

August during days of extreme heat, and these tests (starred in the table) were unsatisfactory because the rats grew poorly and the ovaries of the controls did not respond adequately to the stimulation of the gonadotropic hormone. The other tests were entirely satisfactory. The results are shown in Table I.

TABLE I.
The Average Weights of Ovaries of Rats Tested with Sheep-Pituitary Extracts and with the Sera of 2 Sheep which Received Prolonged Injections of Sheep-Pituitary Extracts.

	The day serum was taken				
	0 day	85th day*	115th day*	145th day	180th day
Controls; no serum; Extract No. 1, 0.5 cc.	59	32	24	54	50
Serum, Ewe No. 1, 0.5 cc. plus Extract No. 1, 0.5 cc.	61	16	23	38	50
Serum, Ewe No. 2, 0.5 cc. plus Extract No. 1, 0.5 cc.	63	16	33	44	38

Summary. Sheep-pituitary extracts, which had produced gonadotropic antihormones in several species of animals, were injected into 2 sheep for 6 months, during which time no gonadotropic antihormone was found in the sheep-sera.

9084

Non-Specificity of Thyrotropic Antihormone.*

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The preparation of an antiserum which inactivated pituitary gonadotropic hormone of several species of animals, including man, has been reported.¹ The present study of the same serum was made in order to extend the observations to include its effect upon pituitary thyrotropic hormone from several species of animals. Along somewhat similar lines, Gregerson, Clark and Kurzrok² injected prolant into rabbits and prepared an antiserum which inhibited the gonadotropic activity of an extract of bovine pituitary glands. Prior

* The experiments were aided by a grant from the Josiah Macy, Jr. Foundation.

¹ Thompson, K. W., and Cushing, H., *Proc. Roy. Soc., London*, s.B., in press.

² Gregerson, H. J., Clark, A. R., and Kurzrok, R., *Proc. Soc. Exp. Biol. and Med.*, 1936, **35**, 193.

to the appearance of these reports, the information available indicated that an antihormone preparation inactivates only the extract that arouses the antagonistic response (Bachman, Collip and Selye).³

Briefly, the tests were devised to determine whether the standard effects of injections of the several pituitary thyrotropic hormone preparations into test animals could be modified by injections of the antiserum.

The thyrotropic extracts used in the tests were the following: (1) a sheep-pituitary extract prepared by a method described by VanDyke and Wallen-Lawrence⁴; (2) an alkaline extract of an acetone-dried powder of whole sheep-pituitaries; (3) a bovine thyrotropic extract kindly contributed by Dr. Arnold Loeser; (4) a thyrotropic extract also of bovine pituitaries supplied by Parke, Davis and Company; (5) an extract of the combined urine samples of 3 men that had complete myxoedema following total thyroidectomy.[†]

The serum was obtained from a mature, female collie dog, which had been injected daily for 16 months with extract No. 1. She showed marked signs of hypothyroidism, namely, obesity, sluggishness, coarse fur, and hypercholesterolemia. Her thyroid gland, as disclosed at biopsy, was activated shortly after injections were started, and it subsequently became completely inactivated. Signs of sexual stimulation, which also appeared shortly after injections were started, rapidly disappeared and did not reappear.

The standard effects of each thyrotropic extract were determined in young male guinea pigs which were subcutaneously injected with the extract twice daily for 3 days and were autopsied on the fourth day. For comparison with these animals, other groups of guinea pigs were given the same tests of the thyrotropic extracts together with injections of the antiserum, which were given twice daily for 2 days before and during the administration of the thyrotropic hormone. Control experiments were made with serum alone. The thyroid glands of the animals were weighed, fixed in Zenker's fluid, and sections were stained with hematoxylin and eosin. The

³ Bachman, C., Collip, J. B., and Selye, H., *PROC. SOC. EXP. BIOL. AND MED.*, 1934, **32**, 544.

