ance of these cells. Also, the question must be raised of the possible participation of these cells in defense against respiratory infection since the creation of a state of hyperadrenocorticalism in rats increases the frequency of respiratory disease.

Summary. Treatment for 21 days with one mg of corticotropin or 5 mg of cortisone acetate daily caused a marked decline in the population of globule leucocytes in the tracheal mucosa of rats. Administration of 6 mg corticotropin or 10 mg cortisone acetate daily caused these cells to disappear almost completely. In this response, the globule leucocyte resembles the lymphocyte.

1. Kent, J. F., *Anat. Rec.*, 1952, v112, 91.
2. Kirkman, H., *Am. J. Anat.*, 1950, v86, 91.
3. Baker, B. L., Ingle, D. J., and Li, C. H., *ibid.*, 1951, v88, 313.
4. Dougherty, T. F., and White, A., *Am. J. Anat.*, 1945, v77, 81.
5. ———, *Endocr.*, 1944, v35, 1.
6. Forsham, P. H., Thorn, G. W., Prunty, F. T. G., and Hills, A. G., *J. Clin. Endocr.*, 1948, v8, 15.
7. Gordon, A. S., Piliero, S. J., Landau, D., *Endocr.*, 1951, v49, 497.

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Effect of Epinephrine on Thyroid Hormone Level in Blood. (20976)

C. D. ESKELSON, H. E. FIRSCHEIN, AND H. JENSEN.
From the Department of Biochemistry, Army Medical Research Laboratory, Fort Knox, Ky.

Thyroid functional activity, employing radioiodide (I^{131}), has been related to the concentration of organic-bound I^{131} in blood. The level of organic-bound iodine in blood is generally regarded as an accurate index of the circulating thyroid hormone.* The concentration of organic iodine in blood represents the difference between the amount of hormone secreted by the thyroid and the amount of hormone metabolized or excreted during the same interval of time. Williams, Jaffe and Kemp(2) found that epinephrine administration to rats produced a lowering of I^{131} concentration in the thyroid and in the organic-bound I^{131} in the blood. Soffer and his associates(3) observed that the parenteral injection of epinephrine into both the intact and the totally thyroidectomized dog resulted in an increase in secretion of thyrotropin (TSH) from the anterior pituitary. Botkin and Jensen(4) reported that while both TSH and epinephrine administration to rats produced a lowering of the I^{131} concentration in the thyroid gland, the organic-bound I^{131} in the blood was increased after TSH injection but decreased after epinephrine administration. This latter response was interpreted as being due to an increased utilization of circulating thyroid hormone caused by the epinephrine.

In order to study further the influence of epinephrine on blood organic iodine the effect of simultaneous administration of TSH and epinephrine or of thyroxin and epinephrine on the level of organic I^{131} in blood was investigated.

Methods and materials. Male rats of the Sprague-Dawley strain, weighing from 200 to 250 g, were used in all experiments. The animals were housed at 25°C ± 1° and were fed Purina checkered dog chow. Food, but not water, was withheld for 18 to 20 hrs before sacrifice. Eighteen hrs before sacrifice the animals receiving TSH† (dissolved in 0.9% saline) were injected with 5 μc I^{131},‡ and those receiving thyroxin (dissolved in NaOH at

* Recently Gross and Pitt-Rivers(1) have presented evidence that the thyroid releases, in addition to thyroxin, another active principle which was shown to be 3:5:3′-triiodothyronine.

† TSH used was obtained from two sources: A Parke, Davis preparation containing 10 J. S. units/mg, and an Armour preparation containing 5 J. S. units/mg. The authors greatly appreciate the generosity of Parke, Davis and Co., Detroit, Mich., and of Armour and Co., Chicago, Ill., in supplying these preparations.

TABLE I. Effect of Simultaneous Administration of TSH and Epinephrine on Organic-Bound I^{131} in Blood.

Treatment	No. of animals	OBI, C/min.	Rat No.	Statistical significance
Exp. 1				
TSH + epinephrine	6	56 ± 18*	1- 6	$p < .01$ $f = 15.96$
TSH	6	68 ± 21	7-12	
Epinephrine	6	24 ± 10	13-18	
Saline	6	37 ± 11	19-24	
Exp. 2				
TSH + epinephrine	4	74 ± 7	1- 6†	$p < .01$ $f = 15.96$
TSH	6	84 ± 17	7-12	
Epinephrine	6	32 ± 3	13-18	
Saline	6	37 ± 10	19-24	

* Mean ± stand. dev.

† 2 samples lost.

All animals received 5 μc I^{131} 18 hr before sacrifice.

No. 1-12 were inj. with 24 J.S. units TSH in 1 ml 0.9% saline 2½ hr before sacrifice.

No. 1-6 and 13-18 were inj. with 0.1 mg epinephrine in 1 ml of 0.9% saline 2 hr before sacrifice.

No. 19-24 were inj. with 1 ml 0.9% saline 2 hr before sacrifice.

pH 11.0) were injected with 30 μc of I^{131}. All injections were given intraperitoneally. Further details as to the amount and time of TSH, thyroxin and epinephrine§ injections are given in the various tables. The animals were sacrificed by ether anesthesia and blood was drawn by heart puncture. The blood was allowed to clot and the serum was obtained by centrifugation. The organic-bound I^{131} content in serum was determined according to the procedure described by Botkin and Jensen (4).

