

enough carbohydrate or, as in this case, dextrose former is given, the gradient tissue sugar  $\rightarrow$  blood sugar, becomes reversed enough to approach normal and permit an increase in dextrose oxidation. The latter is evident in Exp. 2 in the antiketogenic and nitrogen sparing effects of the succinic acid.

*Summary.* In the phloridzinized dog the changes in the D:N ratio indicate that small doses of succinic acid are entirely converted to dextrose (2 mols. succinic acid = 1 mol. glucose). When larger doses are given a smaller percentage is excreted in the urine as sugar but anti-ketogenic and nitrogen sparing activity indicate its conversion to dextrose before being burned.

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#### **Atrophy of Thymus of the Rat Resulting from Administration of Adrenocorticotropic Hormone.\***

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Some time ago publication was made from this laboratory of the rapid atrophy of the thymus on the administration of the gonadotropic hormone in pregnant mare serum.<sup>1</sup> The phenomenon was not seen in males or females after castration and was tentatively referred to the increased production of sex hormones on the part of the gonad. Selye, Browne and Collip<sup>2</sup> have noted atrophy of the thymus following administration of progesterone. Selye, Harlow and Collip,<sup>3</sup> and Schacher, Browne and Selye<sup>4</sup> subsequently produced regression of the thymus by administration of estrogenic, as well as androgenic substances. The preparation of adrenocorticotropic and mammatropic hormones in this laboratory has resulted in their administration under a variety of conditions. It became apparent very soon that invariable prompt reduction in size and almost

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<sup>1</sup> Evans, H. M., and Simpson, M. E., *Anat. Rec.*, 1934, **60**, 423.

<sup>2</sup> Selye, H., Browne, J. S. L., and Collip, J. B., *PROC. SOC. EXP. BIOL. AND MED.*, 1936, **34**, 472.

<sup>3</sup> Selye, H., Harlow, C. M., and Collip, J. B., *Endokrinologie*, 1936, **14**, Heft 1/2.

<sup>4</sup> Schacher, J., Browne, J. S. L., and Selye, H., *PROC. SOC. EXP. BIOL. AND MED.*, 1937, **36**, 488.

complete regression of the thymus occurs<sup>5</sup> after administration of adrenocorticotrophic hormone, while mammotrophic hormone does not produce the atrophy. Although adrenocorticotrophic hormone in large doses causes a stunting of growth or a loss in body weight, the doses used here which were effective in reducing thymus weight were not always associated with loss of body weight.

It is now known that an increase in the production of cortin by the adrenal is provoked by adrenocorticotrophic hormone,<sup>6</sup> as well as a demonstrable increase in its secretion of androgenic and estrogenic substances,<sup>7, 8, 9</sup> and one may naturally inquire as to which of these adrenal functions we may attribute the above mentioned experimental thymic atrophy. The reduction of the thymus by adrenocorticotrophic hormone with equal facility after double ovariectomy would appear to rule out the stimulation of the production of progesterone, or androgenic and estrogenic substances, from the ovary which adrenocorticotrophic hormones could conceivably occasion. Since the sex hormones are known to stimulate the pituitary, which in turn could pour out any one of its secretions, it is desirable to use hypophysectomized animals to simplify explanations of hormonal effects. Hence, it would seem important to note that the thymic atrophy following administration of adrenocorticotrophic hormone was secured in hypophysectomized animals. The accompanying paper shows that thymic atrophy occurs as a direct result of cortin administration.<sup>10</sup> This indicates that the atrophy of the thymus resulting from administration of adrenocorticotrophic hormone is due in part to the increased production of cortin, but does not eliminate the possibility that increased production of male or female sex hormones in the adrenal cortex is a contributing factor.

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<sup>5</sup> Moon, H. D., *PROC. SOC. EXP. BIOL. AND MED.*, 1936, **37**, 34.

<sup>6</sup> Ingle, D. J., Moon, H. D., and Evans, H. M., in preparation.

<sup>7</sup> Davidson, C. S., and Moon, H. D., *PROC. SOC. EXP. BIOL. AND MED.*, 1936, **35**, 281.

<sup>8</sup> Davidson, C. S., *PROC. SOC. EXP. BIOL. AND MED.*, 1937, **36**, 703.

<sup>9</sup> Moon, H. D., *PROC. SOC. EXP. BIOL. AND MED.*, 1937, **37**, 36.

<sup>10</sup> Ingle, D. J., in preparation.