J. med. Genet. (1968). **5**, 286.

Testosterone Excretion Rates in Normal Males and Males with an XYY Complement

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The incidence of males with an XYY chromosome complement in a maximum security hospital was found to be 3% (Jacobs *et al.*, 1965). These males were exceptionally tall, and it was found that 1 in 3 of the men of over 6 ft. (183 cm.) in this hospital had an XYY chromosome constitution. This very high incidence in an over-6 ft. group was confirmed in a special hospital for the subnormal (Casey *et al.*, 1966). Apart from their tall stature no other abnormality has been detected in these XYY males.

The behavioural disorders and pattern of the crime among these XYY males has been extensively investigated (Price and Whatmore 1967a, b). From these studies it was suggested that the extra 'Y' chromosome was a factor contributing to their disorder of personality and their early conflict with the law.

It was thought of some interest to know if the presence of an additional 'Y' chromosome had any influence on the secretion of the male sex hormone, testosterone. In the present study, urinary testosterone excretion rates have been measured in two groups of males with an XY constitution and a third group of males with an XYY constitution.

Materials and Methods

Fifteen males who were detained at the special hospital, Rampton, have been studied. Of these 15, 9 were shown to be XYY constituted (Group 1) (Casey *et al.*, 1966). The remaining 6 subjects had a normal XY complement (Group 2).

In addition, urinary testosterone excretion rates were measured in 6 normal males (Group 3) (members of staff), the results of which have been used as a reference point for the interpretation of the testosterone excretion rates obtained from the 15 male in-patients.

Collections of 24-hour urine specimens were obtained from all the subjects, and aliquots stored at 4° C. until analysed. The testosterone excreted as the glucuronide was hydrolysed with betaglucuronidase enzyme. Preliminary fractionation of the liberated testosterone was accomplished by a modification of the procedure of Ibayashi *et al.* (1964). An additional paper chromatographic step was employed using the light petroleum: dekalin: methanol system of Bush (1961) to ensure the separation of testosterone from epitestosterone.

The testosterone fraction obtained from the paper chromatographic step was acetylated and rerun on a thin-layer chromatoplate in the system ethyl acetate: benzene (1:3). The testosterone acetate fraction was subsequently quantitated by a fluorimetric procedure (Korenman, Wilson, and Lipsett, 1963), using testosterone acetate for the standard curve. The results reported here are expressed in terms of testosterone acetate.

Results

Table I documents the physical parameters and the testosterone excretion rates in the 15 men detained at Rampton (Groups 1 and 2). Table II shows the same parameters obtained from normal men (Group 3).

The mean height was identical in Groups 1 and 2 (184 cm.) and slightly less in Group 3 (176 cm.). The mean age for the XYY males (Group 1) was 29·1 years, for the XY males 25·6 years (Group 2), and for the normal group 31·6 years (Group 3). The means for the body parameters of weight and surface area were similar in all 3 groups.

We were unable to demonstrate a clear correlation between either weight or surface area and the testosterone excretion rate. The Fig. illustrates distribution of testosterone excretion rate in the 3 groups of subjects. The mean excretion rate for Groups 1 and 2 was higher than Group 3, irrespective of the way the data were expressed. In particular, 7 out of 9 (77%) of the men with an XYY complement had excretion rates that were outside +2 SD from the mean testosterone excretion rate found for the normals in Group 3.

Received December 14, 1967.

TABLE I

GROUPS 1 AND 2: RAMPTON DETAINEES

Subject No.	Age (yr.)	Weight (kg.)	Height (cm.)	Body Surface Area ($m.^2$)	Testosterone ($\mu g./24$ hr.)	Testosterone ($\mu g./kg.b.wt.$)	Testosterone ($\mu g./m.^2$ Body Surface Area)
			Group 1 Male Patients with XYY Chromosomes				
1	59	87·7	184	2·12	113	1·3	53·3
2	19	78·6	181	2·00	87	1·1	43·5
3	59	79·5	190	2·08	150	1·9	72·1
4	23	64·5	180	1·84	132	2·0	71·7
5	22	78·2	189	2·07	295	3·8	142·5
6	19	70·9	181	1·92	255	3·6	132·8
7	23	79·5	192	2·11	216	2·7	102·4
8	38	72·7	181	1·95	174	2·4	89·2
9	22	59·1	180	1·77	121	2·0	68·4
Mean	29·1	74·5	184	1·98	171	2·3	86·2
Range	(19–59)	(59·1–87·7)	(1·80–1·92)	(1·77–2·12)	(87–295)	(1·1–3·8)	(43·5–142·5)
			Group 2 Male Patients—Normal (XY) Chromosomes				
1	27½	74·1	181	1·96	117	1·6	59·7
2	25	72·7	183	1·96	204	2·8	104·1
3	23	66·4	182	1·88	115	1·7	61·2
4	21½	72·3	185	1·97	95	1·3	48·2
5	33	78·9	192	2·10	127	1·6	60·5
6	21½	66·8	180	1·86	101	1·5	54·3
Mean	25·3	71·7	184	1·95	126	1·7	64·7
Range	21·5–27·5	(66·4–74·1)	(181–192)	(1·86–2·10)	(95–204)	(1·3–2·8)	(48·2–104·1)

