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EXCHANGE OF CELLULAR POTASSIUM

BY

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Large amounts of potassium are present in the muscle cells and the cells of many other organs. Rabbit muscles contain about 430 mgm. per cent potassium and similar values are found for the muscles of other mammals. Out of the 430 mgm. per cent potassium of the muscle, about 428 mgm. are to be found in the cells and only 2 mgm. are present in the interspaces. The plasma and the extracellular fluid of the rabbit, on the other hand, contain but about 18 mgm. per cent potassium and similar values are found for the plasma of most of the other mammals. In order to investigate whether an exchange takes place between the cellular and the extracellular potassium ions we administered labelled potassium to rabbits and compared the distribution of the ^{42}K ions between plasma potassium and tissue potassium after varying periods of time. Such an exchange would obviously necessitate a passage through the cell wall. The measurements were carried out by comparing the radioactivity of 1 gm. plasma and 1 gm. muscle tissue. If the ^{42}K ions were prevented from penetrating into the muscle cells the extracellular volume of the muscle would contain all the ^{42}K present in the tissue and, assuming this volume to represent 11 per cent of the muscle weight, 1 gm. muscle would only be $^1/_9$ as active as 1 gm. plasma. On the other hand, if the ^{42}K ions penetrate rapidly into the muscle cells a proportional partition of ^{42}K between the potassium of the plasma and the potassium of the muscle would soon take place and we should find 1 gm. muscle to be $\frac{428}{18} = 24$ times as active as 1 gm. plasma.

In previous experiments[1], we found shortly after the administration of ^{42}K the muscle tissue to become much more active than would be expected in case of an impermeability of the cell wall to potassium and, furthermore, the rapid initial influx of some ^{42}K into the muscle cells to be followed by a slow increase only in the later phases of the experiment. Because of the availability of stronger active potassium preparations than previously, we were able to extend the duration of our experiments over several days and to carry out a more detailed study of the rate of penetration of potassium into the tissue cells. The results of these experiments are communicated in the following.

Determination of the exchangeability of cellular potassium.

The partition of ^{42}K between the plasma and the muscle cells can be determined by comparing the activity of 1 gm. plasma with that of 1 gm. muscle. There is, however, also another way of approach which does not involve the investigation of the activity of the muscle tissue. This second method of determination of the extent of cellular exchange is based upon the measurement of loss of ^{42}K from the circulating blood. This loss is mainly due to the penetration of ^{42}K into the tissue cells and, therefore, it is possible to

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[1] L. Hahn, G. Hevesy and O. Rebbe, Biochem. J.. **33**, 1540 (1939). Comp. also M. Joseph, E. Cohn and D. M. Greenberg, J. Biol. Chem. **128**, 673 (1939).

calculate from the decrease of the ^{42}K content of the plasma the extent of ^{42}K penetration into the cells. If the potassium content of plasma and cells is known, we can calculate the percentage replacement of cellular potassium by plasma potassium which takes place in the course of the experiment. In carrying out this calculation due regard must be taken to the potassium content of the plasma as well as to that of the extracellular fluid, since we are faced with the problem of distribution of ^{42}K between cellular and extracellular potassium. The partition of ^{42}K between the plasma and most of the extracellular space was found to be a very fast process[1].

Assuming the extracellular space of the rabbit to amount to 27 per cent of the body weight and the potassium content of the extracellular fluid to be 18 mgm. per cent, the potassium content of the total extracellular space of a rabbit weighing 2.5 kg. is 122 mgm. Taking the muscles to be 40 per cent of the body weight and the muscle tissue to contain 430 mgm. per cent potassium, we arrive at a figure of 4300 mgm. for the total potassium content of the rabbit muscles. This figure refers almost exclusively to cellular potassium, the extracellular potassium present in the muscles making out about 20 mgm. The ^{42}K introduced into the circulation will penetrate besides into the muscle cells also into the cells of other organs. In addition to the 4.3 gm. potassium present in the muscles, about 1.7 gm. potassium are found in the other organs of a rabbit weighing 2.5 kg. The ^{42}K disappearing from the extracellular space will, apart from a small quantity which is excreted, find its way into the red corpuscles and tissue cells containing in all about 6 gm. potassium.

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[1] L. Hahn and G. Hevesy, Acta Physiol. Scand. **1**, in print.

