THE EXCRETION OF 17-KETOSTEROIDS AND GONADOTROPHIN IN CHILDREN: NORMAL AND ABNORMAL CASES*

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Normal development in childhood, and the sex differentiation in growth which is a feature of this development, is essentially a matter of the activity of the anterior pituitary gland and the ability of the peripheral endocrine organs to respond to its stimulation. Developmental anomalies in childhood, as in adult life, may be due to abnormalities either of pituitary secretion or of the gonads, adrenals, or other endocrine glands. The techniques which are available for the study of sex anomalies in the adult are applicable to an investigation of the sex mechanism of childhood, but relatively little work has been done in this field and it tends to be of a conflicting nature. Nathanson et al. (1941) have carried out a fairly elaborate investigation of the secretion of oestrogen and 17-ketosteroids in a group of normal girls and boys, and have been able to detect small, though fairly constant, amounts of both hormones in children between three and seven years of age. At about seven years the excretion of 17-ketosteroids, which up to then had ranged from 1.5 to 4.5 mg. in twenty-four hours, rose in both sexes to between 3 and 7 mg. a day. Boys from nine to eleven years tended to increase in androgen output more rapidly than girls, whose oestrogens increased more rapidly than in boys. Hormone output was correlated with physical development rather than with chronological age. Cycles in oestrogen excretion became obvious in girls at about the age of ten or eleven, and the rate of excretion greatly increased after eleven up to the menarche. This finding confirmed that of Frank (1935). That there is considerable divergence in the figures reported for androgen excretion in children is shown in table 1. Owing to the difficulty of comparing the biological unit with the colorimetric, data expressed in the former have not been given.

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TABLE 1
DATA REGARDING DAILY EXCRETION OF
17-KETOSTEROIDS BY CHILDREN

Author	Age of children : yrs.	Range of excretion: mg.
Patterson et al.	1 $\frac{1}{2}$	less than 0.6*
Oesting and Webster	3	0.3
Chou and Wu	14	1.5 to 2
Koch	under 10	0.2 to 1.1
	6 $\frac{1}{2}$ -10 (boys)	0.07 to 0.2*
	8-10 (girls)	0.18 to 0.2*
Talbot et al.	under 7	0.8 to 2.6 (aver. 1.3)
	7-12	1.8 to 5.0 (aver. 4.0)
	12-15	5.0 to 11.3 (aver. 8.2)
Nathanson et al.	3-7	1.5 to 4.5
	7-9	3.0 to 7.0
	9-12 (boys)	4.0 to 12.5
	9-12 (girls)	3.0 to 12.0
	12-15 (boys)	6.0 to 18.0
	12-15 (girls)	6.0 to 17.0

* = per litre of urine.

Review of the Literature

The result of investigations in the last few years has been to show that the excretion of 17-ketosteroids is an imperfect index of the androgenic activity of the gonads, and that, although there is some degree of correlation of androgen excretion with sex and age, a considerable proportion of the androgen found in urine is secreted by the adrenal cortex (Callow and Callow, 1940; Callow et al., 1940), so that after castration the androgen content is only slightly below normal values. Evidence in support of this observation is afforded by the greatly enhanced excretion of 17-ketosteroids recorded in cases of hyperplasia and tumour of the adrenal cortex. It follows that a knowledge of the 17-ketosteroid excretion is of value in cases of excessive or deficient sexual development, especially if due to adrenal disease; and, when combined with a knowledge of pituitary activity, as reflected in the gonadotrophin excretion, it may provide an important aid to diagnosis.

An efficient and inexpensive method of measuring gonadotrophin excretion has not been forthcoming until recently. Using the ethyl alcohol precipitation method of Aschheim and Zondek, Nathanson et al. (1941) were unable to detect below 20 mouse units of gonadotrophin in a twenty-four hour output of urine, and consequently failed to detect follicle-stimulating hormone in girls under eleven and in boys under twelve to thirteen years old. They expressed the opinion that more efficient methods might demonstrate its excretion at an earlier date. Using a tungstic acid precipitation method, and taking uterine weight as their mouse unit instead of ovarian stimulation (which Nathanson et al. employed), Catchpole et al. (1938), and Catchpole and Greulich (1940) were able to detect as little as two mouse units of gonadotrophin in twenty-four hours; yet they failed to detect any in the urine of boys under eleven, and only between two and ten mouse units in twenty-four hours in the urine of twelve out of fifteen boys between the ages of twelve and sixteen years. They considered ten mouse units to be 'essentially an adult figure.' Prepubertal and adolescent girls had a daily excretion which ranged from three to ten mouse units, and excretion became more frequent and increased to 20 mouse units as the menarche was approached. Gonadotrophic activity was demonstrable for at least a year prior to the menarche. In this they confirmed the observations of Katzman and Doisy (1934) and of Frank (1935). The latter stated that just before the menarche the amount of follicle-stimulating hormone excreted was half the adult amount. Frank was able to detect its secretion at four years of age, and found that at nine the value had doubled. As in the case of oestrogen and ketosteroids, the amounts of gonadotrophin recovered were related to developmental status rather than to actual age.

