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The Sodium, Potassium, and Water Contents of Red Blood Cells of Healthy Human Adults *

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Intracellular sodium and potassium concentrations in man can only be measured with ease and accuracy in red blood cells (RBC). Although there are many published reports of RBC sodium and potassium concentrations, the number of healthy subjects studied has been small, indirect methods of measurement have often been used, and biological sources of variation have not been defined. This paper describes the results of a study of 142 healthy adults and delineates some of the factors influencing RBC sodium and potassium concentrations.

Methods

Blood was drawn with minimal venous compression into plastic syringes containing ammonium heparin [1] in isotonic glucose (0.005 ml of solution containing 0.25 mg heparin per ml of whole blood). Five-g samples of blood were immediately centrifuged in cellulose nitrate tubes (i.d. 11 mm) [2] for 1 hour in a governed hematocrit centrifuge.[3] The relative centrifugal force (RCF) at the base of the tubes was 1,460 g; mean RCF applied to the cells thus depended on hematocrit and varied from approximately 1,330 to 1,370 g. Two or three tubes were used for estimation of plasma and RBC sodium and potassium concentrations and one or two tubes for water and hemoglobin content.

After spinning, a weighed plasma sample was removed and the centrifuge tubes containing a layer of plasma and the packed cell column were frozen in an ethanol-CO_2 mixture and sectioned 0.5 to 1.0 mm below the buffy coat-RBC interface by an electric saw.[4] The cut centrifuge tube containing red blood cells was transferred to a glass beaker and weighed. The weight of red blood cells sampled was obtained by reweighing the beaker and cut centrifuge tube after washing clean and oven drying.

Plasma and RBC water content was estimated by washing the contents of the beakers into weighed plastic Petri dishes, which were dried at 45° C to constant weight. Plasma and RBC samples for sodium and potassium estimation were diluted to appropriate concentrations and stored in polythene containers at 4° C for 1 to 4 days before analysis.

All water used for washing equipment and diluting had an electrical resistance of 10^6 ohms.

Sodium and potassium concentrations were determined with a flame photometer [5] with standards made from P.V.S. sodium chloride [6] (an especially pure grade for volumetric standardization) and analytical grade potassium chloride.[6] Two plasma reference standards (Versatol [7] and Wellcome [8]) were routinely used. Potassium and iron, at concentrations found relative to sodium in red blood cells, did not influence the sodium flame. Plasma potassium was estimated against a standard containing sodium.

Hemoglobin was estimated (1) by adding 1 ml of the cell hemolysate prepared for sodium determination to 10 ml of a modified Drabkin's reagent, prepared by dissolving one Aculute [9] pellet in 250 ml water. After 15 minutes the optical density at 540 mμ of the cyanmethemoglobin solution was compared in a spectrophotometer [10] with that of a reference standard [11] that conformed to the International Standard.

The method of estimating plasma sodium trapping, which is fully described elsewhere (2), is based on the use of sucrose-^{14}C and ^{24}Na as plasma markers. This method was developed when it was found that iodinated human serum albumin (IHSA) underestimates the amount of trapped extracellular sodium in the packed

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[1] Evans Medical, Liverpool, England.

[2] International Equipment, Needham Heights, Mass.

[3] Measuring & Scientific Equipment, London, England.

[4] Apparatus specially constructed by the Department of Physics, King's College Hospital.

[5] Evans Electroselenium, Harlow, England.

[6] Hopkins & Williams, Chadwell Heath, England.

[7] William Warner, Eastleigh, England.

[8] Burroughs Wellcome, London, England.

[9] Ortho Pharmaceutical, Saunderton, England.

[10] Optica Cf4, Baird & Tatlock, London, England.

[11] C. Davis Keeler, London, England.

cell layer. Plasma trapping in the packed RBC column was obtained for each sample from the regression equation $y = 2.8214 + 0.2398\ x$, where y is the percentage trapping of plasma and x the weight in grams of red blood cells sampled.

