THE DIAGNOSIS AND TREATMENT OF HERMAPHRODITISM*

BY

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Until recently the determination of the sex of an individual was mainly based upon the gonadal structure, and the sexual individuality identified with this finding. Accordingly a person having testes was a man and one having ovaries a woman. In the hermaphrodites certain anomalies inside the genital tract were considered more or less as anatomical variations from the normal without more profound changes in the sexual structure of the organism.

Clinical investigations into the various problems of hermaphroditism have, however, changed this picture completely and have shown how much more complicated these things are and how many different factors are working together to build up the harmonious sexual individuality of a human being. Today, in cases where the sex of the child is dubious, thorough investigations must be performed before any determinations as to the sex are made or any treatment can be instituted. The investigations should determine five different aspects of the organisms: (1) the genetic sex, (2) the gonadal sex, (3) the somatic sex—including the external and internal genitalia and the secondary sexual character, (4) the hormonal status, and (5) the psychic structure, including the rearing and gender role of the patient. Only then can a satisfactory decision be made.

The present paper is intended as a short introduction to some of the clinical aspects of hermaphroditism based on a personally known group of human hermaphrodites.

Investigation

In the years 1948-1959, 31 cases of hermaphrodites were investigated at the University Clinic of Paediatrics in Copenhagen. Fourteen of these were found to be female and 17 male pseudohermaphrodites. There were no true hermaphrodites, i.e. patients with both ovarian and testicular tissue inside the same organism.

Female Pseudohermaphrodites.

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<thead>
<tr>
<th>TABLE I</th>
<th>FEMALE PSEUDOHERMAPHRODITES</th>
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<tr>
<td>Adrenogenital syndrome</td>
<td>Origin unknown</td>
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All but one of the patients in the group of female hermaphrodites suffered from the adrenogenital syndrome. Nuclear sexing (Barr, 1955) showed female chromatin pattern. The clinical examination displayed more or less virilized external genitalia with a large phallus and some fusion of the labioscrotal folds (Fig. 1). A vagina and a uterus could be demonstrated either by inspection, endoscopy or radiography (Fig. 2). In three doubtful cases laparotomy was performed. The anatomy of the internal genital tract turned out to be of three different types. In the most common type—11 cases—the vagina and the uterus opened into the posterior urethra. In one case the vagina had a normal opening into the perineum and in another it was completely closed off from the urinary tract.

High 17-ketosteroid excretion in the urine gave the exact diagnosis with minimum 5 mg./24 hours in the newborn and maximum 12 mg./24 hours when the children reached the age of 1 year or more.

A high familial incidence in the group of adrenogenital syndrome was found in our investigation with three pairs of siblings, one pair being twin girls, the other two a boy and a girl. The two boys were also suffering from the adrenogenital syndrome but, not being pseudohermaphrodites, they are excluded from this group of female pseudohermaphrodites.

The last patient in the group did not suffer from the adrenogenital syndrome, the 17-ketosteroid excretion being 0·5 mg./24 hours. Nuclear sexing showed chromatin positive pattern indicating that genetically the child was female. The external genitalia were rather virilized (Fig. 3). Endoscopy

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showed a vagina and a uterus. Gonads were not palpable. Laparotomy was unfortunately not performed, but would have been necessary in order to eliminate the possibility of true hermaphroditism. The history of the mother’s pregnancy revealed no androgen treatment of any sort, as is sometimes the case in these patients (Wilkins, 1957). No reason for the virilism of this child could be demonstrated.

Male Pseudohermaphrodites.

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<th>TABLE 2</th>
<th>MALE PSEUDOHERMAPHRODITES</th>
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<td>Female appearance</td>
<td>Male appearance</td>
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<td>Male appearance</td>
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In the first group of male pseudohermaphrodites all seven patients were members of two families with ‘testicular feminizing syndrome’, with three in one family and four in the other. In six of the cases nuclear sexing was performed showing chromatin negative pattern. Gonadal biopsy showed testicular tissue as it is seen in cryptorchism. The external appearance, especially the external genitalia, were completely feminine (Figs. 4 and 5). A small vagina and no uterus was all that was found of internal genitalia.

The oldest of these patients, a 17-year-old ‘girl’, showed typical feminine development at puberty (Fig. 6) with normal breast development but with amenorrhoea as must be the case in a person lacking a uterus, and with the characteristic phenomenon seen in these patients, namely, lack of pubic hair.

