

During the 4 months the rabbit was observed no metastatic lesions were detected.

The 2 guinea pigs remained vigorous and healthy for 4½ months after inoculation. At the end of this time there was no evidence of disease in the viscera or serous membranes of the 2 animals. No acid-fast organisms were seen in stained tissue preparations from the lungs, spleen, liver and inguinal lymph node in one animal, and from the spleen in the other.

This single observation supports the opinion that sarcoids in syphilitic patients are syphilitic in origin. Although a blood-stream infection was not eliminated as a possible source of the organisms recovered from the animal developing syphilis, its occurrence in an infection of 8 years standing is unlikely. It seems reasonable to assume that although the tumors described by Boeck and by Darier and Roussy belong to a more or less distinct clinical group, they do not represent a common etiologic entity.

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Exophthalmos in Thyroidectomized Guinea Pigs by Thyrotropic Substance of Anterior Pituitary, and the Mechanism Involved.

DAVID MARINE AND S. H. ROSEN.*†

From the Montefiore Hospital, New York City.

We pointed out¹ that chronic, progressive, bilateral exophthalmos, produced in immature (2-3 months old) rabbits, maintained on a diet of alfalfa hay and oats, by the daily intramuscular injection of 0.05-0.1 cc. methyl cyanide, occurs in association with thyroid insufficiency (that is, (a) marked hyperplasia of the thyroid or (b) thyroidectomy). It is obvious, therefore, that exophthalmos is not dependent upon either a normal or abnormal thyroid secretion. Neither do the medulla and cortex of the suprarenal gland have any specific or initial relation to exophthalmos.

To obtain further information on the nature of exophthalmos we have produced it in young normal and thyroidectomized guinea pigs by using acetic acid extracts of anterior pituitary powder (Ar-

* Fellow of Montefiore Hospital.

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¹ Marine, D., Rosen, S. H., and Cipra, A., *PROC. SOC. EXP. BIOL. AND MED.*, 1933, **30**, 649.

mour) that Spaul,² Uhlenhuth and Schwartzbach,³ and Loeb and Bassett⁴ have shown to contain the thyrotropic hormone and with which Loeb and Bassett have produced exophthalmos in guinea pigs. The data are given in the following table.

TABLE I.

Guinea Pig No.	Thyroid intact			Amount thyrotropic† hormone injected intraper. daily	Examination for Exophthalmos by Days						
	Wt.	Age	Sex		2nd	4th	6th	8th	10th	12th	14th
	gm.	days		cc.							
1	276	28	M	2	—	—	+?	+?	+	+	+
3	241	16	M	2	—	+	+	+±	+	+	+
9	206	16	F	2	—	—?	+±	+	+	+	+
10	175	16	M	2	—	—	—	—	—	—	—
13	184	19	M	1 cc. for 10 days then 2 cc.	—	+	+	+	+	+	+±
14	240	24	M	”	—	—?	—?	+	—?	+?	+
	Thyroidectomy										
5	159	16	F	2	—	+	+?	+±	+±	+±	+
6	184	16	M	2	—	+	+	+	+?	+	+
7	141	16	F	2	—	—?	+	+±	+	+	+
8	160	16	M	2	—	—?	—?	—	+?	+	—?
11	213	19	F	1 cc. for 10 days then 2 cc.	—	—	+?	—	—	—?	+
12	187	19	M	”	—	—?	—?	+?	—	—?	+±
15	169	19	M	”	—	—	—	—	—	—?	—

† Prepared after the method of Loeb and Bassett.

It is clear that acetic acid extracts of ox anterior pituitary powder produce exophthalmos as well in thyroidectomized guinea pigs as in those with intact thyroids. Also, as in the case of methyl cyanide, the exophthalmos does not appear in guinea pigs with intact thyroids until they have developed thyroid hyperplasia (thyroid insufficiency), and to both cyanide and anterior pituitary extract some animals are resistant. Since both thyroidectomy and thyroid hyperplasia cause hypertrophy of the anterior pituitary, and since both methyl cyanide and the thyrotropic factor of the anterior pituitary cause exophthalmos in the absence of the thyroid, it is probable that the exophthalmos caused by methyl cyanide is due to its stimulating effect on the anterior pituitary which in turn stimulates the centers in the mid-brain controlling the sympathetic innervation of the eye (the pupillo-dilator muscle and the muscle of Müller). It also appears probable that cyanides act indirectly to cause thyroid hyperplasia by stimulating the anterior pituitary to

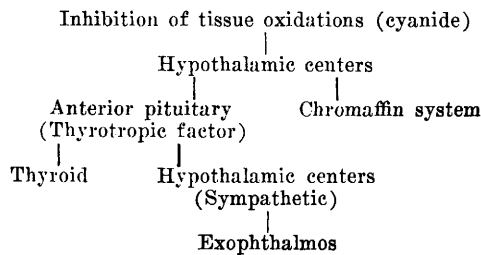
² Spaul, E. A., *Brit. J. Exp. Biol.*, 1924, **2**, 33.

³ Uhlenhuth, E., and Schwartzbach, S., *Brit. J. Exp. Biol.*, 1927, **5**, 1.

⁴ Loeb, L., and Bassett, R. B., *Proc. Soc. Exp. Biol. and Med.*, 1929, **27**, 490.

an increased production of the thyrotropic hormone. Whether the stimulation of the anterior pituitary is a direct cyanide action or an indirect result of stimulation of the autonomic nerve centers in the hypothalamus caused by the general tissue oxidation inhibiting effect of cyanides is unknown, although there is abundant evidence in favor of the latter view; that is, that the thyroid response, the pituitary response, the adrenal response, and the exophthalmos are the expressions of the organism's attempt to overcome the metabolism depressing action of HCN.

Our present view of the mechanisms involved in the production of thyroid hyperplasia and of exophthalmos by cyanides and by the thyrotropic hormone may be presented schematically as follows:



Cyanides appear to act by inhibiting metabolic processes. This inhibition stimulates the hypothalamic centers, which in turn stimulate the pituitary to produce the thyrotropic hormone, which in turn powerfully stimulates the thyroid gland and independently the sympathetic centers in the mid-brain causing exophthalmos.

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Respiratory Quotient of Cerebral Cortex in B₁ Avitaminosis.

H. E. HIMWICH, J. F. FAZIKAS, N. RAKIETEN AND R. SANDERS.

From the Laboratory of Physiology, Yale University, School of Medicine.

The investigation of Peters and his coworkers¹ has shown that the ability of the brain to oxidize lactic acid is decreased in polyneuritic pigeons. Since the respiratory quotient of the cerebral cortex of normal animals is unity,² probably due to the oxidation of

¹ Gavrilcscu, N., Mieklejohn, A. P., Passmore, R., and Peters, R. A., *Proc. Roy. Soc.*, 1932, **110** B, 431.

² Himwich, H. E., and Nahum, L. H., *Am. J. Physiol.*, 1932, **101**, 446. Dickens, F., and Simer, F., *Biochem. J.*, 1930, **24**, 1301.