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A Comparison of the Effects of Cortisone and Deoxycorticosterone on Various Aspects of Organic and Inorganic Metabolism

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Since Hartman, Spoor & Lewis (1939) first demonstrated that adrenal cortical extracts contained at least two hormones, one of which they termed a 'sodium factor', it has been customary to divide adrenal cortical hormones into two functional groups: 'mineralo-corticoids' of which 11-deoxycorticosterone is considered a typical example, although it appears to have been isolated only once from the adrenal cortex (Reichstein & von Euw, 1938), and 'gluco-corticoids' such as the corticosterone group. It was considered that the deoxycorticosterone type of hormone had no appreciable action on carbohydrate metabolism or on glycogen deposition in the liver (Thorn, 1944; Kendall, 1941; Ingle, 1945; Olson, 1944; Grollman, 1947; Reinecke & Kendall, 1943; Olson, Thayer & Kopp, 1944), and that the gluco-corticoid hormones, e.g. cortisone, had no appreciable effect on mineral metabolism, and would be expected to have little or no influence on the inorganic levels of the blood plasma. Montigel & Verzá (1943) concluded that the difference in action on carbohydrate metabolism of these two groups of hormones is not qualitative, but rather one of velocity, deoxycorticosterone acting more slowly. Wang & Verzá (1949) showed that deoxycorticosterone is capable of restoring to normal the liver and muscle glycogen content of adrenalectomized rats and Sass-Kortsak, Wang & Verzá (1949) found that in long-term experiments the difference in action of deoxycorticosterone and cortisone in this respect is not marked. Similarly, Nissim (1952) has recently demonstrated the glycogenic effect of large doses of deoxycorticosterone acetate in adrenalectomized mice. Recent studies (Roberts & Pitts, 1952; Tait, Simpson & Grundy, 1952) have indicated the efficiency of cortisone in decreasing the renal excretion

of sodium in adrenalectomized animals. Much evidence has also appeared from the clinical side (Hartman & Brownell, 1949; Forsham *et al.* 1949; Perera, Pines, Hamilton & Vislocky, 1949; Sprague & Power, 1950; Sprague *et al.* 1950; Fourman *et al.* 1950), that the so-called gluco-corticoid hormones may in fact exhibit considerable effect on sodium retention and potassium excretion.

The present communication gives the results of a study of the comparative effect of the two representative hormones, cortisone and deoxycorticosterone, on the levels of various carbohydrate intermediates in the skeletal muscle of normal and adrenalectomized rats (Conway & Hingerty, 1946), on the sodium and potassium levels of the plasma and muscle, with low- and high-sodium diets, and on growth rate and nitrogen metabolism. Finally, some permeability studies were carried out with the hormones on frog muscle, using ^{24}Na and ^{42}K .

METHODS

Treatment of animals

Young albino rats of the Wistar strain about 6 weeks old and weighing about 80–90 g. were used; for the effects on growth rate and nitrogen metabolism only female rats were used. The rats were maintained for a few weeks before and throughout the experimental period on a diet of the following composition: oatmeal, 44.4; oat flour, 44.4; Bemax, 3.9; baker's yeast, 1.7; cod-liver oil, 5.6%. When the effects with a diet rich in Na were being examined, 12 g. NaCl/kg. was added to the basal diet.

Adrenalectomies were performed under ether-air anaesthesia in a single-stage operation, after which the animals were maintained at constant temperature. Cortisone and deoxycorticosterone were used in the form of cortisone acetate prepared by Merck & Co., Inc. and deoxycorticosterone acetate (DOCA) prepared by Organon

Laboratories. The hormones were injected intramuscularly at the same time each day, being administered as a single 2 or 2.5 mg. injection of the acetate, whilst adrenocorticotrophic hormone (ACTH) (Armour Laboratories) was given in two divided doses, one every 12 hr. An amount equivalent to 0.5 i.u. was injected twice daily in one series, and an amount equivalent to 1.0 i.u. was injected twice daily in a second series. Urine was collected at the same time each day from groups of 7 rats, in a metabolism cage, in flasks containing thymol and citric acid as preservatives. The total daily volume was measured and made up to 50 ml., from which samples were taken for the various analyses. In obtaining samples of blood and muscle the rats were stunned and bled directly into paraffined centrifuge tubes following which about 0.25 g. of fat-free muscle was removed into a weighed platinum crucible and dried overnight at 105° to obtain the water content. The muscle was ashed for Na and K determinations. In estimating the phosphate compounds in muscle, about 1 g. of the tissue was removed immediately into ice-cold trichloroacetic acid.