Red cell sodium, potassium, and water contents were corrected for trapped plasma sodium, potassium, and water by application of the following formula: Corrected RBC content = (observed RBC content − T × plasma content)/1 − T, where T is the fraction of plasma trapped in the packed cell layer. Results were expressed in terms of plasma and RBC wet weight, water, and solids.

Calculations were performed by digital computer, which was also used for many of the statistical analyses. Standard statistical techniques were applied.

The standard errors of the mean of two blood samples (from 12 subjects) were as follows: for plasma sodium, potassium, and water, respectively, 0.25 mEq, 0.10 mEq, and 0.21 g per kg plasma, and for RBC sodium, potassium, water, and hemoglobin, respectively, 0.08 mEq, 0.42 mEq, 0.16 g, and 2.6 g per kg RBC.

Three groups of subjects were studied. All were healthy and at work and none was taking medication.

Sodium and potassium concentrations only were measured in the first group, who were studied sequentially over a period of 2 months. A significant correlation was found between potassium concentration (in both plasma and red blood cells) and the date of sampling. Because this correlation was probably due to technical factors, only the sodium results from this group were used.

The samples in the second and third groups of subjects were collected, processed, and analyzed as groups. Because analysis of the results from the first group suggested the existence of age and sex effects, the second group was balanced for these factors, and in the third group they were eliminated. The sex and age composition of the groups is shown in Table II.

In the second and third groups of subjects, water content, and in the third group, cell hemoglobin concentration, were also measured.

Results

Subject-to-subject and day-to-day variation

Red cell sodium and water contents were measured in six men and four women and potassium content in three men and three women, on three to seven occasions over a period of 9 months. The results are listed in Table I. It can be seen that RBC sodium concentration was relatively constant in individual men and women throughout this period. Subject-to-subject variation was significantly greater than the day-to-day variation for an individual ($p < 0.001$).

Subject-to-subject variation of RBC potassium concentration was also significantly greater than the day-to-day variation ($p < 0.001$), and day-to-day variation was significantly greater in women than in men ($p < 0.05$). When the values in women were related to days of the menstrual cycle, they suggested that potassium concentration in red blood cells falls during the cycle. Thus the average change in potassium concentration from the highest levels (mEq per kg cells) was as follows: day 3, 0; day 10, − 2.3; day 19, − 2.97; and day 26, − 3.94. These results were not obtained during single cycles.

For RBC water content, subject-to-subject variation was no greater than day-to-day variation.

TABLE I

*The sodium, potassium, and water contents of red blood cells from ten subjects estimated on three to seven occasions to illustrate variation among subjects and among occasions**

Subject:	1	2	3	4	5	6	7	8	9	10	
Sodium, *mEq/kg cells*	6.09 6.44 6.02	10.52 11.13 10.61	6.89 6.94 7.23	5.53 6.19 5.57	7.55 6.71 6.51	5.15 5.18 5.20	7.19 7.22 7.33 6.71	5.94 6.36 6.24	8.25 8.30 8.04	4.57 5.20 4.76 4.68	5.06 5.07 4.49
Potassium, *mEq/kg*	92.52 91.52 91.96	85.69 85.05 85.33	87.01 87.64 87.12				93.01 92.16 92.30 84.85	93.83 89.52 91.81		98.30 96.23 91.97 98.73	
Water, *g/kg*	642.5 629.5 625.5	637.8 637.7 638.0	634.0 625.2 624.1	645.2 630.0 637.0	640.9 641.9 642.1	631.8 651.8 651.4	640.6 651.4 618.2 656.5	643.3 651.4 649.7	655.0 644.2 652.0	632.6 677.3 642.6 654.5	649.5 651.4 652.0

* Each value given is the mean of two or three estimations made on a single occasion. The average interval between occasions was 31 days (range, 8 to 203 days). Subjects 1 to 6 were men; subjects 7 to 10 were women.

