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Hypophysis and Detoxification.

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Previous work has shown that the removal of the anterior lobe of the hypophysis not only prevents further growth of the normal tissues of the animal, but diminishes the rate of growth of tumors.[1] Yet in spite of the small size of the tumors the animals very often do not live any longer than the controls. Animals with the hypophysis removed also succumb to pneumonia and other infections more frequently than normal.

Providing the anatomical changes are associated with similar changes in function, this result would be expected from the work of Smith[2] demonstrating that pituitary removal causes atrophy of the adrenal cortex. Lewis[3] first showed that adrenalectomy lowered the resistance of the animals to toxins. Recently Perla and Marmorston-Gottesman[4] have shown that extracts of the adrenal cortex which preserve life in adrenalectomized animals also increase the bodily resistance to toxins. On the other hand, Cutler[5] reported that removal of the hypophysis had no effect on the immune reaction of guinea pigs to *bacillus typhosis*. However, with his method of operation no animals survived which had complete operations. The immunity studies were therefore carried out with partially hypophysectomized animals. The following experiments were undertaken to determine the detoxifying ability of completely hypophysectomized rats as compared with similar normal animals.

The toxin used was a solution of crystalline cobra venom. Doses of this toxin can be accurately duplicated over a long period of time, a condition not true for the bacterial toxins. The crystalline cobra venom was dissolved in normal physiological saline solution to make a concentration of 100 mg. of venom per litre. This solution was injected intraperitoneally into albino rats raised in our own colony. Preliminary experiments with normal animals established the mini-

[1] Ball, Howard A., and Samuels, L. T., *Am. J. Cancer*, 1932, **16**, 351.

[2] Smith, P. E., *J. Am. Med. Assn.*, 1927, **88**, 158.

[3] Lewis, J. T., *Am. J. Physiol.*, 1923, **64**, 506.

[4] Perla, D., and Gottesman, J. M., PROC. SOC. EXP. BIOL. AND MED., 1930, **28**, 474.

[5] Cutler, E. C., *J. Exp. Med.*, 1922, **35**, 243.

mum lethal dose at slightly more than 0.075 mg. per 100 gm. body weight. The ratio of minimum lethal dose to body weight was constant over a wide range.

The hypophysectomized rats were prepared by the method of P. E. Smith, the sphenoid being trephined through the nasopharynx. The entire gland was aspirated without touching the brain. All of the animals had been operated at least 3 weeks before the tests and were definitely free from any post-operative complications. Thirteen operated animals were used; 8 of these received one-sixth grain of thyroid twice a week for 2 weeks previous to injection of the toxin to maintain the basal metabolic rate and eliminate the thyroid changes as a possible factor. Operated rats given doses of 0.043 mg. per 100 gm. body weight all survived, but when the total injection was 0.05 mg. per 100 gm. body weight, 10 animals died and 3 survived. Upon autopsy all of the animals which died were found to have complete operations. One of the surviving animals had portions of the anterior lobe still present. The minimum lethal dose for hypophysectomized animals was 0.05 mg. per 100 gm. body weight.

The detoxifying ability of hypophysectomized rats is therefore only ⅔ that of similar normal animals. The difference is even greater than the figures would indicate since the hypophysectomized animals had much smaller amounts of body fat. This effect of removal of the hypophysis is not due to the indirect effect of a lowered thyroid function but may be due to a reduced function of the adrenals.

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Sexual Variation in the Carbohydrate Metabolism of Rats.

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A distinct variation exists in the rate of development and the extent to which ketosis occurs in normal men and women during the early days of fasting.[1] The present investigation was undertaken to determine whether such a difference can be ascribed to a more rapid depletion of the carbohydrate supply of the female.

[1] Deuel, H. J., Jr., and Gulick, M., *J. Biol. Chem.*, 1932, **96**, 25.