

reaches a peak at 4 days and lasts for at least 10 days. The degree of increase depends upon the dose of toxoid used. The local eosinophilia does not occur in non-immunized mice or in mice passively immunized with heterologous antibody. 2. The experiments suggest that the local eosinophilia is due neither to the antigen-antibody reaction nor to the accompanying inflammatory syndrome, but to an early stage of antibody formation during the secondary response.

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1. Speirs, R. S., and Dreisbach, M. E., *Blood*, 1956, v11, 44.
2. Speirs, R. S., Wenck, U., and Dreisbach, M. E., 1956, v11, 56.
3. Speirs, R. S., *Ann. N. Y. Acad. Sci.*, 1954, v59, 706.
4. Speirs, R. S., *Blood*, 1952, v7, 550.
5. Speirs, R. S., and Meyer, R. K., *Endocrinol.*, 1949, v45, 403.
6. Speirs, R. S., *J. Lab. Clin. Med.*, 1952, v39, 963.
7. Randolph, T. G., *Am. J. Clin. Pathol.*, 1944, v14, 48.
8. Menkin, V., *Physiol. Rev.*, 1938, v18, 366.
9. Kahn, R. L., *Ann. N. Y. Acad. Sci.*, 1955, v59, 281.

10. Opie, E. L., *J. Immunol.*, 1924, v9, 231, 255, 259.
11. Hankin, E. H., *Zentr. Bakteriolog. Parasitenk.*, 1892, v12, 781.
12. Foster, G. B., *J. Med. Research*, 1908, v19, 83.
13. Schlecht, H., *Arch. exp. Pathol. Pharmacol.*, 1912, v67, 137.
14. Weinberg, M., and Sequin, P., *Ann. Inst. Pasteur*, 1915, v29, 323.
15. Panzenhagen, H., and Speirs, R., *Blood*, 1953, v8, 536.
16. Dreisbach, M., Snell, G., and Speirs, R., in preparation.
17. Schwarz, E., *Ergab. Allg. Path. u. path. Anat.*, 1914, v17, 137.
18. Essellier, A. F., and Koszewski, B., *Klin. Univ. Zurich*, 1951, v106, 10.
19. Samter, M., *Blood*, 1949, v4, 217.
20. Godlowski, Z. Z., *J. Endocrinol.*, 1952, v8, 102.
21. McNeil, C., *Am. J. Pathol.*, 1948, v24, 1271.
22. Libby, R. L., and Madison, C. R., *J. Immunol.*, 1947, v55, 15.
23. Koshland, M. E., *Fed. Proc.*, 1955, v14, 469.
24. Harris, S., and Harris, T. N., *J. Exp. Med.*, 1954, v100, 269.
25. Coons, A. H., Leduc, E. H., and Connolly, J. M., *ibid.*, 1955, v102, 49.
26. White, R. G., Coons, A. H. and Connolly, J. M., *ibid.*, 1955, v102, 73.
27. Wenck, U., and Speirs, R. S., papers in preparation.

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Thyroidal I¹³¹ Collection in Normal and Adrenalectomized Rats, Effect of Desoxycorticosterone Acetate and Physiological Saline.* (22102)

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Although it has often been suggested that changes in extrathyroidal distribution of iodine such as would be caused by body fluid shifts or variations in extracellular fluid volume will alter thyroidal I¹³¹ collection, little specific information on this point is available.

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Boatman *et al.*(1) reported an increase in thyroidal I¹³¹ concentration ratio 3 hours after injecting I¹³¹ in rats treated chronically with desoxycorticosterone acetate (DCA). It was postulated that this may have been due to the observed increase in blood radioactivity. In contrast to this, chronic treatment of rats with DCA was reported to cause no change(2) or a decrease(3) in 24 hour thyroidal I¹³¹ collection. In man(4) a decrease was also observed. Except for the report(5) that an increased amount of NaCl in the diet

TABLE I. Effects of DCA and 0.9% NaCl on 3 Hr Thyroid Uptake of I^{131} in Adrenalectomized Rats. 10 rats in each series.

