 1960, 28. 9.-18. 11. 1961, and 18. 3.-7. 5. 1962.

The patient's pedigree is given in Fig. 1. and was kindly provided by the University Institute of Human Genetics. It shows a few cases of feeble-mindedness and deaf-mutism which are, however, probably not of any significance with regard to the patient's disease.

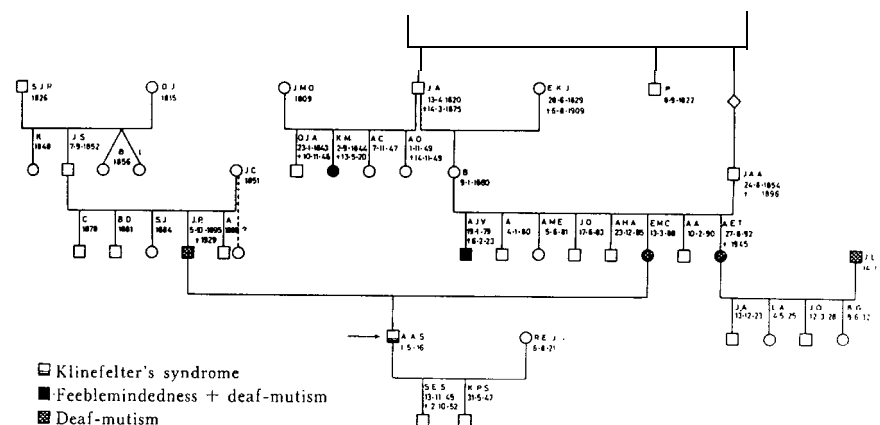


Fig. 1.
Pedigree.

Even as a draftee, the patient was so overweight that he was rejected for military service. There was no history of orchitis following mumps, of gonorrhoea, or of testicular trauma. He had been admitted to another hospital in 1955 as a case of cardiac neurosis, pectoral myalgia, and obesity.

When he was referred to us in 1956, his own doctor had made a diagnosis of endocrine insufficiency, possibly myxoedema. The B. M. R. was -22 % and -19 %, protein-bound iodine 4.4 µg/100 ml serum (normal). His weight was 99 kg, height 185 cm. He was complaining of headache, dizziness, fatigue, and lack of initiative. His muscular strength was rapidly decreasing, he was unable to lift heavy objects at his place of work and required help from his fellow workers. On major exertion he was severely dyspnoeic. He had often had chest pain radiating to the arms, most often after he had gone to bed in the evening. This pain was aggravated on exercise, and nitroglycerin was ineffective. There had been two attacks of auricular fibrillation. He had become so short of breath that he had to stop after walking 100 m, and he had applied for a disablement pension.

The patient had masturbated like other boys. He had not had any homosexual tendencies, had had his first intercourse at the age of 15 and the second at 16. He had only known a very few women, and at the age of 25 he married his first girl.

His first child was born when he was 29 (his wife was 26), i. e. after 4 years of married life, the second when he was 31.

In 1955, when the patient was 38-39 years of age, he began to lose his libido and potentia coeundi, and his wife became dissatisfied. Since November 1957, he had been treated constantly with injections of a long-acting testoste-



Fig. 2.
The heart in 1962.

rone preparation (during the past few years 250 mg testosterone ester every 3 weeks). This had made him fully potent and capable of satisfying his wife a couple of times a week. However, during the past year he no longer could do this and felt that great demands were being made on him.

Objective findings: 89.7 kg in weight, 189 cm in height, with a somewhat feminine distribution of fat (cf. Fig. 3), with ample subcutaneous fat on the hips.

No cyanosis or dyspnoea when resting. The facial skin is rather soft, as in women, but had been softer before the treatment. Voice masculine. Rather bald. Breasts rather large and glandular tissue palpable. Areolae not pigmented.

Cardiac auscultation: Normal sounds. Second pulmonic louder than 2nd aortic. Action regular. No congestive heart failure.

X-ray, Fig. 2: Heart slightly enlarged.

Abdomen normal, liver not palpable.

Penis and scrotum well-developed, but both testes are merely of cherry size and perhaps of a rather soft consistency. Prostate of normal size and consistency.

Hair on abdomen (cf. Fig. 4), in the axilla, and around the anus normal, but had been fairly scanty before testosterone therapy was instituted.