TABLE II

*Mean sodium and potassium concentrations and water content of red blood cells**

Age (years): Group		20–25	26–35	36–45	46–55	56–65	Age effect	Sex effect	Pooled data
Na, *mEq/kg cells*									
Men	1	7.510 (8)	7.897 (7)	7.287 (3)	7.658 (11)	8.013 (4)	NS		
	2	7.710 (12)			7.122 (12)		NS		7.446 (87)
	3	7.174 (30)						p <0.01	
Women	1	6.669 (10)		6.354 (2)	7.114 (12)	7.397 (7)	p <0.10		<45 years >45 years
	2	6.332 (12)			7.361 (12)		p <0.05		6.500 (24) 7.304 (31)
									p <0.01
K, *mEq/kg cells*									
Men	2	88.46 (12)			89.71 (12)		NS		88.42 (54)
	3	88.23 (30)						p <0.001	
Women	2	92.20 (12)			92.64 (12)		NS		92.41 (24)
H_2O, *g/kg cells*									
Men	2	638.4 (12)			634.7 (12)		NS		636.1 (54)
	3	635.7 (30)						p <0.05	
Women	2	638.5 (12)			649.3 (12)		p <0.05		

* Age and sex effects are summarized. The number of subjects contributing to each mean is given in parentheses. Where appropriate, results have been pooled; these are listed on the right. p values for age effects were derived from correlation coefficients and for sex differences from *t* tests. The standard deviations for each mean in the pooled results, based on the largest number of degrees of freedom available, were as follows: for sodium, 1.246 mEq per kg cells; for potassium, 2.863 mEq per kg; and for water, 11.22 g per kg cells.

Day-to-night variation

Blood samples were collected from six men between 12 midday and 6 p.m.; a further sample from each subject was collected 12 hours after the first. Analysis of variance showed no significant differences of sodium, potassium, or water contents of the cells, attributable to the times of sampling. Mean values for the six subjects (per kg RBC) were these: sodium content by day, 8.151 mEq, and at night, 8.164 mEq; potassium content by day, 86.46 mEq, and at night, 85.13 mEq; water content by day, 651.0 g, and at night 651.0 g.

The time of blood sampling was recorded in all the studies subsequently described. No correlation was observed between any of the parameters and the time of blood sampling.

The effects of age and sex

The effects of age and sex on RBC sodium, potassium, and water contents are summarized in Table II.

Red cell sodium concentration. Age did not affect RBC sodium concentration in men, but in women concentration in middle age was higher than in youth ($p < 0.01$). Values for middle-aged women were similar to those for men, but the cells of young women contained less sodium than those of men ($p < 0.01$).

Red cell water content. Age did not affect the water content of red blood cells of men, but the cells of older women contained more water than those of younger women ($p < 0.05$) or of men ($p < 0.05$).

The second group of subjects was balanced for age and sex, and the results obtained from it were suitable for analysis of the variance attributable to these two factors. Such analysis showed that sodium content in terms of RBC dry weight was lower in young women than in young men ($p < 0.001$) or in middle-aged women or men ($p < 0.001$).

Thus the water content of red blood cells was similar in young men and women, but the sodium content was lower in young women. The sodium concentration in cell water was therefore lower in young women than in men. Analysis of the derived data confirmed this ($p < 0.01$). In middle age, the water content of red blood cells of women was greater than in youth, but sodium content was still greater, and sodium concentration in cell water was similar in the two sexes.