The 10 patients belonging to the group male pseudohermaphrodites of male appearance were found to be a very heterogeneous group, being genetically males with chromatin negative pattern, having tested positive by biopsy but with ambiguous external genitalia and persistent Müllerian ducts of various sorts. Figs. 7 and 8 show such a patient, a boy with vulval hypoplasia and with both vagina and uterus.

In four cases a sudden strong virilism at puberty was the first sign which aroused the doubt about whether a correct decision of sex had been made at birth. The genitalia until then were of such a feminine character that neither midwife, family physician nor parents had had any suspicion of dealing with a hermaphrodite. Figs. 9-13 show one of these children, who had been followed up in our department from the age of 3 until the age of 14 years. The final examination was delayed because of disease in the family. Investigation at puberty (Figs. 12 and 13) proved the patient genetically to be a boy. The gonads were testes with no ovarian tissue and the hormonal status displayed an explosive hyperactive puberty with very high estrogens (>200 <400 Mouse/U./24 hours) and androgens (42%).

Finally the psychological investigation revealed both male and female elements in spite of the patient having been reared as a girl since birth.

Figs. 14-16 demonstrate the three other patients with female legal sex from birth, but with strong virilism near puberty. These difficult cases raise the important question of adequate approach to treatment, i.e. whether to change the sex, or remove the gonads. The problem will be discussed later in this paper.

Discussion

It is now possible, as a result of these detailed examinations of patients with ambiguous genitalia, to classify most hermaphrodites and to assemble them in different clinical groups.

The study of the chromatin pattern is an easy procedure: a buccal smear is enough for examination and, together with an analysis of the hormones in the urine, should always be undertaken, when doubt arises about the sex. Chromosomal counting, on the other hand, is still a rather complicated technique which only a few can master at present but in those cases where it can be done, the results are of great scientific and clinical value.

Gonadal biopsy as well as explorative laparotomy should be performed in almost all cases of pseudohermaphroditism except those with the adrenogenital syndrome, when other examinations have failed to give a clear answer. With the present state of paediatric surgery these procedures can safely be done in infancy. The increasing number of true hermaphrodites described in the literature demonstrates the importance of these explorations, especially with regard to gonadal biopsy, which should include incision throughout the whole length of each gonad found in the individual (Innes Williams, 1958).

The high familial incidence found in male and female hermaphrodites is well known (Morris, 1953; Holmer, quoted by Everse, 1958) and is illustrated in this material. In one of our two families with the testicular feminizing syndrome, where the parents were first cousins, no less than four out of eight children suffered from this syndrome (Fig. 17). The other four children were normal. In a branch of the same family another type of male pseudohermaphroditism was found (see Fig. 16).

Clinically two problems are met with in these patients: (1) Determination of sex at birth; (2) Decision regarding later medical and surgical treatment
Fig. 1—Adrenogenital syndrome.

Fig. 2—Same patient, hysterosalpingography.

Fig. 3—Girl with normal 17-ketosteroid excretion and virilized genitalia.
FIGS. 4 and 5.—Testicular feminizing syndrome. Appearance, including genitalia, completely feminine.

FIG. 6.—17-year-old patient suffering from the testicular feminizing syndrome. Feminine breast development but no pubic hair.
Figs. 7 and 8.—Boy with vulvar hypospadia. Urethrography reveals both vagina and uterus.

Fig. 8

Fig. 9

Fig. 10

Figs. 9 and 10.—Male pseudohermaphrodite of feminine appearance.
Figs. 11, 12 and 13.—Male pseudohermaphrodite of feminine appearance until puberty where strong virilism sets in (same patient as in Figs. 9 and 10.)
Figs. 14, 15 and 16.—All patients with female legal sex at birth, but with strong virilism at puberty.

Fig. 17.—Familial incidence of pseudohermaphroditism.
when signs of abnormal development appear in later childhood.

Regarding sex determination, in many cases the decision regarding the sex of the patient can be based on the findings of the genetic, gonadal and somatic sex. On the other hand the general opinion seems to favour following the anatomy of the external genitalia. If these are mainly female, the child should be registered as a girl (Fig. 18) in spite of being genetically a boy and having testes. Such a patient is easier to adapt to the female role than to the male. But the decision must be made at birth or in the first months of life.

Regarding a decision on medical and surgical treatment in infancy and later childhood this will vary considerably from case to case and must depend on what kind of hermaphrodite it is and upon the age of the patient when seen.

**Adrenogenital Syndrome.** Seen at birth the right sex can be chosen in accordance with nuclear sexing and hormonal status. When cortisone treatment (Wilkins, 1957) is started and continued throughout life these girls will develop into normal women, will menstruate and can give birth to children.

