

## THE IODINE CONTENT OF THE BLOOD FOLLOWING THYROIDECTOMY.

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The presence of iodine widely distributed in animal tissues has been well established. The occurrence of iodine in certain essential constituents of the thyroid gland has long been known, and there is evidence that the administration of iodine produces changes in the organ. Little is known concerning the relation of the thyroid to the iodine metabolism of the body.

Baumann<sup>1</sup> first showed that the thyroid gland contains iodine in amounts sufficient for quantitative determination, and obtained evidence that iodine forms an essential constituent of the gland. He found that the thyroids of twenty-six adults from Freiberg contained amounts of iodine varying from 0.22 mg. to 7.2 mg., the average iodine content of these twenty-six glands being 2.5 mg. The thyroids of four others contained 10.8, 14.9, 29.9, and 35.3 mg. respectively. Of thirty-four adults from Hamburg, the thyroids of thirty contained amounts of iodine varying between 0.3 and 9.7 mg. per gland, the average iodine content of the thirty glands being 3.83 mg. The thyroids of the other four individuals contained amounts of iodine in excess of 10 mg. per gland, the greatest amount being 27.6 mg. The thyroids of eleven adults from Berlin had an iodine content of less than 10 mg. per gland, the average content per gland being 6.6 mg. Two other thyroids contained 14.1 and 22.7 mg. respectively. Oswald<sup>2</sup> has also found a considerable variation in the average iodine content of the thyroid in different localities. Baumann found that the thyroids of children usually contained little or no iodine, and that the presence or absence of iodine and the amount, when present, varied according to the locality from which the glands were obtained. Wells<sup>3</sup> analyzed the thyroids of six children under 4 years of age from Chicago; three contained only traces and the other three contained from 0.011 to 0.092 per cent of iodine.

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<sup>1</sup> Baumann, E., *Z. physiol. Chem.*, 1895-96, xxi, 319; 1896-97, xxii, 1.

<sup>2</sup> Oswald, A., *Z. physiol. Chem.*, 1897, xxiii, 265.

<sup>3</sup> Wells, H. G., *J. Am. Med. Assn.*, 1897, xxix, 954.

Marine and Williams<sup>4</sup> and Marine and Lenhart<sup>5</sup> have arranged a series of thyroid glands from minimum to maximum in accordance with their iodine content and have found that they are at the same time arranged in series according to their histology, their colloid content, and their weight. In other words, the weight of the glands varied directly with the degree of hyperplasia and inversely with the iodine content. Marine and Lenhart<sup>6</sup> have found that thyroid hyperplasia in fish in any stage is diminished by addition of iodine to the water; they state that hyperplasia may be similarly prevented by iodine.

Loeb<sup>7</sup> observed hyperplasia in the thyroids of guinea pigs following the removal of part of the gland. He thought that there was evidence of a certain quantitative relation between the degree of hyperplasia and the amount of thyroid removed. Iodine did not diminish the intensity of the hyperplastic changes and he thought indeed that there was some indication that preparations of iodine might increase hyperplasia. Feeding of thyroid preparations, on the contrary, prevented hyperplasia.

Barell<sup>8</sup> found iodine in the ovaries, adrenal, and spleen of swine and cattle and in various commercial preparations of these organs. Howald<sup>9</sup> says that under normal conditions iodine is not found in human hair, dog's hair, or feathers of roosters; but following the administration of iodides the hair and feathers contain iodine. There was no iodine in the hair of a cretin 4 years of age, or of a woman with an extensive carcinoma of the thyroid.

Bourcet<sup>10</sup> has studied the distribution of iodine in the tissues of the rabbit. His figures obtained by examination of three rabbits are as follows: 200 gm. of blood contained 0.005 mg. of iodine; 60 gm. of heart, 0.0005 mg.; 400 gm. of liver with bile ducts, 0.71 mg.; 82 gm. of kidney, 0.027 mg.; 400 gm. of fat, none; 50 gm. of hair, 0.9 mg.; 500 gm. of muscle, 0.025 mg.; 40 gm. of lung, 0.03 mg.; 30 gm. of brain, 0.012 mg.; 10 gm. of pancreas, none; 200 gm. of skin without fur, 0.12 mg. Similar results were obtained with the tissues of a dog, iodine being recovered from the thymus, pituitary, and medullary tissue of the brain, mammary gland, and gravid uterus. Bourcet believes that all of the glands of the body contain iodine, though the amount is much less than that which is present in the thyroid. Iodine is excreted through the skin, the hair being the chief agent of elimination. Gley and Bourcet<sup>11</sup> find that the blood of dogs contains between 0.013 and 0.06 mg. of iodine per liter, which they think is in combination with protein.

