corpus luteum if injected into a rabbit immediately after hypophysectomy, since in this species fully mature follicles are almost continuously present in the ovary. It further explains why the injection of A.P.L. into guinea pigs does not lead to the formation of corpora lutea except in the presence of a large follicle. Since this species responds to A.P.L. in a manner similar to the hypophysectomized rat or rabbit, one may assume that the hypophysis of the guinea pig does not participate with the injected A.P.L. in follicular stimulation. This interpretation would also make Engle's[9] experiments on monkeys more comprehensible. The monkey seems to react very much like the guinea pig, in that here again A.P.L. produces luteinization only after the follicle has responded to hypophyseal stimulation.

It seems necessary at the present time to postulate 2 hypophyseal gonadotropic hormones, one follicle-stimulating and one that luteinizes the theca and the mature granulosa while it has no effect on the immature granulosa cells. The so-called "Prolan A" of menopausal urine appears to consist chiefly of the former, or at least to resemble it closely, whereas the placental hormone "A.P.L." of pregnancy urine ("Prolan A plus Prolan B" of Zondek's original terminology) is more comparable, in its biological relations, to the luteinizing fraction.

7867 C

Effect of Iodine and Desiccated Thyroid on Anterior Pituitary of Goitrous and Thyroidectomized Rabbits.*

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It has been known for nearly a century[1] that individuals and animals with endemic goiter or cretinism have hypertrophy of the anterior pituitary. In man pituitary weights up to 3 gm. have been recorded, while in rabbits of approximately 2 kg. body weight with large parenchymatous goiters we have observed pituitary weights of 0.070 gm., whereas our normal average weight of the pituitary of rabbits of this size is 0.020-0.022 gm. Rogowitsch[2] first demon-

9 Engle, E. T., *Endocrinol.*, 1934, **18**, 513.

*Aided by a grant from the Ella Sachs Plotz Foundation.

1 Nièpce, B., *Traité du goître et du crétinisme*, Paris, 1851.

2 Rogowitsch, N., *Ziegler's Beitrag.*, 1889, **4**, 453.

Rabbit No. and Sex	Wt. at Autopsy gm.	KI or Des. Thyroid No. and Size Doses mg.	Duration Exper. days	Thyroidec. Dura. Life After days	Wt. Pituitary mg.	Histology Pituitary*	Wt. Thyroid mg.	Histology Thyroid
				TABLE 1 A				
1312-F	2910	12—1.25	42	42	52	Mod. hypertrophy Acid. greatly reduced	None found	
1331-F	2287	12—1.25	43	43	45	Mod. hypertrophy Acid. greatly reduced	None found	
1327-M	2128	12—1.25	43	43	61	Mod. hypertrophy Acid. reduced	None found	
1352-F	2978	12—1.25	42	42	39	Mod. hypertrophy Acid. reduced	Small fragment	Colloid early
				TABLE 1 B				
1431-M	1363	24—150	25	220	19	Not hypertrophied Acid. normal	None found	
1436-M	1058	38—150	39	244	22	Not hypertrophied Acid. abundant	None found	
1441-M	1477	39—150	40	221	23	Not hypertrophied Acid. abundant Pars interm. active	Small fragment	Colloid
1442-F	1688	38—150	39	220	25	Not hypertrophied Acid. abundant Pars interm. active	Small fragment	Colloid
1447-F	1723	39—150	40	221	18	Not hypertrophied Acid. abundant Pars interm. active	Large fragment	Colloid

TABLE 1 C

1297-M	2095	1—2.5	3	—	39	Mod. hypertrophy Acid. greatly reduced	657	Colloid early
1298-F	1965	2—2.5	6	—	30	Mod. hypertrophy Acid. possibly reduced	424	Nearly colloid
1299-M	1799	3—2.5	9	—	19	Very sl. hypertrophy Acid. abundant	252	Colloid
1329-F	1771	4—2.5	12	—	22	Very sl. hypertrophy Acid. abundant	343	Colloid
1332-M	1535	5—2.5	15	—	15	Not hypertrophied Acid. abundant	398	Colloid
1325-F	1556	6—2.5	18	—	19	Not hypertrophied Acid. abundant	354	Colloid

