of measurements indicate that for any particular fundal level there is up to eight weeks' variation in gestational age. In practice, therefore, the clinical detection of a baby "large for dates" or "small for dates" necessitates at least four to six weeks' difference between the traditional level of the fundus and the fundal height observed.

No standard rate of uterine growth was discovered in this study and sometimes no detectable increase in the level of the fundus occurred throughout four weeks of pregnancy. The most informative index of fetal maturity was the size of the whole uterus when assessed by pelvic examination in the first trimester of pregnancy. At a later stage neither the level of the uterine fundus nor its relationship to abdominal landmarks provided a reliable guide to gestational age.

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Preliminary Communications

Endocrine Function in Male and Female Homosexuals

Summary: Serial assays of hormones and their metabolites are reported in the urine of three male and four female homosexuals. Urinary testosterone levels were abnormally low in the two men who practised exclusive homosexuality and were within the normal range in the third, who had both homosexual and heterosexual relationships. In the women assays were generally performed throughout one menstrual cycle; in three the pattern of hormone excretion was ovulatory in character, while in the fourth evidence for ovulation was equivocal. Levels of testosterone and luteinizing hormone (L.H.) were raised in the female homosexuals, while those for oestrogens, particularly oestrone, were below the range for normal heterosexual subjects during their reproductive life; readings of follicle-stimulating hormone (F.S.H.) and pregnanediol were normal in three women. The data reported here are in keeping with the view that abnormalities in endocrine function may occur in both male and female homosexuals.

INTRODUCTION

It is now recognized that overt homosexuality is not a rare occurrence in the general population and that the condition is more prevalent in men than in women. There remain, however, considerable differences of opinion among authorities in this field as to the precise incidence of homosexuality in either sex (Kinsey *et al.*, 1948; Bancroft, 1970; Kenyon, 1970). Traditionally the condition has been regarded as essentially psychogenic in origin, and a very extensive literature now exists with respect to the psychological factors which are believed to be responsible for its causation.

The emphasis on the psychogenic aspects of homosexuality has tended to obscure the possibility that abnormalities in endocrine function, and in particular some form of hormonal imbalance, might be present and might conceivably play a part in its pathogenesis. At the time of writing the literature contains little reliable information on the endocrinology of homosexuality, and detailed hormone assay studies in men and women with this condition have been reported to a very limited extent indeed.

The aim of the present paper is to contribute to this field by comparing hormone excretion patterns in three male and four female homosexuals with those of normal heterosexual men and women.

CLINICAL MATERIAL

CONTROLS

The heterosexual men and women used as controls were mainly members of the scientific and technical staff of this unit. The findings in these subjects are reported elsewhere (Ismail *et al.*, 1969; Cooper *et al.*, 1970; Papanicolaou *et al.*, 1970; Adamopoulos and Loraine, 1970). All were volunteers and none admitted to any homosexual inclination or activity. All claimed to be involved in regular heterosexual activity, and none had received medication during the period of investigation.

HOMOSEXUALS

The three men and four women studied were involved in regular homosexual activity throughout the period of study. Only one of them (a man, Subject 3) also admitted to random heterosexual inclinations and experience during this time.

Males.—The ages of the three men were 19, 29, and 33 years. The homosexual role adopted varied in each case, being active and passive at different times, though, in general, one role was preferred. In two subjects buccal smears were taken, and were of the normal male type. The duration of the investigation ranged from 19 to 26 days.

Females.—The four women studied were two pairs of sexual partners; their ages were 23 and 20 years and 21 and 20 years respectively. All were engaged in very active sexual relationships involving daily activity except at the time of menstruation. One of the four admitted to previous heterosexual experience, but at the time of the investigation had become exclusively homosexual, both in inclination and in activity. In three (Subjects 1, 2, and 4) there was a history of irregular menstrual cycles, while in Subject 3 cycles were regular. In Subject 4 a tentative diagnosis of the Stein-Leventhal syndrome had been made. As with the men sexual roles varied, being both active and passive at different times. In Subjects 1, 2, and 4 the period of investigation was one complete menstrual cycle, while in Subject 3 the study continued for 44 days.