Because the age distribution of women studied was bimodal, it was not possible to determine whether the rise of RBC sodium concentration was a gradual process from youth to middle age or whether it was localized and occurred more rapidly at the time of the menopause. Although the menstrual status of all subjects was recorded, the numbers of pre- and postmenopausal women be-

TABLE III

Significant correlations between the parameters measured

Variates		Reference weight	Correlation coefficients			
			Group 2			Group 3
			Men	Women	Both sexes	Men
RBC* hemoglobin	Sum of RBC Na + K	Whole cells				−0.5741†
RBC hemoglobin	RBC water	Whole cells				−0.4560‡
RBC potassium	RBC water	Cell solids	0.7792†	0.8073†	0.8112†	0.8908†
Sum of RBC Na + K	RBC water	Cell solids	0.8057†	0.8463†	0.8447†	0.9331†
RBC sodium	RBC potassium	Cell water	−0.3112	−0.2232	−0.3461§	−0.6007†
Plasma water	RBC water	Plasma and RBC solids	0.1665	0.4946‡	0.3903‡	0.1433

* RBC = red blood cell.
† $p < 0.001$.
‡ $p < 0.01$.
§ $p < 0.05$.

tween the ages of 46 and 55 were too small to allow worthwhile comparison.

Red cell potassium concentration. No significant correlation between RBC potassium concentration and age was found, either for men or for women. At all ages, potassium concentration was greater in the cells of women than in those of men. These differences were significant whether the values were expressed in terms of cell weight ($p < 0.001$), of cell water ($p < 0.01$), or of cell solids ($p < 0.001$).

Plasma sodium, potassium, and water contents. Mean sodium concentrations per kg plasma in the subjects of group 2 were as follows: for young men, 141.1 ± 1.98 mEq; for middle-aged men, 138.4 ± 3.04 mEq; for young women, 138.5 ± 1.86 mEq; and for middle-aged women, 137.4 ± 2.11 mEq. Mean water content was 901.45 ± 3.96 g per kg plasma in young men and was significantly lower than the mean value of 904.35 ± 3.96 g per kg plasma found in middle-aged men ($p < 0.05$). In women the water content of plasma did not alter significantly with increasing age; the mean value was 904.66 ± 4.4 g per kg plasma. Two factor analysis of variance showed that sodium concentration in plasma water was significantly higher in men than in women ($p < 0.01$) and in youth than in middle age ($p < 0.01$).

Plasma potassium concentration was not influenced by age or sex. The mean value was 4.15 ± 0.32 mEq per kg plasma.

Red cell hemoglobin concentration. Hemoglobin concentration was measured in the third group of 30 young men. Mean concentration was 342.6 ± 17.07 g per kg cells, or 8.36 millimolal (assuming a molecular weight for hemoglobin of 64,458).

Interrelationships. Correlation matrixes relating each parameter to all the others were con-

TABLE IV

*Regression equations relating the parameters measured**

Dependent variable	Reference weight	Equation no.	Regression equation	% variation of dependent variable accounted for	p
H_2O, *g/kg*	Cell solids	1	$H_2O = -268.1 + 23.33\ Hgb + 9.942\ Na + 6.104\ K$	91.22	<0.001
H_2O, *g/kg*	Cell solids	2	$H_2O = -250.6 + 23.74\ Hgb + 6.302\ Na + 6.302\ K$	90.02	<0.001
K, *mEq/kg*	Cell solids	3	$K = 61.96 + 0.002631\ H_2O - 1.427\ Na - 3.215\ Hgb$	89.35	<0.001
Na + K, *mEq/kg*	Cell solids	4	$Na + K = 60.42 + 0.002550\ H_2O - 3.142\ Hgb$	89.37	<0.001
Na, *mEq/kg*	Cell solids	5	$Na = 7.793 + 0.000791\ H_2O - 0.2589\ K$	43.87	<0.001
Na, *mEq/kg*	Cell water	6	$Na = 47.78 - 0.2630\ K$	36.08	<0.001
K, *mEq/kg*	Cell water	7	$K = 154.2 - 1.372\ Na$	36.08	<0.001

* All independent variables are expressed as milliequivalents or millimoles per kilogram. In equation 2, sodium and potassium have been constrained to exert the same effect. The variance ratio F attributable to this constraint was 3.521 and was not significant ($0.10 > p < 0.05$). Hgb = hemoglobin.

structed for each group of subjects, with the sexes separated and combined. Significant interrelationships are listed in Table III.

