Section of Endocrinology

President—C. N. ARMSTRONG, M.D., F.R.C.P.

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The Clinical Diagnosis of Sex

PRESIDENT'S ADDRESS

By C. N. ARMSTRONG, M.D., F.R.C.P.

I HAVE chosen the problem of sex for this Address because of present-day interest in the subject, and I propose to make a clinical approach to the problem.

CLINICAL PROBLEMS OF SEX

The *physical abnormalities* seen often concern the external genitalia, but other situations arise. Most frequently the sex decided at birth becomes questioned when supposed hypospadias requires repair; signs of precocious puberty appear; a young girl develops male pattern hair or primary amenorrhœa; or a young male has testicles which fail to descend, possibly together with signs of deficiency of secondary male characteristics. Occasionally the surgeon questions the true sex fortuitously at operation. For example, a colleague operated for acute appendicitis on an 11-year-old girl who was found to have no uterus due to the presence of the Testicular Feminization syndrome. Lastly the true state may emerge from the exercise of "sixth sense". An elderly "woman" was admitted to the general ward of a hospital from an old people's home, and one of the patients objected on the grounds that she thought that the patient was a man. This patient turned out to be a case of true hermaphroditism.

The psychological problems fall mainly within two groups. *Transvestism* or *Eonism* can be present in a male who may have more or less pronounced male physical characters, and the opposite situation may arise in the female. *Homosexuality* includes individuals whose emotional libido is directed to another person of the same sex. The behaviour may be active or passive, or both active and passive.

It is in these forms that various clinical problems have reached me. The correct sex diagnosis in itself may be important to the patient for determining the pathology and treatment in appropriate instances, or for legal reasons associated with inheritance or athletic competition.

THE CRITERIA OF SEX

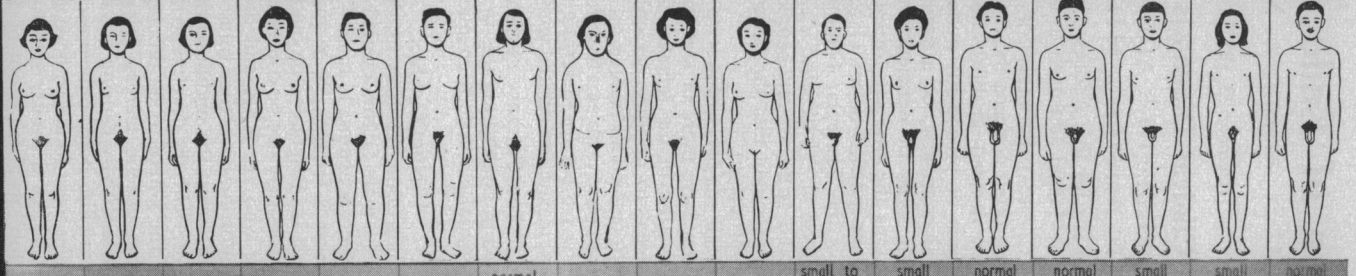
Certain criteria may be applied in establishing the final diagnosis which I would say are: (1) Nuclear sex pattern; (2) gonadal status; (3) chemical evidence; (4) external anatomy; (5) psychological sex.

NUCLEAR SEX

Normally, an X or Y spermatozoon fertilizes an X ovum. The female factor X is represented by 1 and there are $1\frac{1}{2}$ male factors carried in the autosomes; the Y is blank. Thus XX amounts to 2 female factors against $1\frac{1}{2}$ male—this gives a predominance of 2 : $1\frac{1}{2}$ in favour of female and the result is female. X Y amounts to 1 female against $1\frac{1}{2}$ male and the result is male. The basic sex is female, the male being a further development from this. Sometimes the genetic factors may not be constant; for example it has been suggested by Sachs that there are women who are XXX and there may be individuals, both male and female, who carry in the autosomes a higher value of male factors than is represented by $1\frac{1}{2}$. It is not known by what means the undifferentiated gonad in the fœtus at 7 weeks is influenced to develop into a testis with the development of subsequent male characteristics. XX causes the cortical part of the gonad to be differentiated and the XY the medullary part. It is highly probable that genetic factors determine the sensitivity of tissues to hormones, abnormality of such sensitivity causing some types of intersex. Barr noted in nervous tissue an intranuclear satellite body only present in the female. In other tissues 50% to 70% of the cells of females were found to have a small body adjacent to the nuclear membrane compared with only 5% of a similar structure in males. Later Davidson and Smith found a projection or "club" in about 6 out of 500 polymorph nuclei from females and none in those from males. This work is important in the problem of intersexes since those individuals with chromatin positive cells would, if the theory that Barr's bodies are hetero-chromatin derived from two X chromosome is correct, seemingly have XX chromosomes. The presence of this body would thus indicate the genetic sex of the individual whatever might have been the ultimate somatic or psychological development.