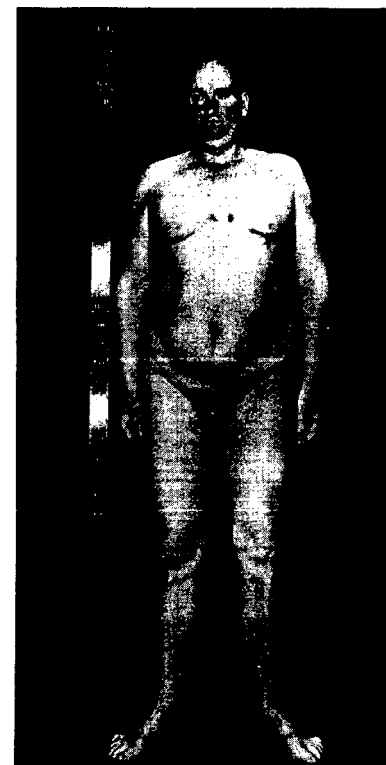


Fig. 3.

The patient in 1957. Note the fat padding on the hips, the horizontal demarcation of the pubes, and the sparse abdominal hair.

In 1957, the pubic hair line had been horizontal, an almost constant finding in Klinefelter's syndrome, but after treatment the pubes extended up towards the umbilicus.

Before the treatment he had shaved only once a week, now every day or every other day.

Special investigations:

ECG: Now normal.

Muscle biopsy (Eskelund): Some perivascular round-cell infiltration, otherwise normal.

Electromyography (J. W. Hansen): (Right rectus femoris): normal.

Electroencephalography (Pr of. Buchthal): During and after hyper ventilation some admixture of slow waves, but the total result did not show any definite abnormalities (borderline case).

Ophthalmological study: Colour vision, visual field, and ophthalmoscopy normal.

Otological investigation: Hearing and balance normal.

Since the patient exhibited certain mental peculiarities, he was investigated, in 1956

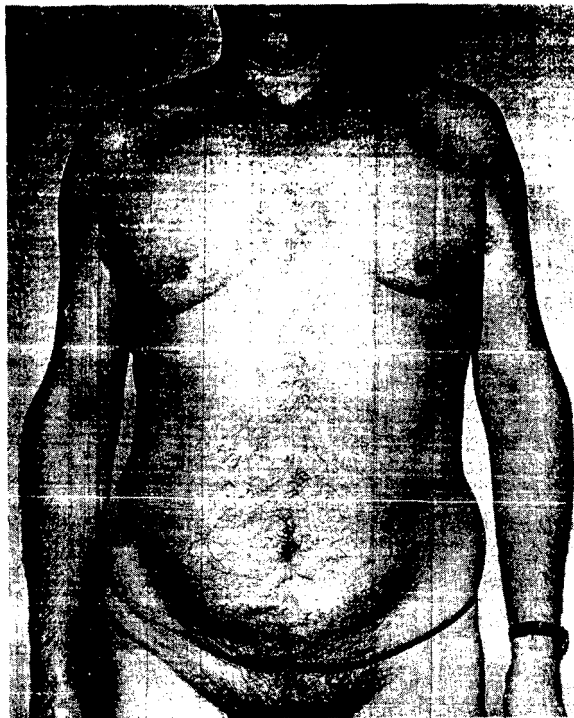


Fig. 4.

1960. Note the abundant hair on the abdomen

and 1961, by the psychiatrists in the psychiatric out-patient department and examined by the psychologist. The statements of the psychiatrists have been abbreviated. They found the patient to be unobtrusive, conscientious, patient, helpful, over-obliging, and very susceptible to his environment. At school he had attended a class for backward children, but did not feel ashamed of it. During a period when he had been feeling insufficient, uncertain, and slightly depressed, he had taken to drinking quite a lot, but not later. His depression, he said, had started in 1952 when his elder son, who was a great favourite of his, had died of poliomyelitis. The psychiatrists obtained good contact with the patient, emotionally as well as intellectually, and they did not find him to be intellectually impaired. On the other hand, the psychologist found that he was a weak, good-natured, anti-aggressive man who had difficulties, sexually as well as socially, in living up to a masculine role. He seemed to be suffering from character neurosis with incipient intellectual impairment. »As to the cause, it was of course difficult to make a statement from the psychiatric point of view, as it might have been due to cerebral arteriosclerosis or an endocrine psychosyndrome which in severe cases is indistinguishable from mild dementia«.

