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Experimental Hyperthyroidism and Sympathetic Irritability.

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The object of this experiment was to make a study of the results of Goetsch's "Epinephrin Hypersensitiveness Test" upon dogs rendered experimentally hyperthyroid by feeding desiccated thyroid.

Goetsch's[1] test is based upon the theory that an oversecretion of the thyroid hormone renders the sympathetic nervous system more sensitive to the action of epinephrin. His method is as follows: In a patient at rest such subjective and objective manifestations as nervous symptoms, temperature, pulse, size of pupil, blood pressure, respiration, etc., are noted. Five-tenths cc. of 1-1000 epinephrin is then injected subcutaneously and deeply and the same observations are repeated. Goetsch states that there is usually an early rise in systolic and fall in diastolic pressure, a rise in pulse rate, and an increase of subjective symptoms, if the patient is hyperthyroid. There is no reaction whatever in other patients. Tests were made upon patients with known exophthalmic goitre to test the method, and the results were positive, parallel to the severity of the cases. Saline injections gave no reaction.

Luckhardt and Koppányi,[2] working with dogs, found that subcutaneous injections of epinephrin caused a rise in blood pressure in normal animals if massage of the area followed injection. The reaction was decreased by deep anesthesia and increased by peripheral dilatation (as from local injection of Na No_2). Light paraldehyde anesthesia or deep morphine analgesia did not interfere. These facts were made use of in our experiment.

The present experiments were performed in two series. In Series 1, 28 small dogs were used: 14 normal and 14 dogs previously made hyperthyroid by feeding desiccated thyroid—1 gm. per kilo body weight per day for one week. The dogs were lightly anesthetized with paraldehyde and the blood pressure recorded from the carotid upon a smoked drum. Two to 3 cc. of epinephrin were injected subcutaneously over the thorax and the area lightly massaged every minute until the first response, then at 10 minute intervals for 2 hours. Controls were made with saline. Averages of the results

[1] Goetsch, Emil, *Penn. Med. J.*, 1920, xxiii; *N. Y. State J. Med.*, 1920, 1921, 1922.

[2] Luckhardt and Koppányi, *Am. J. Physiol.*, 1927, lxxxi.

were calculated for the 14 normal and the 14 hyperthyroid dogs, as follows:

TABLE I.

	Normal	Hyperthyroid
Average time before first response	9.5 min.	9.4 min.
" height of first response	17.4 mm. Hg.	16.6 mm. Hg.
" time before highest response	51.6 min.	38.3 min.
" height of highest response	36.6 mm. Hg.	35.8 mm. Hg.
" " of all responses	22 " "	25 " "

Control injections of saline were negative in all cases.

Although these results seemed consistently negative, we were not entirely satisfied, because of possible individual differences in dogs and in depth of anesthesia. We therefore performed a second series of experiments, in which 6 dogs were used. The animal was operated upon aseptically under ether to isolate one carotid and insert a three-way cannula. The dog was then allowed to recover for at least 1 hour from the ether, and was made analgesic with one-fourth grain of morphine sulphate. He then lay quietly upon the table, and a blood pressure record was made from the isolated carotid. At intervals intravenous injections of 1-500,000 epinephrin were made in doses of 1/10, 2/10, 5/10 and 1 cc.; blood pressure response was recorded upon the drum. The dog was then allowed to recover and fed thyroid, 1 gm. per kilo per day for 1 week, after which the same procedure was repeated, using the other carotid. Controls were made upon 4 dogs to compare the epinephrin reaction when one and when both carotids were ligated. An average of the results from the dogs in the normal and in the hyperthyroid state was as follows:

BLOOD PRESSURE RISE FOLLOWING EPINEPHRIN.

	0.1 cc.	0.2 cc.	0.5 cc.	1.0 cc.
Average of 6 dogs, normal	7 mm. Hg.	11.6	18.3	27.3
Average of same dogs, hyperthyroid	7 " "	9.3	15.3	25.0

The controls comparing the reactions when one or both carotids were ligated showed no difference.

Kunde's work[3] with thyroid medication has demonstrated the fact that dogs fed with 1 gm. per kg. body weight of desiccated thyroid per day for one week are unquestionably hyperthyroid. According to Goetsch's theory, such dogs should show greater sensitiveness to epinephrin than normal dogs would, or than the same dogs would before having been made hyperthyroid. Our results, however, do not support the theory, since they show no increase in blood pressure response to epinephrin in the hyperthyroid groups over that in the normal groups.

[3] Kunde, M. M., *Am. J. Physiol.*, 1928, lxxxii, 195.