

# The Relationship Between Potassium Utilization and Nitrogen Balance

By LAURENCE E. FRAZIER, M.S.,\* RANDOLPH H. HUGHES,† AND PAUL R. CANNON, M.D.‡

THE PRESENCE of potassium deficiency in the tissues as a whole cannot be determined directly but must be inferred from such clinical findings as a decreased level of serum potassium, an abnormal electrocardiogram, or a recently developed muscular weakness. These findings presumably are the resultants of a preceding period of negative potassium balance, due either to an inadequate intake or an excessive output of the ion. Treatment usually consists in the administration of potassium salt. This ignores the fact, however, that in most instances the patient has also undergone a period of negative nitrogen balance, during which a tissue-deficit of both potassium and nitrogen has occurred.

Metabolic experiments in man have indicated that nitrogen and potassium generally follow parallel courses of excretion.<sup>1</sup> For example, Howard and Bigham, in a study of patients undergoing treatment for fractures, concluded that "under the conditions of these experiments, nitrogen and phosphorus move together in and out of cells, and that potassium, though with rather more leeway, follows along as a close member of the team."<sup>2</sup> Albright and Reifenshtein came to essentially similar conclusions, viz., "that nitrogen and potassium are moving together in a fixed relationship to each other."<sup>2</sup>

In view of these indicated relationships of nitrogen and potassium under conditions of excretion, a similar relationship might be anticipated in the processes of tissue reconstruction. Moreover, in view of the fact that during catabolism both elements are being continuously excreted in the course of a continuing cellular degradation, it would not seem likely that such a process would be favorable for potassium retention, despite the liberal administration of potassium salts. In short, it seems unlikely that the therapeutic use of potassium salts is completely justified in the catabolic state; on the contrary, for purposes of nutritional repletion, it would seem that a positive nitrogen balance is a prerequisite for effective tissue utilization of potassium. It should be added, however, that even in the course of severe catabolism presumably not every cell is equally affected; therefore, not all cells should be unable to utilize potassium ion even under such adverse conditions.

Because of the many difficulties associated with metabolic studies in man designed to clarify these questions, we have subjected normal and protein-depleted adult male albino rats to varying periods of positive and negative nitrogen and potassium balances. Our purpose was to attempt to elucidate further the relationships of anabolism and catabolism to the processes determining the tissue utilization of potassium. In four experiments an effort was made to ascertain (1) the ability of protein-depleted rats to undergo effective protein repletion while eating rations containing or lacking nitrogen, and while receiving potassium salts parenterally; and (2) the interrelationships of nitrogen and potassium in normal rats similarly treated. The rations used were variants of a basal ration devoid of both nitrogen and potassium. These rations varied

From the Department of Pathology, The University of Chicago, Chicago, Ill.

\* Assistant in Pathology.

† Technician.

‡ Chairman, Department of Pathology.

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TABLE I  
Composition of Rations, in Per Cent

Diets →	1	2	3	4	5	6
Amino acid mixture	—	11.7	—	—	—	22.75
Cellulose	5.0	5.0	6.82	5.77	9.38	9.38
Choline 50%	0.6	0.6	0.82	0.69	1.12	1.12
Corn oil	4.0	4.0	29.73	20.0	20.0	20.0
Dextrin	70.0	58.3	40.91	44.23	53.12	30.37
Oleum percomorphum	0.3	0.3	0.41	0.35	0.56	0.56
Salt mixture without K	3.73	3.73	5.09	4.30	7.0	7.0
Vitamin mixture	1.0	1.0	1.36	1.15	1.88	1.88
Water	15.67	15.67	15.27	23.86	7.5	7.5
Amount fed daily, in g	15	15	11	13	8	8

<i>Composition of Amino Acid Mixture</i>					
DL-Alanine	4.19	L-Histidine HCl	3.25	DL-Phenylalanine	5.03
L-Arginine HCl	3.71	DL-Isoleucine	12.55	L-Threonine	3.76
DL-Aspartic acid	4.72	L-Leucine	11.68	DL-Tryptophan	1.73
L-Glutamic acid	17.77	L-Lysine HCl	9.13	L-Tyrosine	4.78
Glycine	0.37	DL-Methionine	3.80	DL-Valine	13.53

