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Androgen Function in "Psychogenic" and "Constitutional" Types of Impotence

ALAN J. COOPER,* M.D., D.P.M. ; A. A. A. ISMAIL,† B.PHARM., PH.CH.(HON.), PH.D.

C. G. SMITH,* M.R.C.P.I., D.P.M. ; J. A. LORAINE,‡ D.SC., F.R.C.P.ED.

Summary: Androgen function was studied in twenty-five physically healthy "primarily" impotent males classified on clinical criteria into "psychogenic" or "constitutional" groups. The mean urinary testosterone level in the former was significantly higher than in the latter group (P<0·005). Important variables associated significantly with higher urinary testosterone levels (P<0·05) were (a) "late onset" impotence, (b) shorter duration than two years, (c) stronger "sex drive," and (d) an alternative sexual outlet to orgasm and ejaculation in the three months preceding referral; the last-mentioned appeared to be the single most important discriminatory feature.

It is suggested that testosterone excretion patterns—namely, high, average, and low—may be one method of classifying impotence.

Introduction

The role of the central nervous system and the endocrine glands, especially the testes, in the aetiology of male potency disorders has been largely neglected. This has perhaps been due to two factors—namely (a) the widely held view that most cases of impotence are of psychogenic origin (for example, Simpson (1950), Strauss (1950), and Stafford-Clark (1954), are among many who consider that "at least 90% of all cases of impotence are psychogenic"), and (b) the technical difficulties in assaying various hormones and their metabolites in body fluids in health and disease. Recently, however, some elegant animal experiments (Michael, 1968) as well as observations in man (Kinsey, 1953; Masters and Johnson, 1966) have redirected attention to the important functional interaction of the brain and the sex hormones in regulating libido and copulatory behaviour. In man probably some hypothalamic structures, perhaps initiated and controlled by a "sex centre"§ located deep within the temporal lobes, have an important role in the production and release of "sexual" trophic hormones (notably gonadotrophins) from the anterior pituitary; in turn these may influence testicular syntheses and secretion of testosterone and other C19 steroids and ultimately sexual behaviour.

The technical problems of assaying C19 steroids such as testosterone (17β-hydroxy-androst-4-en-3-one), the most potent naturally occurring androgen so far known, and its 17α-epimer epitestosterone (17α-hydroxy-androst-4-en-3-one) have now been largely overcome; thus the possible role of these substances in the pathogenesis of impotence can be examined.

Cooper (1968, 1969b, 1969c) has inferred two main aetiological types of impotence, designated as predominantly "constitutional" and predominantly "psychogenic," which differ in development, clinical features, and prognosis. In a search for non-clinical objective criteria to support this classification a study of androgen function was undertaken in an impotent population. Additionally, to identify any possible relationship between levels of the C19 steroids, testosterone and epitestosterone, and important clinical variables, appropriate statistical analyses were made. This communication presents some of the findings.

Patients and Methods

Impotence was defined as the persistent inability to develop and/or maintain a penile erection sufficient to conclude coitus to orgasm and ejaculation (Hastings, 1963). A total of 25 subjects who presented in a psychiatric outpatient department with a primary complaint of impotence were studied; these were made up of (a) 20 who suffered predominant (>50% of the time) erectional insufficiency which precluded penetration, and (b) five who, generally able to penetrate (>50% of the time) despite adequate intravaginal thrusting, lost their erection before orgasm and ejaculation could be attained (impotentia ejaculandi) (Johnson, 1965). At the time of presentation all were physically healthy and ambulant, there was no evidence of organic disease, and apart from some anxiety symptoms in five individuals no significant psychiatric disorder was elicited. At least one week before the endocrine investigation each patient was clinically typed (by A.J.C. or C.G.S.) as either predominantly constitutional or predominantly psychogenic according to the relative dominance of the distinguishing features summarized in Table I. At this time two psychological tests, the Eysenck Personality Inventory (E.P.I.) (Eysenck and Eysenck, 1964) and the hostility scale (Foulds, 1965), were also made; these measure respectively "neuroticism" and extroversion-introversion, and degree and direction of punitiveness. It should be emphasized, however, that the psychological test findings played no part in the classification process; this was done on purely clinical grounds. Table II sets out some important clinical data on the 25 impotent subjects of study.