If I were called upon to judge between the psychiatrists and the non-medical psychologist, I would be inclined to think that the latter was right. Some defect in intelligence seemed to be present.

A fractionated 17-ketosteroid analysis was carried out on 2. 4. 1956:

Total excretion	11.5 mg
»U« fraction	0.30 mg
Dehydroisoandrosterone fraction	0.90 mg
Androsterone fraction	2.58 mg
Etiocholanolone fraction	3.20 mg
Rest fraction	4.52 mg

Various fractions in per cent of total:

»U« fraction	3 %
Dehydroisoandrosterone fraction	8 %
Androsterone fraction	23 %
Etiocholanolone fraction	40 %

Gonadotrophins 17. 4. 56: 50 mouse units, 13. 11. 57: 50 mouse units, *i. c.* elevated.

The Central Laboratory performed a large number of investigations, but found only (slightly) abnormal results in respect to hepatic function and blood-sugar regulation. Thymol reaction: 4. 4. 56: 0.16, 1. 11. 57: 0.18, 14. 3. 60: 0.20, 23. 3. 60: 0.18; the normal values in the technique used are a maximum of 0.15.

Blood sugar tolerance test using 99 g glucose (mg/100 ml, Hagedorn & Norman Jensen method) :

Date	Initial value	Maximum	Minimum
1. 4. 56	78	148	50
23. 4. 56	87	175	63
12. 11. 57	90	155	81
6. 4. 60	70	140	45

The patient's *semen* was investigated by Dr. Hammen prior to the institution of treatment in 1956. The total sperm count was 200 000 or about 1/1000 of normal.

Testicular biopsy (Fig. 5) (Dr. Klinken Rasmussen): All tubules **almost** completely hyalinized. In a few tubules Sertoli cells and possibly spermatogonia, but no fully differentiated spermatocytes. In the interstitial tissue, clusters and strands of Leydig cells. No inflammatory cells and no signs of malignancy.

The patient was **chromatin positive**. Dr. Eskelund, who **has had** extensive experience of these studies, reported on 11. 4. 60: »Oral mucosa smears showed bacteria and squamous cells. In the nuclei of the well-preserved epithelial cells sex chromatin, in most of the cells of a typical peripheral arrangement. The percentage ranged from 33 to 66 %. Thus, the patient is *chromatin positive*«.

New sections of the testicular biopsy from 1956 have been prepared. Although the fixation had been unsuitable, a considerable number of the cells showed sex chromatin of a peripheral arrangement«.



Fig. 5.
Testicular biopsy. Most of the seminiferous tubules are missing.
There are 3 clusters of Sertoli cells.

Oral mucosa smears **and** leukocytes have also been studied for sex chromatin by Drs. Frøland and Margareta Mikkelsen who reported: »Oral smear showed numerous typical Barr bodies. On counting 1000 polymorphonuclear leukocytes 8 showed typical 'drumsticks'«. They also studied the chromosome number from peripheral blood and skin biopsy. In the preparation of the specimen from peripheral **blood** they used the technique of *Moorhead et al.* (1960) and in culturing skin cells the technique of *Frøland* (1961).

After culture of white cells from peripheral blood, the chromosomes in 64 mitoses were counted. 53 contained 47 chromosomes, 8 contained 46 chromosomes, one cell contained 44, and 2 cells 45 chromosomes. More detailed analysis of 10 cells containing 47 chromosomes revealed a pattern corresponding to chromosomal constitution XXY. Five cells containing 46 chromosomes were analysed, and 3 showed a distribution pattern corresponding to a normal male sex chromosome constitution, XY, **while** 2 cells showed a completely abnormal pattern.

So far, 16 cells cultured from skin biopsy have been studied. Of these 14 had 47 chromosomes, one 46, and one 44.

Survey of counts.

	Number of chromosomes:					Total
Blood	44	45	46	47	48	64
Skin	1	-	1	14	-	16
Total	2	2	9	67		80

Fig. 6 illustrates the patient's karyotype.

Preliminary result: The predominant proportion of the patient's cells, in the blood as well as skin, contain 47 chromosomes, and presumably sex chromosomes XXY. There is a small number of cells containing 46 chromosomes.

