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# Potassium Uptake of Normal and Low Potassium Human Red Corpuscles* (17945)

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Experiments with radioactive potassium ($K^{42}$) have demonstrated the continuous exchange of this ion between the intra- and the extracellular phase of most tissues including the red cells of the blood(1). Within the limits of this exchange a considerable net transport of potassium across the membrane of the erythrocytes would be possible. A net transport of potassium into the red blood cells is most likely to occur in erythrocytes with abnormally low potassium concentration. Low potassium concentration of the erythrocytes is an unusual finding even in potassium deficiency but was encountered by the authors in a case of extreme persistent potassium depletion. A quantitative estimation of the exchange of potassium in normal cells and in potassium deficient cells and an evaluation of the rate of potassium net transport into potassium deficient cells would be of great clinical interest providing a measure of the optimal rate of therapeutic supply of potassium to patients with an intracellular potassium deficiency.

In the present study such estimations were performed in *in vitro* experiments with blood samples from normal non-hypopotassemic persons and from a case of severe persisting hypopotassemia. The factors limiting the net uptake of potassium, *i.e.*, the possible exchange of Na or other cations with K moving into the cells have not been investigated in this study.

*Experimental.* Blood samples from non-hypopotassemic persons and from a case of severe persisting hypopotassemia were used. In the controls (Experiment A and B) the plasma potassium concentrations were 5.12

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1. Hevesy, G., Radioactive Indicators, New York, 1948, 483.

TABLE I.
Potassium Uptake of Human Red Blood Cells Incubated for 6 Hours at 37°C in Plasma with Different Concentrations of Potassium. For calculations and the potassium concentrations of the erythrocytes, see text.

| Exp. | Pl-K (mEq/L) | $K^{42}$-decrease, % | Hematocrit | K-uptake (mEq/L R.B.C.) |
|---|---|---|---|---|
| B | 5.09 | 72.0 | 38.5 | 5.8 |
| A | 5.12 | 53.3 | 30.0 | 6.3 |
| B | 7.56 | 60.7 | 37.8 | 7.5 |
| C | 9.05 | 34.1 | 21.5 | 11.3 |
| A | 9.20 | 38.0 | 29.1 | 8.5 |
| B | 9.36 | 52.4 | 38.7 | 7.7 |
| B | 13.95 | 39.2 | 38.2 | 8.8 |

and 5.09 mEq/L and the potassium concentration of the erythrocytes 98.6 and 100.2 mEq/L respectively. The corresponding values for the hypopotassemic blood sample (Experiment C) were 1.84 mEq/L in plasma and 87.2 mEq/L in the corpuscles. Blood clotting was prevented in all samples by addition of heparin 2.5 mg per 10 ml of blood. As the hypopotassemic blood was rather anemic the controls had to be diluted with plasma from the same donors thus establishing more adequate hematocrit values. In each experiment aliquots of blood with an added amount of $K^{42}$ were used; in some of the aliquots the plasma potassium concentration was raised by addition of KCl: in Experiment A from 5.12 to 9.2, in B from 5.09 to 7.56, 9.36 and 13.95 in separate experiments, and in C from 1.84 to 9.05 mEq/L. The entrance of potassium into the cells during 6 hours at 37°C was determined in all samples except the 1.84 specimen, which was lost. The total amounts of potassium ions having entered the red blood cells (K influx) from plasma were calculated from estimations of the plasma potassium concentration at the start of the experiment and the decrease in plasma $K^{42}$ activity during the 6 hour period neglecting the simultaneously emigrated labelled potassium ions. By use of the relative plasma-corpuscle ratio these figures were converted into the potassium entrance into 1000 ml corpuscles. In Experiment C a net transport of potassium into the cells was calculated from a decrease in plasma potassium concentration. In the controls (Experiment A and B) no demonstrable net transport of potassium into the cells occurred.

*Technic.* Potassium analyses were performed in a flame photometer with a lithium internal standard. Hematocrit readings were carried out directly on capillary glass tubes at 3000 r.p.m. until constant volume; the blood column was 60 mm, bottom 170 mm from axis of the centrifuge. Each estimation is the mean of 6 readings.

Specific activity of the $K^{42}$ used was about 1 million counts per minute per mg K. The $\beta$-emission was determined directly on samples of plasma in open special cuvettes; the layer thickness of plasma was 4 mm(2). The incubation of blood samples was performed in stoppered vials placed 11 cm from the axis of a gramophone disc rotating at 80 revolutions per minute; the disc was placed with an inclination of 45°. With this technic a gentle but thorough mixing was secured and no demonstrable hemolysis occurred. Plasma glucose and lactic acid was not measured but the pH at the end of the experiments was found to be 7.3.

*Results.* Potassium uptake of the red cells (mEq/L) was derived from the following figures: plasma K at the start of the experiment (Pl-K), the percentage decrease in $K^{42}$-activity of plasma ($K^{42}$-decrease) and the hematocrit (H%) using the following formula:

$$\text{K-uptake (mEq/L. R.B.C.)} = \text{Pl-K} \times \frac{K^{42}\text{-decrease}}{100} \times \frac{100-H\%}{H\%}.$$

The figures are given in Table I.