Hormone Assays.—Urinary testosterone and epitestosterone

* Lecturer, Department of Psychiatry, University of Edinburgh, Edinburgh, EH10 5HF.
† Member of Scientific Staff, Medical Research Council, Clinical Endocrinology Research Unit, Edinburgh, EH1 2QW.
‡ Director, Medical Research Council, Clinical Endocrinology Research Unit, Edinburgh, EH1 2QW.

§Recent observations suggest that the temporal lobes have a special significance in mediating and maintaining libido and potency. It has been postulated that the different modalities of sensory sexual input are processed in the temporal lobes which via the limbic system initiate a sexual response (Cooper, 1969a).

Reprints from Alan J. Cooper.

TABLE I.—*Some Important Clinical Features Which Distinguish Predominantly Constitutional from Predominantly Psychogenic Impotence**

Distinguishing Clinical Features	
Psychogenic Impotence	Constitutional Impotence
(1) Acute onset	Insidious onset from previous competency, or present constantly since 1st coital attempt (if ever made)
(2) Temporal relationship to specific stress — e.g., bereavement, marriage, fatigue, etc.	
(3) Selective, intermittent, and transient—e.g., present on some occasions and situations, but not others	Generally persistent and progressively worsening
(4) Evidence of potential to respond erotically—e.g. (*a*) the exhibition of alternative sexual outlets to orgasm and ejaculation, such as masturbation, etc. (*b*) regular morning erections on awakening, and/or spontaneous erections to sexual stimulating fantasies, etc.; (*c*) presence of erotic desire in sexual situations	Evidence of progressive and "premature" (i.e., may begin in early 30s or even before) generalized waning of sexual interest and activity over months or years—e.g. (*a*) absence of, or only rarely practised, alternative sexual outlet; (*b*) absence or reduced morning and/or spontaneous erections, etc.; (*c*) absence of diminished erotic desire in sexual situations, etc.
(5) Higher "sex-drive"	Lower "sex-drive"

*It should be stressed that constitutional and psychogenic disorders are seen only comparatively rarely in pure culture. Aetiological overlap may occur, and in individual cases, phenomenologically, this may be reflected in various admixtures of clinical features. It is, however, generally possible to classify patients as either predominantly constitutional or predominantly psychogenic according to the relative dominance of the respective pathognomonic features.

TABLE II.—*Some Clinical and Psychological Data According to Typing of Impotence as Psychogenic or Constitutional*

Variable	Clinical Type of Impotence					
	Constitutional n = 16		Psychogenic n = 9		Combined n = 25	
	Mean	Range	Mean	Range	Mean	Range
Duration of impotence in years	8·4	¼–20	3·7	1–19	6·7	¼–20
Age of puberty (1st ejaculation) in years	13·9	11–16	13·1	11–15	13·6	11–16
No. of all types of sexual outlet to orgasm and ejaculation in 1st year of marriage (strength of sex drive) ..	1·7	0·25–4	3·3	1–7	2·3	0·25–7
Neuroticism score, E.P.I.	n = 12 11·3	2–20	n = 8 14·6	4–21	n = 20 12·6	2–21
Extroversion introversion score, E.P.I. ..	10·7	5–16	12·0	4–18	11·5	4–18
Hostility score (Foulds, 1965)	15·4	5–25	19·3	5–27	17·0	5–17

were determined by the method of Ismail and Harkness (1966) as modified by Ismail *et al.* (1968a). Assays were made on 24-, 48-, and 72-hour pools of urine, the results being expressed as μg./24-hour sample. The ratio of the two isomers testosterone/epitestosterone was also calculated.

Results and Discussion

The results are summarized in Tables III and IV.

Testosterone.—At the time of writing the estimation of urinary testosterone has been accepted as a satisfactory means of reflecting both plasma testosterone concentration and androgenic status in men. This is because the major proportion of the hormone in blood results from direct secretion by the testes rather than peripheral interconversion from other steroids, such as androstenedione (androst-4-en-3, 17-dione) and dehydroepiandrosterone (3β hydroxy-androst-5-en-17-one), secreted mainly by the adrenal cortex (Ismail and Loraine, 1968). An obvious advantage of estimating the hormone in urine is that it reflects overall production for a period of at least 72 hours. The mean testosterone excretion value found

in the 25 patients is significantly lower than that found in 14 sexually normal laboratory personnel of comparable age (Table III). Testosterone levels in this group, which are similar to those of previously reported normal men (Ismail and Harkness, 1967; Ismail *et al.*, 1968b), have been detailed elsewhere (Ismail *et al.*, 1968c).