Treatment	Body wt, g	Thyroid wt, mg	Thyroid I^{131} , % dose	Urine I^{131} , % dose	Plasma I^{131} , % dose/g	Muscle I^{131} "space,"† %
Controls	161	19.4	5.6	10.0	.75	19.3
DCA, 1.25 mg/100 g	162	17.4	8.8*	9.5	.69	19.4
0.9% NaCl, 5 cc/100 g	163	19.7	7.6	22.0	.52*	24.4*
" " , 10 "	164	18.3	9.6*	19.4	.45*	24.2*

* By analysis of variance significantly different from controls at 5% level.

† % dose/g muscle

× 89.2.
% dose/g plasma

of mice enhances the goitrogenic properties of the Remington iodine deficient diet, no reference to the effect of salt administration on thyroid function has been found. The present experiments were undertaken to determine the acute effect of DCA and physiological saline solution on short term thyroidal uptake of I^{131} . Concomitant measurements of blood plasma radioactivity and total urinary I^{131} output were made to determine the effect of the treatments on the extrathyroidal distribution of radioactive iodide.

Materials and methods. Eight to 10 days before the experiment, adult male albino rats received *ad libitum* an iodine deficient diet† with tap water to drink. The adrenals were removed at this time by a dorsal approach. The rats were given a daily subcutaneous dose of 0.25 mg DCA in corn oil. Completeness of operation was ascertained by gross examination for adrenal tissue at autopsy. Each rat received intravenously in a femoral vein exposed under light ether anesthesia 0.5 ml solution containing 20 uc I^{131} with 8.5 ug carrier I^{127} as NaI. Food and water were removed immediately before I^{131} injection. DCA, as a suspension in 0.1 to 0.2 ml corn oil and 0.9% NaCl solution (Merck Reagent), warmed to approximate body temperature, were injected intraperitoneally immediately after I^{131} . Exp. I contained 4 groups of adrenalectomized rats (Table I). The rats were placed by groups in metabolism cages for collection of urine; before removal of each rat from the metabolism cage the bladder urine was expressed manually. Rats

were sacrificed by decapitation 3 hr after administration of I^{131} , and freely flowing blood collected into a beaker containing a drop of heparin. A muscle sample was obtained from the non-injected thigh. Exp. II contained 6 groups of rats (Table II). The animals were sacrificed 1½ hr after I^{131} injection, and blood was collected as before. Plasma and urine samples were weighed to the nearest mg in 1-in. pyrex dishes. A few drops of solution containing 1% NaI, 1% casein, 1% phenol and 1% NaHSO₃ were added to each sample to inhibit oxidation and sublimation of iodine. Thyroid glands were dissected cleanly, weighed rapidly to 0.1 mg and placed in the center of similar pyrex dishes. Aliquots from the injection solution were mixed with plasma for use as standards. After drying to constant weight, all samples were counted with an end-window Geiger-Muller tube and a laboratory scaler. Counts were corrected for physical decay, and in the case of plasma, urine and muscle, for self absorption of beta radiation. Results are expressed as % of injected dose.

Results. Rats receiving both DCA and the larger dose of physiological saline accumulated significantly increased amounts of I^{131} in their thyroids at 3 hr (Table I). DCA treated rats did not differ from controls in plasma radioactivity, % of dose found in their urine or in their muscle iodide space. The increased thyroidal I^{131} accumulation occurred in saline-treated rats despite the fact that their plasma radioactivity was significantly less and their muscle iodide space and urinary excretion of I^{131} was significantly greater than in either the control or DCA-

† "Iodine Deficient Diet," General Biochemicals, Chagrin Falls, O.

TABLE II. Effects of DCA and 0.9% NaCl on 1½ Hr Thyroid Uptake of I¹³¹ in Adrenalectomized and Intact Rats.