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<sup>4</sup> Marine, D., and Williams, W. W., *Arch. Int. Med.*, 1908, i, 349.

<sup>5</sup> Marine, D., and Lenhart, C. H., *Arch. Int. Med.*, 1909, iv, 440.

<sup>6</sup> Marine, D., and Lenhart, C. H., *J. Exp. Med.*, 1911, xiii, 455.

<sup>7</sup> Loeb, L., *J. Med. Research*, 1919, xl, 199; 1919-20, xli, 485; 1920-21, xlii, 77.

<sup>8</sup> Barell, E., *Chem. Centr.*, 1897, lxviii, pt. 1, 608.

<sup>9</sup> Howald, W., *Z. physiol. Chem.*, 1897, xxiii, 209.

<sup>10</sup> Bourcet, P., *Compt. rend. Acad.*, 1900, cxxxi, 392.

<sup>11</sup> Gley, E., and Bourcet, P., *Compt. rend. Acad.*, 1900, cxxx, 1721.

Rogoff<sup>12</sup> found in two dogs that blood coming from the hyperplastic thyroid glands which had a very low iodine content did not cause the developmental changes which occur in tadpoles fed with thyroid. Blood of a third dog obtained during massage of the gland or during sympathetic stimulation produced the characteristic developmental changes. The samples of blood from this dog contained less than 0.005 mg. of iodine per gm. of dried blood. Later Rogoff and Goldblatt<sup>13</sup> used specimens of blood obtained from the glands of fifteen individuals on whom thyroidectomy had been performed. In this group were included instances of exophthalmic goiter, colloid goiter, and adenoma of the thyroid. They obtained no evidence of the presence of the active principle of the thyroid gland when these specimens of blood were fed to tadpoles. Examination of the specimens when sufficient amounts of blood were available failed to show the presence of iodine. Kendall<sup>14</sup> has separated the iodine of the thyroid into two parts. Part A is soluble in alkaline media and produces the same effects as thyroid when administered to patients; Part B is soluble in acids and does not produce the reactions of thyroid when administered to patients. When Marine and Feiss<sup>15</sup> perfused thyroids with solutions of potassium iodide they found that iodine was quickly taken up and fixed and was not readily removed by washing the gland with Ringer's solution. They obtained the same results by injecting the iodine into the circulation. Although, according to Marine and Rogoff,<sup>16</sup> iodine is quickly fixed in the thyroid for a time, it does not alter the influence of the thyroid tissue on the metamorphosis of tadpoles, but after several hours this property is distinctly increased. They regard the fixation of iodine and the formation of metamorphosis-promoting substance as distinct processes and think that the formation of this substance is dependent upon the amount of mother substance present in the gland rather than upon the amount of iodine, provided, however, that iodine is present in the usual quantity.

#### EXPERIMENTAL.

Observations recorded above concerning the relation of iodine to the thyroid gland have suggested the possibility that the thyroid might modify the iodine content of the blood. A quantitative study of the iodine in the blood has seemed desirable. Kendall<sup>17</sup> has

<sup>12</sup> Rogoff, J. M., *J. Pharmacol. and Exp. Therap.*, 1918-19, xii, 193.

<sup>13</sup> Rogoff, J. M., and Goldblatt, H., *J. Pharmacol. and Exp. Therap.*, 1921, xvii, 473.

<sup>14</sup> Kendall, E. C., *J. Biol. Chem.*, 1915, xx, 501.

<sup>15</sup> Marine, D., and Feiss, H. O., *J. Pharmacol. and Exp. Therap.*, 1915, vii, 557.

<sup>16</sup> Marine, D., and Rogoff, J. M., *J. Pharmacol. and Exp. Therap.*, 1916, viii, 439; 1916-17, ix, 1.