Let us consider an example of the calculation of the extent of cellular potassium replacement from the decrease of the ^{42}K content of the plasma. After the lapse of 210 min., 1 cc. of the plasma of a rabbit weighing 2.4 kg. was found to contain 0.0269 per cent of the ^{42}K administered. From this figure it follows that the total extracellular fluid of the rabbit contains 17.5 per cent of the ^{42}K administered. The amount of ^{42}K excreted was found to be 1.66 per cent. The amount of ^{42}K present in the extracellular space plus that excreted in the course of 210 min. being 19.2 per cent, the amount present in the tissue cells will be 80.8 per cent. The cells contain, thus, 4.2 times more ^{42}K than the total extracellular space of the rabbit.

We shall now calculate the ratio which would be found in case of a proportional partition of ^{42}K between cellular and extracellular potassium. As such we shall take the ratio of the total potassium content of the cells to that of the extracellular fluid, i. e. $\frac{6000}{122} = 49$. We arrive thus at the result that in the course of 210 min. $^{1}/_{12}$ part of the cellular potassium was replaced by extracellular potassium.

Experimental method.

We are much indebted to Dr. J. C. JACOBSEN and Mr. O. N. LASSEN for preparing radio-potassium by bombarding about 200 mgm. potassium chloride with a deuterium beam in the Copenhagen cyclotron. Along the path of the beam the salt becomes intensely coloured; only the strongly coloured part of the salt was used in our experiments. Under the action of the deuterium beam on potassium chloride in addition to ^{42}K also ^{38}Cl is produced. The activity of the radio-chloride has, however, entirely decayed at the time when the activity of the tissue samples is measured. We administered to rabbits radio-potassium having a β-activity of about 1/500 mgm. radium. The tissue samples were treated with concentrated nitric acid and ashed below 350°. Ash samples having the same weight (100 mgm.) were used in the activity measurements. The activity of the "natural" potassium present in the tissue samples was determined after the decay of their ^{42}K content. The correction due to the "natural" activity of the potassium was always less and, most frequently, much less than 10 per cent of the total activity measured.

Determination of potassium.

We determined the potassium content of the plasma and tissue samples by the method of SHOHL and BENNET[1] modified by NORBERG[2]. The main steps involved in this determination are the following: a) Ashing of the sample in the presence of barium hydroxide, b) removal of the barium excess by adding ammonium carbonate, c) driving-off of the ammonium salts, d) precipitation of the potassium as potassium chloroplatinate, e) washing of the precipitate with alcohol and dissolving it in a buffer solution, f) addition of potassium iodide and titration of the iodoplatinate formed with thiosulphate. We controlled the results of our analyses by using a radioactive indicator. A trace of ^{42}K of known activity was added to the sample to be analyzed and it was investigated whether, after one of the above procedures, the ^{42}K was quantitatively recovered or not.

[1] A. T. SHOHL and H. B. BENNET, J. Biol. Chem. **78**, 643 (1928).

[2] B. NORBERG, Comptes Rendus Travaux Carlsberg, **21**, 233 (1938).

We found that the washing of the dry potassium chloroplatinate precipitate with alcohol cannot be carried out without a quite appreciable loss of ^{42}K. The alcohol centrifuged off contained 4 per cent of the 0.2 mgm. potassium present in the precipitate when using the alcohol volume suggested by Norberg.

Determination of the extent of cellular exchange by following the decrease of the ^{42}K content of the plasma.

We shall now consider an example in which the first plasma volume is obtained from the carotis of the rabbit as early as 0.6 min. after the injection of 15.7 mgm. labelled potassium as potassium chloride into the jugularis. The injection took 2 sec. As seen in Table 1, 0.6 min. does not suffice to obtain a proportional partition of ^{42}K between plasma and extracellular fluid. In case of a proportional partition, 1 cc. plasma would contain 0.149 per cent or less of the ^{42}K injected; in fact, 1 cc. plasma contains 0.19 per cent of the ^{42}K injected. After the lapse of 2 min., we find in 1 cc. plasma only 0.082 per cent of the ^{42}K injected; thus, we have to conclude that an appreciable part of the ^{42}K administered is present in the cells after the lapse of 2 min. We cannot decide whether at that time a proportional partition of ^{42}K between plasma and extracellular fluid is obtained since it is conceivable that before this proportional partition an intrusion of quite appreciable amounts of ^{42}K into the cells had taken place. The amount of ^{42}K present in the cells after 2 min. can, therefore, not be calculated. It can be stated, however, that the amount of ^{42}K present in the cells must be about as large as or larger than that

Table 1.

Rate of disappearance of ^{42}K after intravenous injection from the plasma of a rabbit weighing 2.5 kg. (Rabbit A).