TABLE II

GROUP 3: NORMAL MALES (CLINICAL AND LABORATORY STAFF)

Subject No.	Age (yr.)	Weight (kg.)	Height (cm.)	Body Surface Area ($m.^2$)	Testosterone ($\mu g./24$ hr.)	Testosterone ($\mu g./kg.b.wt.$)	Testosterone ($\mu g./m.^2$ Body Surface Area)
1	32	72·7	179	1·91	98	1·3	51·3
2	31¾	74·5	171	1·84	54	0·7	29·3
3	25	56·8	167	1·65	94	1·6	57·0
4	35	80·7	172	1·96	94	1·2	48·0
5	32	82·6	185	2·08	76	0·9	36·5
6	34	82·7	184	2·06	63	0·8	30·6
Mean ± 2SD	31·6	75·0	176	1·92	80·0 ± 37·0	1·1 ± 0·7	42·1 ± 22·7
Range	(25–35)	(72·7–82·7)	(167–185)	(1·84–2·08)	(54–98)	(0·7–1·6)	(29·3–57·0)

A statistical evaluation of the data using the Student 't' test (Brownlee, 1960) revealed that the values for the testosterone excretion rates were significantly higher for Group 1 as compared with Group 3 ($p < 0·01$). Furthermore, the values for Group 2 were also significantly higher than the values in Group 3 ($p < 0·05$). In addition, those patients with an XYY complement (Group 1) had excretion rates that were *not* significantly different from those patients with a normal XY complement (Group 2).

Discussion

A physiological role for testosterone is well established for the male from the foetal stage of development (Goldman, Yakovac, and Bongiovanni, 1966) and again when puberty intervenes.

Sex reorientation to the female type has been most elegantly demonstrated in the rat when an anti-androgenic agent is administered at the early stages of male foetal development (Neumann and Elger, 1965).

A role for testosterone that influences behavioural patterns not associated with the sexual drive of males is less evident. The present investigation has not elucidated whether or not a clear relation exists between antisocial behaviour and increased testosterone excretion. There is evidence, however, from this study, that patients with an XYY complement and patients with normal sex chromosomes can produce more testosterone than normal men who are not under detention.

It has been demonstrated that the levels of plasma testosterone in normal males show a diurnal variation (Resko and Eik-Nes, 1966). The increased excretion of testosterone found in the patients with XY and XYY chromosomes might be attributable to a loss of the normal diurnal variation. It could be postulated that the enforced detention is a sufficient factor contributing to a loss of diurnal rhythm.

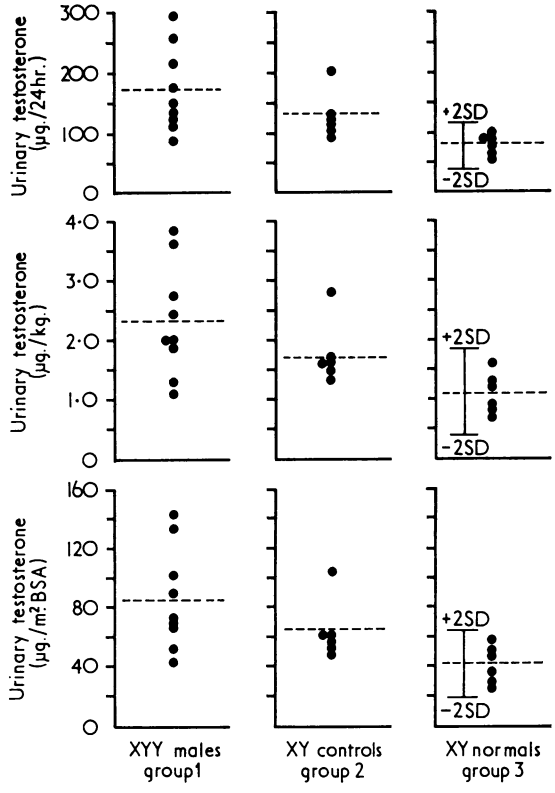

FIG. Testosterone excretion rates.

Such a loss of normal rhythm may result in an increased and variable excretion of testosterone in the urine of these patients.

The proportion of the excreted testosterone which was biologically active also remains unknown. The measurement of the non-conjugated fraction circulating in plasma under conditions of adrenal suppression using analogues of cortisol might be revealing, as has been shown in other studies of androgen excess (Vermeulen, 1965).

Summary

Urinary testosterone excretion rates have been measured in 15 patients detained at the special hospital, Rampton. Of these patients, 9 had an XYY chromosomal complement and the remaining 6 had a normal male sex chromosome pattern. Almost all these patients had higher excretion rates of testosterone when compared to normal healthy men. It has been postulated that patients under detention have increased testosterone excretion rates due to changes in the mechanisms controlling the diurnal rhythm of testosterone. The results do not suggest that an additional 'Y' chromosome has an influence on the excretion of the male sex hormone.

We are particularly indebted to Dr. D. R. K. Street, the Medical Superintendent, and the nursing staff of the Special Hospital at Rampton, for their close co-operation throughout these studies. Our grateful thanks are due to Professor D. V. Hubble for the facilities to pursue this work and to Dr. J. H. Edwards for his constructive criticism.

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