<i>Composition of Vitamin Mixture</i>			
Nicotinic acid	0.4	Riboflavin	0.2
Calcium pantothenate	0.2	Thiamine HCl	0.1
Pyridoxine HCl	0.1	Sucrose	99.0

TABLE II  
Composition of Salt Mixtures (in Per Cent)

<i>A</i>		<i>B</i>	
<i>Usual Mixture</i>		<i>Mixture without Potassium</i>	
Calcium carbonate	6.89	Calcium carbonate	7.39
Calcium citrate	30.97	Calcium citrate	33.22
Calcium phosphate, monobasic	11.33	Calcium phosphate, monobasic	12.15
Magnesium carbonate	3.34	Magnesium carbonate	3.58
Magnesium sulfate, anhydro	3.85	Magnesium sulfate, anhydro	4.13
Potassium chloride	22.40	Potassium chloride	0.00
Potassium phosphate, mono H	10.44	Potassium phosphate, mono H	0.00
Sodium chloride	0.00	Sodium chloride	18.84
Sodium phosphate, mono H, anhydro	9.40	Sodium phosphate, mono H, anhydro	19.21
Trace salts	1.38	Trace salts	1.48

<i>Trace Salts</i>		<i>Trace Salts</i>	
Copper sulfate	0.99	Copper sulfate	0.99
Ferric citrate	92.31	Ferric citrate	92.53
Manganese sulfate	1.15	Manganese sulfate	1.15
Potassium iodide	0.29	Sodium iodide	0.26
Potassium aluminum sulfate	0.66	Aluminum sulfate	0.46
Sodium fluoride	3.61	Sodium fluoride	3.62
Zinc chloride	0.99	Zinc chloride	0.99

with respect to amino acid content, fat content, and caloric potentials. Their compositions are given in Tables I and II, together with those of the amino acid mixtures, the vitamin mixture, and the salt mixtures used. The animals (Sprague-Dawley) were kept in metab-

olism cages, with collections of urine and feces daily or on alternate days. For the potassium determinations a Janke Internal Standard Flame Photometer was used. The nitrogen determinations were made by a micro-Kjeldahl procedure.

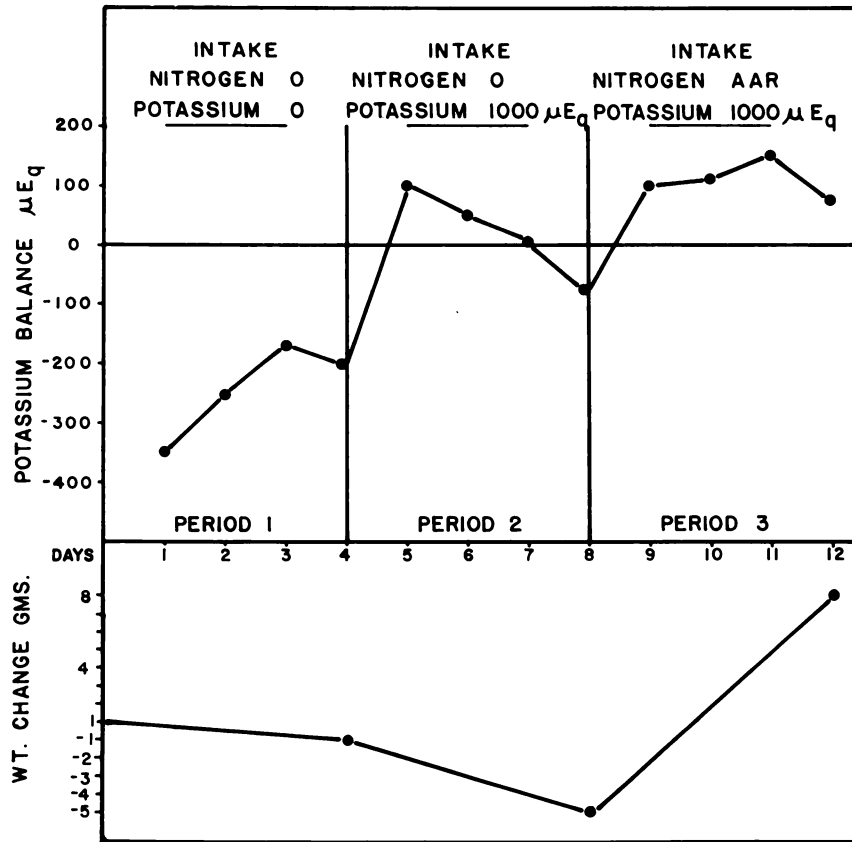


Fig. 1. Potassium balances and weight changes in protein-depleted rats with varying intakes of nitrogen and potassium.

