Some Factors Influencing Thymus Nitrogen Content of the Immature Male Mouse. (18733)

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White and Dougherty(1) have demonstrated that the adrenal cortex is involved in regulating the nitrogen content of lymphoid tissue. It is to be noted, however, that their results were obtained on pooled lymphoid tissue which included the thymus, spleen, and lymph nodes. No studies have been reported on the changes in nitrogen content of each individual type of lymphoid organ. Apparently, it has been assumed that all lymphoid tissues respond in an identical manner although the data of Andreasen(2) suggest that differences between the various lymphoid tissues may be expected.

We wish to report certain observations on the mouse thymus gland which reveal that neither the stress resulting from a 48 or 60-hour fast nor the short term administration of cortisone acetate has a significant effect on the total nitrogen content of the thymus, despite the fact that both the fasting and the cortisone administration produce a marked decrease in the weight of this organ. On the other hand, data are presented which indicate that certain other steroids can cause a significant decrease in the total nitrogen content of the thymus.

Immature male mice (Manor Farms), weighing between 13-17 g at the beginning of the experimental period, were used. Animals had access to water during the fasting period. Cortisone acetate was employed as an aqueous suspension; the other steroids were administered in oil solutions. The dosage and injection schedules are given in Table I. At the end of the experimental period, the mice were anesthetized with ether and the thymus and spleen of each animal were removed, weighed, and each organ used for Kjeldahl digestion. Semi-micro Kjeldahl analysis for total nitrogen was employed. Table I contains the data obtained from typical experiments. The fact that no significant decrease in thymus nitrogen occurs following fasting or cortisone administration, despite the marked weight loss, and raises the question as to what components are responsible for this loss. Preliminary observations indicate that it cannot be accounted for by a change in glycogen or "lipid" content.

White and Dougherty(1) observed a decrease in pooled lymphoid tissue nitrogen which occurred after fasting or after administration of adrenal cortical extract and this may be explained by the fact that the various lymphoid organs do not respond in the same manner or to the same degree. This is clearly evident from the data on the effect of fasting and cortisone treatment on spleen weight and total nitrogen content (Table I). A significant decrease in the total nitrogen content, as well as in the weight, occurs following both experimental situations.

It is particularly interesting that the steroids which reduce thymus nitrogen, in addition to their well-known endocrine effects, are also known protein anabolic compounds (3). These steroids do not appear to affect the nitrogen content of the spleen in any predictable manner as compared to their effect on thymus nitrogen. It is possible that a change in dosage or duration of administration will resolve this matter since the difference observed in the response of the two organs may be one of degree rather than kind.

The decreasing order of effectiveness of the various steroids, at the one dose level studied, in reducing the thymus nitrogen content (methylandrostanediol > testosterone propionate > β-estradiol > estrone > desoxycorticosterone acetate > methylandrostenediol > progesterone) is remarkably similar to the decreasing order of renotrophic (anabolic) effectiveness as reported by Kochakian(3) and confirmed in this laboratory (unpub-

1. White, A., and Dougherty, T. F., *Endocrinology*, 1947, v41, 230.

2. Andreasen, E., *Acta Path. et Microbiol. Scand.*, 1943, vXLIX, 11.

TABLE I. Influence of Fasting and Certain Steroids on Wt and Total Nitrogen Content of Thymus and Spleen.*

Treatment†	No. mice	Daily dose, mg	Total thymus N	Thymus wt	Total spleen N	Spleen wt
Control, fed	10	—	9.4 ± .7	250 ± 23	13.8 ± .7	410 ± 18
Fasted, 48 hr	10	—	10.0 ± .5	*153 ± 18*‡	*10.9 ± .9*	*265 ± 18*
Control, fed	10	—	10.6 ± .3	322 ± 20	13.8 ± .5	438 ± 32
Fasted, 60 hr	10	—	10.4 ± .7	*111 ± 19*	*11.4 ± 1.0*	*258 ± 32*
Control, saline	9	0.1 ml	7.3 ± .3	312 ± 10	11.7 ± .4	352 ± 14
Cortisone acetate	10	3.0	7.1 ± .7	*125 ± 7*	*7.3 ± .5*	*230 ± 21*
17-methylandrostane-3β, 17β-diol	8	1.5	*8.6 ± .2*	*158 ± 5*	*16.9 ± 1.2*	439 ± 31
Testosterone propionate	7	1.5	*5.2 ± .5*	216 ± 15	11.3 ± 1.2	365 ± 29
β-estradiol	8	1.5	*5.2 ± .3*	*159 ± 17*	13.4 ± 1.2	362 ± 36
Estrone	7	1.5	*6.1 ± .3*	*151 ± 18*	11.0 ± 1.0	293 ± 20
Desoxycorticosterone acetate	7	1.5	*6.4 ± .3*	*192 ± 13*	*8.6 ± 1.0*	302 ± 24
17-methyl-Δ⁵-androstene-3β, 17β-diol	7	1.5	7.6 ± .3	207 ± 23	13.6 ± 2.3	445 ± 74
Progesterone	7	1.5	7.8 ± .4	219 ± 22	9.4 ± .7	299 ± 19
Testosterone succinate	6	1.5	7.9 ± .5	221 ± 16	12.2 ± 1.0	383 ± 19
Control, oil	7	0.1 ml	8.0 ± .6	255 ± 15	11.9 ± .8	337 ± 21

* Thymus and spleen wt expressed in mg/100 g body wt; thymus and spleen N as mg N/total organ/100 g body wt.

† All steroids inj. subcut. daily for 3 days.

‡ Italicized values are significantly different from their controls at the 5% level of confidence. Values reported are mean ± standard error.

lished). It appears quite possible that these results may form the basis for a suitable screening procedure for protein anabolic compounds. The physiological significance of this apparent relationship between thymus nitrogen depletion and protein anabolic steroid activity is being currently investigated.

Summary. Neither the stress resulting from a 48 or 60-hour fast nor the administration of cortisone acetate has a significant effect on the total nitrogen content of the mouse thymus gland. On the other hand, it appears that the protein anabolic steroids induce a significant decrease in the thymus total nitrogen content.

Addendum. After this work was completed, the paper by Adams and White(4) came to our attention. Their data, in agreement with our results, show that a 48-hour fast has no effect on the protein content of the thymus nodes.

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3. Kochakian, C. D., *Am. J. Physiol.*, 1944, v142, 319.

4. Adams, E., and White, A., PROC. SOC. EXP. BIOL. AND MED., 1950, v75, 590.

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A Purified Fraction of Thioflavine-S (Vasoflavine): Valuable Agent for Visualization of Blood Vessels.* (18734)

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A method for the visualization of blood vessels and lymphatics under ultraviolet light,

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