It follows that in developmental irregularities, e.g. dwarfism, Fröhlich's syndrome, sexual and somatic precocity, and sexual retardation (as in cases of undescended testes), it is helpful for the clinician to know whether there is excessive or reduced function of the pituitary. As sexual precocity may be due to a tumour in the gonads or adrenals or to a lesion in the brain, or may be merely of the constitutional type (of which examples have been given by Novak, 1944, and by Hain, 1947b) a knowledge of hormone excretion may supply valuable aid in differentiating between these conditions.

Excretion in Normal Children

In order that the data obtained in pathological cases might be compared with a standard of normals based on the same methods, and also with other standards, the excretion of 17-ketosteroids and of gonadotrophin was ascertained in a number of normal children of both sexes (tables 2 and 3). The methods of hormone extraction were those

TABLE 2
EXCRETION OF 17-KETOSTEROIDS AND
GONADOTROPHIN BY NORMAL GIRLS

Case No.	Age in yrs.	17-ketostds., mg./24 hrs.	Gonadotrophin, M.U./24 hrs.
K32	5	{ 2.5 1.4	not done
K206	6½	2.2	4.5
K217	7	1.3	<2
K209	7	1.8	10
K205*	8	7.1	4.5
K216	8	2.6	not done
K211	8½	{ 1.3 1.7	<2
K210	8½	2.0	<2
K207	9	2.7	3
K208	9	2.2	4.5
Range	5-7 8-9	1.3 to 2.5 1.3 to 7.1	<2 to 10

* appendicitis.

described by Hain (1947a): that is, for 17-ketosteroids, the method of Patterson et al. (1942), in which hydrolysis of 20 c.cm. urine with 3 per cent. sulphuric acid was followed by ether extraction and subsequent separation of the oestrogens from the androgens. The final product in alcohol was used for colorimetric estimation with *m*-dinitrobenzene,

TABLE 3
EXCRETION OF 17-KETOSTEROIDS AND
GONADOTROPHIN BY NORMAL BOYS

Case No.	Age in yrs.	17-ketostds., mg./24 hrs.	Gonadotrophin M.U./24 hrs.
K31	2	0.6 (1.8*)	not done
K218	8	not done	<2 (only 110 c.cm. urine passed)
K203	8	4.1 (5.5*) (4.1*)	18
K219	8½	2.4	<2
K214	9	3.6	2.3
K204	9½	3.0	18
K201	10½	(3.6*)	14
K202	11½	3.8	17
		4.8	6
		3.3	4
		2.0	2
		2.6	10
		5.3	3
K213	14	6.0	14
		5.9	28
Range	8-11½ 14	2.4 to 5.3 6	< 2 to 18 14 to 28

* = per litre of urine.

readings of the colour intensity being made in a Spekter absorptiometer. The ketosteroids value was assessed from a calibration curve constructed from standard solutions of androsterone. For gonadotrophin estimation, the twenty-four-hours output of urine was brought to pH4 with glacial acetic acid, and the hormone adsorbed on 20 per cent. kaolin. After centrifuging, the kaolin was extracted with strong alkali and the supernatant made weakly acid before injection into immature mice. The mouse unit was based on uterine weight plus vaginal response.

The values for 17-ketosteroids are in agreement with those of Talbot et al. (1940) for the age groups covered. A discordant note is struck by the girl K205, whose rather high output of androgen may have been the result of general hyperaemia in the abdomen (due to appendicitis) causing temporarily increased adrenal cortical activity. It can be seen that boys tend to excrete more androgen than girls of the same age.

Gonadotrophin excretion could be detected before the seventh year in girls, and before the ninth year in boys; the tendency was for the output to be higher in boys than in girls up to the tenth year. A boy of fourteen excreted as much as many adults (Werner, 1943).