HORMONE ASSAY METHODS

Estimations were performed on 48-hour pools of urine, the results being expressed per 24-hour sample. Testosterone and epitestosterone assays were conducted by the method of Ismail and Harkness (1966) as modified by Ismail *et al.* (1968). Estimations of pregnanediol and of oestrone, oestriol, and oestradiol were performed using the techniques of Klopper *et al.* (1955) and Brown (1955) respectively. Assays for follicle-stimulating hormone (F.S.H.) and luteinizing hormone (L.H.) were conducted by the rat augmentation test of Steelman and Pohley (1953) and the ovarian ascorbic acid depletion test of Parlow (1958) respectively, incorporating the modifications described by Loraine and Adamopoulos (1970). The results of gonadotrophin assays were expressed in international units (i.u.) in terms of the Second International Reference Preparation for Human Menopausal Gonadotrophin. The mean index of precision λ ($\pm$ S. D.) was 0.15 ± 0.03 for the F.S.H. assays and 0.26 ± 0.06 for the L.H. determinations.

RESULTS

MALE HOMOSEXUALS

Results of assays of testosterone and epitestosterone in the three homosexuals and in 14 heterosexual males are shown in Table I.

It will be noted that the mean excretion values for the two C19 steroids in Subjects 1 and 2 were significantly lower than in the individuals constituting the normal group. In Subject 3, who indulged in both homosexual and heterosexual activities, such a difference with respect to testosterone was not noted, but his mean excretion of epitestosterone was significantly lower than that of the controls. The table also shows that L.H. excretion values in the three homosexuals were in the same range as in seven heterosexual men recently studied by Adamopoulos and Loraine (1970).

FEMALE HOMOSEXUALS

The mean excretion values for steroids and gonadotrophins in the four female homosexuals as compared with their heterosexual counterparts are shown in Tables II and III. In the latter group steroid assays were performed in 14 individuals and F.S.H. and L.H. determinations in six.

It will be noted (Table II) that the mean excretion of oestrone was significantly lower in all the homosexuals (P<0.05—0.001); however, in the case of oestradiol and oestriol a significant difference was observed in only two out of the four subjects. Pregnanediol output was within the normal range in all except Subject 2, in whom levels were raised. In all four homosexual women the mean testosterone excretion was significantly higher than in the controls (Table III); in the case of epitestosterone a significant difference was encountered only in Subject 2. F.S.H. output was within the normal range in Subjects 1, 2, and 4 and was abnormally low in Subject 3. The mean L.H. excretion was within the normal range in Subject 1, but was significantly raised in the remaining three. In Subjects 1, 2, and 4 the pattern of excretion of L.H., oest-

rogens, and pregnanediol was characteristic of the normal ovulatory cycle in women (see Loraine and Bell, 1968). In Subject 3, however, evidence for ovulation was equivocal, the rise in pregnanediol output in the luteal phase of the cycle being ill-defined.

Hormone assay data in one of the female homosexuals (Subject 1), who generally adopted the active role in sexual activities, are shown in the Chart. It will be noted that an ovulatory peak of oestrogen excretion occurred on days 15 and 16 of the study and that this was followed by a luteal phase rise in pregnanediol output, maximal on days 19 to 21. Levels for testosterone and epitestosterone were higher in the luteal than in the follicular phase of the cycle. Excretion values for L.H. were high from days 13 to 20, while a rise in F.S.H. output occurred between days 9 and 15 and between days 21 and 26.

DISCUSSION

In the present series of homosexual men and women abnormalities of endocrine function were observed in all cases apart from one. Thus, in the two men with exclusively homosexual activities urinary excretion values for testosterone were abnormally low, while in the third subject, who maintained both homosexual and heterosexual relationships, levels of this hormone were at the lower end of the normal range. In all male homosexuals L.H. readings in urine were normal, suggesting that an abnormality of pituitary gonadotrophic function was not a feature of the condition.

Endocrine abnormalities were also present in the four female homosexuals. Thus in all of them the testosterone levels were raised over those found in heterosexual controls. Furthermore, excretion values for oestrogens, especially oestrone, were low, while readings for pregnanediol were normal in three and raised in one. In three female homosexuals the L.H. output was significantly raised as compared with the heterosexual group.

TABLE I.—*Mean Testosterone, Epitestosterone, and L. H. Excretion in Male Homosexuals and in Normal Heterosexual Men*

	Testosterone	Epitestosterone	L.H. (i.u./24 hours)
	μg./24 hours + S.D.		
Homosexuals:			
Subject 1	39·6±14·6 (9)*<0·001†	13·6± 5·3 (9) <0·001	17·0±12·0 (7) N.S.
" 2	48·2±21·9 (21) <0·001	16·1±10·6 (21) <0·001	23·5±26·9 (10) N.S.
" 3	56·7±34·3 (21) N.S.	24·7± 5·7 (20) <0·001	15·4± 9·8 (7) N.S.
Heterosexual subjects	73·1±34·3 (38)	35·4±19·7 (38)	18·5±14·7 (28)

*Number of observations. †P value. N.S. = Not significant.