Chemical methods

The Barclay flame photometer with internal lithium standard was used for the Na and K determinations. N and Cl were determined by microdiffusion methods (Conway, 1950) and blood glucose by a modification of the Folin & Malmros (1929) method. The various organic phosphate compounds in the muscle were estimated after fractionation of a trichloroacetic acid extract as previously described (Conway & Hingerty, 1946) with some modifications.

In the tracer experiments, frogs were injected with ⁴²K or ²⁴Na in sufficient radioactive strength to give easily determinable counts from the sartorii excised the following morning. Such sartorii were immersed with gentle shaking at 18° in a relatively large volume of Ringer fluid and the count curves, suitably corrected for decay, compared with similar curves obtained from frogs injected with cortisone in doses of up to 3.75 mg., administered in three separate injections of 1.25 mg. 24, 18 and 6 hr. before removing the muscles.

RESULTS

Effects on the phosphate distribution in muscle of normal and adrenalectomized rats

The following determinations were made: total phosphate (TP), acid-soluble phosphate (ASP), residual phosphate (RP; TP-ASP), phosphocreatine (PC), adenosine triphosphate (ATP), glucose 6-phosphate (G 6-P), glucose 1-phosphate (G 1-P) and fructose 6-phosphate (F 6-P). The experiments were carried out on normal and adrenalectomized rats, untreated and injected with cortisone or deoxycorticosterone.

The average results (each figure being obtained from 7-11 experiments) are shown in Table 1, together with the mean differences and probability values.

It will be seen that treating normal rats with deoxycorticosterone or cortisone has no significant effect on the various substances examined. Adrenalectomy causes a very marked fall in glucose

Table 1. *Changes in phosphorylated compounds in skeletal muscles of normal and adrenalectomized rats*

(Cortisone or deoxycorticosterone given as five daily injections of 2.5 mg. All values are m-moles P/kg. muscle. P values given in brackets after mean differences.)							
	ASP	RP	PC	ATP	G 6-P	G 1-P	F 6-P
Normal	55.6	25.2	25.2	19.5	4.48	2.61	0.95
Change after adrenalectomy	-0.8 (0.70)	+0.9 (0.17)	+3.4 (0.06)	+1.2 (0.06)	-4.1 (0.01)	+0.27 (0.45)	-0.73 (<0.01)
Change after cortisone injection	-1.4 (0.86)	+0.8 (0.71)	-0.5 (0.57)	-0.7 (0.52)	-0.22 (0.70)	+0.53 (0.14)	-0.11 (0.14)
Change after deoxycorticosterone injection	-2.0 (0.83)	+4.9 (0.74)	+0.6 (0.40)	+0.3 (0.22)	-0.12 (0.56)	+0.20 (0.72)	-0.21 (0.11)
Adrenalectomized	54.8	26.1	28.6	20.7	0.77	2.88	0.22
Change after cortisone injection	-0.2 (0.80)	+1.2 (0.21)	-2.5 (0.28)	-1.2 (0.49)	+2.07 (<0.01)	-0.06 (0.44)	+0.28 (<0.01)
Change after deoxycorticosterone injection	-0.6 (0.64)	+1.5 (0.66)	-1.1 (0.88)	-0.5 (0.64)	+1.42 (0.11)	+0.30 (0.07)	+0.20 (0.01)

6-phosphate (to 16 % of normal level) and in fructose 6-phosphate (to 23 %); an increase in phosphocreatine, which is probably significant, also occurs. Although the phosphocreatine level is increased by only 13 %, this represents an absolute increase of 3.4 m-moles phosphorus/kg. as compared with an absolute fall in glucose 6-phosphate of 4.1 m-moles phosphorus/kg. This is in agreement with previous work (Conway & Hingerty, 1946). In addition there is an increase in the ATP level after adrenalectomy, which is probably significant.

38 %, respectively. Deoxycorticosterone, although qualitatively similar in action, is appreciably less effective, restoring glucose 6-phosphate and fructose 6-phosphate only 34 and 27 %, respectively.

