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EDITORIAL

Hormones and sexual behaviour[1]

Psychiatrists react to the complexity of human nature in two principal ways; they either take it as justification for their ascientific humanism, or, with unwavering optimism, they accept the challenge and seek scientific explanations. 'Hormones and behaviour' has been a favourite hunting ground for such hopefuls, and it is perhaps the sexual part of our natures that we are most ready to attribute to chemistry.

Following the spate of research in the 1940s, enthusiasm was dampened by the technical problems of biological assays and the conflicting results they provided, but new and superior assay methods have rekindled interest and it is timely to review the situation. To what extent are sexual drive and responsiveness, gender identity and sexual preference determined by hormones?

Endocrine studies of impotent men have produced conflicting results; plasma testosterone levels are either normal (Lawrence & Swyer, 1974) or low (Raboch *et al.* 1975). Ismail *et al.* (1970) found an impaired testosterone response to HCG in impotent men, whereas Delitala *et al.* (1977) reported normal response to both HCG and LH–RH. In most of these studies 'impotence' has been treated as a homogenous category, which with small numbers involved is likely to be misleading. Ismail *et al.* (1970) did find lower testosterone levels in males whose impotence was of gradual onset and associated with lack of sexual interest, in contrast to impotent men with continuing sexual interest. Racey *et al.* (1973), on the other hand, failed to show this hormonal distinction.

The responses of impotent men to exogenous androgens offer an alternative source of evidence. Two studies (Bruhl & Leslie, 1963; Jakobovitz, 1970) claim significant benefits though both are inadequately reported. Cooper *et al.* (1973) reported a small and transient effect with a low dose of androgens. In all these studies the androgen has been the only method of treatment. The possibility that otherwise inadequate or equivocal responses to exogenous androgens may usefully interact with psychological methods of treatment should be considered, and the proper evaluation of androgen therapy awaits its use in such a combination. Even if hormonal deficiency is the primary cause, secondary psychological factors are highly likely to aggravate and perpetuate the problem.

So far, attempts to predict response to androgen therapy by endocrine assessment have proved disappointing (Cooper *et al.* 1970) except where there is clear evidence of late onset primary testicular failure (Heller & Myers, 1944). The possibility that in those cases with low testosterone *and* low gonadotrophin it is not the testosterone deficiency *per se* that is responsible but a deficiency in LH–RH release from the hypothalamus, was suggested by the findings of Mortimer *et al.* (1974). They noted an increase in sexual responsiveness in hypothalamic hypogonadal males in response to LH–RH which preceded any increase in circulating androgens. Once again, studies of LH–RH treatment of impotence have shown equivocal results (Benkert *et al.* 1975; Davies *et al.* 1976), but in both cases impotent men with apparently normal androgen function were involved.

The introduction of cyproterone acetate, a potent anti-androgen, offers a further source of evidence. So far, this is confined to the treatment of antisocial sexual behaviour. Although drug-induced reduction in such behaviour in large numbers of men has been claimed (Laschet & Laschet, 1975; Davies, 1974), the evidence is of an uncontrolled and unsystematic kind, when adequate control and measurement is crucial. In one controlled study (Bancroft *et al.* 1974) cyproterone acetate and ethinyl oestradiol produced very similar effects, more marked in affecting self-report measures (i.e. of masturbation and frequency of sexual thoughts) than physiological responses to erotic stimuli in the laboratory. The pattern of these effects was very similar to that observed in a similar study comparing Benperidol and placebo, but the circulating hormone levels while on cyproterone acetate, ethinyl oestradiol and Benperidol were quite different (Murray *et al.* 1975). These results remind us not only

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that it is the level of free unbound hormone rather than the total hormone in the circulation that is important, but also that hormonal mechanisms may not be usefully reflected in the circulating levels.

While there are strong clinical impressions of the importance of androgens in restoring sexual function to men with post-pubertal primary hypogonadism, evidence of a systematic and detailed kind is hard to find. The variable response of men to castration (Bremer, 1959) indicates that the relationship is complex and the extent to which androgens are necessary or sufficient for male sexual responsiveness remains obscure.

When we turn to the human female, the evidence is even more sparse, with a more or less total absence of endocrine data from sexually dysfunctional women. The cyclical nature of the female endocrine system, and the relatively low levels of circulating testosterone have increased methodological difficulties. But considering the vast number of women receiving steroidal contraceptives or post-menopausal hormone replacement therapy, this lack of evidence is remarkable, and in large part results from reluctant or inadequate behavioural assessment. Our most relevant data are from sub-human primates. Androgens are necessary for the normal sexual responsiveness (i.e. proceptivity and receptivity) of the female monkey (Everitt & Herbert, 1971), whereas the attractiveness of the female to the male is oestrogen dependent. Oestrogens may also be necessary (though not sufficient) for female proceptivity (i.e. sexual approach behaviour by the female) (Baum *et al.* 1977).