Epitestosterone.—This was isolated for the first time from normal human urine in 1964 (Korenman *et al.*, 1964) and from blood in 1967 (Dray *et al.*, 1967). The role of this biologically inert isomer in health and disease is not, so far, understood. The source and precursors of epitestosterone are not yet known with certainty, but it seems that only a very small fraction is derived from the parent hormone, testosterone. Also, the view that epitestosterone is formed during the metabolism of the potent hormone testosterone and represents a mechanism to neutralize its activity is not supported by recent investigations (Ismail and Loraine, 1968).

Testosterone/Epitestosterone Ratio.—The groups differed significantly in respect of this ratio (P<0·05), this was due almost entirely to the difference between the testosterone levels. In the light of these findings it seems unlikely that epitestosterone is functionally important in impotence.

Psychometric Test Results

On the E.P.I. and hostility scale results only the psychogenic group scored definitely "neurotic" (mean score 14·6≡ to a group of mixed neurotics (Eysenck and Eysenck, 1964) and hostile (mean 19·3, normals score in the range of 13±6). (Foulds, 1965). These tests, however, did not discriminate between the two clinical subgroups. Interestingly, both psychogenics (mean score 12) and constitutionals (mean score 10·7) show up as decidedly extroverted (mean score of a group of hysterics was 11·7) (Eysenck and Eysenck, 1964). In a previous study Cooper (1969b) drew attention to the association between potency disorders and clinically diagnosed hysterical personality or hysterical personality disorder. The present objective test findings are in accord with these earlier observations.

Disorder, Clinical Variables, and Androgen Levels

Of 16 patients who on clinical grounds (see Table I) were grouped as predominantly constitutional only three had testosterone levels above the mean (45·7 μg./24 hours), while only one of the nine patients classified as predominantly psychogenic had a level below the mean. The difference is highly significant statistically (P<0·005). In interpreting the present findings an examination of some of the specific clinical variables was informative. Thus (*a*) early onset, (*b*) lower sex drive, (*c*) a disorder of greater duration than two years, and (*d*) absence of an alternative sexual outlet to orgasm and ejaculation, which characterize constitutional impotence, were all significantly associated with lower testosterone levels than (*a*) a late onset (P<0·05), (*b*) higher sex drive (P<0·005), (*c*) a disorder of less than two years' duration (P<0·05) and (*d*) an alternative sexual outlet (P<0·001).

On careful scrutiny of the former four variables early onset and absent alternative sexual outlet seem especially relevant; both indicate the non-occurrence of orgasm and ejaculation for at least three months (range three months to five years) before referral. This feature was seen, however, in two different settings:

(1) Most of the patients who were unable to maintain the physical response of an erection adequate to conclude coitus were still generally experiencing the "psychological response" of sexual desire to varying degrees, including in some cases a "heightening of desire" in the coital situation.

(2) A few patients, however, formerly competent, had been un-

TABLE III.—*Mean Urinary Testosterone (T) and Epitestosterone (ET) Levels and the T/ET Ratio in Impotent Men According to Clinical Typing as Psychogenic or Constitutional and in a Control Group of Laboratory Personnel*

Variable	Constitutional n = 16		Psychogenic n = 9		Combined n = 25		Control Group Laboratory Personnel. n = 14	
	Mean	Range	Mean	Range	Mean	Range	Mean	Range
T level (µg./24 hours)	34·1	5–80·4	62·2	47–127·9	45·7	5–127·9	73·1	35·4–147·4
ET level (µg./24 hours)	25·1	10·8–107·8	38·2	9–43·8	29·8	9–107·8	35·4	4·7–52·4
T/ET ratio	1·35	0·1–2·8	1·73	0·2–5·2	1·53	0·1–5·2	2·6	0·9–3·6
Mean age (years)	33·8	18–47	32·8	24–45	33·4	18–47	33	17–59