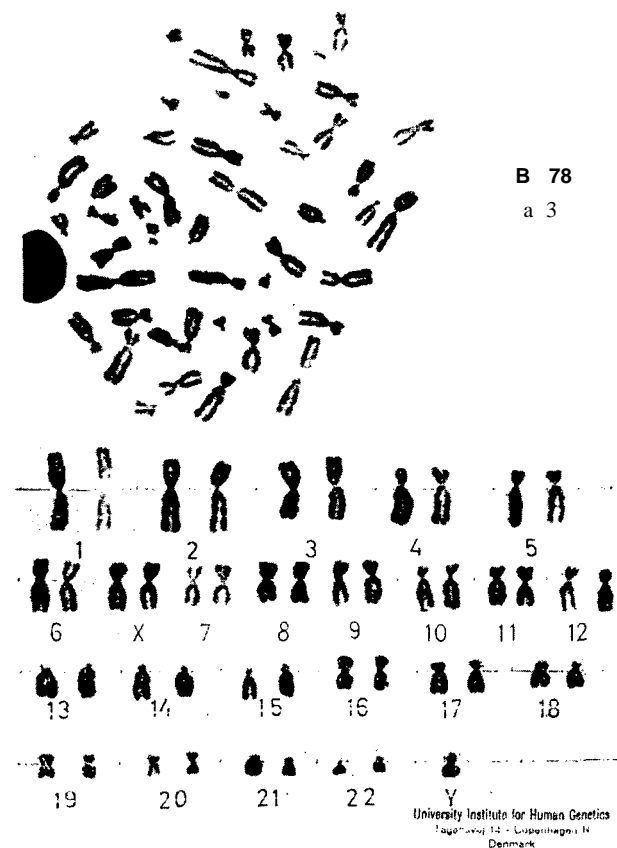


Fig. 6.

The karyotype found by Frøland and Mikkelsen. There are 47 chromosomes. The two chromosomes which make up the second pair in the 2nd row are presumably X chromosomes. The small chromosome in the bottom right hand corner in the last row is presumably a Y chromosome.

some of which presumably have sex chromosomes XY, while others again are entirely abnormal. There is a possibility, therefore, that the patient represents a mosaic of the type 47 (XXY)/46 (XY), with a marked preponderance of the former type.

The chromosome counts in the wife and in (the surviving) son were also studied by Drs. Frøland and Mikkelsen:

»Investigation of oral smears from the wife, born 6. 8. 21, showed typical Barr bodies. Out of 500 polymorphonuclear leukocytes 10 were found to contain typical 'drumsticks'. After culture of white cells from peripheral blood, the chromosomes in 20 mitoses were counted. 18 were found to contain 46 chromosomes, one 45, and one 47 chromosomes. Out of the cells containing 46 chromosomes 4 were submitted to a more detailed analysis which showed the usual pattern for normal women.

Cytological diagnosis: Chromatin positive subject with 46 chromosomes and presumably of the XX constitution.

Examination of oral mucosa smear from the son, born 31. 5. 47, showed no Barr bodies. After culture of white cells from peripheral blood the chromosomes in 40 mitoses were counted, and 36 were found to contain 46 chromosomes, two 45, and two 47 chromosomes. More detailed analysis of the 7 cells containing 46 chromosomes showed the normal pattern for males.

Cytological diagnosis: Chromatin negative subject with 46 chromosomes and presumably of the XY constitution«.

The patient is convinced that he is the father of the two children born in the marriage, and his wife definitely asserts that he is. In order to prove or disprove this, the University Institute of Forensic Medicine obliged me by investigating the family. The result was as follows:

»At the request of Medical Department B, Rigshospitalet, we have performed an anthropological study of patient A. A. S., his wife, and a son born in the marriage with a view to the paternity. This study, which was performed on April 30 and May 5, 1962, by Dr. Hans Giirtler, comprised:

A. Abstract of record:

The patient is married. In this marriage there have been two sons, one of whom died of poliomyelitis at the age of 6 years in 1952, while the other one is alive, now almost 15 years of age. The mother is reported to have definitely denied any other possibilities of paternity than the patient.

In order to assess the possibility that the patient is the father, a number of blood and serum group determinations on the three subjects were carried out on March 23.

B. Investigation for total likeness.

Between the mother and the child there is an unmistakable *physiognomic total* likeness, while between the child and the patient there is no convincing *physiognomic total* likeness.

C. Investigation for detail likeness.

The *length-width indices* of the skulls are: Mother: 1.32, child 1.34, patient 1.27.

The mother has dark blond, wavy *head hair*, the child has dark blond, rather straight head hair, the patient has dark, rather straight head hair.