Quantitative relationships among the hemoglobin, water, sodium, and potassium contents of red blood cells were further investigated by performing multiple regression analyses on the data (in terms of cell dry weight and of cell water) from the 30 young men of group 3, with each variable in turn dependent on the other three. If any of the three independent variables failed to contribute significantly ($p < 0.05$) to the variation of the dependent parameter, it was rejected and the regression recomputed. Thus when hemoglobin content was made the dependent variable, all three independent variables (sodium, potassium, and water contents) were rejected, indicating that variation of hemoglobin content could not be explained in terms of the other parameters measured. The regression equations, the percentages of the variation of the dependent variables accounted for by the independent variables, and the statistical significance of the findings are listed in Table IV.

Discussion

Red cell sodium concentrations found in this study are lower than those given in most recent reports. This is due to the use of a different method for estimating trapped plasma sodium. A description of the method used and a critical examination of results obtained by other methods are given by Beilin, Knight, Munro-Faure, and Anderson (2).

Red cell potassium concentrations found in this study are similar to several previous estimates. Most of the recently published results are given in Table VII of the paper by Valberg, Holt, Paulson, and Szivek (3) and need not be duplicated here. Part of the variation of the reported results can be attributed to one or more of the following factors: derivation of RBC potassium concentration from measurement of whole blood and plasma potassium concentrations (4, 5); failure to allow for plasma trapped in the red cell column (6); the use of hospitalized patients as normal control subjects, particularly if some are anemic (7, 8); and the use of a part only of the packed cell column for potassium estimation (3), since young cells at the top of the column contain more potassium than older cells at the bottom (9).

Mean values for RBC water content found in this study are compared with other reported values in Table V. General agreement is good, but lower levels were found in this study than in the others; of these Valberg and his associates (3) report the highest levels. Two factors may be partly responsible for this difference. First, we used a lower temperature for drying. This temperature was selected because decomposition and volatilization of organic material appeared to occur at 100° C. Second, the mean hemoglobin content of the cells may have been greater in the subjects of this study than in the subjects of the other reported series. Valberg and his colleagues, for instance, found a mean hemoglobin concentration of 289 g per kg cells in the subjects they studied. The concentration found in the 30 young men of group 3 was 342 g per kg cells. Since hemoglobin forms such a large proportion of the cell solids, a negative correlation between hemoglobin and water content of the cells can be anticipated and was in fact found (Table III). It is probable that some of the variation of RBC water content in different published reports is thus attributable to variation of hemoglobin content in the cells of the subjects studied.

Potassium is the principal intracellular cation, and a positive correlation between the potassium and water contents of cells can also be anticipated. A close correlation was found, the r rising in the third and most homogeneous of the groups to 0.8908, a value similar to that noted for the correlation between the sodium and water contents of plasma (0.8459). When sodium content was added to the potassium content, the r between the combined cation and the water content of the cells was 0.9331. That 87% of the variation of cell water content of this group of 30 subjects could be explained by variations of the sodium and potassium contents of the cells (rising to 91% if hemoglobin concentration was also included), is a reflection of the constancy of the plasma osmolarities of this group. It can be noted in Table III that RBC water content was influenced to a trivial extent in men by the plasma water content, but that in the group of women studied the plasma water content exerted a significant effect.

The regression equations for the water content

TABLE V

*Estimates in the literature of red blood cell water content**

Authors	No. of subjects	Method	Temperature of oven	Mean water content
			°C	*g/kg cells*
Maizels (7)	6 patients (some anemic)	Not stated	Not stated	648
Hutt (8)	14 patients (some anemic)	Indirect	100	652
Nichols and Nichols (10)	21	Indirect	Not stated	658
Keitel, Berman, Jones, and MacLachlan (11)	11 men 11 women	Direct	105	660
Kessler, Levy, and Allen (4)	24	Indirect	105	650
Czaczkes, Ullmann, Ullmann, and Bar-Kochba (12)	20	Direct	85	648
Valberg and associates (3)	50	Direct	105	681
Funder and Wieth (13)	61 men 67 women	Direct	105	664 667
Present study	54 men 24 women (20–25 years) 12 women (46–55 years)	Direct	45	636 638 649

