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Maintenance of Life in Adrenalectomized Animals with Flavin Phosphate.

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The recent work of Verzář and Laszt¹ has suggested that the possible function of cortin in the animal body is to convert provitamin B₂ (Flavin) to Vitamin B₂ (Flavin phosphate). The mortality rate of their adrenalectomized animals was materially reduced by injections of Flavin phosphate. It is the purpose of this communication to confirm the work of Verzář and Laszt¹ and to present additional data.

Normal rats were adrenalectomized and divided into several series of 15 rats each as follows: (1) Rats receiving 0.15 cc. Flavin phosphate daily, (2) rats receiving 0.03 cc. Flavin phosphate daily, (3) rats receiving 0.03 cc. Flavin phosphate and 50 mg. ascorbic acid daily, (4) those receiving 0.25 cc. cortin and those (5) receiving no medication. There were also control series. The Flavin phosphate was prepared by the method of Karrer, Salomon, Schopp and Benz² and Kuhn and Rudy³ and also by applying Kuhn's method to yeast which Stern⁴ used to extract photoflavins from liver. The rats were placed on the Flavin free diet of Verzář and Laszt¹ whereas another group was placed on the ordinary preoperative rat diet. The results can be summarized as follows: Rats receiving 0.15 cc. daily of Flavin phosphate maintained normal weight and activity for 3 weeks and were finally autopsied to confirm adrenalectomy. Seventy-five per cent of the rats receiving the smaller dose of 0.03 cc. of Flavin phosphate died within 10 days, the remainder dying within 3 weeks. The rats receiving 0.03 cc. of Flavin phosphate and 50 mg. ascorbic acid (Hoffman-LaRoche) survived 3 weeks, losing weight gradually and died at the end of 4 weeks. Those receiving 0.25 cc. cortin died on the Flavin free diet, but maintained fairly good health on the ordinary diet. Those receiving cortin and ascorbic acid behaved as those receiving cortin alone. Those receiving no medication died within 4 days.

The data suggest that there is a synergistic action between

¹ Verzář, F., und Laszt, L., *Pflüger's Arch. Physiol.*, 1936, 476.

² Karrer, P., Salomon, H., Schopp, K., and Benz, F., *Naturwiss*, 1935, **23**, 355.

³ Kuhn, R., and Rudy, H., *Ber. Deutsch. Chem. Ges.*, 1935, **68**, 383.

⁴ Stern, K. G., *J. Biochem.*, 1934, **28**, 949.

ascorbic acid and Flavin phosphate (Vitamin B₂) and that cortin cannot maintain the life of adrenalectomized rats on a Flavin-free diet. Adrenalectomized rats can be maintained in good condition with Flavin phosphate. Young adrenalectomized rats furthermore have normal growth curves if given Flavin phosphate. Studies are being carried out in cats and dogs after adrenalectomy in the relation of Flavin phosphate to maintenance of life and general metabolism.

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Thyro-Parathyroidectomy and Pregnancy in the Rat.

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In studying the metabolism of thyro-parathyroid deficient rats it was found that a number of the animals which had become pregnant died at term, often during labor, death being preceded by convulsive seizures, occurring at intervals. This recalled the remarkable observation published by Halsted¹ in 1896, before the function of the parathyroids was known. Working with dogs, Halsted performed piecemeal extirpation of the thyroid and studied the changes produced in the remnants of the gland. He was particularly interested in determining the validity of Munk's contention that the thyroid was a superfluous organ. The dogs usually survived repeated operations and did not develop the fatal symptoms resulting from complete removal of the gland. However, 2 of the partly "thyroidectomized" dogs which had become pregnant developed tremors and convulsions at term, these symptoms subsiding after the pups were born.

Our observations seemed of sufficient importance to justify more detailed investigation and accordingly the study was extended to a group of 62 thyro-parathyroidectomized rats, this series being the basis of the present report. Total extirpation of the glands was performed at a relatively early age (less than 110 days, except in 6, operated at 135-140 days). The very young were allowed to ma-

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¹ Halsted, W. S., *Johns Hopkins Hosp. Reports*, 1896, **1**, 373.