#### EXPERIMENTS

##### Experiment 1

In the first experiment, five protein-depleted rats underwent potassium balance determinations during three successive, four-day, diet periods as follows: In period 1, 15 grams of ration No. 1 were fed daily; in period 2 this ration was continued in conjunction with subcutaneous injections of a solution of potassium chloride, 250 microequivalents per day; in period 3 the ration supplemented with the amino acid mixture (ration 2) was used and the injections of potassium chloride were continued. The results with reference to weight changes and potassium balances are shown in Figure 1.

In period 1 there was a slight loss of weight, a reduction in consumption of the ration (approximately 20 per cent) and a continuous negative potassium balance. In period 2,

during which potassium chloride was being injected, and while weight loss was continuing the potassium balance became positive on the first day but then decreased, becoming negative on the fourth day. In period 3, during which the amino acid ration was fed, the rats immediately began to gain weight, ate the ration completely, and went into positive potassium balance. It should be added that the decision to inject 250 microequivalents of potassium daily was based on earlier experiments which had demonstrated that under similar conditions of nutritional repletion approximately 20 milligrams of potassium chloride daily sufficed to ensure optimal repletion.<sup>3</sup>

##### Experiment 2

In order to compare the findings of the preceding experiment with those which might occur in well-nourished animals, ten normal rats,

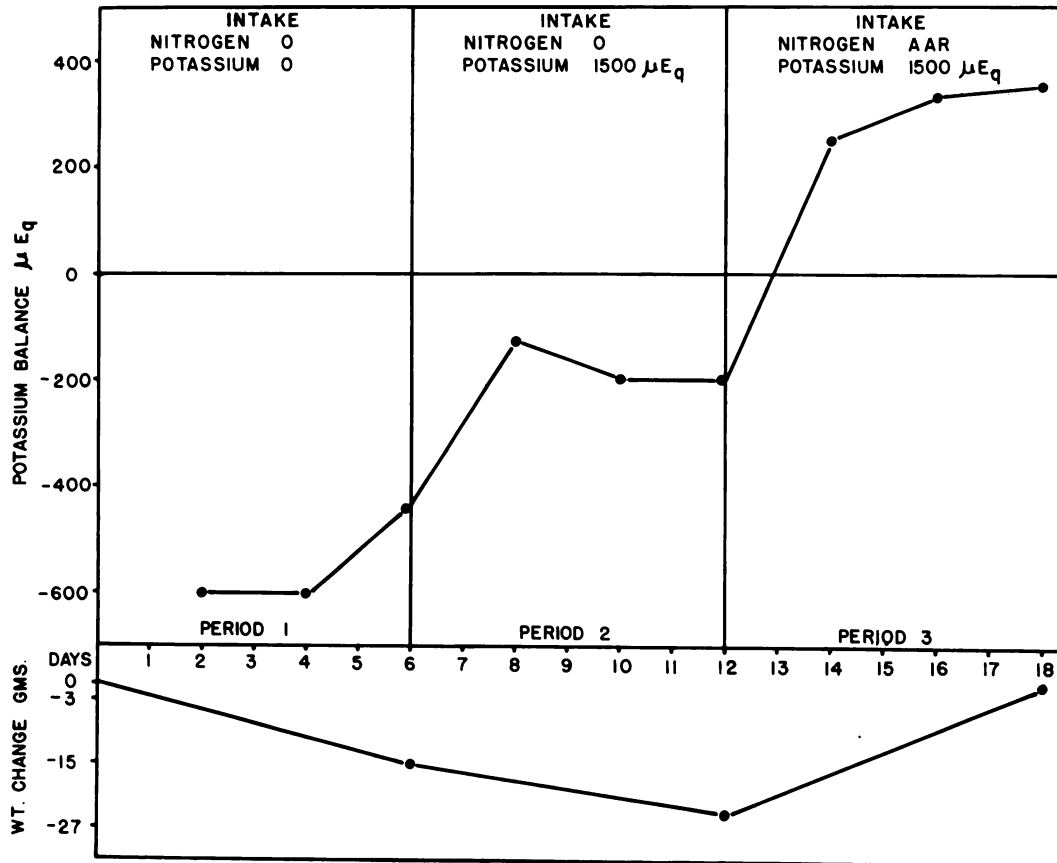


Fig. 2. Potassium balances and weight changes in normal rats with varying intakes of nitrogen and potassium.