TABLE 1 D

1470-M	2221	48—100	49	—	18	Not hypertrophied Acid. normal	236	Colloid
1471-M	2140	48—100	49	—	18	Not hypertrophied Acid. normal	219	Colloid
1473-M	1960	48—100	49	—	17	Not hypertrophied Acid. normal	152	Colloid
1459-M	2022	48—100	49	—	18	Not hypertrophied Acid. normal	169	Colloid

*Sections stained with (1) H & E and (2) Mallory's Connective Tissue.

strated that the anterior pituitary cells of rabbits underwent hypertrophy following thyroidectomy, an observation which has been confirmed by most subsequent observers for many species of mammals including man, as well as lower orders (amphibians, reptiles). Pituitary hypertrophy following thyroidectomy is most pronounced in young rabbits and may be overlooked in old adults.

During the past 4 years we have readily produced large parenchymatous goiters in prepuberal rabbits by maintaining them on a diet of alfalfa hay of low iodine content, whole oats, tap water and the daily injection of methyl cyanide up to 0.1 cc. in 20% solution intramuscularly. This material has made it possible to compare in the same breeds of rabbits under similar environmental conditions the hypertrophic changes in the anterior pituitary associated with parenchymatous goiter with similar changes following thyroidectomy.

As Rogowitsch has pointed out, all the cells of the anterior pituitary undergo hypertrophy following thyroidectomy and coincident with this there is a progressive relative increase in the chromophobic and a decrease in the stainable acidophilic cells, which in the rabbit attains its maximum between the 30th and 60th day. Contrary to the opinion expressed by Bryant,[3] we believe that the apparent increase in chromophobic cells is due to a degranulation of acidophilic cells.

Histologically the changes in the anterior pituitary in parenchymatous goiter and following thyroidectomy are practically identical and comprise 2 major alterations: (1) an increase in the size of all the glandular cells and (2) a decrease of the stainable acidophilic granules which may progress to complete disappearance.

Effect of iodine on the hypertrophic anterior pituitary of thyroidectomized rabbits. We have given iodine in doses of 1.25 to 2.5 mg. KI intraperitoneally 2 and 3 times weekly for one month or more, both beginning at the time of thyroidectomy and beginning approximately one month after thyroidectomy. Iodine in these large amounts does not arrest or prevent the hypertrophy of the anterior pituitary, nor does it arrest or prevent the loss of acidophilic granules, provided the thyroidectomy is complete. Iodine, when administered after hypertrophy of the pituitary has occurred, does not restore the acidophilic granules nor does it bring about a shrinkage in the size of the hypertrophic cells or reduce the weight of the pituitary. (Table 1 A.)

Effect of desiccated thyroid on the hypertrophic anterior pituitary of thyroidectomized rabbits. We have given desiccated thyroid in

[3] Bryant, A. R., *Anat. Rec.*, 1930, **47**, 131.

doses of 0.1 gm. 3 times weekly and up to 0.2 gm. daily beginning both at the time of thyroidectomy and also after a month or more following thyroidectomy. Desiccated thyroid in these doses completely prevents the hypertrophy of the anterior pituitary following thyroidectomy and also prevents the loss of acidophilic granules. If desiccated thyroid is given after the hypertrophy of the anterior pituitary caused by thyroidectomy has occurred, it brings about a restoration of the acidophilic secretion granules and causes a decrease in the size of the anterior pituitary cells individually and in the weight of the gland as a whole. (Table 1 B.)