The statistical significance of the figures in

2. Davidsen, H. G., and Kjerulf-Jensen, K., *Scand. J. Clin. and Lab. Invest.* 1950, in press.

the last column (K-uptake) is sufficient in regard to the methodical error. The standard deviation of each estimation of the 6-hourly K-uptake amounts to 5% of the stated values. This figure was derived from the highest occurring standard deviation of each of the factors in the formula, *i.e.*:

| | |
|---|---|
| Standard deviation of single plasma potassium estimations calculated from 13 tenfold estimations under identical conditions (4) | 3 % |
| Standard deviation of estimations of $K^{42}$–decrease | 3.5% |
| Standard deviation of $\frac{100-H\%}{H\%}$ (in this experiment) | 1 % |

The preceding figures (Table I and Fig. 1) indicate that the potassium uptake of normal red blood cells increases with increasing plasma potassium concentrations (Experiment A and B) ranging between 5.09 and 9.36 mEq/L, *i.e.* within concentrations which may be found in clinical conditions. Experiment C, however, demonstrates a potassium entrance into low potassium red blood cells, which seem to be definitely higher than the corresponding values obtained from the controls, Fig. 1. The net transport of potassium into the cells encountered in Experiment C, calculated from the decrease in plasma potassium concentration from 9.05 to 8.34 mEq/L, amounted to 3.0 mEq per liter of cells when corrected for an increase in hematocrit from 21.5 to 22.5.†

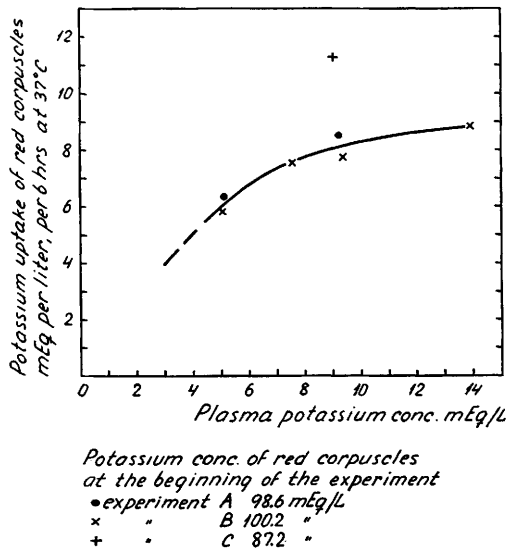


FIG. 1.

Potassium immigration into normal and low potassium human red blood cells at different plasma potassium levels. For calculation, see text and Table I.

*Discussion.* When potassium deficient cells are suddenly given the possibility of free potassium assimilation it would be decisively interesting to know whether the increased potassium assimilation is the result of an increased potassium uptake (K-influx) or a reduced potassium extrusion during the general exchange of ions across the cell membrane. In the preceding calculations the dilution of $K^{42}$-ions passing into the cells with the preexisting potassium ions of the cell interior was presumed so considerable that the number of $K^{42}$-ions returning to plasma was negligible. This assumption should be permissible for the following reasons: assuming a uniform exchangeability of all potassium ions in the cells and that no net transport takes place (as in Experiment A and B) a mathematical analysis reveals that only 3.7% of all emigrating ions are originating from plasma during an exchange including 7.5% of all potassium ions in the cells (the mean degree of exchange in Experiment A and B). In the case of Experiment C where in addition a net transport of potassium was demonstrated about 6% of all emigrated K-ions would be expected to be returning $K^{42}$-ions originating from plasma. These corrections if used in the calculations would heighten the calculated potassium uptake with 3.7 and 6% respectively. Thus the net transport in Experiment C is sufficiently explained as the result of the demonstrated increased potassium influx while the potassium emigration from the erythrocytes (K-influx — K-net transport) was quantitatively comparable with that of the controls.

The rate of penetration of labelled potas-

† $(9.05 \times \frac{100-21.5}{100} - 8.34 \times \frac{100-22.5}{100}) \times \frac{100}{21.5} = 3.02.$

4. Ryssing, E., personal communication to the authors.

sium into the red blood cells of human beings is relatively low compared with that of other tissue cells(3). Provided a total body cell K/red cell K ratio of 15 the calculated minimal 24 hour total cellular potassium uptake would be about 14 g (358 mEq) K. Actually this patient in a well controlled period prior to the experiment received 23 g (588 mEq) K during 2 days; within this period the potassium concentration of plasma increased from 2.28 to 3.45 mEq/L and of the red blood corpuscles from 94.4-99.8 mEq/L. The potassium concentration of the muscular tissue was extremely low at the time of the experiment: 50.9 mEq/kg; Na:107 mEq/kg.

*Summary.* The potassium exchange of normal human erythrocytes *in vitro* increased with increasing plasma potassium concentration and approached a constant level at concentrations above 9 mEq/L.

In an experiment with low potassium erythrocytes from a case of persistent hypopotassemia in which the plasma potassium concentration was raised the potassium uptake (K-influx) was found to be increased by 40% of the corresponding values for normal erythrocytes. This increase in the K-influx corresponded quantitatively to a demonstrated net transport of potassium into the low potassium red blood cells. The simultaneous emigration of K-ions, however, was not reduced, and therefore the net transport of potassium could not be considered a result of a reduced potassium emigration from the cells.

The low potassium concentrations of the erythrocytes in this particular case seemed to reflect the potassium depletion of the body cells.

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3. Moore, F. D., *J.A.M.A.*, 1949, v141, 646

## *In Vitro* Sensitivity of Bacteria to Sulfonamide Combinations as Compared to Single Sulfonamides.* (17946)

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The therapeutic advantages of a mixture of several sulfonamides over a single effective sulfonamide are said to be due to the following: (1) A given volume of fluid (*e.g.* urine) is capable of retaining several sulfonamides in solution up to their individual maximum solubilities, so that larger doses of a mixture than the maximum for any one sulfonamide may be given without producing crystalluria. (2) On a weight for weight basis, such mixtures in a large series of cases have been given with a markedly reduced incidence of renal toxicity(1-9) and of sensitization reactions such as drug rash and fever(7). It is claimed further that mixtures are as effective antibacterial agents *in vitro* as an equivalent amount of a single sulfonamide and may in some instances exert a potentiat-

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