Excretion in Abnormal Children

The data given in tables 4 and 5 (p. 157, 158) relate almost entirely to children with developmental abnormalities. Generally the excretion of both 17-ketosteroids and gonadotrophin was ascertained, but in a few instances an A.Z. test was done instead of a gonadotrophin estimation, for reasons to be explained. In cases of adrenal cortical tumour or hyperplasia, the pregnanediol output was generally estimated in preference to that of gonadotrophin, as the adrenal cortex secretes progesterone; in one case (K181) the excretion of both pregnanediol and gonadotrophin was ascertained.

Girls: table 4. Menstruation occurred in six girls between the ages of two and ten years, and in a seventh girl aged eleven, in whom breast development was very marked. But for this last feature, this case might have been considered within normal limits. Precocious menstruation may be due to any one of six causes: granulosa-cell tumour; lesions of the hypothalamus and third ventricle; adrenal cortical tumour, ovarian cysts, and tumours other than granulosa-cell; the Hand-Schüller-Christian syndrome, in which bone cysts are present; and, finally, 'natural' or 'constitutional' precocity for which no known pathological cause has been found. The occurrence of 'constitutional' precocity in girls and boys has recently been described by the author (Hain, 1947b), who also cited instances of all the above varieties reported in the literature. In all cases of precocious menstruation it is necessary to test the urine (a) for an excess of oestrogen, which in granulosa-cell tumours is excreted so abundantly that less than 3.0 c.cm. of urine causes the maximum

oestrogenic reaction in an ovariectomized mouse, and (b) for an excess of luteinizing gonadotrophin. In cases of ovarian carcinoma and teratoma and embryonic tumours, a positive A.Z. result is obtained with less than 3.0 c.cm. of urine; and in cerebral tumours, other than those of embryonic type, 5.0 c.cm. of urine causes marked uterine enlargement without a macroscopic effect on the ovaries of the mouse injected. If an A.Z. test is entirely ineffective, an excess of oestrogen is excluded at the same time as an excess of chorionic gonadotrophin, thus restricting the number of possible causes of the precocity. The excretion of normal or only slightly raised amounts of 17-ketosteroids rules out adrenal cortical involvement, with which very high values are usually associated. We are then left with 'constitutional' precocity as the most likely cause of the condition. The cause of constitutional precocity is not known; but, from the few facts collected so far, it seems that pituitary secretion, as measured by gonadotrophin output, starts at an earlier date or in larger amounts than in the average child of the same age. That this is not the whole story is suggested by the following: (1) no gonadotrophin was recovered in the two youngest children with vaginal bleeding: K339 and K319, aged two and a quarter and two and a half years respectively; (2) one of the 'precocious' girls (K158, aged six and a half years) excreted eight mouse units gonadotrophin in twenty-four hours, whereas K209, aged seven, who excreted ten mouse units a day, was 'normal'; (3) two girls (K294 and K317), though secreting as much gonadotrophin as adults, did not menstruate although their development in other respects was in advance of their age. It seems likely, therefore, that in cases of precocity of the 'constitutional' type there is not only premature pituitary secretion (or secretion at levels above normal) but also premature gonadal response. The latter was manifest in the formation of ovarian cysts as well as menstruation in at least four of the cases in table 4, and in almost adult development of the gonads and sex characters in two of the boys, P519 and K263, in table 5. This difference in tissue response possibly accounts for one patient showing rapid skeletal development whereas another developed menstrual function under the same stimulus.

Enlargement of the breasts may be the result of abnormal response to normal stimuli in some cases, or may have a pathological etiology. Tests performed with the natural urine showed no excess of oestrogen or of gonadotrophin excretion in the two girls with this anomaly (P516, K303), and the only feature was a 17-ketosteroid output above normal limits. The possibility of an adrenal basis for the condition might therefore be considered. The following facts support such a possibility. (a) Van Heuverswyn et al. (1939) state that desoxycorticosterone acetate caused mammary development in both normal and castrated male mice, a finding which was confirmed by Chamorro

(1940), who considers that the action may be by way of the pituitary as doca had no effect on the mammae of hypophysectomized mice. (b) In two women with mastitis and two men with gynaecomastia a 'pregnan α derivative' was recovered which was in every way similar to that excreted by a woman with adrenal carcinoma, who, prior to its recovery, had excreted large amounts of pregnanediol (Hain, 1947a). (c) The association of adrenal tumours with gynaecomastia in men has been recorded in at least five cases.