Effects on the levels of potassium and sodium, in plasma and muscle, of normal and adrenalectomized rats

The results with high-Na and low-Na diets are shown in Figs. 1 and 2. Fig. 1 illustrates graphically the effects of cortisone and deoxycorticosterone injections (five daily injections of 2.5 mg.) on the Na and K levels of plasma and muscle for the normal rat with low-Na and high-Na intakes. Also shown in Fig. 1, are the effects of 20 daily injections of 2.5 mg. of cortisone and deoxycorticosterone with the high-Na diet. With low-Na intake both cortisone and deoxycorticosterone increase the

Fig. 1. Effects of cortisone (C) and deoxycorticosterone (D) injections on the K and Na levels in plasma and muscle of normal rats on low-Na and high-Na intakes. Ordinates: mean increase or decrease in concentration in m-moles/kg., compared with normal.

It therefore appears that two substances of major consequence containing labile energy-rich phosphate groups in muscle (ATP and phosphocreatine) are increased by adrenalectomy, while glucose 6-phosphate, the product of the phosphorylation of glucose by the hexokinase system, is greatly decreased. So also is fructose 6-phosphate. The question then arises as to how far the injection of cortisone or of deoxycorticosterone replaces the total loss of adrenal hormones in restoring these metabolites to the normal level. Cortisone in the dosage given restores the glucose 6-phosphate and fructose 6-phosphate levels 50 and

Fig. 2. Effects of adrenalectomy (A) and of subsequent cortisone (C) and deoxycorticosterone (D) injections on K and Na levels in plasma and muscle of adrenalectomized rats on low-Na and high-Na intakes.

plasma Na levels but the relative effect of cortisone is greater. With much Na in the diet the hormones have no appreciable effect on the plasma Na, even after 20 daily injections. With plasma K the effect of each hormone is to lower the level but the relative effects of the hormones when the diet is poor in Na is reversed when the Na content of the diet is high. The effects of the two hormones on muscle Na and muscle K are also conditioned by the Na intake. With a low-Na diet, cortisone markedly increases the level of muscle Na whereas deoxycorticosterone lowers it somewhat and the reverse applies when the diet is rich in Na. Finally with regard to the muscle

K, this is lowered by each hormone, the relative effects again being reversed on changing to the Na-rich diet.

Some effects on the muscle water also occur, but even on expressing the quantities per kg. dry matter the above relations are not significantly affected.

The different effects of cortisone and deoxycorticosterone, depending on the level of Na intake, illustrates very strikingly the intricate nature of the picture presented. In this respect the findings of Selye, Stone, Timiras & Schaffenburg (1949) and of Fourman & Kepler (1949) that the storage of sodium chloride in overdosage of deoxycorticosterone is dependent on conditioning by simultaneous sodium chloride administration are of interest. Similarly, Ransohoff *et al.* (1950) found that many of the metabolic and physiological effects of ACTH may be strikingly influenced by the Na intake.

The effects of cortisone and deoxycorticosterone on Na and K levels of muscle and plasma after adrenalectomy are shown in Fig. 2. The well-known effect of adrenalectomy in lowering plasma and muscle Na while increasing plasma and muscle K is shown, being much greater with the Na-poor diet than with the Na-rich diet. Both cortisone and deoxycorticosterone reverse the post-adrenalectomy changes, the relative effectiveness of the hormones being again dependent on the level of dietary Na. With low-Na intake, cortisone shows a much greater effect than deoxycorticosterone and with the dosage used the levels are markedly over-restored. In these experiments the daily urine volume and urinary excretion of Na, K and Cl were followed over a 5-day period and over a 20-day period, the results being compared with those from control animals. Taking the first few days' results in the present series as least affected by variations in dietary intake, they confirm what might be deduced from the blood picture with regard to the action of the hormones on the retention or release of K.

Where a statistically significant effect has been observed, the changes in levels of K and Na in muscle and plasma have been recorded in Table 2

simply as + and - signs, representing increases or decreases compared with the normal values. Also included are the effects of a prolonged K-free diet and of the return to a high K diet (Conway & Hingerty, 1948).