TABLE II.—*Mean Oestrogen and Pregnanediol Excretion in Female Homosexuals and in Normal Heterosexual Women*

	Oestriol	Oestrone	Oestradiol	Pregnanediol (mg./24 hours ±S.D.)
	μg. per 24 hours ±S.D.			
Homosexuals:				
Subject 1	11·0+6·0 (15)* N.S.†	6·7+2·9 (15) <0·01	3·9±1·7 (15) N.S.	1·4±0·7 (7) N.S.
" 2	6·5±4·4 (16) <0·01	7·1±4·5 (16) <0·05	3·7±3·2 (16) N.S.	2·0±1·5 (8) <0·001
" 3	13·6±9·7 (15) N.S.	1·5±2·9 (15) <0·001	1·1±2·4 (15) <0·001	0·5±0·5 (9) N.S.
" 4	3·8±2·2 (23) <0·001	1·1±2·2 (23) <0·001	0·5±0·5 (23) <0·001	1·0±1·0 (7) N.S.
Heterosexual subjects	9·7±6·5 (133)	9·5±4·8 (132)	3·5±2·4 (79)	1·2±1·7 (94)

*Number of observations. †P value. N.S. = Not significant.

TABLE III.—*Mean Testosterone, Epitestosterone, and Gonadotrophin Excretion in Female Homosexuals and in Normal Heterosexual Women*

	Testosterone	Epitestosterone	F.S.H.	L.H.
	μg./24 hours ±S.D.		(i.u./24 hours ± S.D.)	
Homosexuals:				
Subject 1	11·0±1·8 (11)* <0·05†	9·2± 6·5 (13) N.S.	9·0± 7·3 (13) N.S.	12·4±22·3 (13) N.S.
" 2	17·3±2·6 (14) <0·001	18·2± 7·5 (14) <0·001	10·4±13·1 (11) N.S.	26·0±23·2 (12) <0·05
" 3	16·0±2·5 (22) <0·001	14·1±10·5 (17) N.S.	3·6± 2·0 (15) <0·001	37·1±31·2 (14) <0·01
" 4	30·0±5·3 (10) <0·001	14·1±10·2 (7) N.S.	6·0± 4·9 (6) N.S.	30·7±29·5 (10) <0·05
Heterosexual subjects	7·3±4·3 (146)	8·9± 4·8 (51)	7·3± 1·8 (77)	11·1± 4·1 (81)

*Number of observations. †P value. N.S. = Not significant.
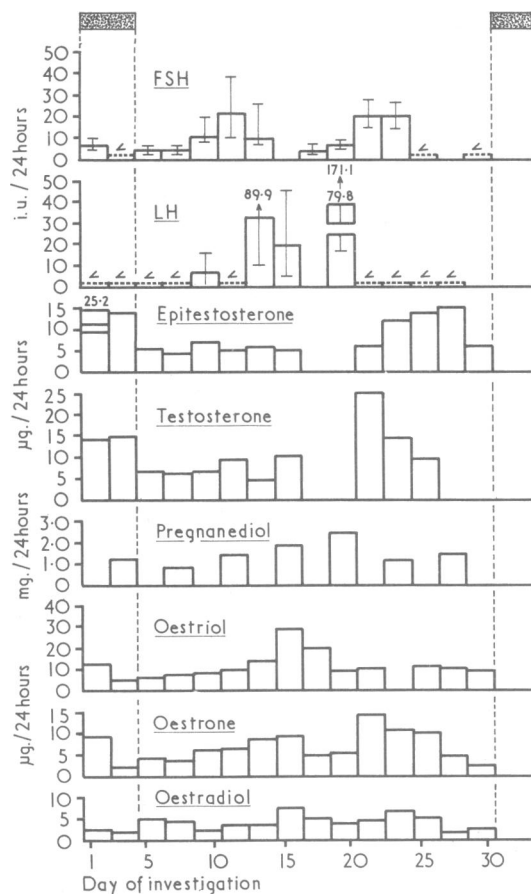
Hormone excretion pattern in a female homosexual (aged 23, para 0 + 0) with the active role.