<sup>17</sup> Kendall, E. C., and Richardson, F. S., *J. Biol. Chem.*, 1920, xliii, 161.

recently published a method for determining iodine in the blood; this method is in reality a modification of his original<sup>18</sup> method of determining iodine in the thyroid gland. With this method, suitable for the determination of very small amounts of iodine, I have first determined the iodine content of the blood of normal dogs kept under laboratory conditions and then removed the thyroids of these animals in order to ascertain whether the iodine content of the blood is changed.<sup>19</sup> Determinations of the iodine in the blood have usually been made in duplicate by Kendall's method; occasionally in order to economize blood single determinations have been made at short intervals. After removal of a thyroid gland the animal has been kept under conditions identical with those before operation. The experiments are described in the order in which they were performed.

Determinations of the iodine in the blood of seventeen dogs have been made before the removal of the thyroid. The lowest amount of iodine found in normal blood is 0.0029 mg. in Experiment 10 and the highest amount is 0.0145 mg. in Experiment 8. The average amount of iodine in the blood of the seventeen dogs before the removal of the thyroid is 0.0079 mg. per 100 cc. of blood. Kendall gives 0.013 mg. of iodine as the average iodine content of the blood. He does not state whether or not the blood was human and does not give its source.

*Experiment 1.*—No determination of iodine in the blood was made before operation.

June 19, 1921. Both lobes of the thyroid were removed, a small tab being left at each lower pole with the parathyroids.

- July 19. 100 cc. of blood contain 0.039 mg. of iodine.  
100 cc. of blood contain 0.0383 mg. of iodine.  
Oct. 3. 100 cc. of blood contain 0.03 mg. of iodine.  
100 cc. of blood contain 0.0283 mg. of iodine.

Oct. 20. Animal killed. The small pieces of thyroid tissue at the lower poles are found to be very much enlarged and quite firm. Microscopic sections show active hyperplasia.

*Experiment 2.*—

- July 16, 1921. 100 cc. of blood contain 0.0116 mg. of iodine.  
Aug. 26. 100 cc. of blood contain 0.01 mg. of iodine.

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<sup>18</sup> Kendall, E. C., *J. Am. Chem. Soc.*, 1912, xxxiv, 894.

<sup>19</sup> All operations were performed under ether anesthesia.

Oct. 26. 100 cc. of blood contain 0.01 mg. of iodine.

Nov. 1. Both lobes of the thyroid are completely removed, leaving the parathyroid *in situ* at each lower pole.

Nov. 7. 100 cc. of blood contain 0.0141 mg. of iodine.

100 cc. of blood contain 0.014 mg. of iodine.

Nov. 9. The animal is found dead in its cage. At autopsy a large hematoma is found filling the space from which the left thyroid lobe had been removed. There is no suppuration of the wound.

*Experiment 3.—*

Aug. 25, 1921. 100 cc. of blood contain 0.0083 mg. of iodine.

100 cc. of blood contain 0.0066 mg. of iodine.

Sept. 3. The gland is removed completely, leaving the parathyroids at the lower poles *in situ*.

Sept. 17. 100 cc. of blood contain 0.02 mg. of iodine.

100 cc. of blood contain 0.0208 mg. of iodine.

The animal is very much emaciated and its hair is falling out in considerable quantities. It is killed with ether. The two parathyroids at the lower poles of the thyroid lobe are found intact.

*Experiment 4.—*

Sept. 15, 1921. 100 cc. of blood contain 0.0041 mg. of iodine.

100 cc. of blood contain 0.005 mg. of iodine.

Oct. 6. Both lobes of the gland are removed with the exception of a small tab at each lower pole.

Oct. 12. 100 cc. of blood contain 0.0166 mg. of iodine.

100 cc. of blood contain 0.0157 mg. of iodine.

*Experiment 5.—*

Sept. 20, 1921. 100 cc. of blood contain 0.0075 mg. of iodine.

100 cc. of blood contain 0.0083 mg. of iodine.

Oct. 4. Both lobes of the thyroid are completely removed.

Oct. 10. 100 cc. of blood contain 0.025 mg. of iodine.

100 cc. of blood contain 0.0216 mg. of iodine.

The animal is killed with ether. Its operative wound has healed by first intention.