From this it appears that there exists a constant relationship between the changes in plasma K and muscle Na, any alteration in plasma K level, however brought about, being accompanied by a change in muscle Na in the reverse sense. In the four groups in which there was a considerable fall in the plasma K (over 30%, indicated by - -) there was a considerable rise (indicated by + +) in the muscle Na. From a consideration of such facts it would appear that the plasma changes which take place in adrenal insufficiency or following hormone administration could of themselves bring about the muscle changes.

It may be noted that the largest changes in muscle Na, such as those occurring after deoxycorticosterone injections into normal rats on a high-Na diet, can occur without any change in the plasma Na.

Effects on muscle-water content

The effects of five daily 2.5 mg. injections of cortisone or deoxycorticosterone on the muscle-water content of normal and adrenalectomized rats on low-Na and high-Na intakes were investigated. The results are shown in Table 3 from which it appears that: (a) on the high-Na diet the water content of muscle from normal rats is higher than in muscle from animals on the low-Na diet. (b) Adrenalectomy raises the water content of muscle both on low-Na and on high-Na diets, the effect being more marked on the low-Na diet. (c) On the low-Na diet both cortisone and deoxycorticosterone are effective in reducing the water content of muscles of adrenalectomized rats, cortisone being more effective in this respect. (d) On the high-Na diet cortisone reduces the water content of muscle from adrenalectomized rats but deoxycorticosterone is ineffective.

The greater efficacy of cortisone in reducing the muscle water may be related to the findings of

Table 2. *Sodium and potassium changes in plasma and muscle under various conditions*

(+ and - signs indicate statistically significant changes compared with normal level; + + and - - indicate changes of 30% or greater; 0 indicates no significant change.)

Diet	Conditions	Plasma		Muscle	
		Na	K	Na	K
Low-Na	Adrenalectomy	-	+	-	+
Low-Na	Adrenalectomy + cortisone	+	-	+	-
High-Na	Adrenalectomy	-	+	-	+
High-Na	Adrenalectomy + deoxycorticosterone	0	- -	+ +	-
Low-Na	Cortisone injections into normal rat	+	- -	+ +	-
High-Na	Deoxycorticosterone injections into normal rat	0	- -	+ +	-
K-free		0	- -	+ +	-
K-free followed by K-rich		0	+	-	+

Table 3. *Changes in water content of rat muscle following adrenalectomy and injections of cortisone or deoxycorticosterone into normal and adrenalectomized rats on low-Na and high-Na diets*

(Five daily 2.5 mg. injections of cortisone or deoxycorticosterone. All values given as g. water/100 g. muscle. *P* values in brackets.)

	Low-Na diet	High-Na diet
Normal	75.87	77.01
Change after adrenalectomy	+1.81 (0.01)	+0.58 (0.20)
Change after cortisone injections	+0.90 (0.67)	-1.33 (0.12)
Change after deoxycorticosterone injections	+0.27 (0.71)	-0.17 (0.85)
Adrenalectomized	77.68	77.59
Change after cortisone injections	-2.15 (<0.01)	-2.34 (<0.01)
Change after deoxycorticosterone injections	-1.54 (<0.01)	+0.35 (0.53)

Eversole, Gaunt & Kendall (1942) who found cortisone to be at least 3 times as effective as deoxycorticosterone in protecting adrenalectomized rats against water intoxication.

Effects of cortisone, deoxycorticosterone and ACTH injections on the growth rates of young rats

Fig. 3 summarizes the effects of the injections on body weight for both normal and adrenalectomized rats, over a 5-day period, each point being the mean

Fig. 3. Effects of cortisone and deoxycorticosterone injections on growth rates of normal and adrenalectomized young rats and of ACTH on growth rate of normal young rats.

for seven rats. It will be seen that in the normal rats both deoxycorticosterone and ACTH increase the rate of growth but cortisone markedly decreases it. After adrenalectomy the cortisone-treated rats tend to a small decrease in weight (the untreated animals show practically no change) but the decrease is much less than in the normal rats. The injection of deoxycorticosterone into the adrenal-

ectomized rats enables them to maintain a practically normal weight increase.

Fig. 4 shows the effects on weight over a much longer period, each point being the average for seven rats. The very pronounced effect of cortisone in decreasing the weight is manifest, the result being strikingly different from that of deoxycorticosterone.

Fig. 4. Effects of cortisone (·) and deoxycorticosterone (○) injections on weight changes in normal young rats; each animal received 2 mg. of the hormone/day for 20 days. Each point represents seven rats.

