

statistically analyzed for the preliminary run and for each of the subsequent periods.

Results. Five pairs of animals were carried through successfully. In 4 pairs no significant effect of the thyroxine could be noted. In the fifth a rise of 28% was found at the 9th to 12th day after the first injection. This animal, however, suffered a severe tail lesion at the time of introduction into the respiratory chamber. Since the standard error of the mean of each period varied from 3 to 7% of the mean, it is apparent that a change of even 25% in the standard level would be clearly brought out in the present study. The absence of such a rise in all but one case (where its significance is perhaps doubtful) leads the authors to the opinion that, in the toadfish, thyroxine, even in heavy doses, does not materially increase the oxygen consumption of the normal animal. At the end of the experiment in 3 cases 2 to 2.5 mg. of 2-4 dinitrophenol were injected into the experimental animals. This resulted in a rise of almost 100% in the oxygen consumption, showing that the animals were capable of responding to an effective agent.

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Low-Iodine Goiter and the Resistance of the Rat to Thyreotropic Stimulation.

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The rat thyroid is peculiarly resistant to stimulation by the anterior lobe thyreotropic hormone.¹ Anderson and Collip¹ found that rats showing spontaneous goiters of unknown etiology developed a more severe hyperthyroidism after thyreotropic injections than did normal animals, which suggests that the stress of hyperplasia of the thyroid in some way alters this resistance. Severely hyperplastic thyroids can consistently be produced in the rat by means of a diet with inadequate iodine intake.² In this work, the modified low-

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¹ See review in Anderson, E. M., and Collip, J. B., *J. Physiol.*, 1934, **82**, 11.

² Levine, H., Remington, R. E., and Von Kolnitz, H., *J. Nutrition*, 1933, **6**, 325.

iodine diet of R. E. Remington³ was used in an effort to determine whether rats bearing hyperplastic goiters of known origin would show an augmented susceptibility to thyreotropic stimulation.

Three methods of pituitary administration were used: (1) implants of freshly ground anterior lobes of beef pituitaries into the thigh muscles; (2) injections of an alkaline extract of sheep anterior lobes;† (3) injections of a more purified extract, "Phyone".‡ Treatment was continued for one week. The potency of all 3 materials was established by the injection of similar doses into immature guinea pigs. The beef implants were the most effective of the 3.

The criteria for judging thyroid response were the fresh weight, dry matter content, iodine content, and histological picture. Techniques used were those of R. E. Remington.³‡

(a) *Normal Animals* (Table I, Series A). Two groups of normal animals receiving pituitary substance showed a slight increase in thyroid weight, of questionable significance. Dry matter and iodine content showed a significant decrease. Histological study showed a rather wide variation in degree of response, but in general there was a heightening of epithelial cells, a partial softening and disappearance of colloid, and a tendency toward hyperplasia.

(b) *Goitrous Animals* (Table I, Series B, C, D). In none of the groups was there a significant increase in thyroid fresh weight or decrease in dry matter and iodine content following pituitary administration. No gross external signs of the development of a thyrotoxic condition were evident, and no difference could be seen between histological pictures of the thyroids of treated and untreated animals.

Since the lack of response of goitrous animals to pituitary stimulation might in part be due to an inadequacy of available iodine, 1 γ iodine per day (a minimal protective dose⁴) was given to 2 groups of rats, with and without pituitary administration (Series E). The untreated goitrous rats of Series D served as controls. The iodine induced an average decrease of approximately 6 mg. per 100 gm. body weight, with a partial return of the dry matter and iodine content toward normal levels. There was no significant difference in degree of recovery between the 2 groups. Histological study showed no difference between thyroids of the group receiving pituitary and those of the group which did not.

³ Remington, R. E., *J. Nutrition*, 1937, **13**, 223.

† The sheep extract was kindly supplied by Dr. Oliver Kamm, of Parke, Davis and Company, and the Phyone by Dr. David Klein, of the Wilson Laboratories.

‡ Iodine analyses were made by Mr. Cecil L. Smith.

⁴ Levine, H., Remington, R. E., and Von Kolnitz, H., *J. Nutrition*, 1933, **6**, 347.

TABLE I.