Results. As can be seen from the data of Table I, the increased organic I^{131} blood level, observed after TSH injection alone, became lowered on simultaneous administration of TSH and epinephrine. The highest to lowest organic I^{131} level in blood respectively was observed with TSH only, TSH and epinephrine, saline control, and lowest with epinephrine alone.

‡ The radioactive iodide, I^{131}, was supplied by the Oak Ridge National Laboratory on allocation from the Isotope Division, U. S. Atomic Energy Commission.

§ Soluble Salt, The Upjohn Co., dissolved in saline.

The data of Table II indicate that there was no difference in the response of the gland with regard to the I^{131} distribution whether TSH was administered alone or in combination with epinephrine.

The data of Table III illustrate that the highest organic I^{131} values in blood were observed in the saline control group and the lowest values in the thyroxin-epinephrine group. It is interesting to note that thyroxin alone exerted a greater effect on lowering the organic I^{131} blood level than did epinephrine alone. The highest to lowest organic I^{131} level in blood respectively was found with saline, epinephrine, thyroxin, and lowest with thyroxin-epinephrine.

Discussion. The data presented indicate that epinephrine administration produced a lowering of the organic-bound I^{131} in blood. This response was observed on administration of epinephrine alone as well as in combination with either TSH or thyroxin. These findings support the postulation of Botkin and Jensen (4) that epinephrine produced an increased utilization of circulating thyroid hormone by the peripheral tissues.

The estimation of the blood organic I^{131} level is, therefore, inadequate in itself as a test of thyroid function. It merely measures the amount of circulating thyroid hormone at a certain time period.

Summary. Administration of epinephrine alone or in combination with either TSH or

TABLE II. Effect of Simultaneous Administration of TSH and Epinephrine on I^{131} Distribution in the Thyroid.* Four animals in each series.

Treatment	Rat No.	Gland — Total Cpm × 10^3	Gland — Organic Cpm × 10^3
		Mean	
TSH + epinephrine	1- 4	16.30	10.95
TSH	5- 8	16.25	11.35
Epinephrine	9-12	22.19	15.96
Saline	13-16	25.87	20.92

* Distribution of I^{131} was determined according to the method of Morton and Chaikoff (*J. Biol. Chem.*, 1943, v147, 1).

All animals inj. with 5 μc I^{131} 18 hr before sacrifice.

No. 1-8 received 2.4 mg TSH (24 J.S. units) 2 hr before sacrifice.

No. 1-4 and 9-12 received 0.1 mg epinephrine 1½ hr before sacrifice. No. 13-16 received saline 2 hr before sacrifice.

TABLE III. Effect of Simultaneous Administration of Thyroxin and Epinephrine on Organic-Bound I^{131} in the Blood.

Treatment	No. of animals	OBI, C/min.	Rat No.	Statistical significance
Exp. 1				
Thyroxin + epinephrine	5	91.8 ± 30.2*	1- 5	f = 38.91
Thyroxin	5	94.8 ± 28.2	6-10	p <.01
Epinephrine	5	132.0 ± 18.5	11-15	
Saline	3	152.0 ± 25.7	16-18	
Exp. 2				
Thyroxin + epinephrine	5	117.8 ± 10.6	1- 5	f = 9.37
Thyroxin	5	186.0 ± 46.5	6-10	p <.01
Epinephrine	5	196.0 ± 65.8	11-15	
Saline	3	299.7 ± 17.7	16-18	
Exp. 3				
Thyroxin + epinephrine	5	189.0 ± 33.0	1- 5	
Thyroxin	5	242.0 ± 82.0	6-10	
Epinephrine	5	246.0 ± 64.0	11-15	
Saline	1	318.0	16-18†	

* Mean ± stand. dev. † 2 samples lost.

Each animal inj. with 30 μc I^{131} 18 hr before sacrifice.

No. 1-10 inj. with 0.5 mg of thyroxin 2½ hr before sacrifice. No. 1-5 and 11-15 inj. with 0.1 mg epinephrine 2 hr before sacrifice. No. 16-18 inj. with a normal saline solution 2 hr before sacrifice.

thyroxin has been found to produce a lowering in the blood level of thyroid hormone (organic-bound I^{131}). This response to epinephrine is interpreted as being due to the increased utilization of circulating thyroid hormone caused by epinephrine. The significance of this finding is discussed.

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1. Gross, J., and Pitt-Rivers, R., *Biochem. J.*, 1953, v53, 645.

2. Williams, R. H., Jaffe, H., and Kemp, C., *Am. J. Physiol.*, 1949, v159, 291.

3. Soffer, L. J., Volterra, M., Gabrilove, J. L., Pollack, A., and Jacobs, M., PROC. SOC. EXP. BIOL. AND MED., 1947, v64, 446.

4. Botkin, A. L., and Jensen, H., *Endocrinology*, 1952, v50, 68.

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The First Heart Sound in Ventricular Contractions Arising from the Apex and Base.* (20977)

ROY D. SCHAEFER† AND ROBERT C. LITTLE.

From the Divisions of Physiology and Medicine, University of Tennessee, Memphis.

The first heart sound has been reported to be delayed in ectopic ventricular beats in humans(1,2) and in dogs(2). This delay was attributed to the mechanism of closure of the A-V valves. No attempt was made in these reports to differentiate between ectopic beats arising from the apex and those originating from the base. The mode of contraction may be different in beats arising from one or the other of these locations; therefore, variations in closure of the A-V valves and timing of the first sound might occur. The present study was undertaken to investigate this pos-

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† Public Health Service Research Fellow of the National Heart Institute.