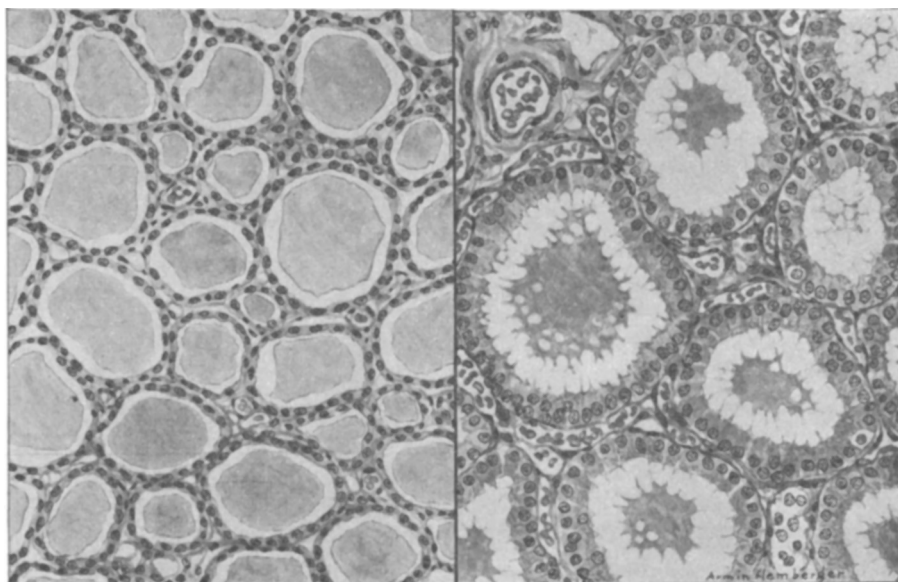
⁴ VanDyke, H. B., and Wallen-Lawrence, Z., *J. Pharm. and Exp. Therap.*, 1933, **47**, 163.

[†] The operations for total thyroidectomy were performed by Dr. Elliott C. Cutler of the Peter Bent Brigham Hospital. Not one of these patients had taken thyroid in any form within a year prior to the time the urine was tested, and each had the classical signs and symptoms of myxoedema. The extracts were made by precipitation of the urine with 80% acetone.

histological signs which were used in comparison to the control findings for estimation of the thyrotropic effects were diminution in the amount of stainable colloid, elevation and proliferation of the epithelium of the acini, and increased vascularity.

Special precautions were taken to have the guinea pigs' cage at a constant temperature of 29°C. Two weeks before testing, the animals were placed in this cage where they remained until autopsied. Such regulation of temperature has been reported by Englemann⁵ and by Schoeller⁶ to be an aid in securing uniformity of results. The further precaution was taken to inject the serum into one side of the guinea pigs and the extract into the other side, in order to prevent mixture of the materials at the site of injection.

Study of the average weights of the thyroid glands and the histological preparations revealed that injections of the dog's serum into guinea pigs produced an effect resembling hypophysectomy, and substantial doses of each of the thyrotropic preparations were inactivated in these test animals by the antiserum. The results are illustrated in Fig. 1 and are listed in Table I.



A

B

FIG. 1.

- A. Thyroid gland of guinea pig treated with serum and Extract No. 3.
 B. Thyroid gland of guinea pig treated with Extract No. 3 alone.

⁵ Englemann, B., *Arbeitsphysiol.*, 1930, **2**, 387.

⁶ Schoedel, W., *Arch. f. exp. Path. u. Pharmacol.*, 1933, **173**, 314.

TABLE I.
Inactivation of Thyrotropic Hormone from Different Species of Animals Produced in Guinea Pigs by the Serum of a Dog which Had Been Injected for Sixteen Months with a Sheep-Pituitary Extract (No. 1).

Source of Hormone	Thyroid glands of guinea pigs: Hormone alone		Thyroid glands of guinea pigs: Hormone plus Serum	
	Wt.	Activity	Wt.	Activity
Extract No. 1 (Sheep), 1.0 cc.	56	Activated 2 plus	24	Inactivated
Extract No. 2 (Sheep), 0.5 cc.	81	" 3 "	25	"
Extract No. 3 (Beef), 0.5 cc. (Looser)	75	" 3 "	17	"
Extract No. 4 (Beef), 1.0 cc. (P. D. & Co.)	96	" 4 "	47	Partially inactivated
Extract No. 4 (Beef), 0.25 cc. (P. D. & Co.)	63	" 3 "	29	Inactivated
Extract No. 5 (Man), 3.0 cc.	25	" 1 "	25	"

Summary. Daily injections of sheep-pituitary extract into a dog produced an antihormone which inactivated in guinea pigs substantial test doses of thyrotropic hormone from sheep and bovine pituitary glands and from human urine of myxoedema. Injections of the serum alone into guinea pigs produced upon their thyroids an effect which resembled hypophysectomy.

9085

The Augmentary Factor in Animal Sera After Injections of Pituitary Extract.*

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There has recently appeared a most timely report of the preparation of a pituitary gonadotropic antagonist by Evans, Korpi, Pencharz, and Simpson.¹ According to these workers this pituitary fraction, representing what Sharpey-Schafer would have called a chalone, is probably present in considerable amounts in most crude pituitary extracts, and accounts for the strange lack of activity shown by certain gonadotropic extracts from which greater potency would have been expected. Such an extract has been the subject of inves-

* The experiments were aided by a grant from the Josiah Macy, Jr. Foundation.

¹ Evans, H. M., Korpi, K., Pencharz, R. I., and Simpson, M. E., *Univ. of Calif. Pub. in Anat.*, 1936, 1, 237.