Series	No.	Treatment	Aver. final wt., gm.	Thyroid Glands		
				Wt. per 100 gm. body wt., mg.	Dry Matter, %	Iodine, dry basis, %
	27	Normal ¹	102	10.0±0.5 5.7-14.6	33.3	.200
A	14	ASE ²	115	11.8±0.2 10.6-14.0		
	18	PI ³	102	11.3±0.3 8.2-15.6	26.9	.178
B	15	Untreated Goitrous ⁴	150	14.8±0.3 12.1-18.0	25.6	
	12	ASE ⁵	159	15.3±0.4 11.7-19.1	25.1	
C	9	Untreated Goitrous ⁶	87	22.1±0.9 15.1-27.7	20.2	
	9	PI ⁷	88	20.9±1.0 15.6-28.0	19.4	
D	9	Untreated Goitrous ⁶	115	25.4±0.7 22.0-40.0	20.6	.008
	9	PI ⁷	117	26.6±0.8 21.5-32.3	20.2	.012
	9	Phyone ⁸	110	23.0±0.7 17.5-26.5	21.0	.015
E	9	PI+NaI ⁹	118	19.0±0.9 12.8-26.3	22.2	.056
	9	NaI ¹⁰	115	20.0±0.9 16.5-28.6	22.8	.055

¹ From table of normal thyroids for colony used: Remington, R. E., Remington, J. W., and Welch, S. S., *Anat. Rec.*, 1937, **67**, 367.

² Alkaline Sheep Extract, 0.8 cc. per day for 7 days.

³ Beef Pituitary Implants, daily for 6 days.

⁴ Placed on Diet No. 342 (Remington, R. E., *J. Nutrition*, 1937, **13**, 223) when approximately 60 gm. in weight, injections begun at end of 35 days.

⁵ Alkaline Sheep Extract, 1 cc. per day for 6 days.

⁶ Born of goitrous mothers, on low-iodine diet from time of conception.

⁷ Beef Pituitary Implants, daily for 7 days.

⁸ Phyone, 1 cc. per day for 6 days.

⁹ Beef Pituitary Implants daily for 7 days, with 1 γ iodine per day, in an aqueous solution of NaI, injected interperitoneally.

¹⁰ 1 γ iodine per day for 7 days, injected interperitoneally.

Summary. 1. Normal rats receiving pituitary stimulation showed a slight positive thyroid response, as determined by differences in fresh weight, dry matter content, iodine content, and histological picture. 2. Rats with hyperplastic goiters, produced by an iodine-deficient diet, were just as resistant to pituitary stimulation as were the normals. 3. Iodine administration at a level which will just protect the normal rat against thyroid hyperplasia does not affect this resistance. 4. On the basis of the criteria used, the low-iodine hyper-

plastic goiter seems to differ from the reported spontaneous goiter, in that it does not alter the natural resistance of the rat to thyreo-tropic stimulation.

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The Purpuric Reaction Produced in Animals by Derivatives of the Pneumococcus.

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Julianelle and Reimann¹ have described the purpura that develops in white mice following the intraäbdominal injection of pneumococcal autolysates. This reaction is most evident in those portions of the skin on which hair is either scanty or absent. They concluded that some autolytic derivative of the bacterial cells damaged the endothelium of the capillaries in these areas.

The experiments of Julianelle and Reimann have been largely repeated and extended. One of the most striking features of the reaction is that the purpura produced is seldom evenly distributed over the ears, feet, tail, snout, and genitalia. Even on the ears the distribution may be splotchy while along the tail the reaction is always most irregular, certain points showing a very intense reaction while others may be completely negative. These irregularities as well as the anatomical distribution of purpura suggested that some factor such as a mild trauma might be involved in the localization of the reaction. As a test of this hypothesis several experiments have been carried out of which 2 typical examples may be cited.

Experiment 1. An area of one sq. cm. of the abdominal skin of a mouse was carefully shaved. Immediately thereafter 0.5 cc. of an autolysate of rough pneumococci prepared by the method of Julianelle and Reimann was injected intraäbdominally at a point removed from the shaved area. At 24 hours the shaved lesion was markedly purpuric but the removal of hair from neighboring areas showed these to be free of purpura. A second injection of the autolysate was then given. Twenty-four hours thereafter the freshly shaven areas were purpuric but further removal of hair showed that the adjacent skin was completely clear. It seems reasonable to

¹ Julianelle, L. A., and Reimann, H. A., *J. Exp. Med.*, 1926, **43**, 87, 97; 1927, **45**, 609.