Time in minutes	Per cent of ^{42}K injected present in		Volume of diluting fluid	
	1 gm. plasma	total plasma	in cc.	in per cent of body weight
0 (extrapol.)	1.4	100	—	—
0.6	0.19	13.2	526	21
2	0.082	5.7	1220	49
3	0.068	4.7	1470	59
5	0.058	4.0	1720	69
15	0.035	2.4	2860	115
120	0.0206	1.4	4850	194
∞ (assumed extracellular intrusion, only)	0.149	10.4	674	27
∞ (assumed proportional partition between extracellular potassium and cellular potassium)	0.0029	0.20	33000	1320

present in the interspaces. To dilute the ^{42}K introduced into the circulation to this low level, 1220 cc. of body fluid had to take part in the dilution process. The volume of diluting fluid thus calculated for different times is shown in the fourth column of Tables 1—3, while in column 5 the volume of the diluting fluid is stated, expressed in percentage of the body weight. While, after the lapse of 2 hours, the volume of the diluting fluid is found to be seven times larger than that of the extracellular fluid, showing a very appreciable intrusion of ^{42}K into the cells, it is still only $^1/_7$ of that which would be expected in case of a proportional partition of ^{42}K between extracellular and cellular potassium.

Table 2.

Rate of disappearance of ^{42}K after intravenous injection from the plasma of a rabbit weighing 2.3 kg. (Rabbit B).

Time in minutes	Per cent of ^{42}K injected present in		Volume of diluting fluid	
	1 gm. plasma	total plasma	in cc.	in per cent of body weight
0 (extrapol.)	1.6	100	—	—
0.26	0.354	22.7	283	12.3
0.50	0.220	14.1	455	19.8
1.05	0.129	8.3	775	33.7
3.05	0.057	3.65	1755	76.4
7.55	0.029	1.85	3450	150
∞ (assumed extracellular intrusion, only)	0.161	10.3	620	27
∞ (assumed porportional partition between extracellular potassium and cellular potassium)	0.0033	0.21	30500	1320

The figures of Table 3 show a similar trend to those of Table 1, but after the lapse of 210 min. 1 gm. plasma still contains 0.0269 per cent of the ^{42}K injected while, in the first mentioned case, after the lapse of 120 min. only 0.0206 per cent of ^{42}K was present. The cellular uptake in the case of rabbit C was, thus, less than that in the case of rabbit A and also less than in the case of rabbit B. These differences in the cellular uptake cannot be due to analytical errors since the results of duplicate analyses have shown only small variations. To some extent at least they may be explained by a difference in the size of the extracellular space of the rabbits. We assumed the extracellular volume to be 27 per cent of the body weight. This is the average value found for rabbits. The deviation from this average

Table 3.

Rate of disappearance of ^{42}K after intravenous injection from the plasma of a rabbit weighing 2.4 kg. (Rabbit C).

Time in minutes	Per cent of ^{42}K injected present in		Volume of diluting fluid	
	1 gm. plasma	total plasma	in cc.	in per cent of body weight
0 (extrapol.)	1.5	100	—	—
5	0.058	3.9	1730	72
10.5	0.048	3.2	2080	87
20.5	0.038	2.5	2640	110
40.5	0.031	2.1	3230	135
80	0.028	1.9	3580	149
210	0.027	1.8	3710	155
∞ (assumed extracellular intrusion, only)	0.154	10.3	650	27
∞ (assumed proportional partition between extracellular potassium and cellular potassium)	0.0032	0.21	31500	1320

^{42}K content of urine produced between 0 and 80 min. 1.18 per cent.
^{42}K content of urine produced between 81 and 210 min. 0.48 per cent.

value is quite marked, as found by several experimenters. In another paper, the results of experiments on the exchange of cellular potassium in animals kept in intense motion are described[1]. Such animals were found to exchange their cellular potassium at an enhanced rate. It is quite possible that several of the rabbits experimented with performed some muscular work which influenced the rate of ^{42}K exchange between the extracellular and the cellular space.

In Tables 4—7 the results of experiments of longer duration are shown.

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[1] L. Hahn and G. Hevesy, Acta Physiol. Scand., in print.

Table 4.

Rate of disappearance of ^{42}K after subcutaneous injection from the plasma of a rabbit weighing 2.5 kg. (Rabbit D).