Two of the three girls described as undersized may have been deficient in pituitary function, as no gonadotrophin was recoverable; in the third case—K344—excretion was normal.

With one exception (P323), all the girls with virilism excreted excessive amounts of 17-ketosteroids; P323 excreted four or five times as much as the average three-year-old, but surprisingly little for one with an adrenal tumour (which was found at operation), and as compared with K30, a child of almost the same age whose output was over 300 mg. in twenty-four hours. K30 excreted no pregnanediol, whereas P323 did. On the basis of 17-ketosteroid output it was not possible to discriminate either between hyperplasia and a tumour of the adrenal cortex, or between these and a virilizing tumour of the ovary (K181). In this latter case not only were large amounts of pregnanediol excreted, but also of gonadotrophin (fifty-five mouse units in twenty-four hours), which suggests that the absence of normal ovarian function had so reacted on the pituitary as to cause heightened secretion of gonadotrophin. A similar case will be described later, a cryptorchid male: K161. It would be interesting if virilizing ovarian tumours could be distinguished from adrenal cortical tumours by means of an excessive gonadotrophin output in cases of the former.

Boys: table 5. Precocious development occurred in five boys under eleven years old, of whom the youngest was only twelve months old. Such precocity can be due to one of four causes: cerebral tumour; testicular interstitial cell tumour; hyperplasia or tumour of the adrenal cortex; or 'constitutional' precocity. Three cases of the last named occur in table 5: K345, who, though only twelve months old, excreted almost seven mouse units of gonadotrophin in twenty-four hours; and P519 and K263, who, at five and six and a half years of age respectively, excreted as much gonadotrophin as adult men, and almost as much 17-ketosteroid. In each case the A.Z. test had been negative, making it unlikely that a cerebral tumour or tumour of embryonic type was responsible for the condition. These cases are described by Hain (1947b).

The case of P510, in whom sexual precocity was due to an interstitial cell tumour of the testis, is of special interest as only nine others have been reported in the world literature since 1895; it has been the subject of a special report by Horne et al. (1947). The 17-ketosteroids excreted by this infant,

though equal to the output of an adult man, were not so high as frequently occurs in cases of adrenal tumour. Owing to the rarity of testicular tumours in children, adrenal hyperplasia or tumour was suspected, and it was only post mortem that the testicular abnormality was found. It would appear that in neither sex can differentiation be made between adrenal and gonadal virilizing tumours on the basis of 17-ketosteroid output. In the case of the boy the urine received was not sufficient to permit of an estimation of the gonadotrophin excreted, as was done for K181, who had an ovarian tumour. That the output was not such as occurs in presence of a seminoma or teratoma was shown by the negative reaction to the A.Z. test.

The only boy with an adrenal cortical tumour (K148) excreted 84 mg. 17-ketosteroids, and was in every way (except mentally) as developed as a man of eighteen. His case is described in a report on adrenal tumours (Hain, 1947a).

P512, whose abdominal tumour proved to be a neuroblastoma, had a normal 17-ketosteroids output.

Sexual under-development comprised a large group, in which complicating features were present in some cases. In two of the three 'dwarfs' the excretion of 17-ketosteroids was satisfactory; in the third, whose dwarfism was of the Lorain type, total pituitary function was undoubtedly impaired, and as a result adrenal cortical activity also was reduced. With the possible exception of K170 the boys of Fröhlich type had a satisfactory excretion of 17-ketosteroids but a low gonadotrophin output, suggesting deficient pituitary secretion in one direction. In K68, whose sexual under-development was associated with diabetes of long standing, the excretion of corticotrophic hormone was probably reduced, as well as that of gonadotrophin, as the result of impairment of total pituitary function, since both the ketosteroids and the gonadotrophin were low.

The boy with gynaecomastia (K342, aged eleven), excreted normal amounts of ketosteroids but gonadotrophin was excessive, so that blood-spots (which denote a high concentration of luteinizing hormone) formed in the ovaries of the mice injected with the urinary extract. Klinefelter et al. (1942) describe a syndrome characterized by gynaecomastia and hypogonadism (small testes and aspermatogenesis but normal phallus, prostate, and pubic hair) plus increased excretion of follicle-stimulating hormone (F.S.H.) and usually low 17-ketosteroids. Oestrogen excretion was not above normal. They considered it likely that the condition was due to the excessive secretion of F.S.H. and the absence of luteinizing hormone; testosterone failed to cause an improvement, and they suggested that luteinizing hormone might be tried. Their findings confirmed those of Bronstein (1939) and Turner (1939). In the boy K342 there does not seem to have been any deficiency of luteinizing hormone but rather an excess, as it is rarely that

one can detect its excretion in cases other than those in which chorionic tissue is present. Its excretion by menopausal women and by people of both sexes with hypertension and obesity is not uncommon (Hain, 1947c).