whose weights ranged between 229 and 246 grams, were fed the test rations in three metabolic periods of six days each. Potassium balances were determined as before. These animals were fed rations 3 and 4, of higher fat content than ration 1, in order to minimize "food-scattering." Ration 4 was used only because ration 3 contained too much fat for convenience in measuring diet intakes. Both rations, however, were isocaloric. In period 3 the amino acid ration 2 was fed.

The results (Fig. 2) demonstrate that in period 1 all animals receiving ration 3 remained in negative potassium balance and all lost weight. The injection of potassium chloride in period 2 again failed to induce positive potassium balances and the animals continued to lose weight. In period 3, however, when the amino acid ration 2 was fed while potassium was being administered, the animals all started

to gain weight and all went quickly into positive potassium balance.

### Experiment 3

In order to ensure as completely comparable conditions as possible with respect to food intake, five additional normal rats were subjected to forced feeding over four metabolic periods of four days each during which both nitrogen and potassium balances were determined. As a preliminary step each animal was accustomed gradually to the procedure, starting with intragastric feedings, twice daily, of 3 ml of ration 5 suspended in an equal quantity of distilled water, and increasing the amounts daily until, by the fifth day, all were receiving the amounts necessary to ensure ingestion of the complete ration during the metabolic studies. The results of the balance studies are shown in Figure 3.

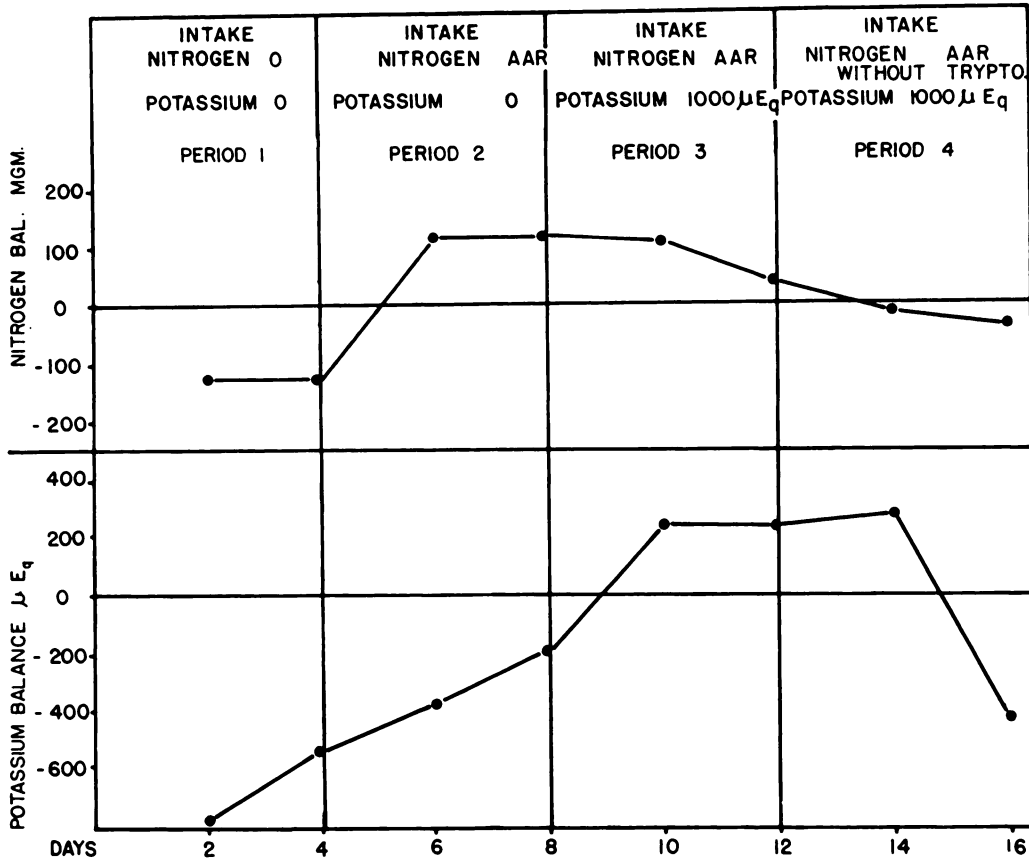


Fig. 3. Nitrogen and potassium balances in normal rats force-fed with varying intakes of nitrogen and potassium.