*Experiment 6.—*

July 21, 1921. 100 cc. of blood contain 0.01 mg. of iodine.

Aug. 1. 100 cc. of blood contain 0.01 mg. of iodine.

Aug. 15. 100 cc. of blood contain 0.01 mg. of iodine.

Sept. 15. 100 cc. of blood contain 0.01 mg. of iodine.

100 cc. of blood contain 0.00833 mg. of iodine.

Oct. 21. Both lobes of the gland are removed, leaving the parathyroids at the lower poles *in situ*.

Oct. 30. 100 cc. of blood contain 0.03 mg. of iodine.

100 cc. of blood contain 0.0316 mg. of iodine.

The animal is killed with ether. The wound has healed by first intention.

*Experiment 7.—*

Oct. 19, 1921. 100 cc. of blood contain 0.0125 mg. of iodine.

100 cc. of blood contain 0.0133 mg. of iodine.

Nov. 8. Both lobes of the thyroid are removed, leaving the parathyroid at the lower pole *in situ*.

Nov. 13. 100 cc. of blood contain 0.025 mg. of iodine.

100 cc. of blood contain 0.0266 mg. of iodine.

Nov. 15. The animal is found dead in its cage. There was no clonic convulsion of tetany before death. There is slight suppuration of the wound at autopsy.

*Experiment 8.—*

Nov. 15, 1921. 100 cc. of blood contain 0.015 mg. of iodine.

100 cc. of blood contain 0.0141 mg. of iodine.

Dec. 1. The usual operation for removal of the thyroid is performed, leaving the parathyroid at each lower pole.

Dec. 3. 100 cc. of blood contain 0.0166 mg. of iodine.

Dec. 5. 100 cc. of blood contain 0.015 mg. of iodine.

There is slight suppuration of the wound.

Dec. 7. 100 cc. of blood contain 0.0066 mg. of iodine.

There is considerable discharge from the wound and the animal does not eat.

Dec. 9. 100 cc. of blood contain 0.0066 mg. of iodine.

The animal is killed with ether because its wound is suppurating and it does not eat.

*Experiment 9.—*

Dec. 3, 1921. 100 cc. of blood contain 0.00833 mg. of iodine.

100 cc. of blood contain 0.0075 mg. of iodine.

Dec. 3. The usual operation for removal of both lobes of the thyroid is performed, leaving a small tab of thyroid tissue with each parathyroid at the lower pole.

Dec. 5. 100 cc. of blood contain 0.02832 mg. of iodine.

Dec. 7. 100 cc. of blood contain 0.0375 mg. of iodine.

Dec. 8. The animal is found dead in its cage, symptoms of tetany having been present during 24 hours. Autopsy shows a small tab of thyroid tissue at each lower pole. These tabs of tissues are deep red in color. The parathyroids are not identified.

*Experiment 10.—*

Dec. 10, 1921. 100 cc. of blood contain 0.0033 mg. of iodine.

100 cc. of blood contain 0.0025 mg. of iodine.

Dec. 12. The usual operation for removal of both lobes is performed, leaving a small tab of thyroid tissue at each lower pole with the parathyroids.

Dec. 14. 100 cc. of blood contain 0.01 mg. of iodine.

Dec. 18. 100 cc. of blood contain 0.0116 mg. of iodine.

Following the operation this animal has eaten little. Immediately after removal of blood there are clonic convulsions of tetany and death occurred on Dec. 21.

At autopsy the wound is closed and there is no suppuration but the deeper tissues about the remaining bits of thyroid are red and indurated.

*Experiment 11.—*

Dec. 13, 1921. 100 cc. of blood contain 0.01 mg. of iodine.

100 cc. of blood contain 0.01 mg. of iodine.

Jan. 30, 1922. 100 cc. of blood contain 0.00833 mg. of iodine.

Feb. 1. The thyroid is removed as usual, leaving a small tab of thyroid tissue at each lower pole.

Feb. 6. The wound has healed by primary intention but there has been somewhat more edema than usual for several days. The animal has had today clonic convulsions of tetany. It is given 15 cc. of a 30 per cent solution of calcium lactate intraperitoneally and convulsions have disappeared within  $\frac{1}{2}$  hour.

Feb. 8. The calcium lactate is repeated because of clonic convulsions of tetany.

