calculations and which should be of importance in the experimental and clinical use of pellets. Theoretical considerations indicate that the absorption rate may have decreased rapidly after 90 per cent. absorption had occurred.

Within a week after implantation each pellet became closely invested with a thin, non-adherent tissue capsule. Histologically, the capsules consisted of circumferentially and compactly arranged connective tissue cells and fibers. The capsules were of fairly uniform structure but varied in thickness roughly according to their age. In a few instances, perhaps as a result of local infection, the capsules were markedly thickened and vascular; in these cases the absorption rate showed after the first 10 days either moderate increase or a moderate decrease.

Stilbestrol invariably caused losses in body weight; such losses ranged from 0.3 to 3.6 gm (average) for each day the pellet was *in situ*. Weight losses occurred in some but not all of the other rats.

The results of additional observations, now in progress, on the relative absorption rates of several other steroid hormones indicate that estrone and alpha-estradiol show relatively very slow absorption and that, like testosterone propionate (see above), esterified alpha-estradiol and desoxycorticosterone are absorbed more slowly than the corresponding free forms.

T. R. FORBES

DEPARTMENT OF ANATOMY,
JOHNS HOPKINS UNIVERSITY

ANTAGONISTIC ADRENAL AND PITUITARY EFFECTS ON BODY SALTS AND WATER*

IN a number of papers published during the past four years we have described important related effects on electrolyte and fluid balance brought about through adrenal and hypophyseal activities.[1,2,3,4,5,6] In 1938 it was shown that a hormone contained in our cortico-adrenal extracts acted as a diuretic agent and antagonized the anti-diuretic hormone of the posterior lobe of the pituitary.[4,5] The conditions proposed by Smith[7] for a diuretic factor were shown in our experiments to be fulfilled in every respect by the cortico-adrenal hormone.[4] Recently we have extended our experiments and tested the more specific adrenal substance, desoxycorticosterone, in its possible relationship to water intake and urinary chloride and fluid output under different conditions. Some experiences with this crystalline factor reported recently by other workers[8,9] confirm our earlier results obtained with whole extracts of the adrenal cortex.

Observations have been made in the present experiments on normal, adrenalectomized and hypophysectomized rats, amplifying our previous work on opossums. Operated animals were allowed several days for recovery before metabolism tests were run, and then studied at intervals for periods up to 30 days (adrenalectomized rats) and 80 days (hypophysectomized animals) after operation. Two to four "rest" days were given between runs. Adrenalectomized animals were occasionally given weak saline and small amounts of cortico-adrenal extract on off-test days, sufficient to keep them in a state of chronic insufficiency; hypophysectomized rats also were observed in the chronic condition, *i.e.*, when showing only slight diabetes insipidus. The 12-hour tests were made with water allowed *ad. lib.*, usually without previous fasting; in a few series in which runs were carried out after a 6-hour fast, no significant differences were observed. Results and other experimental details are shown in Table 1.

TABLE 1

EFFECTS OF DESOXYCORTICOSTERONE† AND POST-PITUITARY EXTRACT‡ ON WATER INTAKE AND URINE AND CHLORIDE OUTPUT IN RATS UNDER DIFFERENT CONDITIONS

Experimental conditions	No. of cases	Water intake cc/100 gm rat	Urine cc/100 gm rat	Urinary chlorides mg/cc
Unoperated rats, no treatment	34	1.7	1.5	2.78
Unoperated rats, desoxycorticosterone-treated	12	2.9	1.9	1.50
Unoperated rats, post-pituitary extract	10	0.6	1.1	16.20
Adrenalectomized, untreated	10	3.4	2.1	3.30
Adrenalectomized, desoxycorticosterone-treated	11	7.8	5.0	1.11
Adrenalectomized, post-pituitary extract	6	0.9	1.3	8.25
Hypophysectomized, untreated	26	2.3	1.9	2.12
Hypophysectomized, desoxycorticosterone-treated	52	5.9	5.2	0.38
Hypophysectomized, post-pituitary extract	10	0.8	1.7	6.40
Hypophysectomized, desoxycorticosterone and post-pituitary extract	12	1.9	1.9	6.09

† Desoxycorticosterone acetate ("Cortate"), kindly supplied by the Schering Corporation.
‡ Post-pituitary extract ("Solution," U.S.P.), kindly supplied by Squibb and Sons.
Metabolism tests in each case extended over 12 hours. Small doses of the above preparations were administered every two hours.

It is clear at a glance that in all groups of animals, normal, adrenalectomized and hypophysectomized, the effects of desoxycorticosterone are of opposite sign to those of post-pituitary extract. Desoxycorticosterone invariably increased water intake and urine output,

* Aided by a grant from the National Research Council.

1 H. Silvette, *Am. Jour. Physiol.*, 117: 405, 1937.

2 H. Silvette and S. W. Britton, *Am. Jour. Physiol.*, 121: 528, 1938.

3 H. Silvette, *Proc. Am. Physiol. Soc.*, fiftieth annual meeting, Baltimore, 1938, p. 188.

4 H. Silvette and S. W. Britton, SCIENCE, 88: 150, 1938.

5 H. Silvette and S. W. Britton, *Am. Jour. Physiol.*, 123: 630, 1938.

6 E. L. Corey, H. Silvette and S. W. Britton, *Am. Jour. Physiol.*, 125: 644, 1939.

7 H. W. Smith, "The Physiology of the Kidney," New York, 1937, p. 229.

8 C. Ragan, *et al.*, *Am. Jour. Physiol.*, 131: 73, 1940.

9 M. Schweizer, *et al.*, *Am. Jour. Physiol.*, 132: 141, 1941.

and at the same time reduced urinary chlorides, both in concentration and total amount excreted. Entirely reversed effects were observed after post-pituitary extract administration. Further, when post-pituitary extract and desoxycorticosterone were injected together, the action of the former substance always appeared dominant. The increased chloride output in untreated adrenalectomized rats, and decreased output along with increased water intake and urine secretion in untreated hypophysectomized animals, may be noted. Young normal rats about 125 gms. in weight responded to desoxycorticosterone better than older animals.