TABLE IV.—*Relationship of Some Clinical Variables to Urinary Testosterone (T) and Epitestosterone (ET) Levels; the T/ET Ratio and Significan Levels, Where Applicable, Derived from 25 Impotent Males*

Variable	Method of Measurement or of Comparison	Relationship and Significance Levels		
		Urinary Testosterone	Urinary ET	T/ET Ratio
Type of disorder	Predominantly psychogenic. Predominantly constitutional	Psychogenic significantly higher level than constitutional (Fisher test); $P < 0·005$	N.S.	N.S.
Time of onset	"Early" (impotent from 1st coital experience) versus "late" (previously competent)	"Early onset" significantly lower level (Fisher test); $P < 0·05$	N.S.	N.S.
Age	"Younger" versus "older"	N.S.	"Younger" significantly higher than "older" (Kendall's Tau); $P < 0·05$	N.S.
Duration of disorder	<2 years versus >2 years	Duration <2 years significantly higher level (Fisher test); $P < 0·05$	N.S.	N.S.
"Strength of sexual drive" (mean 2·3 outlets per week)	Above the mean ("stronger") versus below the mean ("weaker")	Above the mean significantly higher level (Fisher test); $P < 0·05$	N.S.	N.S.
Direction of sex drive	Heterosexual versus other	N.S.	N.S.	N.S.
Presence of an alternative sexual outlet (masturbation), culminating in orgasm and ejaculation, within 3 months of referral	"Present" or "absent"	Alternative sexual outlet significantly higher level (Fisher test); $P < 0·005$	N.S.	N.S.
"Neuroticism" (E.P.I.)	More "neurotic" versus less "neurotic"	N.S.	N.S.	N.S.
Extroversion—Introversion (E.P.I.)	More extroverted versus less extroverted	N.S.	N.S.	N.S.
"Hostility" (Foulds)	More "hostile" versus less "hostile"	N.S.	N.S.	N.S.

able to generate either feelings or erection despite stimulation from their spouse which technically would clearly have been highly provocative to a normally responsive male. The pattern of development suggested that these two types of reaction might represent different stages along the same continuum in a progressive decline in sexual capacity and responsivity. This progressive decline in erotic responsivity, which is also commonly seen, but much later, in normal ageing males, is thought by Kinsey *et al.* (1953) to be due mainly to psychological fatigue, specifically the repetition of the same sort of stimuli, with the same sexual partner over many years. Kinsey also comments on the probability of diminished androgen function in older males; however; he does not offer any specific views on its significance.

Comment should be made about the retention of or even "heightening" of the capacity to become emotionally if not physically roused; this was noted in some cases in the present series. On a psychodynamic level this may represent a striving towards the unattainable ("physiologic release in orgasm"). This is probably also the case in the psychologically analogous situation of some types of nymphomania, where, despite frequent and exhaustingly repeated sexual encounters, orgasm is never reached; the sexual tensions in such women may reach almost unbearable proportions. A neurohumeral basis for this phenomenon is suggested by Masters and Johnson's (1966) work on sexual responsivity in pregnant women. These workers found that in the three or four months immediately post partum, though sexual desire was often of normal (pre-pregnant) or even heightened intensity, the essential physiological precursors of pelvic and genital vasocongestion, vaginal lubrication, dilatation, etc., were lacking; coitus culminating in orgasm was therefore impossible

for most. Masters and Johnson (1966) suggested that this was due to oestrogen deficiency, which may persist post partum for several months; psychological sexual tension may be related to other, largely non-humeral factors, especially the cerebral cortex.|| An important but not necessarily an exclusive relation between testosterone and male erection and ejaculation may likewise exist.

The present findings, which support this premise, additionally point to qualifications. Thus the precise modus of the sexual stimuli, whether coital or non-coital (most often masturbation) seemed irrelevant; the crucial point was the physical occurrence of ejaculation. Furthermore, there was a clinical suggestion that the response had to be a specific "sexual one," occurring in consciousness (a cortically initiated response). Thus two individuals who had never ejaculated in the waking state and who experienced nocturnal seminal emissions fairly regularly, every two to three weeks during vivid sexual dreams, had exceptionally low testosterone levels (10·5 and 29·0 µg./24 hours). This observation may support the notion that nocturnal erections and emissions may generally be non-sexual-non-specific-midbrain mediated-physiological responses (Fisher *et al.*, 1965; Karacan *et al.*, 1966) associated especially with rapid eye movement (R.E.M.) sleep (Jouvet, 1961). When they occur "sexual dreams" may in fact be secondary to the erections and emissions. Further definitive studies are necessary, however,·to clarify this point.

||This, however, may be an oversimplification, since testosterone may be relatively important in determining female sexual desire; which may be greatly increased following its use (Kupperman, 1967).