Thus, in period 1, with the animals receiving basal ration No. 5, devoid of potassium and nitrogen, all remained in both negative nitrogen and potassium balance. In period 2, when approximately 1.8 grams of amino acid mixture daily replaced an equal amount of dextrin in the ration, but in which potassium was still lacking, the animals went into positive nitrogen balance. The potassium balances, however, remained negative, although somewhat less so than in period 1. In period 3, during which 250 microequivalents of potassium were added to the ration, the animals remained in positive nitrogen balance and also went into positive potassium balance. Finally, in period 4, one essential amino acid (tryptophan) was omitted from the amino acid mixture in order to induce a catabolic state. All the animals went promptly into negative nitrogen balance, followed, after a two-day lag, by a negative potassium balance.

*Experiment 4*

In the final experiment, ten protein-depleted rats were fed test-rations 1 and 2 in four diet periods of six days each, with nitrogen and potassium balances being determined as before. The results are shown in Figure 4. The purpose of this experiment was to determine whether or not considerably larger intakes of potassium might have a greater influence upon the possible attainment of a positive potassium balance.

As can be seen in the chart, all animals receiving rations devoid of nitrogen and potassium in period 1 remained in negative nitrogen and potassium balance. This ration was continued throughout period 2, but with the animals being divided into two groups. Those in one group received a daily supplement to the ration of one milliequivalent of potassium; those in the other group received two and one half milliequivalents. All, however, continued