The *physiognomic width-length indices*: Mother: 1.25, child: 1.22, patient: 1.26.

Planimetric measurements of colour photographs of the irides revealed that the *inner zones of the irides* in the mother, child, and patient made up 0.28, 0.18, and 0.18 respectively of the radial area of the irides, corresponding to a genetic paternity index of 1.3.

The *mother* has blue irides (Martin 1 a) with delicate radial streaking of the inner zones and no pigmentations. The limits towards the outer zones are delicately serrated and without pigmentations. The outer zones are the seat of quite dense radial streaking and without crypts, nodules, or pigmentations. The *child* has blue irides (Martin 1 c) with delicate radial streaking of the inner zones without pigmentations. The limits towards the outer zones are delicately, somewhat irregularly serrated and have a sparse yellowish pigmentation. The outer zones are rather dense, show somewhat irregular radial streaking and are devoid of crypts and pigmentations. Peripherally in the outer zones there are occasional whitish nodules. The *patient* has blue irides (Martin 1 c) with delicate radial streaking of the inner zones which show slight, diffuse, brownish pigmentation with a few more intensely pigmented yellowish-brown spots. The limits towards the outer zones are delicately serrated, with a faint yellowish pigmentation. The outer zones have delicate, rather irregular radial streaking and are devoid of crypts and pigmentations. Peripherally in the outer zones there are numerous whitish nodules.

The *physiognomic ocular indices* of the three subjects are: Mother 0.400, child 0.373, patient 0.398. After the necessary correction for age, this corresponds to a genetic paternity index of 0.821.

With respect to the *periocular structures*, including the *shape and position of the eyebrows*, the child shows some similarity to the mother, but no convincing similarity to the patient.

As far as the *shape and structure of the nose* is concerned, the child shows a marked similarity to the mother and a distinct difference from the patient.

The *physiognomic nose-lip indices* of the three subjects: Mother: 0.620, child: 0.641, patient: 0.671. After the necessary correction for age this corresponds to a genetic paternity index of 0.778.

With regard to the *perioral structures* including the appearance of the *upper lip* and the *shape of the mouth*, the child on the whole shows a fairly distinct similarity to the mother, and no convincing similarity to the patient.

In the *shape of the chin* the child shows some difference from the mother and a similarity to the patient.

None of the three subjects has *a dimple in the chin*.

With respect to the *shape, position, and structure of the ears* the child shows a similarity to the mother as well as to the patient and they all exhibit a distinct mutual likeness in this feature.

Investigation of the *hands and feet* did not show inherited anomalies of significance in assessing the possibility of the patient's being the child's father.

E. Investigation of finger and palm prints.

Finger and palm prints were taken and assessed **by** the head of the Central Bureau for Identification of the Danish Police, Detective Superintendent C. H. Vogelius Ander-

sen, M. **Sc.**, whose statement of 14. 6. 1962 is given in abstract: There are no features which can be interpreted as contraindicating the patient being the child's father, but also no features giving any stronger evidence of such a paternity. It may be added that with regard to the total number of papillary ridges on the fingers the constellation between the mother, child, and patient corresponded to a genetic paternity index of 0.947. As far as the hypothenar pattern is concerned, the constellation corresponded to a genetic paternity index of 2.440.

F. Supplementary blood and serum grouping.

The study was supplemented by obtaining blood and saliva specimens for blood and serum grouping. The result of all the groupings was as follows:

The mother belongs to group: A₂MS- C+C^w -D+E-c+P+K-Fy(a+) Lu(a-)

Jk(a+) Le(a+) non-secretor Hp 2-1

Gm(a-x-b+) Gc 1-1.

The son: OMS- C+C^w -D+E-c+P+K-Fy(a+) Lu(a-)

Jk(a+) Le(a-) Hp 2-1 secretor

Gm(a-x-b+) Gc 1-1.

The patient: OMS- C+C^w -D-t-E-c+P+K- Fy(a-) Lu(a-)

Jk(a-) Le(a-) Hp 2-2 secretor

Gm(a+x-b+) Gc 1-1.

Accordingly, there is nothing to contraindicate the possibility that the patient was the child's father.

