TABLE II. Distribution of Radioactivity in Tissues of Mammary Tumor Mice Following Administration of Radioiodinated Tetracycline.

Mouse No.	Tissue	Specific activity, cpm/mg wet tissue	μg of tetracycline/g
1*	Liver	.91	
	Femur	.98	
	Tumor	1.19	
2†	Liver	.052	§
	Femur	.161	8.95
	Tumor	.062	§
3‡	Liver	.05	§
	Femur	.16	5.81
	Tumor	.09	1.4
4*	Liver	.26	
	Femur	.08	
	Tumor	.63	
5*	Liver	.12	
	Femur	.06	
	Tumor	.08	
6*	Liver	.009	
	Femur	.03	
	Tumor	.19	
7*	Liver	.83	§
(4 inj.)	Femur	.39	3.55
	Tumor	.095	§
Control* (avg of 4 mice)	Liver	.012	
	Femur	.020	
	Tumor	.027	

* Sacrificed 24 hr after last inj. † Sacrificed 48 hr after last inj. ‡ Sacrificed 72 hr after last inj. § Not detectable.

low specific activity, which in most instances is of questionable significance.

Table II indicates that mouse tumor contained a higher specific activity than did mouse femur or liver. Muscle from mice showed a low specific activity. Control animals flushed out most of the NaI^{131} within 24 hours.

These data indicate that the radioactive product is a labeled tetracycline or degradation product and that it is inactivated by liver, since considerable radioactivity was measured in liver specimens, but in no case was antibiotic activity demonstrated. In some animals thyroid became radioactive, suggesting that the product was contaminated with NaI^{131}. This was partly alleviated by giving the product in a solution of nonradioactive sodium iodide and giving animals sodium iodide in drinking water thus blocking the thyroid.

These studies indicate a possible new irradiation tool for detection and treatment of tumors. Bone tumors may offer greatest possibilities in utilizing this new tool.

Summary. Attempts to radioactivate tetracycline by iodination reaction have evolved a product which resembles tetracyclines when injected into rats and mice. It is sequestered in general by fast-growing tissues and in particular by tumor, liver and epiphyseal plate region of bone. Liver appears to inactivate and excrete the material.

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Comparison of Effect of Desoxycorticosterone Acetate and Cortisone Acetate on Rat Skeletal Muscle Electrolytes. (25710)

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Recently in a study of differences between hypertensive actions of 2 adrenal steroids, desoxycorticosterone acetate (DCA) and cortisone acetate, the electrolyte composition of eviscerated carcasses of rats injected with one or another of these hormones was determined (1). In animals given the former steroid, while maintained on high sodium intake, an impressive retention of sodium and marked depletion of potassium were noted, findings consistent with previous reports of effects of this compound on skeletal muscle(2,3). In rats injected with cortisone, regardless of sodium content of diet, a severe potassium de-

TABLE I. Allocation of Animals, Experimental Regimen, Duration of Observation, Terminal Blood Pressure Readings, and Body Weights at Sacrifice.

Group	Sodium intake	Adrenals	Steroids, mg/day	Duration exp., days	No.	Terminal B.P., mm Hg	Terminal Body wt, g
I	High	Excised	DCA 2.5*	21	8	189 ± 10	181 ± 14
II	"	"	Cort. Ac. 2.5†	21	7	195 ± 2	121 ± 12
III	"	"	nil	21	6	132 ± 12	166 ± 15
IV	"	Intact	"	21	6	149 ± 10	159 ± 9
V	Low	Excised	DCA 2.5	14	8	137 ± 6	150 ± 11
VI	"	"	Cort. Ac. 2.5	14	7	195 ± 17	105 ± 5
VII	"	"	nil	4 to 7	7	87‡	104 ± 9
VIII	"	Intact	"	14	6	150 ± 9	150 ± 16

* Desoxycorticosterone acetate kindly supplied by Dr. Kenneth Thompson of Organon, Nutley, N. J.

† Cortisone acetate kindly supplied by Merck & Co.

‡ B.P. obtainable prior to sacrifice in only 1 rat in group. Remaining 6 rats were moribund.

pletion was also observed, though surprisingly not accompanied by any change in sodium, all measurements expressed in terms of fat free dry tissue. However, rats receiving cortisone while on a liberal sodium intake failed to grow, while animals given this steroid while on restricted sodium intake lost as much as a quarter of initial body weight. In contrast, rats receiving DCA gained, as did normal controls, roughly a third as much as their initial weight during same time interval. Inhibiting effect of cortisone on growth was so striking and so different from DCA that it seemed possible that electrolyte disturbances in cortisone groups were a reflection of this growth suppression rather than representing a true shift in electrolyte content of cells. This study therefore focused on analysis of a single tissue from these same animals, skeletal muscle, as opposed to whole carcass. It was hoped that this would permit a more precise comparison between the 2 steroids, though admittedly a more limited one.