Gonadal status was at one time naturally thought to be the most important. The gonads might seem to determine the correct sex of the individual, and in the past I think that they would have been accepted for the legal definition. Since the detection of the nuclear sex pattern in the various syndromes it can no longer be said that the gonad is the all-important factor.

Chemical evidence.—There is no doubt that hormones play a very large part in the

	Normal female	Simple constitutional masculinism	Adreno-genital masculinism	Female homosexual	Female transvestism	Female intersex I without adrenal disorder	True hermaph-roditism	Turner's syndrome	Swyer's syndrome	Male intersex II "testicular feminisation syndrome"	Klinefelter's syndrome	Male transvestism	Male homosexual	Adreno-genital feminism	Simple constitutional feminism	Male with hypospadias	Normal male
NUCLEAR SEX CHROMATIN	+	+ but lesser % in polymorphs	+	+ occasionally in polymorphs	+	+	+ or −	− rarely +	−	−	+ rarely −	− rarely +	−	−	−	−	−
GONADS	○ ○	○ ○	○ ○	○ ○	○ ○	○ ○	○ ●		?	● ●	● ●	● ● or normal	● ●	● ●	● ●	● ●	● ●
HORMONES: OESTROGENS	normal F.			normal F.	normal F.	normal F.			high	normal M.	not increased	n. to >n. for male	normal M.	probably >n. for male		normal M.	normal M.
HORMONES: ANDROGENS	normal F.	increased for female	increased for female+++	normal F.	normal F.	normal F.	normal or low	low	normal	normal M.	< normal	deficient for male	normal M.	increased++	diminished for male	normal M.	normal M.
EXTERNAL ANATOMY																	
PHALLUS: PENIS							normal penis ... or enlarged clitoris				small to moderate size	small	normal size	normal size	small	small (often mistaken for enlarged clitoris)	normal size
PHALLUS: CLITORIS	normal size	normal size	enlarged	normal to enlarged	normal to enlarged	enlarged++		normal size	normal to enlarged	normal size							
MICTURITION	♀	♀	♀	♀	♀	♀	♀	♀	♀	♀	♂	♂	♂	♂	♂	♀	♂
MENSTRUATION	normal	irregular or amenorrhoea	absent	normal or irregular	normal or irregular	normal	usually absent	absent	amenorrhoea	absent							
FERTILITY	+	+ or −	−	+	+	−	−	−	−	−	−	− or +	+	−	+	−	+
PSYCHOLOGICAL SEX	F.	F.	F.	M. or F.	Neutral or M.	F. or M.	F. or M.	F.	F.	F.	Neutral or M.	Neutral or F.	M, F. or both	M.	M. or rarely F.	M.	M.
AETIOLOGY	genetic	genetic & / or hormone	genetic & / or hormone	genetic or psychological	genetic	genetic	genetic	genetic	genetic	genetic	genetic	genetic	genetic or psychological	hormone	genetic & / or hormone	genetic	genetic

physical development and other features of the individual and their estimation is valuable in certain syndromes, for example the adreno-genital syndrome, and gonadal dysgenesis. I doubt whether it is possible at the present time to say, on purely chemical grounds, what might be the sex of an individual.

External physical characteristics are important in influencing our minds on the nature of an individual's sexual status.