Feb. 11. 100 cc. of blood contain 0.015 mg. of iodine.

100 cc. of blood contain 0.02 mg. of iodine.

The animal has lost much weight and its hair is falling out in considerable quantities. Eats little.

Feb. 16. The animal is found dead in its cage. No suppuration of the wound is observed at autopsy. The bits of thyroid tissue at each lower pole are embedded in scar tissue.

*Experiment 12.—*

Dec. 18, 1921. 100 cc. of blood contain 0.0066 mg. of iodine.

100 cc. of blood contain 0.0066 mg. of iodine.

Dec. 23. The thyroid is removed, leaving the parathyroids at each lower pole.

Dec. 27. 100 cc. of blood contain 0.011 mg. of iodine.

Dec. 29. 100 cc. of blood contain 0.0097 mg. of iodine.

Dec. 31. 100 cc. of blood contain 0.00833 mg. of iodine.

The animal died following the removal of blood. At autopsy no suppuration of wound is found.

*Experiment 13.—*

Oct. 28, 1921. 100 cc. of blood contain 0.005 mg. of iodine.

100 cc. of blood contain 0.00583 mg. of iodine.

Jan. 10, 1922. The thyroid gland is removed.

Jan. 14. 100 cc. of blood contain 0.0233 mg. of iodine.

100 cc. of blood contain 0.02 mg. of iodine.

Jan. 15. The animal is found dead in its cage. No suppuration of the wound is found at autopsy.

*Experiment 14.—*

Jan. 3, 1922. 100 cc. of blood contain 0.0055 mg. of iodine.

100 cc. of blood contain 0.0055 mg. of iodine.

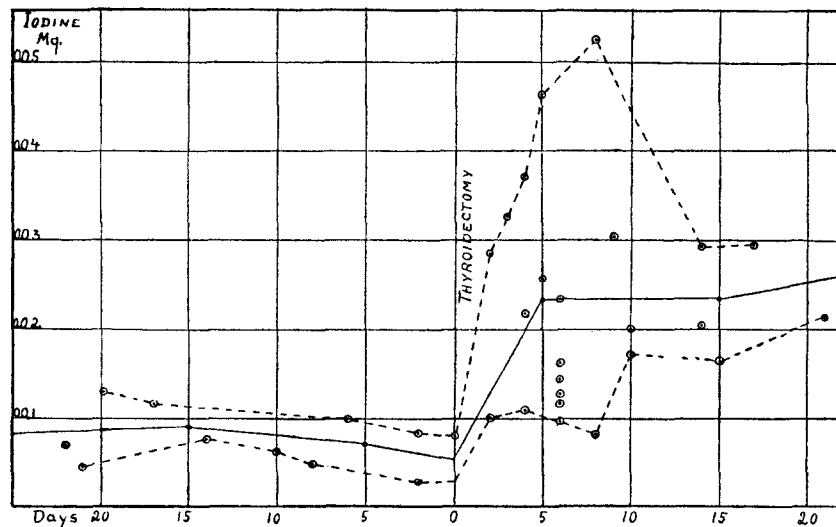
Jan. 11. The thyroid is removed.

Jan. 14. 100 cc. of blood contain 0.0333 mg. of iodine.

100 cc. of blood contain 0.036 mg. of iodine.

The animal died while being bled. No suppuration of the wound is found at autopsy.

This group of experiments demonstrates that the amount of iodine in the blood is greatly increased after thyroidectomy (Text-fig. 1). This increase is seen in all experiments. In Experiment 8 the increase is small and the amount of iodine in the blood soon falls below that found before operation; but this dog has suffered from a badly infected wound and did not eat, so that its store of iodine has not been re-



TEXT-FIG. 1. Composite chart of iodine determinations made before and after thyroidectomy. Maximum and minimum determinations are connected by broken lines to show the degree of variation. Only one determination was made on the day of operation, since it seemed undesirable to draw blood at this time. The date of operation has been crossed by the minimum line at the level of the last determination. The continuous line is an average of all determinations made within a period of 10 days, the date of operation being crossed midway between the minimum and maximum lines.