Time in hours	Per cent of ^{42}K injected, present in				Ratio of ^{42}K content of the tissue cells and the extracellular fluid
	1 gm. plasma	total extracellular fluid	total extracellular fluid + excreta	tissue cells	
0.4	0.0089	6.0	—	—	—
3.5	0.0101	6.9	8.6	91.4	13.2
18.5	0.0064	4.4	10.6	89.4	20.4
24.5	0.0067	4.5	12.5	87.5	19.5
48	0.0057 0.0053 0.0058 0.0052	3.7	18.1	81.9	22.2
∞ (assumed proportional partition of ^{42}K between extracellular potassium and cellular potassium)	..	..	..	..	59

Calculation of the extent of cellular potassium exchange from the ratio of the activity of plasma and muscle tissue of the same weight.

If all the potassium present in the cells had opportunity freely to exchange with the extracellular potassium, 1 gm. cellular potassium would show the same activity as 1 gm. extracellular potassium. Since the cells of 1 gm. muscle contain 24 times as much potassium as 1 gm. plasma, the activity of 1 gm. muscle will, in this case, be 24 times greater than that of 1 gm. plasma. If, in the course of the experiment, the cellular potassium had opportunity only partly to exchange with the extracellular potassium, 1 gm.

Table 5.

Rate of disappearance of ^{42}K after subcutaneous injection from the plasma of a rabbit weighing 2.4 kg. (Rabbit E).

Time in hours	Per cent of ^{42}K injected, present in				Ratio of ^{42}K content of the tissue cells and the extracellular fluid
	1 gm. plasma	total extracellular fluid	total extracellular fluid + excreta	tissue cells	
1.8	0.0159	10.4	11.7	88.3	8.5
17.3	0.0106	6.9	12.9	87.1	12.6
24	0.0091	5.9	13.8	86.2	14.6
41.5	0.0080	5.2	17.6	82.4	15.8
49	0.0105	6.8	21.2	78.8	11.6
64	0.0079	5.1	24.5	75.5	14.8
∞ (assumed proportional partition of ^{42}K between extracellular potassium and cellular potassium)	..	..	..	..	43

muscle would be less than 24 times as active as 1 gm. plasma. If the ratio of the activity of the cells of 1 gm. muscle and of 1 gm. plasma is equal to R, then $\frac{R}{24}$ will measure the extent of exchangeability of the cellular potassium.

The figures given in the 4th column of Table 8 were obtained by comparing the activity of the muscle sample and that of the plasma sample secured at the same time. The ^{42}K content of the muscle sample accumulated continuously in the course of the experiment from plasma the ^{42}K content of which varied. To arrive at a correct measure of the percentage exchange of the muscle potassium we should, therefore, not compare the activity of the muscle sample and the plasma sample secured at the end of the experiment,

Table 6.

Rate of disappearance of ^{42}K after subcutaneous injection from the plasma of a rabbit weighing 2.7 kg. (Rabbit F).

Time in hours	Per cent of ^{42}K injected, present in				Ratio of ^{42}K content of the tissue cells and the extracellular fluid
	1 gm. plasma	total extra-cellular fluid	total extra-cellular fluid + excreta	tissue cells	
16.5	0.0091	6.65	12.2	87.9	13.2
24	0.0091	6.65	14.6	85.5	12.9
26	0.0089	6.50	14.9	85.1	13.1
48	0.00763 0.00765	5.58	20	80	14.3
∞ (assumed proportional partition of ^{42}K between extracellular potassium and cellular potassium)	..	..	..	..	53

Table 7.

Rate of disappearance of ^{42}K after intravenous injection from the plasma of a rabbit weighing 2.1 kg. (Rabbit G).

Time in hours	Per cent of ^{42}K injected, present in				Ratio of ^{42}K content of the tissue cells and the extracellular fluid
	1 gm. plasma	total extra-cellular fluid	total extra-cellular fluid + excreta	tissue cells	
4.6	0.0194	11	13	87	7.9
16.7	0.0081	4.6	10.3	89.7	19.5
24.7	0.0067	3.8	11.8	88.2	23.2
40.7	0.0068	3.8	15.8	84.2	22.2
∞ (assumed proportional partition of ^{42}K between extracellular potassium and cellular potassium)	..	..	..	..	44

as done in column 4 of Table 8, but we should compare the activity of 1 gm. muscle tissue with that of the average activity of 1 gm. plasma during the experiment. Furthermore, due regard must be taken to the fact that more ^{42}K penetrates into the muscle in the early phases of the experiment than in corresponding later intervals. The figures contained in the last column of Table 8 represent, therefore, the upper limit of exchangeability of the cellular potassium. In experiments taking several hours or more, the activity of the plasma does not much decrease with time and the figures given in column 5, so far as they relate to experiments taking several hours, only slightly overrate the exchangeability of the cellular potassium. The figures in the column "Percentage exchange of cellular potassium" are obtained by dividing the figures quoted in the column "Ratio of ^{42}K content of the cells of 1 gm. muscle and 1 gm. plasma" with the ratio of the potassium content of the cells of 1 gm. muscle and the potassium content of 1 gm. plasma.