Psychological sex is of particular importance when it is different from the main physical characteristics indicative of external anatomical sex. Transvestism is also named Eonism after the Chevalier d'Eon de Beaumont, who was a diplomatic agent of Louis XV, and was taken to be a woman, but proved at post-mortem to be a normal man. Transvestism is an inaccurate term for the description of such cases, for the preference to wear feminine dress is only one expression of a strong desire to become identified with women, and to be regarded as a female by society. Other characteristics of eonism are the fantasies of pregnancy, passionate longing for a maternal role, preference for feminine games and activities, and a desire for castration in an attempt to achieve anatomical resemblance to a woman. This preference for the feminine role is evident from early childhood.

The condition is relatively common, but second in frequency to homosexuality. It may be symptomatic of homosexuality or other perversions, but only a small proportion of homosexuals are transvestites. The conditions are probably quite distinct for these reasons: the crucial desire of the homosexual is for sexual relationship with a person of his own sex whereas the eonist is repelled by the physical aspects of such relations and responds with disgust and revulsion. If an active sexual life is led by an eonist it is more often an heterosexual one, as in the case of Chevalier d'Eon and Abbé de Choisy. The evidence for regarding transvestism as being of a constitutional nature, doubtless on a genetic basis, perhaps can be even more readily accepted than in the case of homosexuality, because it is a phenomenon manifested so early in life and, in most instances, there are striking feminine characteristics of physique. There is no sound evidence for accepting the contention of psychiatrists that it is due to a castration complex or other environmental psychological factors, e.g. female dominance in the home.

Homosexuality.—By contrast homosexuals as a rule do not want to change their sex, and identity. I am surprised that even recently published works on endocrinology (e.g. Wilkins) still make the statement that the psychological sex is that according to which the individual has been brought up; if this were so man would be the only animal dependent on his environment both for his sexual libido and for the survival of the race. Surely this is fantastic! To quote Broster, the sexual act is so instinctive that it has not even to be learned but must be of genetic origin. All my cases of boys and men with hypospadias, brought up as "girls" have a male psychological outlook. The present attitude to homosexuality is similar to the attitude in the past to physical and mental illness, although I think scientific opinion is coming round to the view that the condition can be one of genetic and not environmental determination.

Spectrum of Sex

Fig. 1 has been drawn for me by Mr. D. P. Hammersley mainly from photographs of my own cases. It gives his impression of the stances and features of cases of intersex. Beginning at the red end of the spectrum on the left is a normal woman, which is the basic sex, passing to the deviations from the normal, through the intersexes, to the blue end of the spectrum, the normal man. Various intersexes may occur, mostly as a result of purely genetic factors and of hormone influence, itself of genetic origin or acquired, or of failure of the target organ to respond to hormones. Fig. 1 is not intended to be scientifically correct in all details; it does not include all the syndromes, nor have I grouped, for instance, cases of gonadal dysgenesis together. It represents the way the problem of gradation of sex, including psychological sex, impresses me. I have taken permissible licence in a Presidential Address: I know I shall be criticized for including disorders of psychological sex amongst the physical intersexes, but in my opinion it is where they should be and where they will eventually arrive.

The Clinical Diagnosis of Sex and Management

I should like, after the above remarks, to return to the clinical problems. Firstly *the patient with female micturition and large phallus.* Is this individual, in whom often hypospadias is diagnosed, in fact a boy or a girl? The patient will be a boy if the nuclear sex is male, and external male characteristics are present with the exception of the hypospadias; testes may be present or undescended. He should be regarded as of male sex and the hypospadias repaired. The patient will be a girl if the nuclear sex is female, and female external characteristics and ovaries are present. This may not be evident before puberty, particularly in that type of female intersex without endocrine disorder. It is important in such cases to estimate the urinary 17-ketosteroids. If the ketosteroids are normal and the patient has a uterus and ovaries, and is young, I would advise plastic