Up till now the view that homosexuality stems from psychological causes and is not related to abnormalities in endocrine function has received wide acceptance (see Stafford-Clark, 1964; Perloff, 1965). The main basis for this contention has been the observation that when steroid sex hormones are administered either to heterosexual or to homosexual subjects no alteration occurs in the pattern of sexual behaviour which has already been established (Money, 1961; Perloff, 1965). The validity of this hypothesis, however, has been challenged by recent neuroendocrine research concerned with the effects of sex hormones, particularly androgens, on fetal and neonatal hypothalamic development in animals and with the possible repercussions of exposure to these substances on the pattern of sexual behaviour when such animals attain adulthood (Harris and Levine, 1965; Goy, 1968; Dörner, 1968; Dörner and Hinz, 1968).

On the basis of the currently available evidence it now appears probable that, with the exception of the critical periods of late intrauterine and neonatal life, steroid sex hormones produce little, if any, effect on the direction of sexual behaviour. Thus homosexuality is not induced in heterosexual men and women by castration, though libido may be reduced or absent after this operation (Allen, 1962; Roen, 1965). Moreover, if a person is castrated before puberty sexual activity in the adult is abolished but can be re-established by appropriate steroid therapy (Koch, 1936; Foss, 1937; Daniels and Tauber, 1941; Simpson, 1950). No evidence exists that such behaviour is altered from that which would have occurred normally. On the other hand, androgenic steroids given during intrauterine life to some species—for example, monkeys and guinea-pigs—and neonatally to others—for example, rats—produce pronounced effects on the pattern of mating and sexual behaviour which occurs in adulthood. It is tempting to suggest that, at puberty, the increased production

of sex hormones may serve to activate not only physiological mechanisms such as menstrual cycles but also the patterns of sexual behaviour laid down during fetal and neonatal life (see Donovan and Werff ten Bosch, 1965). Thus a hormonal imbalance at this time could conceivably lead to the development of aberrations in sexual behaviour, though definite evidence on this point has not yet been forthcoming.

The precise cause of the endocrine disturbance noted in all but one of the subjects reported here remains to be elucidated. Presumably the abnormalities could have been the result of psychological factors acting through the pituitary-hypothalamic axis, and support for such a concept comes from the finding of abnormally high L.H. levels in three of the female homosexuals. On the other hand, possibly a hormonal imbalance occurring during the critical periods of differentiation of the brain, and particularly of the hypothalamus, could have played a part. Little is at present known regarding the causative mechanisms underlying such an imbalance. There is, however, evidence that drugs administered during pregnancy may lead to disturbances of endocrine function (Money and Ehrhardt, 1968). In addition, it has been shown that hormonally active compounds may be present in the normal diet, and it is conceivable that such substances, if ingested at stages of development at which sexual behaviour patterns are laid down, might upset the delicate balance of the endocrine system. In this latter connexion it is of interest to note that steroids and steroid-like substances have been found in various plant and animal tissues (Zalkow et al., 1964; Tschesche, 1965).

Apart from homosexuality in men and women, deviations from normality in terms of endocrine function have recently been shown in other clinical situations which in the past have been regarded as predominantly psychological in origin. These include incapacitating dysmenorrhoea in women, in which excretion values for oestrogens and pregnanetriol tend to be low (Bell and Loraine, 1965), and impotence in men, in which decreased urinary testosterone levels are not infrequently encountered (Cooper et al., 1970).

The present paper has attempted to emphasize the highly complex nature of the clinical condition of homosexuality in the human. Kenyon (1970), in his recent admirable review, has stressed that the aetiology of homosexuality is essentially multifactorial, and with this concept we are in complete agreement. Psychological factors are undoubtedly of great importance in relation to pathogenesis, while the studies reported here suggest that abnormalities of endocrine function may also be of some significance. The area is one which is peculiarly suited to a collaborative approach between psychiatrists and endocrinologists, and it is to be hoped that, in the future, interdisciplinary studies of this type will become increasingly prevalent.

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Medical Memoranda

Chronic Carriage of Australia Antigen without Symptoms after Renal Transplant

CASE REPORT

A man aged 35 was admitted to the transplant unit, Addenbrooke's Hospital, Cambridge, on 26 June 1968 with renal failure as a result of chronic pyelonephritis. Dialysis was begun. Transplantation on 6 August with cadaver kidney was followed by rejection, allograft nephrectomy on 9 September, and bilateral nephrectomy on 14 October. A second cadaver transplant on 9 November was successful and he was sent home on 24 December. After two more days on the unit he was dischargd on 30 December. He was still symptom free on October 23 1970.