Group	Treatment	No. of rats	Body wt, g	Thyroid wt, mg	Thyroid I ¹³¹ , % dose	Plasma I ¹³¹ , % dose/g
Adrenalectomized	Controls	21	123	12.3	.66	1.20
	DCA, 1.5 mg/100 g	20	120	11.5	.65	1.16
	0.9% NaCl, 10 ml/100 g	20	120	12.1	.95*	.91*
Intact	Controls	21	133	12.9	.46	1.11
	DCA, 1.5 mg/100 g	20	129	11.7	.45	.99
	0.9% NaCl, 10 ml/100 g	19	131	12.1	.55	.83*

* By analysis of variance significantly different from controls at 5% level.

treated groups.

The only significant intergroup difference in thyroid uptake in the second experiment (Table II) is the increase in thyroidal I¹³¹ uptake in the saline-treated adrenalectomized group. Radioactivity of the blood plasma was reduced significantly in both the adrenalectomized and intact saline-treated rats.

Discussion. In view of the precautions taken in these experiments to standardize iodine intake, the increased thyroidal accumulation of I¹³¹ after both DCA and physiological saline solution should represent an increased amount of inorganic iodine fixed. The early uptake of radioiodine by the thyroid is known to be influenced by the thyroid to plasma I¹³¹ ratio, by the rate of conversion of inorganic to organic iodine and perhaps by the rate of blood circulation through the gland. There is no good evidence to suggest from these data which of the 3 may have been augmented in the treated groups. In contrast to earlier observations(1) regarding the effect of chronic DCA treatment on I¹³¹ concentration ratio, the increase in 3 hr uptake of I¹³¹ after administration of DCA was observed without any increase in blood radioactivity. A most interesting situation existed in the saline treated animals in that both the 1½ and 3 hr uptake of I¹³¹ increased despite a significant decrease in plasma I¹³¹ level.

Whether it is valid to compare the effect on the thyroid of DCA and physiological saline solution cannot be shown from the data available. Yet, speculation is attractive as to whether DCA might have a typical inorganic ion or water shifting effect at the level of the thyroid itself that results in a changed capacity to concentrate iodine and that the

saline solution might have simulated the changes produced by DCA.

Summary. Adrenalectomized male rats, fed an iodine deficient diet and maintained on ¼ mg DCA daily, were injected intravenously with I¹³¹ containing 8.5 µg of iodide carrier. Thyroidal collection of I¹³¹ increased at 3 hr after 1.25 mg DCA/100 g, but not at 1½ hr after 1½ mg DCA/100 g, the DCA being given intraperitoneally immediately after I¹³¹ in both groups. There was no change from controls in plasma I¹³¹ level or urinary I¹³¹ excretion. Under similar conditions, adrenalectomized rats showed increased thyroidal I¹³¹ collection 3 hr and 1½ hr after intraperitoneal injection of 10 ml 0.9% NaCl/100 g. This occurred despite decreased plasma radioactivity and increased urinary I¹³¹ excretion. Intact rats studied under the same conditions showed no change from controls in thyroidal I¹³¹ collection, but had less radioactivity in their blood plasma.

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1. Boatman, J. B., Russ, C., Sunder, J. H., Konnerth, A., and Moses, C., *Endocrinology*, 1952, v50, 134.
2. Paschkis, K. E., Cantarow, A., Eberhard, T., and Boyle, D., *Proc. Soc. Exp. Biol. and Med.*, 1950, v73, 116.
3. Money, W. L., Kraititz, L., Fager, J., Kirschner, L., and Rawson, R. W., *Endocrinology*, 1951, v48, 682.
4. Zingg, W., and Perry, W. F., *J. Clin. Endocrinol. Metab.*, 1953, v13, 712.
5. Axelrod, A. A., Leblond, C. P., and Isler, H., *Endocrinology*, 1955, v56, 387.

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