The result of the potassium determinations carried out according to the method of SHOHL and BENNET (comp. p. 7) can be seen in Table 9.

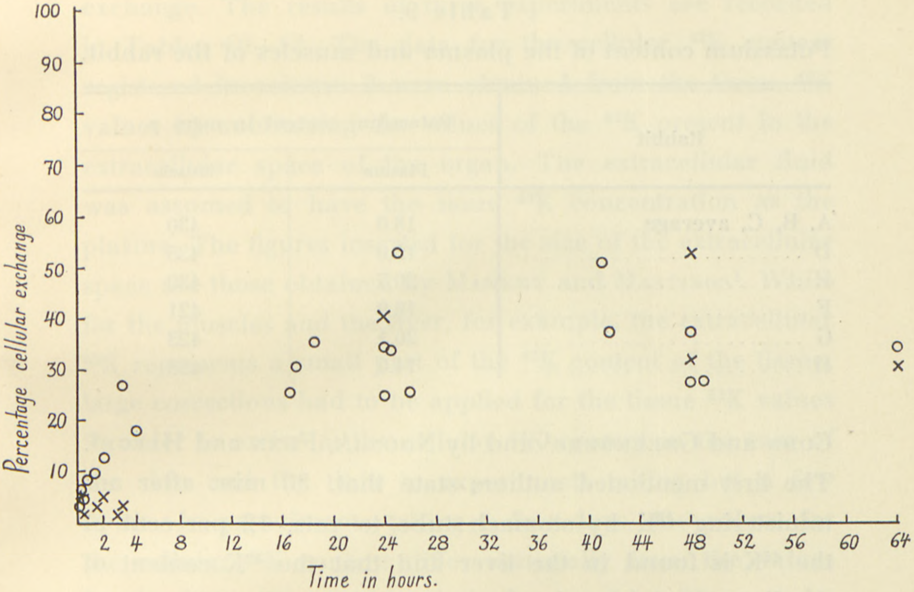
The percentage of cellular potassium which takes part in the exchange process found by both methods is plotted in the figure, where the open circles represent the values obtained by the "disappearance" method described on p. 8 and the crosses indicate the figures calculated from the activity values obtained for plasma and muscle tissue. The experiments lasted from a few minutes up to 64 hours. It is clearly seen that within a few minutes a quite appreciable part of the cellular potassium exchanges with plasma potassium, the amount doing so first increases markedly with increasing time but, after the lapse of a day, the per-

Table 8.

Distribution of ^{42}K between plasma and gastrocnemius of the rabbit.

Time	Per cent of ^{42}K administered, present in 1 gm. muscle	Ratio of ^{42}K content of muscle and plasma of equal weight	Ratio of ^{42}K content of the cells of 1 gm. muscle and 1gm. plasma	Percentage exchange of cellular potassium
Rabbit A.				
5 min.	0.027	0.46	0.35	1.46
120 min.	0.026	1.28	1.17	4.85
Rabbit B.				
1.05 min.	0.023	0.177	0.067	0.21
3.05 min.	0.031	0.549	0.44	1.41
Rabbit C.				
10.5 min.	0.0184	0.38	0.27	1.13
20.5 min.	0.0181	0.48	0.37	1.54
40.5 min.	0.0178	0.52	0.41	1.71
210 min.	0.0265	0.99	0.88	3.67
Rabbit D.				
48 hours	0.0498	9.09	8.98	31.0
Rabbit E.				
64 hours	0.0488	6.18	6.07	29.2
Rabbit F.				
24 hours	0.0765 0.0673	8.49	8.38	39.8
48 hours	0.0840 0.0840	11.0	10.9	51.9
Rabbit H.				
3.5 hours	0.0158	0.86	0.75	3.1

centage of cellular potassium taking part in the exchange process increases only slightly. At the stage when no significant further increase takes place, more than half of the cellular potassium has not participated in an exchange process.



Percentage of the potassium content of the muscle cells which got into exchange equilibrium with the potassium present in the extracellular fluid. ○ represent the values obtained by the "disappearance" method, while × indicate the figures calculated from the activity values obtained from plasma and muscle tissue.