* Results given in terms of cell volume have been divided by 1.096 [Ponder (14)]. When red blood cell water content has been estimated from the difference between the contents of whole blood and plasma, it is termed "indirect"; when estimated in red blood cells themselves, it is termed "direct."

of the cells (no. 1 and 2, Table IV) are of some interest. The size of the regression coefficient b for each of the independent variables reflects the osmotic weightings of the variables.

The values for b in equation 1 suggest that hemoglobin exerts an osmotic effect 3.82 times greater than that exerted by potassium. In this small group of subjects the coefficients b for sodium and potassium do not differ significantly, and in equation 2, where they have been constrained to exert the same effect, hemoglobin has an osmotic effect 3.78 greater than that of the combined cations. If it is assumed that the osmotic coefficient of potassium is 0.95 at the observed mean hemoglobin concentration of 8.36 millimolal, the osmotic coefficient of hemoglobin at this concentration becomes approximately 3.6.

The figure of 3.6 at 8.36 millimolal is slightly lower than the values obtained by McConaghey and Maizels (15) in *in vitro* studies of red blood cells, depleted of cations by incubation in lactose media or suspended in saline solutions of varying tonicities. The size of their published graphs does not allow accurate interpolation, but it is doubtful whether the osmotic coefficients differ significantly.

Conversely, the figure of 3.6 is higher than that obtained from the virial equation of Dick and Lowenstein (16), which gives a value of 3.29 at a hemoglobin concentration of 8.36 millimolal. This equation was based on the results of Adair (17), who studied the osmotic pressures of pure hemoglobin solutions at concentrations up to 7.7 millimolal.

It is difficult to relate these results to those of Savitz, Sidel, and Solomon (18), who were unable to explain RBC volume changes produced in solutions of varying tonicity in terms of a changing osmotic coefficient for hemoglobin. These authors, however, measured cell volume from the hematocrit, corrected for trapped plasma by estimation of IHSA trapping. Beilin and his associates (2) have shown that IHSA underestimates trapped plasma sodium and hence probably trapped plasma water. Red cell water content may thus have been spuriously elevated in the calculations of Savitz and his colleagues.

Although cells of low hemoglobin content must contain more water and hence more potassium and sodium, in biological terms the water content of the cells is a function of the cation content (assuming constant external osmolarity) and not vice versa. The forces controlling the cation and hence the water content of cells have not been

clearly defined, although models have been proposed and tested (19).

Maizels (7) first noted that potassium concentration in the red blood cells of patients with hypochromic anemia is greater than in the cells of normal subjects. The same inverse relationship between potassium and hemoglobin concentrations was noted in the healthy young men of the third group (r, −0.4821). The r was greater (−0.5741) when sodium and potassium together were related to the hemoglobin content of the cells. The regression equations relating these variables (no. 3 and 4, Table IV) indicated that there was a reciprocal change of approximately 3 mEq cation per 1 mmole change of hemoglobin content of the cells. This relationship was only apparent when quantities were expressed in terms of cell weight or weight of cell solids. Cation concentration in cell water is a function of plasma osmolarity and is independent of hemoglobin concentration. This relationship may be due to increased binding of cation by hemoglobin, as the concentration of the latter falls over the observed range.

It has been mentioned that the concentrations of sodium and potassium in cell water were independent of hemoglobin concentration; they were, however, negatively correlated with each other.

From the two regression equations (no. 5 and 6 of Table IV), the change in potassium concentration for a 1 mmole change of sodium concentration could be determined and was found to be between 1.37 and 3.8 mmoles. Over the much greater range of RBC cation concentrations occurring in sheep, Tosteson and Hoffman (19) found that the change in potassium concentration for a 1 mmole change of sodium concentration was approximately 1 mmole.

