These problems, especially the part played by the soil population in the transformation of organic matter in the soil, are at present studied in this laboratory and the results will be published at a future date.

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THE PRECIPITIN REACTION OF THYROGLOBULIN

Specificness; Presence of Thyroglobulin in Human Thyroid Veins; Production by Rabbit of Precipitin for Rabbit Thyroglobulin; Thyroglobulin in the Foetal Thyroid and in Exophthalmic Goiter

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Human thyroglobulin, prepared by Ostwald's method, besides a main specific antigen may contain also elements that call forth precipitins for the thyroglobulins of the beef and the swine.[1] These thyroglobulins, however, so far seem to be species-specific precipitinogens. By means of the precipitin test the presence of thyroglobulin in the thyroid lymph of goitrous dogs has been established, and observations have been made on the amount of thyroglobulin in the thyroid lymph of the blood of normal dogs under various conditions.[2] Like the human, dog thyroglobulin has elements in common with the beef and swine. It has been shown, too, that beef thyroglobulin can be demonstrated in the portal blood of fasting dogs fed beef thyroids.[3] In the course of this work further results have been gathered that now will be reported in brief.

1. *Specificness of Thyroglobulin Precipitins.*—Special care is used in the preparation of thyroglobulins to obtain solutions that are free from blood proteins; in most cases the serum of the immunized rabbits has not had any effect on the normal serum of the species in question, and in the case of beef, dog, horse and human antithyroglobulin serums there was no action on the corresponding serum proteins or hemoglobin. Thyroglobulin precipitins consequently are specific for thyroglobulin, but as shown in table 1 they are not consistently species-specific. In the case of a strong antihuman serum, the precipitins for beef and for swine thyroglobulin were removed completely by specific absorption in each case without noteworthy reduction of the precipitins for human thyroglobulin. Absorption ex-

periments have not been made with any of the other antithyroglobulin serums.

In addition to showing that thyroglobulin may occur in thyroid lymph and blood, the precipitin test also reveals that thyroglobulin is present as such in the colloid material of the thyroid. Consequently it does not seem likely that the method of preparing thyroglobulin materially alters its antigenic properties. We have not been able to detect thyroglobulin in extracts of any of the principal internal organs except that in one instance extracts of calf hypophysis reacted with precipitin serum for beef thyroglobulin and in one case an extract of dog liver seemed to contain thyroglobulin. Further work, however, needs to be done on problems such as now suggest themselves.

2. *Is Thyroglobulin Present in Blood in Human Thyroid Veins?*—Principally through the coöperation of Dr. John deJ. Pemberton of the Mayo Clinic a considerable number of samples of blood from the human thyroid veins have been tested with potent antiserum for human thyroglobulin, and in several instances positive reactions have been obtained (table 2).

3. *Can the Rabbit Produce Precipitin for Rabbit Thyroglobulin?*—Thyroglobulin was prepared from so-called wild rabbits. The strength of the solution was 1 to 1250; 5, 10, 20 and 40 cc. were injected intravenously at intervals of 3 days, and on the fourth day after the last injection the serum reacted with dilutions of this thyroglobulin up to 1 to 10,000, as well as with thyroglobulin prepared from common laboratory rabbits, but not with the thyroglobulins of other species given in table 1.

TABLE 1

RANGE OF SPECIES-SPECIFICNESS OF PRECIPITIN REACTION OF THYROGLOBULIN

	ANTITHYROGLOBULIN PRECIPITIN SERUMS								NORMAL RABBIT
THYROGLOBULINS	BEEF	DOG	HORSE	HUMAN	RABBIT	RAT	SHEEP	SWINE	SERUM
Beef	+	+	+	+	0	0	0	0	0
Dog	0	+	0	0	0	0	0	0	0
Horse	0	0	+	+	0	0	+	0	0
Human	0	0	+	+	0	0	+	0	0
Monkey	0	0		+				0	0
Rabbit	0	0	0	0	+	0	0	0	0
Rat	0	0	0	+	0	+	0	0	0
Sheep	+	0	0	+	0	0	+	0	0
Swine	0	+	0	+	0	0	+	+	0

0 = no reaction + = reaction Tests by contact or layer method; results read after one hour at room temperature.