The enhancing effect of androgens on human female sexual responsiveness has been described many times at an anecdotal level. No systematic or controlled evidence on this point has been published, although a study has recently been completed demonstrating such effectiveness of testosterone when combined with counselling (M. A. Carney, J. Bancroft & A. M. Mathews – unpublished data).

The present state of our knowledge on the effects of steroidal contraceptives on female sexuality can best be described as confused. There is strong clinical evidence of an association between oral contraceptive use and sexual impairment (Royal College of General Practitioners, 1974), but psychological reactions are difficult to distinguish from the pharmacological effects of the steroids (Aznar-Ramos *et al.* 1969), and 'the pill' may often be used as the scapegoat when this problem has other determinants. The two best controlled studies have shown that the distribution of coitus during the 28-day cycle may be altered without the overall frequency being affected (Udry *et al.* 1973), and that sexual side-effects are infrequent and probably secondary to mood changes when they do occur (Cullberg, 1973). While methodological problems in this area are formidable, there is an obvious need to relate behavioural change to hormonal change. Evidence of androgen levels in pill-takers shows a variable picture (Apostolakis *et al.* 1966; Kjeld *et al.* 1976) and there may be important differences between the various progestogens in their effects on androgen levels, because of differential effects on androgen binding (Victor *et al.* 1976).

The effects of hormone replacement therapy on the sexual behaviour of post-menopausal women awaits proper evaluation, but one of the most convincing effects is likely to be the restoration of normal vaginal responsiveness by systematic or local oestrogens.

The current situation with the female is, therefore, even more uncertain and complex than in the male. Androgens are likely to be important, oestrogens have a probable peripheral role, but a very uncertain central role, and the relevance of progestogens is less clear than it seemed to be some years ago. With the growing necessity to evaluate properly steroidal contraceptives and hormonal replacement therapy and with improvements in both behavioural and hormonal assessment, we can hope for greater clarification in the near future.

Two other aspects of sexuality to be considered are gender identity and sexual preferences. In the first case, evidence has been well collected by Money & Ehrhardt (1972). While there is strong evidence for the role of pre-natal androgens in determining masculine gender identity, it remains difficult to distinguish between social learning shaped by anatomical features (e.g. masculinization of external genitalia) and the direct effect of hormones on psychological development. Part of the problem stems from the reliance on the various types of early onset endocrine anomaly such as the adreno-genital syndrome or androgen insensitivity syndrome. One of the most promising lines for future research stems from the finding that normal male infants show marked rises in circulating testosterone between 3 weeks and 3 months after birth (Forest *et al.* 1973). A prospective cohort study of the relationship

between these early androgen levels and later psychological development therefore becomes a possibility.

Hirschfeld in the 1920s suggested that homosexual preferences resulted from hormonal 'intersex states'. Although early endocrine studies failed to support this idea, interest has been renewed recently with a spate of studies comparing the hormonal status of homosexual and heterosexual males (e.g. Loraine *et al.* 1970; Kolodny *et al.* 1971; Doerr *et al.* 1973; Brodie *et al.* 1974; for a fuller review, see Bancroft, 1977). The varied and conflicting results have more or less cancelled each other out, and have revealed methodological naiveties reminiscent of early biochemical studies of schizophrenia. Two studies both reported an abnormal ratio of androsterone to etiocholanolone in the urine (both breakdown products of testosterone) but the relevance of such a finding remains obscure (Margolese & Janiger, 1973; Evans, 1972). The most sophisticated approach has been the search for the typically female positive feedback response of the hypothalamus to oestrogen provocation, as a possible indicator of incomplete masculinization of the male homosexual's brain. Dörner *et al.* (1975) have claimed such a difference between homosexual and heterosexual males, though the effect was not great. This requires replication, but in any case, the relevance of this positive feedback response to sexual differentiation of the primate and human brain is still unclear.

In spite of major technological advances, therefore, our understanding of the relationship between hormones and human sexual behaviour has moved forward very little. What is happening is a greater definition of the relevant questions and awareness of the methodological complexities in answering them. The next phase of research should, therefore, see more real progress, but the relationships so clarified are likely to be highly complex. Those psychiatrists looking for simple biological explanations of human behaviour would be advised to search elsewhere.

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