Intracellular Glycogen and Electrolyte Concentrations in Human Skeletal Muscle.* (23744)

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Values for less than 100 analyses of human skeletal muscle for electrolytes are available in the literature(1-7), and, of these, the largest series was conducted on post-mortem tissues(1). Furthermore, calculation of the intracellular concentrations of ions was carried out by the authors in only 3 series(4,5,7). The only data available on the glycogen content of human skeletal muscle is that of Moscati(8). The present communication presents the intracellular concentrations of sodium, potassium, phosphate, and glycogen obtained in 6 normal human subjects and discusses their possible interdependence.

Methods and calculations. Patients entering the hospital for elective surgical procedures were selected for biopsy studies. Specimens were obtained after the induction of anaesthesia and following the administration of 0 to 400 cc of 5% dextrose intravenously. Blood samples for the determination of water, chloride, sodium, and potassium were drawn one to four hours before the biopsy specimens were obtained. Of 11 patients in whom biopsies were carried out, 5 patients had abnormal serum electrolyte values and are not included in the study. Biopsy specimens weighing 1-2 g were obtained from the rectus abdominis muscle after induction of anaesthesia and before any other surgical procedures had been carried out. Two hundred to 400 mg of tissue were immediately placed in a tared tube containing 2 cc of 30% KOH for glycogen analysis. The remainder of the specimen was placed in a tared weighing bottle, brought to constant weight at 100°C., fat-extracted, and the dry, fat-free tissue analyzed for sodium, potassium, chloride, and phosphate. The methods used in the analysis of the tissues for glycogen, and the plasma and tissues for fat, water, and electrolytes have been previously described by the author(9,10). Calculations of the intracellular concentrations of electrolytes were made assuming the extracellularity of chloride, using the formulae of Hastings and Eichelberger(11). It is unfortunate that blood samples were not obtained simultaneously with biopsy specimens, as this may have introduced errors into the calculations of intracellular values. However, this was not possible.

Results. Table I presents the ages, clinical diagnoses, type of anaesthesia, and amount of

TABLE I. Clinical Data on Patients.

Patient, age and sex	Dx	Operation	Anaesthesia	5% dextrose, cc
(1) M.O. 64 ♂	Duodenal ulcer	2nd stage subtotal gastric resection	Cyclopropane and ether	0
(2) M.R. 49 ♀	Carcinoma of sigmoid	Left colectomy	*Idem*	400
(3) S.R. 50 ♀	Pericolic abscess following exploratory laparotomy	Excision of abscess; closure of colostomy	"	210
(4) P.M. 77 ♂	Carcinoma of sigmoid	Resection of sigmoid	GOE	100
(5) H.A. 55 ♀	Abdominal carcinomatosis	Exploratory laparotomy	Cyclopropane and ether	150
(6) G.C. 60 ♂	Adenocarcinoma of sigmoid	Resection of sigmoid	*Idem*	140

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TABLE II. Basic Data.

Patient	Plasma H_2O, g/l	Plasma Cl^-, meq/l	Plasma Na^+	Plasma K^+	Muscle* H_2O, g/kg tissue	Muscle* Cl^- meq/100 g dry solids	Muscle* Na^+	Muscle* K	Muscle* PO_4, mM/100 g dry solids	Muscle* Glycogen, g/kg wet tissue
1	936	102	149	3.9	778	11.0	16.5	42.4	23.2	5.28
2	940	98	150	4.1	786	10.0	16.8	42.2	25.1	15.68
3	942	104	154	4.2	789	15.0	24.5	39.7	23.5	9.50
4	938	100	143	4.0	778	7.3	14.6	46.1	27.8	13.70
5	938	104	149	3.6	788	14.3	22.4	38.4	23.0	8.62
6	936	100	146	3.9	787	9.6	16.2	43.8	25.9	15.74
Mean	938	101	149	4.0	784	11.2	18.5	42.1	24.8	11.42
S.D.	2.2	2.5	3.5	.2	4.9	3.2	4.0	2.8	1.9	4.2

* All data are expressed in terms of fat-free tissue.