Methods. Details of procedures have been described(1). Table I outlines the 8 groups of rats, number in each group, regimens employed, duration of observation, terminal blood pressure recordings and body weights. At sacrifice the right gastrocnemius muscle was removed, animals eviscerated and muscles and carcass saved for analysis as reported previously. The muscles were kept in frozen state until analyzed. Determination of water content was based on weight differences after 48 hours of desiccation in oven at 100-110°F. After desiccation, muscle fat was extracted with ethyl ether in a Soxhlet apparatus. The tissue was then digested with 3 ml of concentrated nitric acid, the digest diluted to 100 ml in volumetric flask containing 1:200 parts of lithium, and sodium and potassium determined by flame photometry.

Results, with standard deviations, are presented in Table II.*

Water content. Muscles from rats injected with cortisone contained significantly less water than muscles from any other group, while those from adrenalectomized rats on sodium restriction (Group VII) contained excess amounts of water.

Amount of fat was so small that comparisons between groups seem of little import. However, muscles of cortisone injected rats on a liberal sodium intake contained the largest amount of fat.

Sodium content. In spite of normal water content, muscles of sodium loaded DCA rats contained more than twice as much sodium as did muscles from other groups. Restriction of sodium intake prevented influx of excess quantities of this cation into muscles of DCA treated rats of Group V. A significant reduction in muscle sodium occurred in sodium depleted adrenalectomized controls. No variance from normal was noted in muscles from either cortisone injected group.

Potassium content. Muscles of sodium loaded DCA rats sustained a highly significant decrease in potassium content to 75% of values obtained in muscles of control ani-

* We are indebted to Dr. Agnes Berger and Miss Helen Perlstein, School of Public Health and Administrative Med., for statistical examination of the data.

TABLE II. Rat Muscle Analysis.

Group	High sodium regimen	Water, %*	Fat, % dry wt	Na^+ meq/100 g FFDT†	K^+ meq/100 g FFDT†
I	DCA + ADRX	74.2 ± .7	4.0 ± 1.0	17.1 ± .9	33.1 ± 1.3
II	Cort. Ac. + ADRX	72.0 ± 1.9	6.7 ± 1.7	8.2 ± .7	42.1 ± 1.9
III	ADRX	74.6 ± 1.6	3.0 ± 1.0	8.3 ± .7	43.8 ± 1.5
IV	Intact controls	74.4 ± .8	1.0 ± .4	8.2 ± .2	44.3 ± .1
	Low sodium regimen				
V	DCA + ADRX	74.8 ± .8		8.4 ± .3	44.8 ± .8
VI	Cort. Ac. + ADRX	72.3 ± 1.1	1.8 ± 1.5	7.6 ± .6	42.8 ± .8
VII	ADRX	76.4 ± .5	1.6 ± 2.0	6.4 ± .5	45.7 ± .9
VIII	Intact controls	74.7 ± .5	3.1 ± 1.4	7.9 ± .5	44.0 ± 1.1

* For each category of measurements, treatment differences were jointly estimated by 95% simultaneous confidence interval following Tukey(6). (This amounts to listing individual treatment differences more strictly than at 5% level.) Values for water, fat, Na^+ and K^+ differing significantly from intact controls on the same regimen are underlined; those of borderline significance are underscored with a broken line.

† FFDT = fat-free dry tissue.

mals. Restriction of sodium intake, as in the DCA injected Group V, prevented development of this abnormality. Muscles from cortisone rats provided with high sodium intake exhibited a lower average potassium concentration of borderline significance. The slight decrease in potassium values in cortisone rats on low sodium did not prove significant on statistical analysis. It seemed possible that these slight changes in potassium were a reflection of dehydration of these muscles; and indeed when potassium was expressed in terms of fat free wet weight rather than dry weight, the content of this cation was normal (112 meq/kg for Group II *vs.* 112 meq/kg for Group IV).