plenished. Increase of iodine in the blood varies but in a number of experiments is considerable. For example, in Experiment 14 there is an increase after removal of the thyroid from 0.0055 mg. to 0.033 mg. in 100 cc. of blood, and in Experiment 13 the increase is from 0.00583 mg. of iodine before operation to 0.0233 mg. per 100 cc. of blood after thyroidectomy. These variations are too great to be explained by experimental error, for Kendall has shown that there is a constant



loss of about 3 per cent of iodine determined by his method. The change noted after operation cannot be due to difference in the iodine content of the food, for in a number of instances repeated determinations before operation when the food was identical with that received after operation show little variation. For example, Experiment 6 shows a variation from 0.01 mg. to 0.00833 mg. among iodine determinations made on four occasions between July 21 and September 15; during this time the dog received the same diet as after the operation so that an increase from 0.01 mg. to 0.03 or 0.0316 mg. of iodine per 100 cc. of blood within the first 10 days after operation cannot be explained by variation of the iodine in the food.

It is noteworthy that the increase of iodine occurs soon after removal of the thyroid gland; in Experiment 9 there is an increase from 0.00833 mg. to 0.02832 mg. of iodine per 100 cc. of blood, and in Experiment 10 from 0.0033 mg. to 0.01 mg. within the first 48 hours after removal of the thyroid gland. If this sudden increase in the iodine content of the blood were due to injury of the gland during the operation the iodine content of the blood would return to normal in a very short time, but in Experiment 5, 6 days after operation the iodine content of the blood is 0.025 mg. per 100 cc. of blood, or three times that before operation, and in Experiment 3, 14 days after operation it is 0.0208 mg. as compared with 0.0083 mg. before operation; in Experiment 1, 30 days after operation the iodine content of the blood is 0.0386 mg. and 106 days after operation it is 0.0291 mg. per 100 cc. of blood.

The possibility suggests itself that the thyroid influences the metabolism of iodine in much the same way that the pancreas controls the metabolism of glucose. Present knowledge of the subject does not establish any close analogy between iodine and carbohydrate metabolism.

A series of experiments has been performed to determine the effect of thyroid feeding on the iodine content of the blood of dogs of which the thyroids had been removed. Following the operation determinations of the iodine content of the blood have been made and the dogs have then been fed with fresh thyroid of sheep in addition to the usual food. After a number of days, the iodine content of the blood has again been determined. The thyroid feeding has been discontinued and later iodine determinations have been made.

*Experiment 15.*—

July 15, 1921. 100 cc. of blood contain 0.01 mg. of iodine.

Aug. 25. 100 cc. of blood contain 0.0125 mg. of iodine.

Oct. 15. 100 cc. of blood contain 0.0116 mg. of iodine.

Nov. 1. Both lobes of the gland are removed, the parathyroids at the lower pole being identified and left *in situ*.

Nov. 11. The wound has healed by first intention.

100 cc. of blood contain 0.02 mg. of iodine.

100 cc. of blood contain 0.02 mg. of iodine.

Nov. 22. 100 cc. of blood contain 0.0233 mg. of iodine.

100 cc. of blood contain 0.0233 mg. of iodine.

Jan. 5, 1922. 100 cc. of blood contain 0.021 mg. of iodine.

100 cc. of blood contain 0.021 mg. of iodine.

Following the removal of blood the feeding of fresh thyroids of sheep was started. The dog received from two to four lobes each day.

Jan. 19. 100 cc. of blood contain 0.01 mg. of iodine.

100 cc. of blood contain 0.012 mg. of iodine.

*Experiment 16.*—

Dec. 13, 1921. 100 cc. of blood contain 0.0066 mg. of iodine.

100 cc. of blood contain 0.0066 mg. of iodine.

Dec. 20. The thyroid is removed, leaving the parathyroid at each lower pole.

Dec. 25. 100 cc. of blood contain 0.0483 mg. of iodine.

Dec. 28. 100 cc. of blood contain 0.0566 mg. of iodine.

Jan. 3, 1922. 100 cc. of blood contain 0.0333 mg. of iodine.

Jan. 6. 100 cc. of blood contain 0.0333 mg. of iodine.

The feeding of fresh thyroid of sheep was started. The animal receives from five to eight lobes each day.

Jan. 19. 100 cc. of blood contain 0.0066 mg. of iodine.