The remaining two patients, K122 and K161, are male pseudo-hermaphrodites (that is, they had testicles but female external secondary characters); in the older patient, who is being brought up as a girl, the tiny testicles found lying in the internal ring were removed. Her case has been fully described by Hain and Schofield (1947), and stress has been laid on the very high excretion of gonadotrophin (F.S.H.) before operation, which was undoubtedly due to the patient being, to all intents and purposes, a castrate. A boy castrated at the age of twelve was found to be excreting from 100 to 300 mouse units F.S.H. per litre of urine during the two years that Hamburger (1933) observed the case; it would appear that the condition is an exaggeration of that observed at the menopause, and in people of both sexes in whom the gonads make little or no response to pituitary secretion (Hain, 1947c). The excretion of excessive amounts of gonadotrophin in a case of doubtful sex, especially in the absence of a high ketosteroids output and of any pregnanediol, may be regarded as strong presumptive evidence in favour of the patient's being a male pseudo-hermaphrodite, since a similar morphological picture in the female is associated with a hypersecretion of 17-ketosteroids, and sometimes of progesterone also, either by the adrenal cortex or by a similar structure in the ovary.

Fluctuations in Output

Considering the fluctuations in hormone output which occur even in the normal individual, the desirability of estimating gonadotrophin excretion on several occasions in the same person is obvious; its practicability in a laboratory undertaking a variety of hormone analyses is another matter. Since as a general rule the excretion of two hormones was ascertained in each patient, the data provided the clinician with a fair indication of pituitary function in doubtful cases.

Summary and Conclusions

1. A knowledge of the excretion of 17-ketosteroids and gonadotrophin is helpful to the clinician in dealing with developmental anomalies in children.

2. Gonadotrophin can be detected in normal girls before the seventh year, and in normal boys before the ninth year.

3. In children of both sexes in whom development was precocious, gonadotrophin was excreted in amounts considerably above the average for the chronological age. Precocious menstruation without

a pathological background is probably associated with abnormal tissue response as well as premature pituitary secretion.

4. Cases are given illustrating the method of differentiating between precocity due to pathological, and that due to non-pathological causes by means of hormone assays.