surgery if required and the adoption, if necessary, of female sex. If the ketosteroids are unduly high the presence of the adreno-genital syndrome would be indicated; in such cases treatment with cortisone should be begun early so that the normal development of female characteristics can occur. The *patient with female characteristics and primary amenorrhœa with or without pubic hair and normal or slightly enlarged clitoris* may manifest the Testicular Feminization syndrome, Turner's syndrome or Swyer's syndrome. "She" may have male nuclear sex and retained testes, which abnormalities may be considered of academic rather than clinical interest. The fact that pubic hair is absent in the Testicular Feminization syndrome and not made to grow by testosterone suggests that the cause of the Syndrome is lack of response of the target organ to the male hormones for genetic reasons. In my opinion patients of all these types should continue as females but they could raise a difficult legal problem, particularly if inheritance or athletics were involved. Until this question is fought out in the court we do not know the legal position. *Cases of poorly developed male characteristics, poor masculine hair, small penis, small testes, and with or without gynæcomastia.* Like the last group they may be found to have nuclear sex opposite to the external anatomy. In Klinefelter's syndrome the nuclear sex is usually female, suggesting they are masculinized genetic females. Yet in fact the external anatomy is male, and spermatogenesis does rarely occur, so it is better to regard them socially as males. The only legal complication which may arise if they are regarded as males would concern such an individual who is also a transvestite or homosexual. Such patients have been put in prison for following their psychological sex libido, even when the nuclear sex is female. Again thus far all the facts have not been presented in court. Under this general heading there are also patients simply having poor masculine development of genetic origin or due to hormonal deficiency, and those boys with adipose gynandrism (Simpson). *Patients with psychological sex abnormalities* immediately raise immense problems. No one surely will contend, after scanning the whole spectrum of sex with all its physical inconsistencies, that it would be reasonable to assume that the psychological sex must correspond to the other sexual criteria. Prejudice is so deeply embedded that I doubt if we have reached a stage when the general public, or even the medical profession, would accept that psychological sex may differ from physical sex and can be of genetic rather than of environmental origin. If this view is accepted society can hardly be held responsible. I am prompted to ask, which is the more important, the body or the mind? The law of Great Britain, so far, is definite on this: it is the body. The law has no sympathy with the individual who has female psychological sex in a male body, nor has the general public. Without a physical background, it would be too much to expect the law to define sex merely upon psychological grounds. Although it may come to be accepted that there are individuals who are genetically psychologically of one and physically of the opposite sex and should be allowed to follow a life in accordance with their psychological sex, the registered sex of these individuals must, I would say, remain as determined by their physical characteristics.

Conclusions

To sum up, my advice in intersex would be:

In cases of female micturition with large clitoris, always determine the sex by modern methods of nuclear sexing, ketosteroid excretion, &c., and advise that such cases be brought up as their correct sex. If they have been brought up in the wrong sex, carry out the necessary treatment, plastic, hormonal or both and advise that they change to their correct sex, even in adult life.

Those cases of intersex whose nuclear sex or gonads are not consistent with the external sex anatomy should be told nothing, but allowed to continue with the sex already assumed by their external body form which should be enhanced with treatment if possible. I would advise that the legal sex be that of the individual's external anatomical sex.

Where the psychological sex is opposite to that of the body, I think it is the duty of society to allow those individuals to live as their true sex emotion directs, provided it does not interfere with the welfare of other persons, but the legal registered sex should be that of the external anatomy.

In the case of transvestites, I should support the proposal of Dr. Peter Bishop, that a small committee should be set up to investigate such cases and have the legal right to advise any plastic surgery they consider necessary.

I shall conclude by quoting from Milton's "Paradise Lost."

> "For spirits when they please
> Can either sex assume, or both, so soft
> And uncompounded is their essence pure."

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REFERENCES.—Barr, M. L., and Bertram, E. G. (1949) *Nature, Lond.*, **163**, 676. Broster, L. R. (1944) Endocrine Man. London. Davidson, W. M., and Smith, D. R. (1954) *Brit. med. J.*, ii, 6. Klinefelter, H. F., Reifenstein, E. C., and Albright, F. (1942) *J. clin. Endocrinol.*, **2**, 615. Damon, M., and Sachs, L. (1957) *Lancet*, ii, 20. Simpson, S. L. (1948) Major Endocrine Disorders. 2nd Edn., p. 63. London. Swyer, G. I. M. (1955) *Brit. med. J.*, ii, 709. Turner, H. H. (1938) *Endocrinology*, **23**, 566. Wilkins, L. (1957) The Diagnosis and Treatment of Endocrine Disorders in Childhood and Adolescence. 2nd Edn., p. 287. Oxford.