5% dextrose received by the patients. Table II presents the basic data for plasma and muscle in the 6 subjects, together with the mean and standard deviation for each set of values. Plasma water and electrolyte values were all within the range of normal. In the case of the basic values for muscle, there was a wide variation in the values for chloride and sodium, representing considerable differences in the size of the extracellular spaces in the samples. The values for water, potassium, and phosphate fell within a close range. Potassium and phosphate concentrations tended to vary inversely with the concentrations of chloride and sodium. Glycogen content varied from 5.28 to 15.74 g/kg wet tissue.

Table III presents the chloride spaces and the concentrations of sodium, potassium, phosphate, and glycogen in the intracellular water of the muscle cells of the 6 subjects. The chloride spaces ranged from 18.7% of total muscle water to 33.4%. This should not be interpreted as a normal variation for two reasons: (1) the connective tissue content of the samples varied considerably, and (2) all but 1 patient was receiving intravenous fluid at the time of biopsy. Average values in connective-tissue free, normal skeletal muscle are probably lower than the average 27% of total muscle water found in these samples. The values obtained for intracellular phosphate were quite constant, varying only from 90.2 to 95.6 mM/kg of cell water, with a mean value of 92.0. The concentration of intracellular potassium ranged from 152 to 165 meq/kg of cell water, with a mean of 156. Intracellular sodium showed values of from 7.4 to 16.7 meq/kg of intracellular water. Glycogen constituted from 2.4 to 6.8% of the total tissue solids, and was present at concentrations of from 9.3 to 26.6 g/kg of intracellular water.

Discussion. The values obtained by Moscati for the glycogen content of human skeletal muscle ranged from 0.4 to 0.6 g %. These values are considerably higher, and show a greater range. They are similar to values found in rats by the author(12) and others (13). It is of interest to note that patient M. O., who had fasted for 14 hours and had

TABLE III. Derived Data.*

Patient	Chloride space, g H_2O/kg muscle H_2O	Na (meq/kg intrac. H_2O)	K (meq/kg intrac. H_2O)	PO_4, mM/kg intrac. H_2O	Glycogen % total tissue solids	Glycogen g/kg intrac. H_2O
1	272	7.4	165	90.2	2.4	9.3
2	250	10.0	152	90.6	7.2	26.6
3	349	16.6	161	95.6	4.4	18.5
4	187	16.7	154	92.7	5.9	20.7
5	334	13.7	153	91.9	3.9	16.5
6	232	11.7	150	90.8	6.8	26.0
Mean	271	12.7	156	92.0	5.1	
S.D.	68	3.7	5.4	2.0	1.85	6.4

* All data are expressed in terms of fat-free tissue.

TABLE IV. Intracellular Ion Concentrations in Human Skeletal Muscle.*

Ref.	Author	Date	No analyses	Na meq/kg ICW	K meq/kg ICW	P, mM/kg ICW
1	Cullen†	1933	19		121.0	92.0
2	Shohl‡	39		12.4	145.0	110.0
3	Mangun	41	13		145.0	111.7
4	Mudge	49	3	8.6	157.0	
5	Eliel	51	6	11.4	134.3	85.7
6	Baldwin	52	15		164.0	101.6
7	Mokotoff	52	4	11.4	157.0	101.0
8	Nichols	57	6	12.7	156.0	92.0

* Where values for total water, ECF, and/or plasma values were not given, the mean values obtained in this series were used to calculate the $(ion)_i$.

† Post-mortem analyses.

‡ Compiled from literature.

received no glucose had maintained a muscle glycogen content of 0.528 g %. This maintenance of relatively high muscle glycogen levels despite fasting has also been demonstrated in rats by the author. In ten rats fasted 24 hours, muscle glycogen fell only from 0.86 to 0.40 g %. This was in contrast to liver, where glycogen concentrations decreased from 7.43 to 0.13 g % in the same period. There did not appear to be a quantitative correlation between the amount of glucose that had been administered to the patients and glycogen levels in the muscle. Patient M.R. who had received 400 cc of 5% glucose and patient H.A. who had received only 150 cc had almost identical muscle glycogen concentrations. This may have been related to the blood sugar levels which were not determined, or may be due to the individual reactions to the varying stresses to which these patients were subjected.