100 cc. of blood contain 0.0075 mg. of iodine.

Jan. 20. The thyroid feeding is discontinued.

Feb. 14. 100 cc. of blood contain 0.0216 mg. of iodine.

100 cc. of blood contain 0.0233 mg. of iodine.

The animal is killed with ether following the removal of blood.

*Experiment 17.*—

Dec. 29, 1921. 100 cc. of blood contain 0.007 mg. of iodine.

100 cc. of blood contain 0.007 mg. of iodine.

Jan. 20, 1922. The thyroid is removed, leaving a very small tab of thyroid tissue at each lower pole with the parathyroid.

Jan. 27. The animal is losing its hair in considerable quantities.

The feces are very hard, dry, and powdery. The wound has healed by first intention.

Feb. 4. 100 cc. of blood contain 0.0166 mg. of iodine.

100 cc. of blood contain 0.0168 mg. of iodine.

Feb. 9. The feeding of fresh thyroid of sheep is started, the animal receiving from six to eight lobes each day.

Feb. 15. 100 cc. of blood contain 0.0066 mg. of iodine.

The hair has stopped falling out and the animal has somewhat softer feces.

Mar. 1. The feeding of fresh thyroid is discontinued.

Mar. 20. The hair is falling out in considerable quantities, and the feces are hard and powdery.

100 cc. of blood contain 0.015 mg. of iodine.

*Experiment 18.*—

Feb. 1, 1922. 100 cc. of blood contain 0.00583 mg. of iodine.

100 cc. of blood contain 0.0066 mg. of iodine.

Feb. 11. The thyroid is completely removed, leaving only the parathyroids at each lower pole.

Feb. 17. 100 cc. of blood contain 0.0133 mg. of iodine.

100 cc. of blood contain 0.0116 mg. of iodine.

The hair is falling out in considerable quantities and the animal is losing weight. There are mild clonic convulsions of tetany.

Feb. 19. The feeding of fresh thyroid is started, the animal receiving from four to eight lobes each day.

Feb. 23. The hair has stopped falling out and the animal is gaining in weight. There are no symptoms of tetany.

100 cc. of blood contain 0.008 mg. of iodine.

The thyroid feeding is discontinued.

Mar. 5. The animal is losing weight, eats very little, and the hair is falling out.

100 cc. of blood contain 0.0125 mg. of iodine.

The animal is killed with ether. The parathyroids are found embedded in scar tissue at each lower pole.

In this group of experiments the foregoing results are confirmed and further evidence that increase of the iodine content of the blood is due to the removal of the thyroid is obtained. Feeding of fresh thyroid of sheep to thyroidectomized dogs reduces the iodine content of the blood so that it approximates the preoperative level. In Experiment 15 the iodine content of the blood before operation was 0.0125 mg. per 100 cc., and on the day the animal first received fresh thyroid with its food the postoperative iodine of the blood was 0.021 mg.; after 14 days of thyroid feeding the iodine content of the blood had fallen to 0.012 mg.

In Experiment 16 the preoperative iodine content of the blood was 0.0066 mg. with a postoperative iodine content which reached the height of 0.0566 mg. and was still 0.033 mg. after the removal of 400 cc. of blood within a period of 12 days. 13 days after thyroid feeding

had been started the iodine content of the blood was 0.0075 mg. In Experiments 17 and 18 the iodine content of the blood rose again to the former postoperative level when the thyroid feeding was discontinued.

When some substance which the thyroid gland normally supplies is lost as the result of removal of the organ, the iodine content of the blood increases to an abnormal level. This hypothetical substance may be restored by feeding thyroid, and under this influence the normal iodine level is restored. Iodine in the blood decreases even though the thyroid gland is no longer present to remove it from the blood. The thyroid supplies some substance which profoundly influences the metabolism of iodine not only within the thyroid but elsewhere in the body.

#### CONCLUSIONS.

1. After thyroidectomy in dogs the iodine content of the blood is increased.
2. The administration of fresh thyroid gland of sheep by mouth to thyroidectomized dogs causes the iodine content of the blood to fall so that it returns to the normal preoperative level; when the thyroid feeding is discontinued the iodine content of the blood is again increased.

It is with pleasure that I acknowledge the advice and encouragement given by Professor E. L. Opie.