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TOTAL-BODY POTASSIUM AND LEAN BODY MASS IN MALES WITH AN ABNORMAL SEX CHROMOSOME COMPLEMENT

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Total-body potassium and lean-body mass were estimated in 21 male patients at a state mental hospital. Seven of these had an abnormal sex chromosome complement: XXY in three, XYY in two, and XXYY in two. The remainder had a normal chromosome analysis. In the group of patients with chromosome abnormalities considered as a whole, the total-body potassium and the lean-body mass were significantly less than in the "normal" males and they were not significantly different from the corresponding values for healthy females. Within the group, abnormally low levels of total-body potassium and significantly reduced values for lean-body mass occurred amongst the 47,XXY and the 48,XXYY males. For both 47,XYY males, the values were not significantly different from the predicted normal values for men.

Differences between the sexes with respect to the total-body content of potassium and the lean-body mass are well established. It was of interest, therefore, to initiate a pilot study to examine whether males with different types of chromosome intersex exhibited differences from males of normal karyotype.

PATIENTS AND METHODS

The patients examined were 21 male inmates of a state mental hospital, 7 of whom had an abnormal number of sex chromosomes. Of these seven, three (127/69, 358/67, 19/66) had a total of 47 chromosomes, the additional one being an X (47,XXY), two (82/70, 123/65) had a total of 47 due to an extra Y (47,XYY), and two (379/67, 11/61) had both an extra X and an extra Y making a total of 48 (48,XXYY). All of the five men with extra X chromosomes had testicular atrophy and varying degrees of anomalous development of secondary sexual characteristics. One of these men (358/67) also suffered from congestive cardiac failure due to rheumatic aortic and mitral valve disease and had previously had a partial gastrectomy for peptic ulceration. At the time of this investigation, he was digitalized on digoxin (0.75 mg daily). This patient has since died of acute cardiac failure.

Patients at the state hospital are mentally ill or psychopathic with dangerous, violent, or criminal propensities and are detained under conditions of maximum security. Three of the 14 men with normal chromosomes were also epileptic. A high proportion were receiving psychotropic drugs chiefly of the phenothiazine group and usually in combination with orphenadrine to counteract Parkinsonian side effects. Epileptics were also receiving anticonvulsant therapy. None of these patients was receiving or had been given either androgen or estrogen therapy. Additional clinical data on Patients 11/61 and 123/65 are published elsewhere (*1*) and on other patients are available at the M.R.C. Registry of Abnormal Karyotypes*. Total-body potassium was measured using the MERLIN mobile whole-body radioactivity counter (*2*) and the techniques described previously (*3*). The results were compared with "normal" values estimated from the height and age and from the height, weight, and age of the patient and expressed as lean-body mass using regression equations derived elsewhere (*4*). Total-body water was determined by the tritium method and expressed as lean-body mass using the Pace-Rathbun relationship (*5*): lean-body mass (kg) = total-body water (liters) ÷ 0.73. Skinfold thicknesses were

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measured over four sites: biceps, triceps, subscapular, and suprailiac and used to calculate body density (*6*) from which percentage body fat, and hence lean-body mass, were derived using the relationship of Siri (*7*). Lean-body mass was also estimated from the patient's height and weight (*8*).

RESULTS

The karyotype, age, height, and weight of each patient and a summary of the results are given in Table 1. In the group of patients with chromosomal anomalies, the measured total-body potassium was significantly less than the estimated normal male values from weight, height, and age ($t = 3.57$, $p < 0.02$) and from height and age ($t = 3.17$, $p < 0.02$). In four of the seven patients, the individual measured value was significantly less ($p < 0.001$) than the normal male value, in three of these cases being less than both normal values estimated from height, weight, and age and from height and age. Table 2 compares the measured total-body potassium with the normal values for healthy control females (*4*) of corresponding height, weight, and age. The measured values for the whole group of male patients were not significantly different from the estimated normal female values ($p > 0.05$). In patients 27/69, 379/69, and 11/61, the individual measured values are not different from the normal female value but in the remaining individuals the measured value is greater ($p < 0.05$) than, at least, one or other of the corresponding normal female values.