Effect of iodine on the hypertrophy of the anterior pituitary of

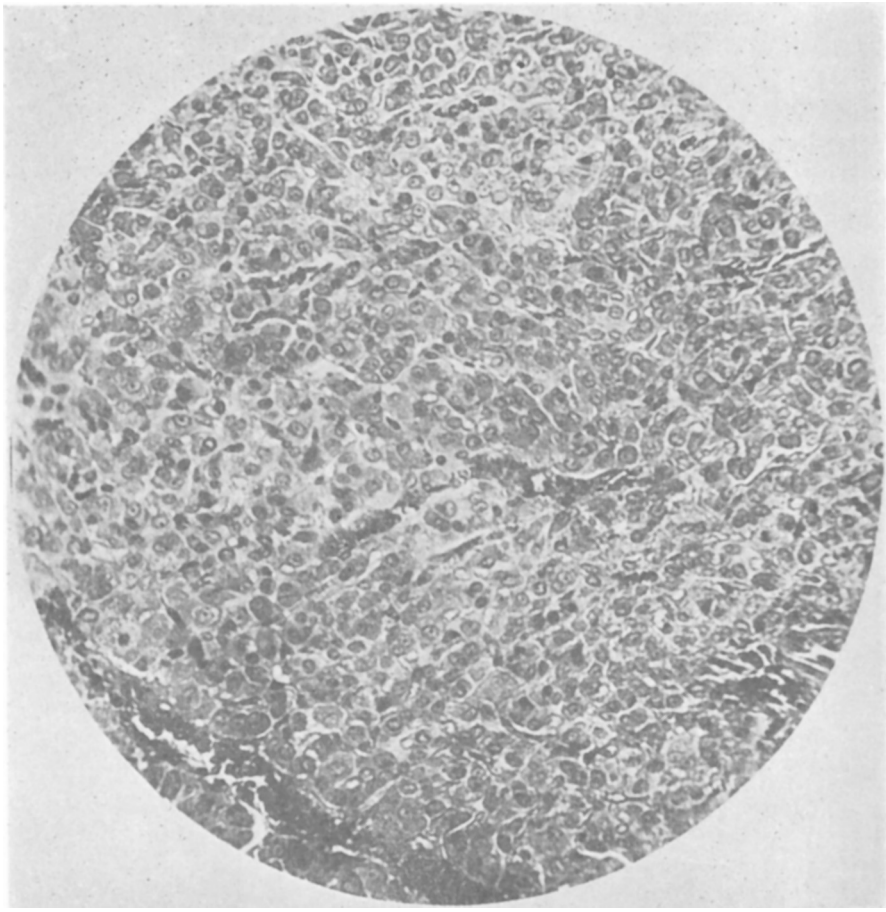

FIG. 1. Rabbit 1297. H and E stain. X 240. 1 injection 2.5 mg. KI, 3 days. Acidophilic granulations beginning to appear, cells large, only few pyknotic nuclei.

parenchymatous goiter. Iodine given in doses of 2.5 mg. KI 2-3 times weekly causes a rapid restoration of the acidophilic secretion granules and a shrinkage in the size of the cells. As determined by the comparative weights of the pituitaries there is also a great decrease in size. These changes in the anterior pituitary are obvious as early as the third day following the first dose of 2.5 mg. KI and by the ninth day the acidophilic granules are practically restored to normal staining intensity. The involution of the cells (shrinkage in volume and weight of gland) is far advanced but may not be complete in this time period. (Table 1 C.)