Table IV presents the data obtained by other workers for intracellular ion concentrations in human skeletal muscle. There is surprisingly good accord between the average values for intracellular sodium, although the individual values in each series show a wide range. Five of the 8 studies show an average intracellular potassium concentration of 145 to 157 meq kg intracellular water, with 2 series (1 and 5) having lower values, and one (6) higher. The extreme values for total intracellular phosphate are 85.7 to 111.7 mM/kg intracellular water, with a mean value of 99 for all of the series.

A number of studies have been made which indicate that the deposition of glycogen is accompanied by a fall in the serum concentrations of potassium and phosphate(14,15,16). Conversely, it has been shown that potassium and phosphate administration can lower the blood sugar(17,18) and prevent the occurrence of the hyperglycemia occurring from glucose administration following fasting(19). There is good evidence in animals that the deposition of glycogen in liver is accompanied by the deposition of potassium(20), which would account for the observed fall in serum levels of this ion. Whether or not potassium also enters muscle during glycogen deposition is not known. Phosphate, on the other hand, does not enter liver cells when glycogen is deposited(9), the level of total liver phosphate declining as liver glycogen rises. Clinical evidence confirms this and suggests(21) that the fall observed in serum phosphorus after glucose administration is due to the entry of phosphate into skeletal muscle(21,22). It seemed of interest therefore to study the correlation between the levels of intracellular muscle glycogen and potassium and phosphate in these 6 patients. Although the glycogen levels ranged from 5.28 to 15.74 g/kg of wet tissue, or 9.3 to 26.0 g/kg of intracellular water, representing a broad physiological span(23), glycogen constituted only 2.4 to 6.8% of the total tissue solids. Assuming muscle glycogen to be deposited with the same amount of water as is found in association with nitrogenous solids(20), the addition of 10.46 g of glycogen (*i.e.* a rise from 5.28 to 15.76 g/kg of wet tissue) to a kilogram of tissue would only command the addition of 7.96 meq of potassium and 4.7 mM of phosphate to maintain the pre-existing level of these ions in the intracellular water. Conversely, non-entry of these ions would only cause a fall in concentration of 7.96 meq of potassium or 4.7 mM of phosphate. It is apparent that these changes are very small, and unlikely to be statistically verifiable in this small series. The correlation coefficient for the addition of potassium to the intracellular water of skeletal muscle for these 6 tissues is −.776, which is suggestive that potassium concentrations fall as glycogen is added to skele-

tal muscle. The standard error of the estimate for this small series shows that there is an 84% chance that this correlation did not occur by accident, but there is less than the 95% chance which is considered the lower limit of significance. It must be borne in mind that these patients were receiving glucose without exogenous potassium, and that the body has no known reservoir for this ion. Had exogenous potassium been available, as is the case in the normal diet, potassium levels in muscle cell water might have remained constant. In contrast to the relation between potassium and glycogen the correlation coefficient for intracellular phosphorus and glycogen is –.027 (no correlation), indicating that the concentration of phosphorus in the intracellular water of skeletal muscle does not fall during the deposition of glycogen. Again assuming the addition of intracellular water to muscle mass as glycogen is deposited, this suggests that phosphate ion is added to skeletal muscle cells in order to maintain a constant level of this ion, even in the absence of an exogenous supply of this ion.

Summary. The composition of human skeletal muscle has been examined in 6 normal individuals. Intracellular concentrations of sodium, potassium and phosphate have been calculated and agreed closely with values reported by other workers. Glycogen levels ranged from .528 g % in a fasted patient to 1.57 g % in a patient who had received glucose. Glycogen levels were not directly correlated with the amount of glucose given. There is some evidence (correlation coefficient of –0.776) that in the absence of exogenous supplies, potassium is not deposited in muscle cells when glycogen is deposited, whereas phosphate may be deposited (correlation coefficient of –0.027).

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