To be emphasized also are the large increments in fluid exchange effected by desoxycorticosterone, and the marked increases in chloride elimination after post-pituitary injection. In the former case the changes in water intake and urine output approximated 100 per cent., and in the latter (chloride output) 100 to 500 per cent. in different series. Extraordinarily large amounts of chloride may thus be forced from the body through post-pituitary action.

The water-intake: urine-output ratios (W/U) were greatly reduced in all cases by post-pituitary extract —by 50, 55 and 70 per cent. in the 3 series. In contrast to the resultant deficits of water in pituitary-treated animals, there were apparently increases in body water in normal rats treated with desoxycorticosterone. Hematocrit readings were in keeping with these findings: in all cases tested in which desoxycorticosterone was given, the total cell volumes fell continuously over a period of 12 hours.

It appears clear from the results above, therefore, that the adrenal cortex and the post-pituitary tissues elaborate principles which specifically counteract each other in their effects on the kidney, and on salt and water balance in the body. In this connection one may recall that desoxycorticosterone has recently been found responsible for severe reactions (edema, hypertension) and some deaths in the clinic because of overdosage or cumulative action. Possible utilization in dangerous situations of the physiological antagonist to desoxycorticosterone, post-pituitary extract, should of course be kept in mind.

It may be observed that desoxycorticosterone does not exactly reproduce the effects that are brought about by cortico-adrenal extract. The action of the latter is much greater, particularly on carbohydrate levels in the body.[10] Moreover, there are surely other hormones besides those controlling body water to be found in whole cortico-adrenal extract and in post-pituitary preparations. The results herein show that the organism is intimately dependent on a balanced relationship between the adrenal and pituitary mechanisms for normal salt and water regulation in probably all body fluids and tissues.

S. W. BRITTON
E. L. COREY

PHYSIOLOGICAL LABORATORY,
UNIVERSITY OF VIRGINIA MEDICAL SCHOOL

[10] S. W. Britton and E. L. Corey, *Am. Jour. Physiol.*, 129: 316, 1940.

NUTRITIONAL FACTORS CONCERNED IN RUSTING OF ALBINO RATS

THERE have been several recent reports in the literature concerning the achromotrichia factor and the rusting factor which offer some differences in observations. Györgyi and his coworkers[1] report that graying of black or piebald animals and, presumably, rusting of albino animals when placed on a suitable diet can be prevented by addition of pantothenic acid to that diet. Dimick and Lepp[2] report that pantothenic acid decreases graying of fur. Unna[3] reports that with 80 μgm of pantothenic acid daily only fleeting signs of fur impairment were observed. Nielsen, Oleson and Elvehjem[4] have published a procedure for the separation of a substance which is not pantothenic acid but which prevents nutritional achromotrichia. Williams[5] has found that nutritional achromotrichia could not be cured by pantothenic acid when butter fat was omitted from the diet.

We have noted the occurrence of rustiness developing in our experimental albino rats during investigations of synthetic diets. It seemed that these results were worth mentioning because, if they are confirmed, they may open another way to attack the question of the relationship of pantothenic acid to nutritional achromotrichia and also the question of the identity of the achromotrichia factor and the rustiness factor.[6] Our observations were purely incidental and the problem will not be investigated further in our laboratories.

The basal diet used contains 68 per cent. sucrose, 18 per cent. vitamin-free casein, 7 per cent. butter fat, 2 per cent. cod liver oil, 1 per cent. Wesson oil and 4 per cent. salts.

In the first experiment a supplement containing 15 μgm thiamin hydrochloride, 20 μgm riboflavin, 250 μgm nicotinic acid, and 20 μgm choline hydrochloride was fed daily six days a week. In every case rustiness was noted in 4 weeks. If 20 μgm of pyridoxine was added rustiness was noted in 4 to 7 weeks. Any sign

[1] P. Györgyi, C. E. Poling and Y. Subbarow, *Proc. Soc. Exptl. Biol. Med.*, 42: 738, 1939; *Jour. Biol. Chem.*, 132: 789, 1940; P. Györgyi and C. E. Poling, SCIENCE, 92: 202, 1940.

[2] M. K. Dimick and A. Lepp, *Jour. Nutrition*, 20: 413, 1940.

[3] K. Unna, *ibid.*, 20: 565, 1940.

[4] E. Nielsen, J. J. Oleson and C. A. Elvehjem, *Jour. Biol. Chem.*, 133: 637, 1940.

[5] R. R. Williams, SCIENCE, 92: 561, 1940.

[6] S. Ansbacher, SCIENCE, 93: 164, 1941, has shown that *p*-aminobenzoic acid is the chromotrichia factor for black or piebald rats. Whether this substance prevents rustiness in albino rats is still to be ascertained.