Fig. 5. Effects of cortisone (·) and deoxycorticosterone (○) injections on urinary N excretion in normal young rats; each animal received 2 mg. of the hormone/day for 20 days. Each point represents seven rats.

Effects on nitrogen excretion

The effects of cortisone and deoxycorticosterone injections on the urinary nitrogen excretion were studied on the group of rats used in Fig. 4, the results being expressed as mg. nitrogen/100 g. body wt./day. The results, which are given in Fig. 5, where each point is likewise the average for seven rats, show the great effect of cortisone in increasing the nitrogen excretion.

Effects of cortisone on the permeability of frog sartorius muscle to sodium and potassium ions

Preliminary studies on the effects of cortisone on the permeability of the frog sartorius were carried out, the relative entry and exit rates of Na and K into and out of the fibres being measured for normal and cortisone-injected frogs. The problem of measuring the relative entry and exit rates was simplified by the use of the radioactive isotopes

Fig. 6. Exit rates of ^{42}K from muscle of normal (·) and cortisone-injected (○) frogs into Ringer solution. Room temperature.

^{24}Na and ^{42}K . In measuring the entry rates of these ions, sartorii from normal and from cortisone-injected groups of frogs were immersed in Ringer solution containing the isotope and the radioactivity of the muscle (expressed as counts/g./min.) measured at short intervals. The results indicated that under the experimental conditions cortisone had no appreciable effect on the entry rates of these ions or on the exit rate into Ringer solution at room temperature. Fig. 6 illustrates a typical experiment with ^{42}K .

DISCUSSION

Phosphate esters of rat muscle

After adrenalectomy cortisone may (depending on the Na intake) be more effective than deoxycorticosterone in restoring the Na and K levels of plasma and muscle; similarly, deoxycorticosterone can act like cortisone in restoring the level of the hexose phosphates and of phosphocreatine and ATP, and in some degree the level of the fasting blood glucose (Harrison & Harrison, 1939). It appears that the classification into mineralo- and gluco-corticoids, as with cortisone and deoxycorticosterone is misleading. It is a question rather of dosage to produce

equal effects and the proportions of the hormones required vary with the conditions and probably differ somewhat with each species.

On the other hand, the effect of cortisone on nitrogen metabolism and growth rate of young rats seems a practically qualitative difference compared with that of deoxycorticosterone, suggesting a unique effect of cortisone and related hormones in suppressing protein synthesis (Clark, 1950; Albright, 1943).

The marked reduction in the level of glucose 6-phosphate after adrenalectomy is related either to a less rapid formation or a more rapid disappearance. With a more rapid disappearance one would expect a marked increase of carbohydrate metabolism; in this respect it may be noted that Ingle & Nezamis (1948) have shown an increased rate of glucose utilization after adrenalectomy. With a slower formation after adrenalectomy it would seem as if, under the conditions examined, the effect is on the hexokinase system and both cortisone and deoxycorticosterone would appear as activators, cortisone being more effective than deoxycorticosterone. This is in contrast to results obtained by Colowick, Cori & Slein (1947) and by Krahle & Cori (1947) who have demonstrated by *in vitro* experiments that the hexokinase activity of muscles of diabetic rats can be inhibited by adrenal cortex extract and that the amelioration of diabetes by adrenalectomy is paralleled by a return of the glucose utilization of the diaphragm to normal.

The level of fructose 6-phosphate is also decreased after adrenalectomy but to a slightly lesser extent, the F 6-P/G 6-P ratio being 0.19 for the normal rat muscle and 0.29 for the adrenalectomized rat muscle; corresponding ratios for adrenalectomized rats treated with cortisone and deoxycorticosterone are 0.17 and 0.19, respectively. These values are somewhat low when compared with that obtained for phosphohexoseisomerase *in vitro* (0.35), possibly due to simultaneous utilization of F 6-P by phosphohexokinase and formation of G 6-P from glycogen and/or glucose.

While the hexose phosphate levels are much decreased, phosphocreatine and ATP are increased by adrenalectomy. The increase may be taken as statistically significant but relatively small compared with the total amounts present.