On the basis of the distribution of blood and serum groups in the Danish population it may be calculated that a constellation of groups as between the mother, the child, and the patient occurs 5.4 times as often in mother-child-man constellations when the man is the child's biological father as when he is not. The present constellation in the subjects, therefore, may be considered as positive evidence in favour of the patient's paternity with a weight of 5.4 to 1 or in per cent 84 0/0 to 16 0/0.

Conclusion.

The anthropological investigation between the mother and the child showed a distinct *physiognomic total likeness* as well as a likeness in respect to a number of *physiognomic detail characters*.

Between the child and the patient there was no convincing physiognomic total likeness or detail likeness, but also no features which might argue against the patient's paternity.

With regard to the *pigmentation and structure of the irides*, including in particular the relative width of the inner zones and the occurrence of nodules in the peripheral areas of the outer zones, the child showed some divergence from the mother and a distinct similarity to the patient.

Finger and palm prints did not reveal any features contraindicating the patient's paternity. In most respects the child showed a distinct similarity to the mother, while in respect to the hypothenar pattern he differed from the mother and showed a similarity to the patient.

Blood and serum grouping did not show any findings which might argue against the patient's paternity.

In a *statistical evaluation of the blood groups*, based on the total findings in the three subjects, the group constellation between the parties was found to argue *in favour of* the patient's paternity with a weight of 5.4 to 1 or in per cent 84 0/0 to 16 0/0.

Thus, the anthropological investigation did not reveal any features not supporting the patient's paternity. To some extent the results support the assumption that the patient is the child's father, as a constellation of such characters between the mother, son, and patient must be assumed to be 10 times more common than in mother-child-man constellations in which the man is not the child's biological father.

(Signed: Harald Gormsen and Hans Görtler).

DISCUSSION

As evident from the above, there is a great likelihood that the present patient exhibiting Klinefelter's syndrome with positive sex chromatin and a karyotype with a preponderance of 47 chromosomes and sex chromosomes XXY has been fertile. How often this phenomenon occurs, we do not yet know, as the present case is to my knowledge unique. Indeed, nothing definite is known regarding the true incidence of Klinefelter's syndrome. As far as I know, only about 15 cases have been published in this country, but there is a great likelihood that a large number of other cases would be found by investigating mentally deficient men - 1 0/0 of whom have been reported to be chromatin positive by *Prader et al.* (1958) and 0.45-2.4 0/0 by *Israelsohn & Taylor* (1961) - and men with childless marriages, especially those who have oligo- and azoospermia. But for this purpose the physicians must always carefully palpate the testes, and I feel that my colleagues - like myself - have been a little remiss in this respect.

I have assumed that only about 1.5 chromatin positive cases have been published in this country. *Riis & Fuchs* (1960) found 11 cases of Klinefelter's syndrome among 150 male patients with malformations, 115 of whom did not have any sexual abnormalities. *Johnsen* (1961, 1962) found 9 among 207, and *Froland & Mikkelsen* (1962) 11 among 55 with congenital and in 24 cases sexual abnormalities. There is no doubt that a number of the patients of these three series are identical. In his last analysis *Riis* (1961) found among more than 150 intersexual subjects, 50 of whom had chromosomal abnormalities, 13 whom he classified as cases of Klinefelter's syndrome. Of these, 12 were sex chromatin positive. *Lennox et al.* (1958) of Mack's male infertility clinic

*) D. J. B. Ashley (Human Intersex, Edinburgh and London, 1962, p. 21.5) found, on adding *Moore's* (1959), *Bergemann's* (1961), *MacLean, Harnden & Court-Brown's* (1961) cases one among 378 babies.

in Glasgow, have reported on 126 cases of sperm counts of less than 40 000 000. Among these patients 10 proved to have chromatin positive oral mucosa smears. Clinically, 17 were judged as cases of Klinefelter's syndrome, 8 were sex chromatin negative (male karyotype) and 6 chromatin positive. It must be mentioned, however, that there was a marked difference between the microscopic testicular findings in the chromatin positive and the chromatin negative cases. *Lennox et al.* (1958) calculated that among men aged 28-37 years in Glasgow there should be one in 18 000 with chromatin positive findings and less than 40 000 000 spermatocytes per ml, while there should be one in 14 000 with chromatin negative findings.

Decourt et al. (1962) have published the results of their study in 21 chromatin positive cases of Klinefelter's syndrome. Gynaecomastia was absent in 10 and was only slightly marked in 4, while in 7 it was very marked. The authors at the same time reported the results of their study in 49 cases of gynaecomastia without any testicular atrophy. Chromatin studies were made in 2.5 cases, none of whom was chromatin positive. In many respects, the patients differed from typical cases of Klinefelter's syndrome.