Discussion. That muscles of hypertensive adrenalectomized rats, on regimen of large daily injections of DCA and liberal sodium intake, sustained marked depletion in potassium along with increase in sodium is quite in keeping with similar changes encountered in analyses of eviscerated carcasses of such animals(1), and confirmatory of many previous studies on effect of the steroid on skeletal muscle.

That muscles of hypertensive adrenalectomized rats, on a regimen of large daily injections of cortisone and either low or high sodium intake, contained normal amounts of sodium is in keeping with previously reported analyses of carcasses of such animals. However, values for potassium in muscle, while showing changes in the same direction as in whole carcass, were by no means as impressively reduced. The more strikingly lowered potassium/unit of fat free dry weight in the carcass could be explained if weight losses induced by cortisone involved greater losses from potassium rich tissues such as muscle, than from potassium poor tissues such as skin. This possibility cannot be confirmed by present data, though the observation that normal rats in which intake is restricted to achieve same weight reduction do not show this depletion(4), suggests that the change is not the result of weight loss *per se*. Dehydration of cortisone rats could also contribute to previously noted low carcass potassium. As mentioned above, when muscle data were expressed in terms of fat free wet tissue potassium depletion was no longer evident. When carcass potassium values are similarly expressed in terms of wet weight, depletion of this electrolyte becomes far less impressive, is no longer demonstrable in the group on a restricted sodium intake.

It seems probable that both of above considerations contributed to the low value for potassium obtained in carcasses of cortisone injected rats, neither one necessarily implying reduction in amount of potassium/cell unit. Using the ratio of amount of potassium to nitrogen as a very rough indicator of this last mentioned variable, the figures listed in Table III were computed from previously reported analyses of whole carcass. (In earlier experiments(5), similarly prepared animals given

TABLE III. Carcass Analyses. Additional calculations.

	Sodium	Chloride	
	meq/kg fat-free wet tissue		Potassium, meq/g N*
High sodium regimen			
DCA + ADRX	56.8	30.4	1.88 ± .11
Cortisone + ADRX	56.4	36.2	2.13 ± .17
ADRX	46.5	34.0	2.39 ± .17
Intact controls	50.4	33.5	2.29 ± .07
Low sodium regimen			
DCA + ADRX	43.3	31.2	2.41 ± .28
Cortisone + ADRX	46.5	26.5	2.21 ± .31
ADRX	38.0	27.2	2.31 ± .04
Intact controls	38.1	28.0	2.30 ± .20

* See footnote to Table II for methods of statistical analysis.

DCA or cortisone acetate have not shown any alteration in serum urea nitrogen values which might disturb this ratio.) In neither cortisone injected group was the ratio significantly reduced; by comparison the decrease in this value in sodium loaded DCA injected rats of Group I was striking and qualitatively different.

Muscle content of sodium in cortisone treated rats was normal, whether this electrolyte was calculated in terms of dry or wet tissue. However, if figures for sodium in total carcass are expressed in terms of wet weight, the value for this cation now appears definitely elevated (Table III). Since skeletal muscle did not participate in this sodium increase, a possible explanation is that cortisone injected rats lost more weight from those tissues high in potassium than from tissues high in sodium.

It appears that selection of a single tissue, skeletal muscle, to study electrolyte effects of cortisone *vs.* DCA has the advantage of reducing the number of variables which must be taken into account in interpreting the analysis. In this single tissue, cortisone in amounts sufficient to produce severe hypertension in adrenalectomized rats, unlike the steroid DCA, was without effect upon electrolyte composition of muscle when dehydration of tissue was taken into account. These findings provide still further evidence of the different nature of hypertension induced by cortisone from that induced by DCA in the rat.

Summary. 1. Analyses of skeletal muscle from adrenalectomized rats given cortisone acetate in amounts sufficient to induce severe hypertension revealed no impressive alteration in sodium or potassium content from normal, when dehydration of tissue was taken into account. 2. In contrast, skeletal muscle from adrenalectomized rats given comparable amounts of DCA and with comparable degrees of hypertension, showed, as anticipated, marked increase in sodium and reduction in potassium content. 3. In rats injected with cortisone, blood pressure and muscle electrolytes were comparable in groups maintained on a low sodium diet and in groups with liberal sodium intake. In contrast, in rats given DCA, both hypertension and shift in electrolyte content were dependent on high sodium intake; neither was encountered when sodium content of the diet was restricted. 4. Muscles from adrenalectomized rats without steroid subsidy were normal in all respects in groups provided with liberal amounts of sodium but were overhydrated and depleted of sodium in the group sustaining sodium restriction.

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