Effect of desiccated thyroid on the hypertrophy of anterior pituitary of parenchymatous goiter. Desiccated thyroid in doses of 0.1

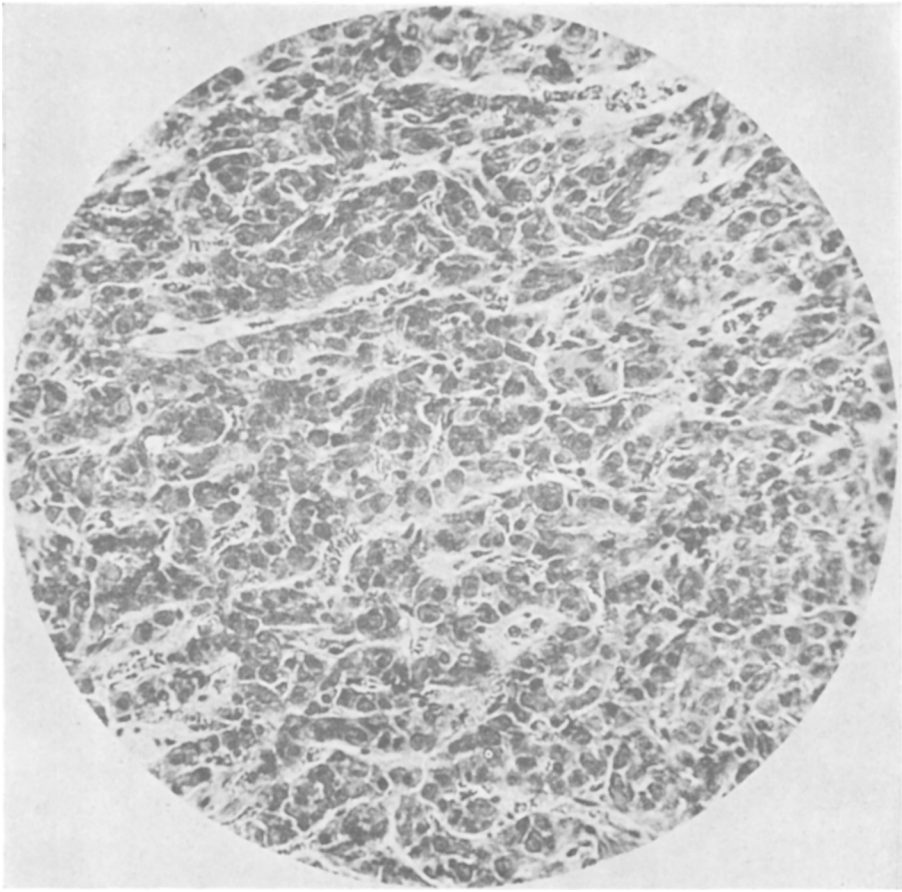

FIG. 2. Rabbit 1298. H and E stain. X 240. 2 injections 2.5 mg. KI, 6 days. Acidophilic granules more numerous. Cells and nuclei are smaller. More pyknotic nuclei.

gm. daily produces changes similar to those caused by iodine and also similar to those which desiccated thyroid in the same doses produces in the hypertrophic anterior pituitary following thyroidectomy. (Table 1 D.) Severinghaus, Smelser and Clark[4] observed that the acidophiles were larger and stained more brilliantly in thyroid fed rats.

It is evident, therefore, that desiccated thyroid will prevent the anterior pituitary changes and if present will restore the gland to the anatomical condition approximating normal, whether the thyroid