Of the 14 patients of normal karyotype, the measured total-body potassium of 4 individual patients was significantly greater ($p < 0.05$) than one or other of the estimated normal male values. In respect of age, height, diagnoses, and therapy this group of four did not differ from the remaining controls. One, Patient 20, was, however, clinically obese. The relevance of the observations will be discussed later. In the remaining patients, individually and collectively, there was no significant difference between the measured and normal total-body potassium ($p > 0.05$).

Lean-body mass estimated by the four methods is also given in Table 1. The values, with the exception of that from total-body water in Patient 5, which was technically unsatisfactory, were intercompared. Lean-body mass estimated from the measurements of skinfold thicknesses was consistently and significantly ($p < 0.001$) higher than estimates from the

TABLE 1. DATA FOR MALE PATIENTS WITH NORMAL AS WELL AS ABNORMAL SEX CHROMOSOME COMPLEMENTS

Patient No.	Karyo-type	Height (cm)	Weight (kg)	Age (yr)	Measured TBK gm K	"Normal" TBK (gm K)		Lean-body mass (kg)			
						Ht, Wt, Age	Ht, Age	TBW	gm K	Skinfold	Ht, Wt
27/69	XXY	173.7	67.5	40	102.2	136.0‡	137.4†	43.4	47.7	53.3	54.6
358/67	XXY	175.0	80.0	48	130.9	145.7	137.1	55.2	53.3	65.7	60.0
19/66	XXY	171.9	73.5	57	121.8	131.1	127.2	49.3	51.5	55.4	56.6
82/70	XYY	179.7	92.4	32	143.7	171.4†	152.9	56.8	55.7	68.9	66.4
123/65	XYY	178.1	61.0	45	129.5	133.6	144.6	57.0	53.0	55.9	53.1
379/69	XXYY	188.0	97.5	27	126.8	189.9‖	172.0‡	59.5	52.5	69.5	70.6
11/61	XXYY	194.8	68.5	27	130.7	172.1‖	186.1‖	48.5	53.2	57.7	60.6
8	N	171.3	69.5	43	154.6	133.1*	131.3	58.8	57.8	60.1	54.8
9	N	170.0	64.5	21	133.4	137.1	137.0	50.7	53.7	53.0	52.4
10	N	170.1	67.5	29	151.1	136.2	134.1	54.4	57.2	58.7	53.6
11	N	176.2	79.0	32	171.3	154.0	145.6*	69.5	61.1	68.0	59.9
12	N	179.8	85.5	47	141.2	157.9	147.4	59.5	52.2	67.5	63.5
13	N	157.8	70.0	48	130.2	112.7	101.4*	53.3	53.1	55.3	51.4
14	N	177.5	74.0	46	140.2	144.4	143.0	57.5	55.0	61.4	58.3
15	N	155.3	70.0	39	140.2	128.6	122.5	47.9	55.1	55.6	53.6
16	N	172.1	67.0	31	150.8	137.6	137.5	56.6	57.1	59.4	54.0
17	N	172.7	83.5	22	151.9	158.1	142.2	46.3	57.3	59.9	60.8
18	N	187.3	83.0	31	171.0	173.4	169.0	69.9	61.0	70.0	64.5
19	N	167.7	63.0	40	129.3	123.5	125.0	49.3	52.9	53.6	51.2
20	N	173.8	92.0	32	177.4	162.8	140.7†	64.4	62.2	69.4	64.6
21	N	181.4	72.0	34	146.4	153.6	155.7	62.6	56.2	62.9	58.5

N = Normal TBK = Total-body potassium

statistical significance of differences between measured and "normal" TBK.

