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Effect of Epinephrine on Adrenal Cholesterol and Ascorbic Acid.*

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It has previously been shown that the injection of pure adrenotrophic hormone into rats is followed by a rapid fall in adrenal ascorbic acid, a slower fall in adrenal cholesterol, and an increase in liver glycogen.[1,2,3] It has been found (unpublished experiments) that exposure of rats to such conditions as cold, scalds, or hemorrhage is also followed by a depletion of adrenal cholesterol and ascorbic acid. However, since the above stresses are without any effect on the adrenal cholesterol and ascorbic acid of hypophysectomized rats, it is evident that a release of adrenotrophic hormone from the anterior pituitary is a preliminary and necessary step in the adrenal cortical response to an increased need for cortical hormone.

The factors, humoral or nervous, that are associated with stress and which lead to an increased secretion of adrenotrophic hormone are not known, but it would appear that one common denominator is an increased degree of activity of the sympathetic nervous system, with a consequent release of epinephrine. We have, therefore, investigated the effect of epinephrine on the cholesterol and ascorbic acid levels of normal and hypophysectomized rats.

Methods. Male rats about 200 g in weight of either Sprague-Dawley or Yale strain were used for this investigation. Non-fasted animals were hypophysectomized by the parapharyngeal approach under ether anesthesia. They were used on the third postoperative day after a fast of 18 hours, while food was withheld from normal rats 24 hours before the experiment.

A 4-hour course of injections was given subcutaneously to both groups. Every hour each animal received 0.02 mg/100 g of epinephrine in physiological saline. One hour following the last injection the rats were quickly anesthetized with nembutal. The adrenals were removed and weighed on a torsion balance. The left adrenal was analyzed for cholesterol and the right one for ascorbic acid. The effect of a single subcutaneous dose of epinephrine of the same concentration was also studied 2 hours after injection.

In another series of experiments the left femoral vein was exposed under nembutal anesthesia, and epinephrine in saline (containing 20 mg% glutathione) was delivered into the circulation at a constant rate of 0.02 mg/100 g/hr for a period of 2 hours, at which time the adrenals were analyzed.

Cholesterol was determined by the Sperry and Schoenhemier method.[4] Ascorbic acid was first determined by Tillman's method and later by the Roe and Kuether procedure.[5]

Results. Table I shows that epinephrine administered subcutaneously causes an unmistakable fall in adrenal cholesterol and ascorbic acid and that this effect is abolished by hypophysectomy. Similar results were obtained with epinephrine administered intravenously. Consequently, the absence of any effect of epinephrine on hypophysectomized rats is not due to failure of absorption from the subcutaneous tissues.

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1 Sayers, G., Sayers, M. A., White, A., and Long, C. N. H., Proc. Soc. Exp. Biol. and Med., 1943, **52**, 200.

2 Sayers, G., Sayers, M. A., Fry, E. G., White, A., and Long, C. N. H., *Yale J. Biol. and Med.*, 1944, **16**, 361.

3 Sayers, G., Sayers, M. A., Lewis, H. L., and Long, C. N. H., Proc. Soc. Exp. Biol. and Med., 1944, **55**, 238.

4 Sperry, W. M., *Am. J. Clin. Path.*, Tech. Suppl., 1938, **2**, 91.

5 Roe, G. H., and Kuether, C. A., *J. Biol. Chem.*, 1943, **147**, 399.

TABLE I.

	No. animals	Duration of experiments hr	Adrenal: Cholesterol, g %	Adrenal: Ascorbic acid, mg %
Normal.				
Controls	23	—	4.03 ± 0.10	370 ± 14
Epinephrine. 1 × 0.02 mg/100 g subcut.	6	2.0	2.88 ± 0.28	210 ± 24
Epinephrine. 4 × 0.02 mg/100 g subcut.	10	4.0	2.26 ± 0.22	216 ± 9
Epinephrine. 0.02 mg/100 g/hr intraven.	6	2.0	2.31 ± 0.18	104 ± 17
Hypophysectomized.				
Controls	4	—	5.74 ± 0.43	398 ± 38
Epinephrine. 4 × 0.02 mg/100 g subcut.	9	4.0	5.34 ± 0.47	411 ± 13
Epinephrine. 0.02 mg/100 g/hr intraven.	2	2.0	6.04	357

At the moment it is not possible to decide whether this effect of epinephrine is due to a direct stimulation of the cells of the anterior pituitary that secrete adrenotrophic hormone or whether it is due to changes in the composition of the blood acting as the exciting agent. Further experiments to clarify this question are in progress.

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The Incidence of Toxoplasmic Infections in the St. Louis Area.*

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Since 1940 8 fatal cases of toxoplasmosis have been observed in the St. Louis area.[1,2,3] Two of the patients were adults, in whom the infection occurred as an acute febrile disease manifested by a skin rash and closely simulating the typhus spotted fever group of diseases. A history of tick bite was obtained from both patients.[1] The other instances of this type of infection have been observed in infants in whom the onset of clinical signs and symptoms was apparent at birth or appeared shortly thereafter.[2,3] Widespread involvement of the central nervous system gave rise to the principal clinical manifestations of generalized convulsions, muscular paralysis and internal hydrocephalus. Cerebral calcification and widespread encephalomyelitis with the formation of many granulomatous lesions were the prominent pathologic changes. Toxoplasma were present in small aggregates or pseudocysts and as free organisms within the central nervous system.

The onset of the disease at birth or shortly thereafter, as well as the advanced nature of the lesions in the central nervous system, led Paige, Cowen, and Wolf[4] to advance the concept of the intrauterine inception of the disease. In the cases reported by these observers, as well as many other instances of the infantile type of toxoplasmic encephalomyelitis, the infection in the mother produced no clinical manifestations of disease although neutralizing antibodies were demonstrated in the peripheral blood.[5,6,7] This would indicate

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1 Pinkerton, H., and Henderson, R. G., *J. A. M. A.*, 1941, **116**, 807.

2 Callahan, W. P., Jr., Russell, W. O., and Smith, M. G., to be published.

3 Pinkerton, H., personal communication.

4 Paige, B. H., Cowen, D., and Wolf, A., *Am. J. Dis. Child.*, 1942, **63**, 474.

5 Cowen, D., Wolf, A., and Paige, B., *Arch. Neurol. and Psych.*, 1942, **48**, 689.

6 Sabin, A. B., PROC. SOC. EXP. BIOL. AND MED., 1942, **51**, 6.

7 Callahan, W. P., Jr., unpublished data.