

## PHYSIOLOGY

## Effect of Hydrocortisone on Thyroid Structure in Albino Mice

It has been shown that adult male albino mice on *ad libitum* diet as well as on restricted isocaloric diet treated with certain doses of hydrocortisone have more fat in their depots than the controls<sup>1,2</sup>. One of the possible causes for this may be a depression of thyroid and a consequent lowering of the metabolic rate. There have been a number of investigations on the effect of ACTH and glucocorticoids on thyroid function in various laboratory, dairy, and wild animals, the results of which support this view<sup>3-6</sup>. Similar observations have also been made in man<sup>7,8</sup>. The findings, however, of the effect of ACTH and cortisone on the structure of the thyroid seem to be quite contradictory. D'Angelo<sup>9</sup> observed that cortisone administration was without effect on thyroid cell height in the albino rat. Likewise, Trabert and Betz<sup>10</sup> did not notice any histological changes in the thyroid of guinea pigs after administration of cortisone. The observations of Stux<sup>11</sup>, on the other hand, indicated stimulation of the thyroid by cortisone treatment in rats. Similarly, Delost and Delost<sup>12</sup> reported a stimulation of the thyroid by cortisone treatment in *Microtus arvalis* and *Pitymys subterraneus*. Baker<sup>13</sup> reported that ACTH with daily doses of 1 and 3 mg, respectively, per rat was without effect on epithelial cell height of the thyroid, but with 6 mg there was a significant reduction in cell height.

The investigation recorded here was undertaken to examine the effect of hydrocortisone on the structure of the thyroid in mice.

The experimental animals were 103-day-old male albino mice raised in this Department. The animals in the treated and the control groups were litter-mates. Each animal was kept in an individual cage a week preceding and during the course of the experiment. Powdered Purina laboratory chow and water was given *ad libitum*. Treatment consisted in daily injection of 0.14 mg hydrocortisone (alcohol) prepared by the Sigma Chemical Co. The hormone was homogenized and suspended in Merck diluent ('CMC'), consisting of 0.5 per cent carboxymethyl cellulose by weight, 1.5 per cent benzyl alcohol by volume, 0.9 per cent sodium chloride by weight, and 0.4 per cent 'Tween 80' by volume, in aqueous medium. The administration was made by subcutaneous injection, daily between 5 and 6 p.m., for a period of 11 days. The volume of injected material per dose was 0.05 ml. Control animals were given the same volume of the vehicle. The number of mice in each group was 4. The morning following the last injection, the animals were killed, their thyroids removed (while remaining attached to the trachea), fixed in Bouin's fluid, complete serial section slides made, and stained in Delafield's haematoxylin-eosin. The epithelium percentage was used in determining the structure of the gland. This was done by projecting the sections on paper, drawing a straight line at random through the follicles, measuring the segments of the line covered by epithelium, and then expressing the total length of these segments as a percentage ratio of the whole length of the line<sup>14,15</sup>. For each animal 15 determinations were done. The projected sections in each case were chosen from about the same region.

The results are indicated in Table 1. The average epithelium percentage in the control is  $57 \pm 3.3$ , while that of the treated is  $49.1 \pm 2.9$ . This indicates a definite reduction in the height of the follicular epithelium.

Table 1. THE EFFECT OF HYDROCORTISONE TREATMENT ON THYROID EPITHELIUM PERCENTAGE

	No. of animals	Average initial body-weight (g)	Average final body-weight (g)	Epithelium percentage
Controls	4	$32.4 \pm 0.4$	$32.7 \pm 0.2$	$57.5 \pm 3.3$
Treatment with hydrocortisone (0.14 mg)	4	$32.0 \pm 0.2$	$32.1 \pm 0.5$	$49.1 \pm 2.9$

From the results of this investigation and the observations of others, it can be concluded that the glucocorticoid used, the dosage, and the duration of treatment seem to have an impact on the thyroidal response. Furthermore, there seems to be quite a variation on the effect of the individual glucocorticoid in different species. The latter might be due to the amount of the particular glucocorticoid found as a normal product of a given species, as it has been reported that there are marked differences in various species<sup>16</sup>.

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## Effect of Sodium Diethyldithiocarbamate on Blood Copper-levels and Pregnancy in the Rabbit

SWAYBACK is a disease of lambs in which lesions in the white matter of the spinal cord are associated with low levels of copper in the tissues. Mills and Fell<sup>1</sup> reported the experimental production of swayback using a high molybdenum, high sulphate diet. Their results indicated that this diet strongly inhibited the transfer of copper from the ewe to the lamb. Any preparation which facilitates the investigation of demyelination associated with reduced copper-levels in a laboratory animal would be of great value. Mür, Záruba and Charamza<sup>2</sup> reported a destruction of myelin in rabbits following the repeated intravenous administration of a solution of either  $\alpha$ -benzoin-oxime or of diethyldithiocarbamate. The administration of  $\alpha$ -benzoin-oxime resulted in a decrease in the blood copper-level in nine out of twelve animals. The effect of diethyldithiocarbamate on the blood copper-level was determined in two rabbits and resulted in a decrease in both. Changes in myelin, particularly in the spinal cord, were recorded after diethyldithiocarbamate had been administered for only three weeks. For these reasons the effect of sodium diethyldithiocarbamate in the rabbit has been further investigated, but it has not been possible, as yet, to confirm the effect on myelin. However, in the course of the work it became clear that sodium diethyldithiocarbamate interfered with the blood copper-level and had a marked effect on pregnancy.

Copper values in whole blood were obtained for duplicate 3-ml. samples using a modification of the method of Eden and Green<sup>3</sup>. The blood was collected from an ear vein into chemically clean bottles using purified ammonium citrate as an anticoagulant. An injection of an isotonic solution of sodium diethyldithiocarbamate given at the rate of 5 ml./kg body-wt. (3 animals), or of a solution containing 0.5 g of the chelating agent in 5 ml. of