Sooner or later corrective surgical procedures, comprising phallectomy and closure of the abnormal opening of the vagina into the urethra with vulvoplasty, should be undertaken. Jones and Scott, (1958) recommend the age of 1 year as being the best age for these procedures.

In the present material six phallectomies were done, the age of the children varying from 1 to 5 years. In one case it was done already in early infancy on account of emigration.

The question of the necessity of phallectomy with its possible injuring sequelae has been discussed a great deal. It is, however, the majority opinion that, as long as the phallus does not diminish in size during cortisone treatment, the operation should be undertaken at least in those cases where the phallus is of considerable size. According to Money, Hampson and Hampson (1955) this procedure does not interfere with the normal mature sexual life.

Adrenogenital syndrome in older female children reared as boys but suddenly found to be girls brings up the question of changing the sex. This is a difficult problem, and the general opinion seems to be crystallizing to the view that, after the age of 1 year, change of sex in this condition as in most other types of hermaphroditism is psychologically hazardous and should not be undertaken (Money et al., 1955).

In the present investigation only one patient, less than 3 years of age, was changed from a boy to a girl and cortisone treatment instituted. This happened five years ago, but overwhelming psychic conflicts are still to be found both in the child and the parents.

In our opinion, patients with the adrenogenital syndrome, being girls from a genetic and gonad standpoint, but reared as boys, should be left as males, have the hypospadias corrected and the ovaries removed. They then feel and act like men and their gender role will clearly be male when they mature.

A patient in the present material demonstrates what can happen to the clinical picture years after puberty, if the gonads have not been removed:

L.C. was reared as a girl until 1935 at the age of 9 years the sex was changed on account of virilization with simultaneous surgical correction of the hypospadias. At the age of 30 years, when the patient was living a well adjusted life as a married man, there was a sudden development of breasts, which were removed. A year later the patient menstruated heavily from the hidden...
vagina and uterus. Laparotomy was performed, a fibroma in the uterus was found and hysterectomy was carried out.

Male Pseudohermaphrodites with Female Appearance. This group includes patients with the testicular feminizing syndrome.

In childhood they are occasionally discovered during herniotomies, when a gonad is found and turns out to be a testis. In each of our two families one patient was primarily discovered this way, giving rise to a thorough examination of the others.

In these very female individuals, in whom it is known that their gender role will be that of a woman in spite of having testes and genetically being males the question arises whether the gonads should be removed or not.

This may be difficult to answer. Left in the groin, as some propose (Wilkins, 1957) they grow, become large and give an unpleasant feeling. If removed, puberty does not develop. Placed within the abdomen there will be a 10% risk for malignant degeneration (Morris, 1953). Jones and Scott (1958) advise that the gonads should be left untouched until the early twenties and then removed.

In most of our cases the gonads have been left or, during herniotomy, replaced in the abdomen and in only two cases have they been removed. The rest of our patients have not yet reached the age of 20 and the decision whether to remove the gonads or not has, accordingly, not been made yet.

Male Pseudohermaphrodites with Male Appearance. In this group the real problems are met at puberty when sudden virilization appears in children reared as girls. No simple answer can be given to the question how best to handle these patients, and many individual factors will affect the final decision. In most cases it is probably advisable to remove the gonads and make corrective plastic procedures and thus let them remain female individuals. This has been the case in three of our four patients at the ages of 13-14 and 15 years.

On the other hand the possibility of changing a girl to a boy at the age of more than 1 year cannot be ruled out. In one of our cases the child, who was reared as a girl but genetically was a boy with testes, virilized at the age of 13 and insisted upon being changed into a boy (Fig. 15). This demand was met, but unfortunately the patient left the country so that no follow-up has been possible.

Conclusion

Patients with ambiguous genitalia at birth must immediately be carefully examined before the legal sex is decided, and in most cases both gonadal biopsy and explorative laparotomy will be a necessary part of the examination with the exception of patients suffering from the adrenogenital syndrome. The choice of sex depends more than anything else on the structure of the external genitalia.

Seen later in childhood, roughly speaking after 1 year of age, all the same examinations must be performed, but from this time it is advisable to leave the patient with the legal sex given at birth. Accordingly, corrective surgical procedures should be undertaken including excision of contradictory sex structures and in some cases removal of the gonads. The change of sex in later childhood will only rarely present a satisfactory solution of the problem.

Summary

The modern concepts of hermaphroditism are discussed based upon 31 cases of pseudohermaphroditism of which 14 were female and 17 male pseudohermaphrodites. The diagnosis and treatment in each group of patients are discussed.

REFERENCES