The present findings perhaps support the role of testosterone in a sexual feedback mechanism. Possibly one stimulus for testosterone production might be orgasm and ejaculation—the usual culmination of coitus. Since testosterone is an essential requirement for the production of functionally mature spermatozoa (Dawson *et al.*, 1957; Dawson and Rowlands, 1959; Bishop, 1961) the biological-adaptive nature of such a feedback mechanism becomes apparent. Some evidence for this interpretation has been provided by Ismail and Harkness (1967), who showed that in two sexually abstinent normal men basal testosterone levels rose markedly when coitus was resumed. While probably endogenous testosterone levels may fluctuate according to ejaculative sexual activity (as well as many other factors) (Ismail and Harkness 1967) it is still far from clear whether the steroid induces or is the consequence of sexual behaviour.

Most of the impotent persons with abnormally low urinary testosterone levels in the present study population failed to respond to exogenous testosterone administered in varying doses (15-30 mg. daily) for up to four months. (These findings will be reported in detail later.) One possible interpretation of this observation is that potency once established is not specifically dependent on testosterone activity, which may be importantly related to ejaculative sexual response instead. Nevertheless, quite possibly the therapeutic failure in these cases might be accounted for by: (*a*) unphysiological dose levels too high or too low, and/or (*b*) enzymic and/or receptor site dysfunction. The elucidation of the precise role of testosterone and other androgens in potency and impotence is clearly important, with aetiological and therapeutic implications.

Conclusion

Though the present series is small and may not necessarily be representative of impotents generally, the data reported here tend to support the clinically derived "constitutional" "psychogenic" impotence classification; these terms, however, may be inappropriate and aetiologically misleading, since the single most important discriminatory feature, clinically, appeared to be the occurrence in the psychogenic impotents of regular alternative sexual outlets (masturbation) to orgasm and ejaculation, up to the time of referral. This, absent in the

constitutional impotents, indicated a definite physiological potential to respond erotically. It may be preferable to classify impotent men as "high," "average," or "low" testosterone excretors. At present, however, it is not known whether such a classification would have aetiological or prognostic significance.

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A Survey of Infantile Gastroenteritis

ALASTAIR G. IRONSIDE,* M.B., CH.B., M.R.C.P.ED. ; ANN F. TUXFORD,† M.D.
BARRIE HEYWORTH,‡ M.B., D.C.H., D.T.M.&H.

Summary: In 1967 we admitted 339 cases of infantile gastroenteritis; one-third of these were dehydrated, and in this group the commonest biochemical abnormality found was hypernatraemia, sometimes with metabolic acidosis. A higher incidence of dehydration was found in the patients who had received oral glucose fluids before admission. Enteropathic *Escherichia coli* were isolated from the faeces of 16% of the cases. Associated infections, especially of the respiratory tract, were common. Treatment was aimed at the restoration of fluid and

electrolyte balance. Usually this was achieved with oral fluids, though intravenous fluids were used in the most severely dehydrated cases. Recovery was complete in 320 cases and a further 14 cases were discharged as carriers of enteropathic *E. coli*. There were five deaths (1·5%) in the series; three occurred immediately after admission.

Introduction

Gastroenteritis of infancy is still common in Great Britain, accounting for about 400 deaths in 1967 in those aged less than 2 years (General Register Office, 1969). Each year some 10,000 cases of infantile gastroenteritis are admitted to hospital, and it is estimated that only 10% of the cases seen in general practice are referred to hospital (Wheatley, 1968).

* Consultant Physician, Department of Infectious Diseases, Monsall Hospital, Manchester 10.
† Lecturer in Bacteriology, University of Manchester.
‡ Assistant Physician, Department of Infectious Diseases, Monsall Hospital, Manchester 10.