Sodium and potassium levels of rat muscle

From the results summarized in Table 2 it appears that such changes are secondary, or very largely secondary, to those of the plasma. When the plasma K falls, there is a secondary marked increase in the muscle Na, for which the following reason may be given. The fall of plasma K induces an increase in the membrane potential across the muscle fibre membrane and if this potential is already poised at

or near its maximum (Conway, 1947) a compensatory change of permeability may well occur with a net entrance of Na ions.

Renal effects. In turn the plasma changes themselves after deoxycorticosterone and cortisone injections arise from effects on the renal functions. This dependence of the tissue and plasma changes on the renal effects has previously been noted by Elkinton & Winkler (1944) and by Winkler, Smith & Hoff (1942) who found that deoxycorticosterone was without effect on the K metabolism of dogs following ligation of the ureters.

If the renal function with respect to Na and K is taken, in accordance with current views, as being reducible to an approximately constant filtration rate at the glomeruli combined with an approximately constant reabsorption rate of Na and of K, then the blood levels will depend on these two processes of filtration and reabsorption. If, for illustration, it be supposed that the reabsorption of K is inhibited by deoxycorticosterone, then deoxycorticosterone will cause a fall of plasma K, which in fact it does and especially with adequate Na intake. The effect on the K absorption under the circumstances (high-Na intake) need not appreciably affect the Na absorption, nor does the plasma Na level alter even after 20 days of deoxycorticosterone treatment, when at the same time the K level is greatly lessened.

After adrenalectomy the normal inhibition of K absorption produced by the cortical steroids is removed and the K level in the plasma markedly increases (cf. Harrison & Darrow, 1939). In turn it may be supposed that this back absorption of K inhibits the back absorption of Na, when the latter is low at the site (e.g. following low-Na intake), possibly by displacing Na from the absorption complex or mechanism. This assumption would serve at least to limit the number of hypothetical processes and receives support from the experiments of Miller (1922, 1926), Hoffman & Post (1933), Harrop (1936) and Kepler *et al.* (1948), who studied the relationships of Na and K intake in the diet to their retention and excretion.

On the other hand, if the diet is rich in Na the high concentration of Na resulting in the tubule lumen, at least below the level of the proximal convoluted tubule, may not only overcome the inhibition produced by this back absorption of K but in turn effectively inhibit it (Harrop, 1936; Wallace, 1948). Adrenalectomy should then produce but little effect on the K and Na levels of the plasma, and this is what in fact happens. Also it is a well-known fact that a high-Na intake can largely replace the action of the adrenal hormones on the cation pattern. Such a view as given above has the merit of correlating a number of leading facts.

The active transport of K^+ or Na^+ by the renal cells may be explained by the 'redox-pump' mechanism (Conway, 1951, 1952*a-c*), and the following paper deals with effects of the hormones on such a mechanism in yeast. It may be added that effects on membrane permeability to the free ions may well have a place. In the present paper permeability experiments were carried out on the isolated frog sartorius muscle using labelled ions but without any positive result. Since, as shown above, the Na and K effects on muscle are of a secondary kind, this is not surprising.

SUMMARY

1. Adrenalectomy causes a fall in the level of hexose phosphates and a rise in phosphocreatine and adenosine triphosphate of rat muscle. The hexose phosphate levels are restored towards normal by cortisone and by deoxycorticosterone, cortisone being more effective. Neither hormone has any effect on the levels of these substances in normal rats.

2. On a low-sodium intake both cortisone and deoxycorticosterone increase the plasma sodium and decrease the plasma potassium levels of normal rats, cortisone showing the greater effect. In a high-sodium intake neither hormone has any appreciable effect on the plasma sodium, even after a 20-day period of injection but both hormones lower the plasma potassium level and here deoxycorticosterone has a greater effect.

3. In adrenalectomized rats both hormones are effective in reversing the changes in plasma and muscle sodium and potassium; here again the relative effectiveness of the two hormones is dependent on the dietary sodium, cortisone being more effective with low-sodium intake. The muscle changes appear to be secondary, or largely secondary, to the plasma changes.

4. Cortisone is more effective than deoxycorticosterone in reducing the increased muscle-water content occurring after adrenalectomy.

5. Cortisone and deoxycorticosterone have opposite effects on the weight changes of normal and adrenalectomized rats, cortisone causing a marked decrease which is probably related to its effect in increasing urinary nitrogen excretion.

6. No apparent effect of either hormone on the permeability of frog sartorius muscle to ^{24}Na or ^{42}K was seen.

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