On 30 April 1970 his blood urea was 40 mg./ml., plasma creatinine 1·5 mg./100 ml., urine output good, haemoglobin 14 g./100 ml., and W.B.C. 8,000/mm.³ His present immunosuppression dosage is 18 mg. of prednisone and 150 mg. of azathioprine (Imuran)—that is 2·5 mg./kg. daily.

Australia antigen (Blumberg, 1964) was found during serum screening after his discharge; the source of infection remains unknown. He has not caused any overt infection on the unit or elsewhere up to the present.

MATERIALS AND METHODS

Agar gel double diffusion was done in protamine-agarose (Prince, 1968). Electron microscopy was carried out after centrifugation of 0·05 ml. of uninactivated serum diluted with phosphate-buffered saline (pH 7·4) at 25,000 r.p.m. for 60 minutes (mean 51,000 g) in the S.W. 39 rotor of a Spinco preparative centrifuge. The completely drained pellet was suspended in 5% sodium phosphotungstate, pH 6·5, and portions were placed on Formvar-carbon coated grids and blotted with filter paper after a few seconds. Specimens were examined in a Philips EM 300 electron microscope. Counts were made on serial photographs at identical magnification standardized with a latex suspension of 5 × 10^{10}/ml. concentration. It was not found necessary to add antiserum to assist the deposition of particles in the centrifugation of the sera.

RESULTS

Electron microscopy was superior to agar gel diffusion for the detection of antigen, and gave positive results three months earlier. Complement fixation tests were not possible because of the shortage of detector serum, but they might have been still more

sensitive (Shulman and Barker, 1969; Cossart and Vahrman, 1970).

The presumptive virus capsid of Australia antigen-associated hepatitis, described by Dane *et al.* (1970), was present in all except the first of the positive sera, which had so little antigen—that is, the long forms and irregular 20-nm. rounded forms of Bayer *et al.* (1968)—that capsids in the proportion found in later specimens would be unlikely to be found, even when present, with the method used.

It seems probable that the capsid is infective by analogy with the work of Bancroft *et al.* (1969), who assembled structurally similar capsids in vitro by aggregation of plant virus proteins around various nucleic acids and found that they were infective. The capsid concentrations found here are consistent with clinical estimates of the highly infectious nature of sera that have produced hepatitis.

The highest concentrations of antigen (3·8 × 10^{11}/ml.) and capsid particles (1·3 × 10^{10}/ml.) were reached about three months after antigen was first detectable, and the antigen has since shown little decline though the capsids were slightly fewer after a year (see Table).

Comparison of Gel Diffusion and Particle Counts by Electron Microscopy

Serum	Gel Diffusion Titre (Reciprocal)	Count/ml. of Serum	
		Capsid	Antigen
3/10/68	0	N.F.	N.F.
14/11/68	0	N.F.	N.F.
5/12/68	0	N.F.	< 2 × 10^8
16/1/69	0	4 × 10^8	3·4 × 10^{10}
13/3/69	8	1·3 × 10^{10}	3·8 × 10^{11}
26/6/69	16	1·1 × 10^{10}	3·4 × 10^{11}
11/12/69	8	6·2 × 10^9	2·1 × 10^{11}
5/3/70	2	1·2 × 10^9	1·1 × 10^{11}
2/4/70	1	2·8 × 10^9	1·2 × 10^{11}

N.F. = None found.

The titre of precipitable material by gel diffusion has approximated to the total particle count (see Table), and SGPT estimations have also shown a similar picture (Figs. 1 and 2).

At no time was there any evidence of antibody attached to antigen or capsids to cause agglutination, nor was there any anticomplementary activity in conventional complement fixation tests. The size of the capsids was 42 nm., as Dane *et al.* (1970) found, and showed little variation in undeformed particles. It was noted that there was often a toothed perimeter to the outer coat with approximately 5·5 nm. spacing (see Fig. 3 A) which gives about 24 projections around the periphery of each particle.

The long antigen particles, average width 21 nm., had transverse striations and marginal projections at intervals of 5·25 ± 0·25 nm. (Fig. 3 B)—that is, slightly closer than on the capsid. This agrees with the suggestion of Dane *et al.* (1970) that the