The application of compartmental analysis to *in vivo* studies of sodium flux between plasma and red blood cells (20) has shown that RBC sodium is distributed in at least two compartments. Considered as compartments in series, 25 to 35% of RBC sodium is in a slowly exchanging inner compartment. Similar studies with potassium (21) indicate that this ion is also distributed in at least two compartments, but suggest that a much greater proportion, approximately 90%, is present in an inner slowly exchanging compartment. Until the relationships between the rapidly and slowly exchanging sodium and potassium compartments and hemoglobin concentration have been defined, it is not possible to evaluate the regressions observed in greater detail.

The results of this study show that red blood cells of young women contain more potassium and less sodium than the cells of young men. Love and Burch (22) found similar differences in potassium but not in sodium concentration. Conversely, Keitel and his colleagues (11), Dowben and Holley (23), and Funder and Wieth (13) noted similar differences in sodium but not in potassium concentration. Czaczkes and co-workers (12) and Valberg and associates (3) were unable to detect any sex effect.

It is possible that the higher potassium content of red blood cells of women than of men is related to a lower hemoglobin content; the latter was not measured in women in this study. Nevertheless, significant sex differences remain when ion concentrations are expressed in terms of cell water, and these appear to be independent of hemoglobin concentration.

The ratio of intracellular potassium to sodium concentration is about 20% greater in young women than in young men (14.18 to 11.88).

In men RBC cation concentrations are not affected by increasing age, but in women both the sodium and water contents of the cells are greater in middle age than in youth. Funder and Wieth (13) also found that sodium content, but not water content, of red blood cells increases with age in women. The net effect of these changes is that the sodium concentration in cell water rises from a mean value of 10.18 millimolal at 23 years to 11.24 millimolal at 50 years, whereas potassium falls from 144.3 to 141.19 millimolal during the same period. It is probable that hormonal factors are responsible for this change with age in women and possible that the same factors cause the sex difference. The observation that red blood cell potassium concentration falls during the menstrual cycle requires confirmation in studies during single cycles.

Although some of the factors influencing RBC sodium and potassium concentrations have been indicated in this study, much of the variation among subjects remains unexplained. Thus in the third and most homogeneous groups of subjects, only one-third of the observed variation among subjects was accounted for. In the second group

of subjects, ABO blood groups were determined, and the results suggested that ion concentrations within the cells were influenced by blood group substances. This finding was not confirmed in the third group of subjects, which was balanced for phenotypes A and O. No clear relationship was found in this group between intracellular ion concentrations and blood groups, secretor status, or any particular isoenzyme of acid phosphatase, phosphoglucomutase, 6-phosphogluconate dehydrogenase, or adenylate kinase.

Summary

1. Red blood cell sodium and potassium concentrations were measured in groups of healthy adults comprising 142 subjects.

2. For both sodium and potassium concentrations subject-to-subject variation was greater than day-to-day variation in an individual. No significant day-to-night variation was observed.

3. Red blood cell sodium concentration was lower in young women (mean 6.50 mEq per kg cells) than in men (mean 7.45 mEq per kg cells) and increased with age (to a mean 7.30 mEq per kg cells at 50 years). No change with age was observed in men. Red blood cell potassium concentration was greater at all ages in women (mean 92.41 mEq per kg cells) than in men (mean 88.42 mEq per kg cells). Age did not affect the concentration in either sex.

4. Ninety-one per cent of the observed variation of water content of the red blood cells of young men was accounted for by the observed variation of sodium, potassium, and hemoglobin contents of the cells. In the women studied, plasma water content also affected red blood cell water content. The osmotic coefficient of hemoglobin at the concentrations found was 3.8 times greater than the coefficients for sodium and potassium.

5. Sodium and potassium concentrations in red blood cell water were negatively correlated. The regression equations relating these variables indicated that for a given change of sodium concentration the change of potassium concentration was 1.4 to 3.8 times as great.

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