4. *Thyroglobulin from the Thyroid of Patients with Exophthalmic Goiter.*—Several samples of thyroglobulin have been prepared from thyroids of patients with well developed exophthalmic goiter, and rabbits immunized therewith. The precipitin serum of such rabbits did not differ from the

serum of rabbits immunized with thyroglobulin from normal human thyroids. No indications have been obtained that exophthalmic thyroglobulin differs in any way from the normal.

TABLE 2

CONDITION OF THYROID IN PATIENTS (DR. JOHN DEJ. PEMBERTON) IN WHOM THE BLOOD FROM THE THYROID VEINS GAVE PRECIPITIN TEST FOR THYROGLOBULIN

1. Small, cystic adenomas in colloid thyroid in woman, age 52.
2. Foetal and colloid adenomas in colloid thyroid in man, age 32.
3. Hypertrophic parenchymatous thyroid in woman, age 20.
4. Hypertrophic parenchymatous thyroid in man, age 43.
5. Foetal and colloid adenomas in colloid thyroid in woman, age 46.

The serums of several exophthalmic patients have been studied with reference to the possible presence of thyroglobulin or of precipitins for thyroglobulin. The number of serums studied in this way is too small to warrant any conclusions. Thyroglobulin has not been found definitely in any serum from exophthalmic patients. In one instance of advanced exophthalmic goiter in the care of Dr. Joseph F. Jaros, Chicago, the serum gave positive precipitin tests with extremely high dilutions of human thyroglobulin, but the amount of serum available was not sufficient to carry out all the properly controlled tests necessary to obtain conclusive results, and we have not had positive results in precipitin tests of other exophthalmic serums with human thyroglobulin.

So far skin tests with thyroglobulin have been negative.

5. *Does the Foetal Human Thyroid Contain Thyroglobulin?*—Definite reactions for thyroglobulin have been obtained in extracts of the thyroid of the human foetus in the third and fourth months. This result suggests that iodine may not be a factor in the antigenic properties of thyroglobulin, but direct tests are required. The precipitin test may be a means of estimating the quantity of thyroglobulin in foetal thyroids.

Summary.—Thyroglobulin precipitins appear to be specific for thyroglobulin but are not consistently species-specific; thyroglobulin is present as such in the colloid of the thyroid gland; the rabbit can produce precipitin for rabbit thyroglobulin; thyroglobulin may occur in the blood from the human thyroid vein; the precipitin test does not indicate any difference between thyroglobulin from the normal thyroid and that from exophthalmic goiter; the foetal human thyroid contains thyroglobulin in the third and fourth months, if not earlier.

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[3] Hektoen, Ludvig, Kanai, Paul H., and Dragstedt, Lester R.: A Study of Protein Absorption from the Digestive Tract by the Precipitin Test, with Especial Reference to Thyroglobulin, *J. Amer. Med. Ass'n.*, **84**, 1925 (114–5).

THE INTERNAL SECRETION OF THE PARATHYROID GLANDS

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The parathyroid glands were first shown by Gley to be vital structures. Since the work of this investigator these glands have been looked upon as organs of internal secretion. It was held by some that they formed part of a detoxicating system while others thought that they functioned by the production and liberation into the blood stream of a specific hormone. Of late years there have been two main theories of parathyroid function. One, the calcium theory based largely on the work of MacCallum, the other the toxin theory based mainly on the work of the Glasgow school. Both theories were entirely compatible with the idea that a specific internal secretion was elaborated by the parathyroid gland.

Many attempts have been made by various workers to obtain definite evidence of the presence in the normal gland of this specific substance. Suggestive results have been reported on numerous occasions by both laboratory workers and clinicians. No definite and absolutely convincing scientific evidence of the existence in extracts of the parathyroid gland which have been used of the specific internal secretion of the gland has, however, been obtained by these investigators. It is thought that this scientific evidence has now been furnished by the work which has been carried out in the University of Alberta during the past year. The results which have been obtained have been so clear cut and readily duplicable that it is evident that the suggestive results of other workers have been due to the existence in certain of their preparations of the active principle. In the absence of any reliable method of testing and standardizing parathyroid gland extracts these workers were consequently unable to place their results on a scientific basis. From the data which is to be found in the writings of Berkeley and Beebe (1909) and Hanson (1924) there can be no doubt that these authors had obtained the active principle of the parathyroid gland in certain of their extracts.

The work which has been carried out in our laboratory has shown conclusively that the specific internal secretion of the parathyroid gland can be obtained in a stable form and in a degree of purity and potency hitherto