* = $p < 0.05$
† = $p < 0.01$
‡ = $p < 0.005$
‖ = $p < 0.001$

TABLE 2. DATA FOR MALE PATIENTS WITH AN ABNORMAL SEX CHROMOSOME COMPLEMENT

Case No.	Karyotype	Height (cm)	Weight (kg)	Age (yr)	LBM (kg)	Measured TBK (gm K)	Normal values (gk)			
							Male		Female	
							a	b	a	b
27/69	XXY	173.7	67.5	40	43.4	102.2	136.0*	137.4*	109.4	109.7
358/67	XXY	175.0	80.0	48	55.2	130.9	145.7	137.1	114.9	109.0*
19/66	XXY	171.9	73.5	57	49.3	121.8	131.1	127.2	105.3*	102.2*
82/70	XYY	179.7	92.4	32	56.8	143.7	171.4*	152.9	131.9	120.0*
123/65	XYY	178.1	61.0	45	57.0	129.5	133.6	144.6	107.7*	113.9
379/69	XXYY	188.0	97.5	27	59.5	126.8	189.9*	172.0*	143.7	132.4
11/61	XXYY	194.8	68.5	27	48.5	130.7	172.1*	186.1*	132.8	141.3

LBM = Lean-body mass.
TBK = Total-body potassium.
a = Normal values estimated from height, weight, and age.
b = Normal values estimated from height and age.
* = Significantly different from measured TBK ($p < 0.05$).

other methods, the mean differences being 5.3, 5.7, and 2.7 kg over the total-body water, total-body potassium, and height and weight methods respectively. Differences between the total-body water method and both total-body potassium and height and weight methods were not significantly different. The significant difference ($p < 0.05$) between the latter two methods disappeared when patients were excluded whose height or weight were outwith the control population for that method. For the purpose of normalizing body potassium to lean-body mass, the values from the total-body water measurements have been taken.

DISCUSSION

A relatively small number of patients with chromosomal anomalies were included in this initial study but it was not obvious at the outset that the study was even practicable in the circumstances. Certainly the measurement of total-body potassium was possible only because the mobile whole-body monitor could be sited within the confines of the hospital grounds. Further, patients with the chromosomal anomalies of interest are comparatively rare. The findings are, therefore, considered preliminary but, as far as we are aware, even these few observations are unique.

Total-body potassium. To decide whether a measured value for total-body potassium lies within the normal range is generally problematical because normalization with body weight or body water embodies the possibility that these parameters themselves are aberrant in the clinical disorder or individual patient. Obesity, edema, and starvation are obvious influencing factors in relation to body weight in particular. For this reason our normal values and ranges were derived from separate regression equations (*4*) correlating total-body potassium with (A) height, weight, and age and (B) with height and age only, as height aberrations are less common. Whether the measured total-body potassium is, or is not, abnormal can then be assessed on a more balanced basis. In three of the patients (27/69, 379/69, and 11/61) of abnormal karyotype the measured total-body potassium was less at a highly significant confidence level ($p < 0.01$ to < 0.001) than both estimated normal male values. The deficits ranged from 34–45 gm K, which are remarkably large. Further, the values for gm K/kg lean-body mass tend to be low despite the tendency of the lean-body mass to be low also. In each of these same cases, respectively, of XXY, XXYY, and XXYY karyotype, the measured total-body potassium was not different ($p > 0.05$) from the normal value in females. Although the measured total-body potassium in Patient 82/70 of XYY karyotype, was significantly less than the normal male value estimated from height, weight, and age, it was not different from the normal value from height and age. This patient's weight was about 14 kg more than the mean for a subject of this height, his lean-body mass (from total-body water) was 61.4% of his body weight, which was lower than the mean value in healthy controls (*4*) of 81.8%, whereas the value of 2.53 gm K/kg lean-body mass was essentially the same as the control mean of 2.52 gm K/kg lean-body mass. These observations suggest that the excess body weight in this patient was largely obesity tissue and the discrepancy between the measured and estimated normal male value is an anomalous consequence. There is suggestive evidence, therefore, that in some patients of XXY and XXYY karyotype total-body potassium is subnormal and corresponds more closely to that of females of the same body habitus and age. There was no firm evidence, how-