5. The earliest age at which gonadotrophin was detected in urine was in a 'precocious' boy aged twelve months.

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TABLE 4

EXCRETION OF 17-KETOSTEROIDS AND GONADOTROPHIN IN ABNORMAL CASES: GIRLS

Case No.	Age in yrs.	Condition	17-ketostds., mg./24 hrs.	Gonadotrophin, M.U./24 hrs.
K339	2½	Sexual precocity; m. twice; breasts and labia enlarged.	0·9 (1·2*)	<3; AZ-ve
K319	2½	Sexual precocity; m.; ovarian cyst; breasts enlarged.	3·15*	<4*; AZ-ve
P478	3½	Sexual precocity; m. since 19 months old; breasts large; pubic hair at 2 mths.; ossific.=12 yrs.	2·4 (5·6*)	AZ-ve; <4 I.U. oestrone
P409	4	Sexual precocity; m. and breast development=17 yrs.; ossific.=6-9 yrs.	2, 3, and 1·4	16; AZ-ve
K158	6½	Sexual precocity; m. for 3 mths.; breasts large; excessive body growth for 6 months.	4·1, 5·0	8; AZ-ve
K498	9½	Sexual precocity; m. and breast enlargement; obesity (91 lb.), 52" tall; ossific.=12; pubic hair; striae; impaired sugar tolerance; enuresis.	3·0 (8·5*)	AZ-ve (excreting pregnanediol)
K172	11	Sexual precocity; m.; very marked breast development.	4·4 (3·5*)	12; AZ-ve
K299	3	Oversized=5 or 6 yrs.; arms very long; hands and feet large; no pubic hair.	2·3	<1
K312	8	=11 yrs. in devt. of mammae and limbs; 60" tall, 92½ lb., abd. 29".	2·2	7
K294	10	Obesity since appendicectomy 2 yrs. ago; weight 90 lb., 53" tall; abd. 31".	4·8 (10*)	22
K317	9½	Developing quickly; pubic hair present for 1 year; axillary hair for 6 months; breasts slightly enlarged.	5·8 (10·5*)	13
K336	8½	Obesity 1 yr.; 6½ st., i.e. almost 3 st. above normal; 52" tall.	4·8 (9·5*)	3 to 4
K350	13	Obesity—13 st. 6 lb., 'has always been obese.'	7·3 (11·9*)	almost 10
P516	6½	Rapid enlargement of one breast.	5·4	AZ-ve
K303	2	Enlargement of one breast.	3·4 (10·5*)	<2; 5 cc. urine no effect
K340	7½	Leucorrhoea.	4·4 (6*)	<3
K321	8½	Dwarfism; 44", 44 lb.; proportions normal.	2·8	<5
K326	9	Undersized: 40", 43½ lb. (i.e. 10" and 10 lb. less than normal); intelligent.	2·8	<3
K344	10½	Undersized: 6" and 20 lb. under normal—of a small-sized family.	6·8	almost 7
K325	7	Virilism: v. large clitoris; growth of pubic hair.	28·7	<10; no pregnanediol
K355	15	Virilism.	28	not done
K139	3½	Virilism; enlarged clitoris, pubic hair; ossific.=7-8; brother had adrenal tumour (K148).	12	" "
K85	1½	Virilism; enlarged clitoris; pubic hair (adr. hyperplasia).	23·5*	no pregnanediol
P323	3½	Virilism; enlarged clitoris, pubic hair (adrenal tumour).	5·9	12 mg. pregnanediol
K30	4	Virilism; enlarged clitoris, pubic hair (adrenal tumour).	375*	AZ-ve
K181	12	Virilism; enlarged clitoris, pubic hair (ovarian virilizing tumour).	116	55; 60 mg. pregnanediol

m. = menstruation.

* = per litre of urine.

TABLE 5
EXCRETION OF 17-KETOSTEROIDS AND GONADOTROPHIN IN ABNORMAL CASES: BOYS

Case No.	Age in yrs.	Condition	ketostds. mg./24 hrs.	Gonadotrophin M.U./24 hrs.
K345	1	Physically and mentally precocious; walked at 4½ mths.	1.5 (4.5*)	Almost 7; AZ-ve.
P510	1½	Sexual precocity due to testicular tumour.	9.4*	AZ-ve
P519	5	Constitutional sexual precocity; enlarged genitalia, pubic hair; 10" above average height; B.P.105/75.	7.5*	40-50
K263	6½	Sexual precocity (constitutional).	5.0	AZ-ve
K148	10½	Sexual precocity (adrenal cortical tumour).	6.0	18, 21
P512	2½	Neuroblastoma.	9.9	AZ-ve
			84	not done
			1.4 (4*)	" "
Sexual underdevelopment				
K292	8½	Lorain dwarf; =4 to 5 yrs.; iron callipers on feet for 2 yrs.	1.5	<2
K311	8	Dwarf; chronic diarrhoea 4-5 yrs.; Hb. 55%; tendency to bed-wet.	4.2	<3
K313	5½	Dwarf (36"; 32½ lb.); bed-wetter, diarrhoea for 2 yrs.; Hb. 70% (only 20 lb. <6 mths. ago).	6.4	<4
K316	10	Severe obesity (105 lb.); only 1 testis palpable (tiny); penis very small.	6.6	<3
K154	11	Severe calcium deficiency.	7.5	<4
K68	15	Diabetes; sexual underdevelopment.	2.3, 1.6	almost 4
K280	11	? Fröhlich's syndrome.	12.0	4-5
K173	12	Fröhlich's syndrome.	6.2	none
K170	14	? Fröhlich's syndrome.	10.0	10
K163	14½	Sexual underdevelopment, amyotonia, obesity.	7.4	not done
K233	15	Undescended testes.	8.0	7.5
K342	11	Gynaecomastia (unilateral, glandular).	7.0; 11.9	25 F.S.H. 5 L.H.
K122	8	Clitoris large; hypospadias; testes not palpable; brought up as female.	<2	20
K161	14	One testicle removed when 2½ yrs. old; vagina 1½ inches long; clitoris size of red end of match; female type urethra; brought up as female; remaining testicle removed.	6.7	>106

* = per litre urine.