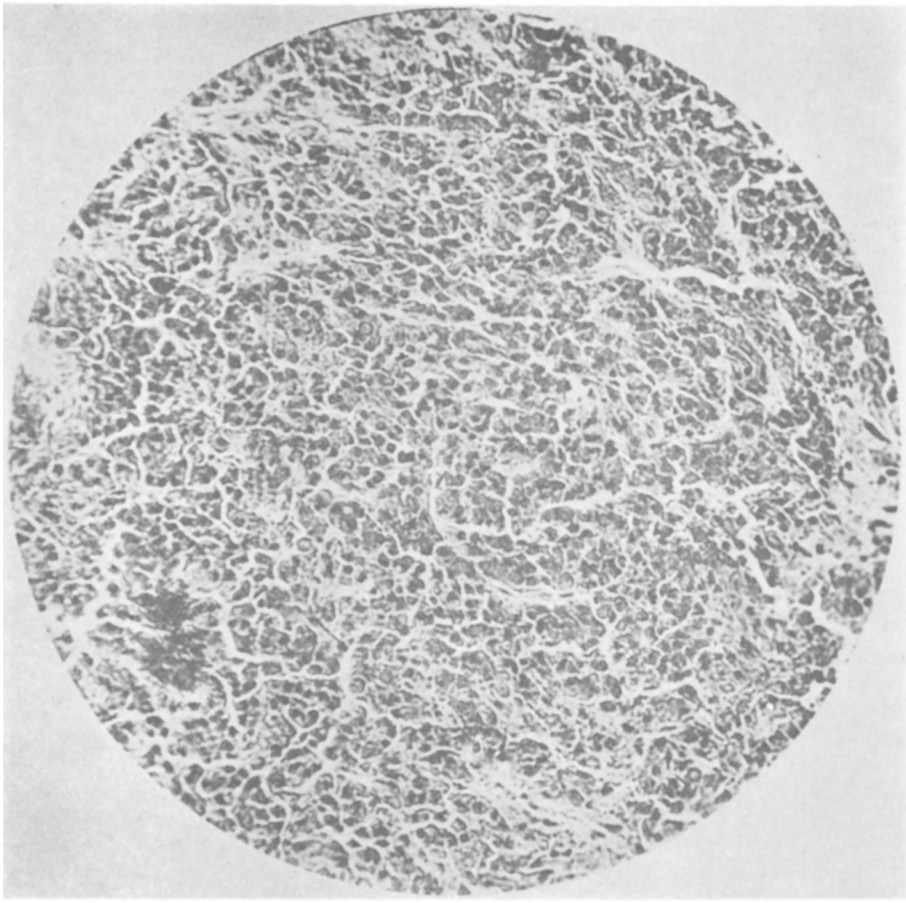

FIG. 3. Rabbit 1299. H and E stain. X 240. 3 injections 2.5 mg. KI, 9 days. Acidophilic granules abundant. Striking decrease in size of cells and condensation of nuclei.

4 Severinghaus, A. E., Smelser, G. K., and Clark, H. M., PROC. SOC. EXP. BIOL. AND MED., 1934, **31**, 1125.

is removed or intact. On the other hand iodine will restore the hypertrophic pituitary of parenchymatous goiter to normal as quickly and as effectively as desiccated thyroid, but it has no detectable effect on the pituitary after thyroidectomy. Evans and Simpson[5] have found that fresh beef thyroid fed to normal rats for 5 weeks caused an appreciable decrease in the weight of the pituitary and Loeser[6] showed that the pituitaries of iodine fed normal rats contained more thyrotropic substance than those of controls.

These facts suggest that only thyroxine is capable of preventing the hypertrophy of the pituitary after thyroidectomy and in parenchymatous goiter, and of restoring such glands to normal, and that iodine is effective only when the animal is capable of utilizing it in the elaboration of thyroxine. The thyroid secretion affects the anterior pituitary as strikingly as the anterior pituitary hormone affects the thyroid. From these results it would appear certain that the acidophilic granules are true secretion granules, decreasing with increased functional activity of the cells and increasing with physiologically decreased functional activity. This evidence could be further interpreted as indicating that the acidophilic granules contain the thyrotropic factor, although direct tests by several investigators have failed to demonstrate that there is a significant decrease in thyrotropic potency of the pituitary after thyroidectomy.

7868 P

Anti-Anemia Potency of Liver After Gastrectomy in Swine.*

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The introduction by Minot and Murphy[1] of liver therapy for pernicious anemia, and the subsequent discovery by Sturgis and Isaacs[2] of the efficacy of desiccated stomach have stimulated interest in the interrelationship between liver and stomach in the etiology

[5] Evans, H. M., and Simpson, M. E., *Anat. Rec.*, 1930, **45**, 215.

[6] Loeser, A., *Klin. Wchschr.*, 1934, **13**, 533.

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