The values obtained for the percentage cellular exchange by the indirect "disappearance" method and by a direct comparison of the activity of plasma and muscle tissue show no great difference in experiments taking several hours. In experiments of short duration, the "disappearance" method supplies much larger exchange values. This discrepancy suggests the assumption that, in the early phases of the experiment, one or several organs take up as large or larger amounts of ^{42}K than are taken up by the muscles. That the liver takes up large amounts of ^{42}K in the earliest phases of the experiment was found by Joseph,

Table 9.

Potassium content of the plasma and muscles of the rabbit.

Rabbit	Potassium content in mgm. p. c.	
	Plasma	Muscle
A, B, C, average	18.0	430
D	15.0	435
E	20.7	430
F	16.9	421
G	20.1	423
H	14.0	438

Cohn and Greenberg[1] and by Noonan, Fenn and Haege[2]. The first mentioned authors state that, 30 min. after administering ^{42}K by stomach tube to rats, 12 per cent of the ^{42}K is found in the liver and that the ^{42}K content of the liver diminishes in the course of the next 210 min. to 4 per cent of the amount administered. The last mentioned authors found as much as 30 per cent of the ^{42}K administered in the liver 30 min. after administration of the labelled potassium.

Exchange of cellular potassium of different organs.

In some cases, we investigated not only the uptake of ^{42}K by the muscles but also its uptake by other organs. From the data obtained and from the known potassium content of the organs we calculated the extent of potassium

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[1] M. Joseph, W. E. Cohn and D. M. Greenberg, J. Biol. Chem. **128**, 673 (1939).

[2] T. R. Noonan, W. O. Fenn and L. F. Haege, Amer. J. Physiol. **129**, 432 (1940).

exchange. The results of these experiments are recorded in Tables 10—13. The data for the cellular ^{42}K content registered in column 3 were obtained from the tissue ^{42}K values by subtracting the values of the ^{42}K present in the extracellular space of the organ. The extracellular fluid was assumed to have the same ^{42}K concentration as the plasma. The figures inserted for the size of the extracellular space are those obtained by MANERY and HASTINGS[1]. While for the muscles and the liver, for example, the extracellular ^{42}K represents a small part of the ^{42}K content of the tissue, large corrections had to be applied for the tissue ^{42}K values in order to arrive at the cellular ^{42}K content in the case of the skin and the tibia in experiments taking but a few hours. In experiments taking a few days, the values for the cellular ^{42}K content differ materially from the values for the tissue ^{42}K content only in few cases as, for example, in that of the tendon.

In experiments taking a few hours only, the percentage potassium exchange taking place in the cardiac muscle and the liver was found to be larger than the percentage potassium exchange in the gastrocnemius. In experiments of long duration this was no longer the case[2]. The lowest exchange took place in the brain. The tibia epiphysis and, to a minor extent, the tibia diaphysis contained much more ^{42}K than can be explained by the potassium present in the extracellular fluid of the tibia, which amounts to 26 per cent of the total weight of the tibia. Presumably, some of the ^{42}K ions are incorporated into the surface layer of the bone apatite. This incorporation provides a not negligible

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[1] J. F. MANERY and A. B. HASTINGS, J. Biol. Chem. **127**, 657 (1939).

[2] Comp. L. HAHN and G. HEVESY, Acta Physiol. Scand. in print, where the problem of the cardiac muscle exchange is discussed.

Table 10.

Exchange of potassium between plasma and different organs of rabbit C in the course of 210 min.

Labelled potassium administered by intravenous injection.

Organ	^{42}K content per gm. tissue	Cellular ^{42}K content per gm. tissue	Potassium content in mgm. p. c.	Percentage cellular potassium exchange
Plasma	100	—	18	—
Gastrocnemius	99	88	430	3.7
Cardiac muscle	281	250	360	14
Liver	228	206	370	11
Skin	78	20	69	5
Tibia diaphysis	45	19	—	—

additional outlet of ^{42}K from the plasma. Assuming the skeleton to amount to 15 per cent of the rabbit's weight and the non-extracellular ^{42}K of 1 gm. bone tissue to be equal to that of 0.3 cc. extracellular fluid, the ^{42}K of the bone apatite corresponds to 17 per cent of the ^{42}K content of the extracellular space of the rabbit. The diluting volume of the rabbit is, thus, increased from 27 per cent (i. e. the value obtained by the thiocyanate and similar methods) to about 32 per cent of the total weight of the rabbit.