There is a difference of opinion as to whether the »true«, sex chromatin positive cases of Klinefelter's syndrome are more common than the »false« ones without sex chromatin. This is not surprising in view of the difference in the diagnostic criteria.

It is remarkable that so few cases of Klinefelter's syndrome have been found, as there is a relatively far larger number of newborn boys with positive sex chromatin. *MacLean et al.* (1961) found sex chromatin in the cells of the oral mucosa of newborn boys in 3 out of 1000 cases, *Moore* (1959) in 5 out of 1911, and *Bergemann* (1961) in 4 out of 1890. According to *Ferguson-Smith et al.* (1960) the incidence is at least 1 in 3000. *Prader et al.* (1958) reported 1 in 1000 and *Penrose* (1961) 1.35 in 1000. Accordingly, there should be several thousand men (and boys) in Denmark with two or more X chromosomes. One cannot but wonder whether all subjects of a male phenotype, but having the above-mentioned chromosomal abnormality, exhibit complete manifestation or perhaps no manifestation until at a somewhat advanced age, i. e. after the subject with such an abnormality has had the opportunity of becoming a father.

It must be emphasized that the present patient was 39 years of age when he was first seen by us, which is considerably older than most of the reported cases of Klinefelter's syndrome.

The possibility that men with (true) Klinefelter's syndrome might be fertile has been briefly discussed previously by *Penrose* (1961) and by *Segal & Nelson* (1957). The explanation as to why fertile patients with Klinefelter's syndrome have not previously been found is perhaps that the majority have sought medical aid because they were infertile.

In the literature there are a few examples of histological findings of complete spermiogenesis in some of the seminiferous tubules. This applies to cases reported by *Bunge & Bradbury* (1956), *Jirásek & Raboch* (1958), and *Segal & Nelson* (1957). The latter state: »It is a long step from the type of a gonad shown in figure 1 to fertility, but a few months ago the occurrence of complete spermatogenesis in a human genetic female would have been regarded as equally unlikely«.*

The great majority of patients with an XO sex chromosome constitution are phenotypically women with Turner's syndrome. In the Danish literature these patients have been accurately described by *Dahm* (1961). They are nearly always infertile, but *Bahner et al.* (1960) have described a phenotypically normal woman who did not have the sex chromatin in the oral smear, but who gave birth to a son at the age of 31 years. This case too gives food for thought.

ACKNOWLEDGEMENT

I would like to thank the numerous colleagues who assisted me during the preparation of this paper.

REFERENCES

- Bahner E., Schwartz G., Harnden D. G., Jacobs P. A., Heinz H. A. & Walters K.:* Lancet 2 (1960) 100.
Bergemann E.: Schweiz. med. Wschr 91 (1961) 292.
Bunge R. G. & Bradbury T.: J. Urol. 76 (1956) 758.
Dahm N.: Ugeskr. Læg. 123 (1961) 1603.
Decourt J., Jayle M. F., Massin J. P., Louchart J., Israël L. & Calmettes C.: Sem. Hôp. Paris 38 (1962) 1266.
Ferguson-Smith M. A., Lennox B., Stewart I. S. & Mack W. S.: Memoirs Soc. Endocrin. Cambridge 7 (1960) 173.
Froland A.: Acta path. microbiol. scand. 53 (1961) 319.
Froland A. & Mikkelsen M.: Ugeskr. Læg. 124 (1962) 421.
Israelsohn W. & Taylor A. J.: Brit. med. J. 1 (1961) G33.
Jirásek J. & Raboch: Endokrinologie 35 (1958) 1.
Johnsen S G: Bibl. f. læger (Dan.) 153 (1961) 335.

*) D. J. B. Ashley (l. c. p. 217) has stated on the subject of Klinefelter's syndrome: »From the foregoing it appears that the only constant feature so far observed in this syndrome is infertility. No case has yet been recorded in which the patient was fertile, although this is a possibility which must be expected. There seems to be no absolute necessity for these patients to be incapable of procreation. It is known that some of them do have spermatozoa in the seminal fluid, and at least one of Turner's syndrome has been found to be fertile. The diagnosis of such a case must arise largely by chance and, of course, rigid proof of paternity would be necessary in view of the unusual nature of the phenomenon«.