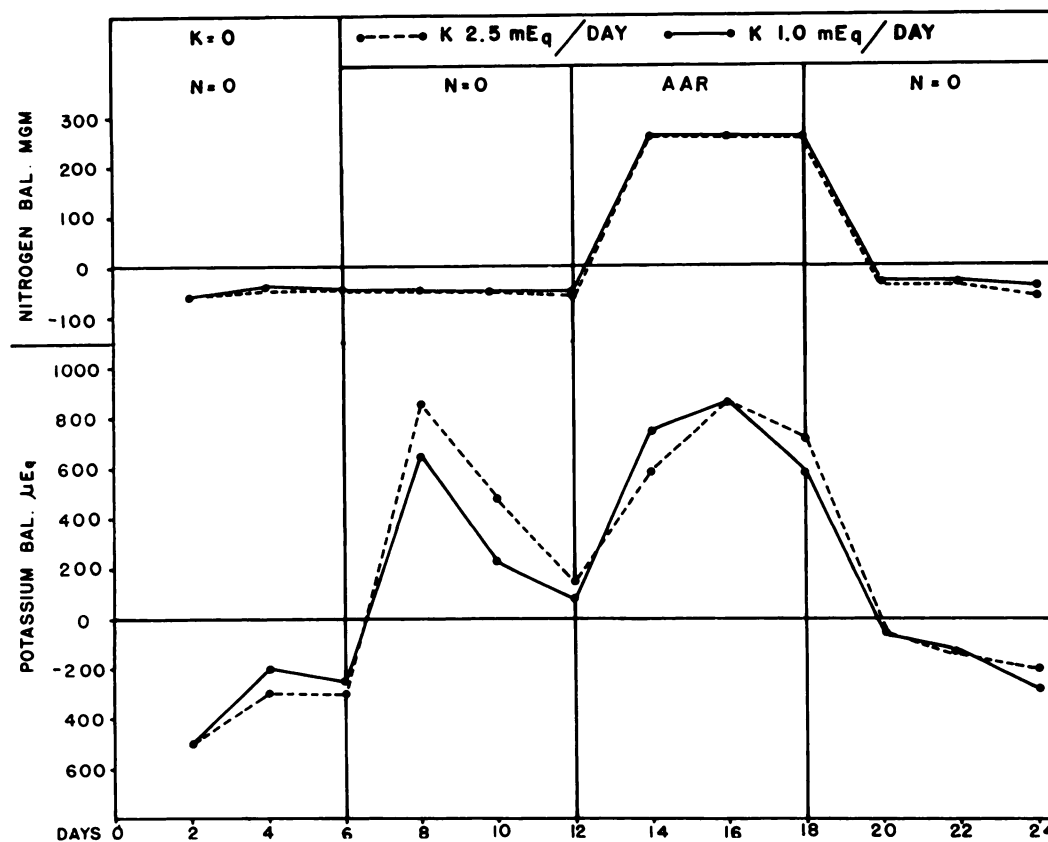


Fig. 4. Nitrogen and potassium balances in normal rats with varying intakes of nitrogen and with large intakes of potassium.

in negative nitrogen balance, but with the larger intakes of potassium, the potassium balances became positive on the second day, only to decrease progressively, approaching the zero line with the third collection sample. In period 3, when anabolism was established by feeding the amino acid ration 2, all animals gained weight, and both nitrogen and potassium balances became strongly positive, remaining so throughout the period. In period 4, when ration 1 devoid of nitrogen was again fed, but with the continuation of intakes of potassium chloride, the animals lost weight slowly and went into both negative nitrogen and potassium balance.

#### DISCUSSION

These experiments strengthen the point of view that the problem of correcting a potassium deficit is a more complicated one than can be solved simply by the administration of a

potassium salt. On the contrary, they indicate that the metabolic state of the tissues largely determines their ability to retain and to utilize potassium ion; they demonstrate, also, that for optimal nutritional replenishment of depleted tissues both nitrogen and potassium are essential, and in a definite relationship to one another. Elevation of the serum potassium level by the administration of potassium alone is not enough, presumably because of the fact that the loss of tissue mass, whether from starvation or as a result of catabolism in general, creates a tissue need for both nitrogen and potassium. Moreover, if tissue loss is actively proceeding as a consequence of a marked catabolic state, it is unlikely that potassium alone can be used effectively by tissue cells for purposes of cellular reconstruction. The basic nutritional problem in such a situation, therefore, would seem to be that of re-establishing an anabolic state. Once this



has been accomplished, potassium utilization by cells should quickly follow.

Unfortunately, in surgical patients conditions often exist which contribute to losses of potassium. These may include dehydration and inanition, as well as losses through renal and gastrointestinal routes. Randall and co-workers<sup>4</sup> have shown that such simple procedures as the administration of salt solution, or glucose and amino acid solutions, may initiate diuresis with a further loss of potassium from cells. Elman and associates<sup>5</sup> have also suggested that postoperative loss of potassium may result from hyperactivity of the adrenal cortex, due both to the excretion of potassium and the retention of sodium. Finally, although transitory retention of potassium may be accomplished in surgical patients even while they are in negative nitrogen balance, as has been shown by Howard and Carey,<sup>6</sup> our results (fourth experiment) indicate that even with comparatively large potassium intakes, but in the presence of a continuing negative nitrogen balance, potassium retention was at best transient, and became continuous only as the animals went into positive nitrogen balance.

#### SUMMARY AND CONCLUSIONS

Experiments were performed in normal and in protein-depleted adult rats, in an effort to determine the metabolic relationships between positive and negative nitrogen balances and the capacity of the tissues to retain dietary potassium. When the animals were fed synthetic rations devoid of both nitrogen and potassium, weight losses ensued and the potassium and nitrogen balances were negative. The administration of potassium chloride to such animals while they were eating a nitrogen-free ration failed to establish positive potassium balances or to promote weight-gains, whereas the addition to such rations of an appropriate amino acid mixture caused the

animals to go into positive nitrogen and potassium balances. Following the elimination of one essential amino acid (tryptophan) from such a mixture, however, the animals went quickly into negative nitrogen and potassium balance. Finally, the feeding of the complete amino acid ration devoid of potassium led to the development of a positive nitrogen balance but a continued negative potassium balance; and increasing the intake of potassium by as much as ten times the amount necessary for adequate repletion seemed to have only a transient effect in achieving a positive potassium balance during catabolism.

These experiments emphasize the importance of anabolism in relation to the overall utilization of dietary potassium. They suggest, also, that in the presence of a general catabolic state, tissue retention of dietary potassium is impaired, and that for optimal cellular utilization of potassium for purposes of tissue synthesis, the anabolic state is an essential requirement.

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