As described on p. 17, the larger part of the potassium present in the muscle cells does not participate in an exchange process and is not, or only at a very slow rate, replaced by plasma (extracellular) potassium. As seen in Tables 10—13, the other organs investigated show a similar behaviour, this fact suggesting that we are faced with a fundamental property of the cellular potassium of all or several organs.

Table 11.

Exchange of potassium between plasma and different organs of rabbit H in the course of 210 min.
Labelled potassium administered by subcutaneous injection.

Organ	^{42}K content per gm. tissue	Cellular ^{42}K content per gm. tissue	Potassium content in mgm. p. c.	Percentage cellular potassium exchange
Plasma	100	—	14	—
Gastrocnemius	86	75	438	2.4
Cardiac muscle	346	315	360	12
Liver	356	334	370	13
Skin	96	38[1]	69	8
Brain, grey ...	48	13	..	..
Brain, white ..	27	— 8[2]	..	..
Tibia diaphysis	54	28	..	..
Tibia epiphysis	99	73	..	..

[1] In view of the very large extracellular space and low potassium content of the skin, the value stated is uncertain.

[2] The minus value indicates that a proportional partition of ^{42}K between the plasma and the extracellular fluid of the white brain tissue was not obtained in the course of 210 min.

Table 12.

Exchange of potassium between plasma and different organs of rabbit D in the course of 48 hours.
Labelled potassium administered by subcutaneous injection.

Organ	^{42}K content per gm. tissue	Cellular ^{42}K content per gm. tissue	Potassium content in mgm. p. c.	Percentage cellular potassium exchange
Plasma	100	100	15	—
Gastrocnemius	909	898	435	31
Cardiac muscle	641	610	360	26
Liver	783	761	370	31
Brain	429	394	400	15

Table 13.

Exchange of potassium between plasma and different organs of rabbit E in the course of 64 hours.

Labelled potassium administered by subcutaneous injection.

Organ	^{42}K content per gm. tissue	Cellular ^{42}K content per gm. tissue	Potassium content in mgm. p. c.	Percentage cellular potassium exchange
Plasma	100	—	20.7	—
Gastrocnemius	618	607	430	29.3
Cardiac muscle	486	455	360	26
Tendon	113	52	38	28
Liver	608	586	370	33
Brain	357	322	400	17

Exchange of the potassium content of the red corpuscles.

The red corpuscles of the rabbit contain about 400 mgm. per cent of potassium, thus about 20 times as much as plasma of the same weight. In our previous experiments, we found that some potassium exchange does take place between the corpuscles and the plasma. A more detailed investigation shows that, in experiments lasting a few days, an appreciable part of the corpuscle potassium of the rabbit, thus a much larger part than found by us previously, is replaced by plasma potassium, though the amount replaced was found in all cases investigated to be less than a third of the potassium present in the corpuscles. The results obtained are shown in Tables 14—18.

In a further experiment, in which ^{42}K was administered by subcutaneous injection to a rabbit, 64 hours later 1 gm. corpuscles was found to contain 5.95 times as much ^{42}K as 1 gm. plasma.

Table 14.

Distribution of ^{42}K administered by subcutaneous injection between the plasma and the red corpuscles of rabbit J.

Time	Per cent of ^{42}K administered, present in 1 gm. corpuscles	Ratio of the ^{42}K content of corpuscle and plasma of equal weight	Percentage replacement of corpuscle potassium
20 min.	0.0041	0.16	0.7
50 —	0.0080	0.29	1.2
102 —	0.011	0.39	1.6
214 —	0.014	0.49	2.0
390 —	0.017	0.68	2.8
∞	..	24	..

Table 15.

Distribution of ^{42}K administered by intravenous injection between the plasma and the red corpuscles of rabbit C.

Time	Per cent of ^{42}K administered. present in 1 gm. corpuscles	Ratio of the ^{42}K content of corpuscle and plasma of equal weight	Percentage replacement of corpuscle potassium
10.5 min.....	0.0077	0.16	0.7
20.5 —	0.0096	0.25	1.1
40.5 —	0.0113	0.37	1.5
80 —	0.0119	0.43	1.8
210 —	0.0160	0.60	2.5
∞	..	24	..

In all the experiments in which the potassium was administered by intravenous injections, a part of the labelled potassium penetrated into the cells in an early stage of the experiment, when the plasma had a high ^{42}K content. The figures contained in the fourth column of Tables 15 and 16 are therefore not quite a correct measure of the

Table 16.