ever, that this was so in patients of XYY karyotype. This finding is consistent with the known hypogonadal status and lower than average testosterone levels of males with extra X chromosomes (*1*), and the reported normal testosterone levels of males with the 47,XYY karyotype (*9–12*). The normal body potassium in two males with the 47,XXY karyotype is also consistent with the overlap that occurs in body habitus and evidence of hypogonadism between males with this karyotype and normal XY males. It is of interest that in the case of Patient 358/67 the XXY karyotype even in the presence of cardiac failure and on treatment with digoxin, both of which have potassium-lowering effects, the total-body potassium was not significantly reduced below the normal. Other evidence is in course of publication to show that in persons of XXY karyotype some characteristics tending towards the female phenotype appear. These are first, mean values of the biacromial diameter and the associated androgyny score which are intermediate between those expected in XX women and XY men. The androgyny score was computed by Tanner (*13*) as a discriminant function to estimate femininity in men or masculinity in women. It separates normal men and women fairly well, with XXY men lying between. Secondly, the mean span-height ratio in XXY men is the same as that found in normal women in whom span approximates more closely to height than it does in normal men. Thirdly the metacarpal cortex is significantly thinner in XXY compared with XY men, the values corresponding more to those expected in women (*14*). In Patients 8, 11, 13, and 20 who were patients of normal karyotype, the measured total-body potassium was apparently significantly greater than the normal values estimated from one or other relationship but not both. The lean-body mass in Cases 8 and 11 was a relatively high proportion of the body weight, which would be compatible with and explain the above-normal total-body potassium measured in these patients. In Patient 13, the lean-body mass was a similar percentage of the body weight as the mean in healthy controls (*4*) but, as his body weight was about 6 kg above the mean for his height, the value of lean-body mass as a percentage may be misleadingly low accordingly. Certainly the value of gm K/kg LBM was unexceptional and it might be, therefore, that his situation is similar to that of Patients 8 and 11. The measured total-body potassium would seem to be higher than the normal value from height and age in Patient 20. It can be argued that the weight, height, and age relationship would tend to overestimate the normal values and hence not show a significant difference with the measured value because this patient was some 18 kg heavier than the mean weight for his height. The relatively low value of 70% for his lean-body mass also suggests the influence of obesity tissue, particularly when the estimates of lean-body mass by the different methods were in fair agreement. The value of 2.75 gm K/kg lean-body mass is at the higher end of the normal range and would tend to support the significance of the high measured total-body potassium.

Lean-body mass. The methods of estimating lean-body mass gave results in reasonable agreement with the striking exception of the skinfold thicknesses. This latter technique gave estimates almost invariably higher than by the other methods, the differences being highly significant statistically ($p < 0.001$). Reasons for this finding are not clear. The measurements of skinfold thicknesses were made by only one person, who had considerable experience with the technique. The reproducibility of measurements of skinfold thickness by this observer can be described by saying that the standard deviation of the mean difference between paired measurements of the skinfold thickness, made on separate occasions, expressed as a percentage of the mean of the dimension concerned (*15*) lay between 1.6% and 3.6% according to the site of measurement. Some patients' ages exceeded those of the control population from which the relevant correlation of skinfold thicknesses and body density, and hence lean-body mass, was derived (*6*). Even when these patients were excluded from the analysis, however, the differences remained highly significant ($n = 11$, $p < 0.01$). An explanation we cannot exclude is that the skinfold thickness correlation, which was derived in healthy controls, is not equally valid in, at least, the present patients.

The mean values of lean-body mass (percent body weight), estimated from total-body water, were intercompared in the patients with chromosomal anomalies, in the patients of normal karyotype, and in healthy male controls (*4*). The mean in the patients of abnormal karyotype, excluding Patient 123/65 whose total-body water estimate was technically unsatisfactory, was significantly lower ($p < 0.05$) than in the patients of normal karyotype and both means were significantly lower than that in the healthy male controls ($p < 0.05$). As the total-body potassium levels in the patients of normal karyotype were not different from normal, and presumably the lean-body masses (kg) were correspondingly normal, the lower percentage of body weight may simply reflect a greater proportion of obesity tissue in these patients than in our normal series. In the patients of abnormal karyotype, the still lower percentage values may have a similar explanation coupled with the influence of the low total-body potassium values, which would

be associated with a smaller absolute lean-body mass (kg).

Although this was a preliminary study, there was evidence suggesting that in some male patients with 47,XXY and 48,XXYY karyotypes the total-body potassium and lean-body mass were more similar to those in healthy female controls than in males. In two males with a 47,XXY karyotype there was no difference from normal men. Further investigation is required and projected.

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