Distribution of ^{42}K administered by intravenous injection between the plasma and the red corpuscles of rabbit G.

Time	Per cent of ^{42}K administered, present in 1 gm. corpuscles	Ratio of the ^{42}K content of corpuscle and plasma of equal weight	Percentage replacement of corpuscle potassium
16.7 hours ...	0.0271	3.36	16
24.7 — ...	0.0270	4.04	19
40.7 — ...	0.0276	4.04	19
∞	..	21	..

Table 17.

Distribution of ^{42}K administered by subcutaneous injection between the plasma and the red corpuscles of rabbit D.

Time	Per cent of ^{42}K administered, present in 1 gm. corpuscles	Ratio of the ^{42}K content of corpuscle and plasma of equal weight	Percentage replacement of corpuscle potassium
18.5 hours ...	0.0240	3.75	14
39 — ...	0.0307	4.06	15
48 — ...	0.0359	6.55	24
∞	..	27	..

Table 18.

Distribution of ^{42}K administered by subcutaneous injection between the plasma and the red corpuscles of rabbit F.

Time	Per cent of ^{42}K administered, present in 1 gm. corpuscles	Ratio of the ^{42}K content of corpuscle and plasma of equal weight	Percentage replacement of corpuscle potassium
16.5 hours ...	0.0405	4.45	19
26 — ...	0.0496	5.52	23
48 — ...	0.0580	7.60	32
∞	..	24	..

extent of replacement of the corpuscle potassium. The figures correctly indicating the extent of replacement are somewhat lower than the figures stated (see p. 15). After subcutaneous injection, the plasma activity increases with time and the potassium exchanged in the earliest phase is but slightly active. The values arrived at by comparing the activity of the plasma and the corpuscles shortly after subcutaneous injection underrates, therefore, the extent of potassium exchange which took place in the corpuscles in the course of the experiment. In experiments taking two days, $^1/_4$ of the corpuscle potassium was found to be replaced by plasma potassium.

Moreover, ^{42}K ions can get into the corpuscles by incorporation during the formation of the corpuscles. In experiments taking only a few hours, the ^{42}K incorporated during the formation of new corpuscles is insignificant. In the course of 3 hours, for example, about 3 per cent of the corpuscle potassium is found to be replaced by labelled plasma potassium while the labelled potassium incorporated into the corpuscles which were formed during that time amounts to about $^1/_2$ per cent of the potassium present in the corpuscles. In experiments taking a few days or more, the amount of labelled potassium incorporated into the corpuscles formed during that time is no longer insignificant and may be responsible for as much as half of the ^{42}K found in the corpuscles. We arrive at this result by assuming that somewhat less than 5 per cent of the corpuscles of the rabbit are destroyed and built up daily. If the building-up takes place in an organism containing labelled potassium the corpuscles formed are bound to contain such labelled potassium.

Summary.

Labelled potassium chloride was administered by intravenous or subcutaneous injections to rabbits and the ^{42}K content of plasma, corpuscles, gastrocnemius and other organs was determined at different intervals. The cellular potassium exchange was followed by two different methods.

a) By comparing the ^{42}K content of plasma and gastrocnemius of equal weight it was found that, in the earliest phase of the experiment, significant amounts of cellular potassium are replaced by plasma (extracellular) potassium. The amount of cellular potassium replaced increases at first appreciably with increasing time, but, after the lapse of about a day no perceptible further replacement takes place. In this phase of the experiment, one half or more of the cellular potassium content was not yet replaced.

b) The exchange of potassium between the tissue cells and the plasma (extracellular fluid) was also determined by following the decrease of the labelled potassium content of the plasma after the administration of radioactive potassium ^{42}K to rabbits. The application of this method led also to the result that the cellular potassium exchange ceases almost or completely at a stage when one-half or less of the cellular potassium has interchanged with plasma potassium.

In experiments taking few hours, a larger percentage of the cellular potassium of the liver and the cardiac muscle exchanges with plasma (extracellular) potassium than of the cellular potassium of the gastrocnemius. The lowest exchange is found to take place in the brain tissue.

In experiments taking a few days, the percentage exchange of gastrocnemius, cardiac muscle and liver potass-

ium is about the same. Though half or more of the cellular potassium had not yet exchanged no further potassium replacement of any significance takes place with increasing time.

After the lapse of two days, 1 gm. corpuscle was found to contain in the average six times as much labelled potassium as 1 gm. plasma, which corresponds to a replacement of about $^1/_4$ of the corpuscle potassium by plasma potassium.

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