A METABOLISM STUDY OF GOITER

WITH THE EFFECT OF THYROID AND THYMUS TREATMENT *

JOHN O. HALVERSON, PH.D., OLAF BERGEIM, PH.D.

AND

PHILIP B. HAWK, PH.D.

PHILADELPHIA

Many studies on the feeding of thyroid and thymus have been made on various animals and man, in normal and in pathologic conditions. The results obtained have in many cases been contradictory, although the majority of observers agree that loss of weight and increase of protein metabolism occur in the feeding of thyroid gland to normal animals and man, and that the effect on metabolic processes is more marked in hypothyroidism and in hyperthyroidism. The results with thymus feeding have so far not been encouraging.

Scholz¹ conducted rather complete experiments with a woman suffering with exophthalmic goiter and with a normal person on the same treatment for comparison. Each subject was studied for two periods of from three to five days each, one without thyroid treatment and the other on dried thyroid gland substance. His goiter patient, without treatment, stored 7.437 gm. and on thyroid substance 7.09 gm. nitrogen per day. For the normal control with thyroid treatment the daily nitrogen retention fell from 3.76 to 2.64 gm. That the data from this patient were typical has not yet been demonstrated, but similar though less marked results have been obtained on animals by Roos and others. Roos,² using a dog weighing 11.943 kg., to which 25 gm. of fresh thyroid were given for six days, records an increase of urinary nitrogen from 4.32 to 6.27 gm. and a diminution of 1.82 kg. in weight. A further dose of 30 gm. fresh gland caused a decrease to 4.09 gm. urinary nitrogen and a lowering of body weight to 9.956 kg. Roos showed that the administration of thyroid substance to a thyroidectomized dog increased the nitrogen and sodium chlorid elimination to a greater degree than when thyroid was given to the normal dog. He concluded that the thyroid has a decided influence on phosphorus and nitrogen metabolism, the nature of which was as yet obscure.

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* From the Departments of Physiological Chemistry and the Practice of Medicine of Jefferson Medical College of Philadelphia.

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1. Scholz: *Zentralbl. f. inn. Med.*, 1895, xvi, 1041, 1069.

2. Roos: *Ztschr. f. physiol. Chem.*, 1895, xxi, 19.

A patient of Matthes,³ who was given her own dried excised gland, showed increased nitrogen excretion. David's⁴ patient, on thyro-iodin, excreted 90 per cent. more nitrogen. Scholz¹ and Hirschloff⁵ in similar cases of exophthalmic goiter report retention of nitrogen and gain in weight.

Magnus-Levy⁶ established the fact that in exophthalmic goiter the energy requirements increased from 50 to 70 per cent. above the normal and he showed in cretinism and myxedema⁷ that the heat production was as much as 45 to 50 per cent. below normal; that thus the respiratory quotient in the above diseases is low, but in exophthalmic goiter⁸ high. Dubois⁹ gave an instance of a cretin whose total energy requirement was increased by thyroid treatment from 18 to 25 per cent. above the normal. Magnus-Levy⁸ and Anderson and Bergmann¹⁰ also found thyroid gland produced marked effects of this nature on normal men.

Schöndorff,¹¹ using a dog as subject, obtained a loss of nitrogen of 0.66 gm. in a twelve days' foreperiod, and of 0.12 and 1.13 gm., with a loss in weight in two periods of forty-six days under the influence of varying doses of dry and fresh gland respectively. Schöndorff considered that the protein metabolism at first was not affected; that the body fat was used up, and that increased nitrogen output was due to an increased excretion of nitrogenous extractives, already formed and retained in the body. He considered that protein metabolism was later upset.

Georgiewsky, Richter, Gluzinski and Lemberger, Voit, and Ostwald¹² also obtained with thyroid feeding loss of weight in dogs. Schäfer¹³ found that the addition of small amounts of thyroid tissue to the diets of white rats greatly increased the food consumption, especially in quite young individuals, and accelerated growth and nitrogen retention. Farrant¹⁴ in a recent paper reports increased appetite and loss of weight in cats and in rabbits after thyroid feeding. Hewitt¹⁵

3. Matthes: *Verhandl. d. Cong. f. inn. Med.*, 1897, 232.

4. David: *Ztschr. f. Heilk.*, 1897, xvii, 439.

5. Hirschloff: *Ztschr. f. klin. Med.*, 1899, xxxvi, 200.

6. Magnus-Levy: *Berl. klin. Wchnschr.*, 1895, xxx, 650.

7. Magnus-Levy: *Ztschr. f. klin. Med.*, 1904, lii, 201.

8. Magnus-Levy: *Ztschr. f. klin. Med.*, 1897, xxxiii, 269; *Ibid.*, 1906, ix, 177.

9. Dubois: *Jour. Am. Med. Assn.*, 1914, lxiii, 827; *THE ARCHIVES INT. MED.*, 1916.

10. Anderson and Bergmann: *Skand. Arch. f. Physiol.*, 1898, viii, 326.

11. Schöndorff: *Arch. f. d. ges. Physiol.*, 1897, lxxvii, 385.

12. Georgiewsky: *Ztschr. f. klin. Med.*, 1897, xxxiii, 153. Richter: *Centralbl. f. inn. Med.*, 1896, xxii, 65. Gluzinski and Lemberger: *Centralbl. f. inn. Med.*, 1897, xviii, 89. Voit: *Ztschr. f. Biol.*, 1897, xxxv, 116. Ostwald: *Ztschr. f. physiol. Chem.*, 1899, xxiv, 39.

13. Schäfer: *Quart. Jour. Exper. Physiol.*, 1912, v, 203.

14. Farrant: *Brit. Med. Jour.*, 1913, ii, 1363.

15. Hewitt: *Quart. Jour. Physiol.*, 1914, viii, 113.

found that 0.5 gm. doses of thyroid administered to rats gave a greater nitrogen retention than larger doses.

Scholz, Richter, and Gluzinski and Lemberger obtained a diminished positive nitrogen balance after thyroid administration. Cramer and Krause¹⁶ found that the administration of thyroid gland affected carbohydrate metabolism. A further proof of this action on carbohydrate and also on fat metabolism is afforded by the observations of Thiele and Nehring and Stüve¹⁷ that in the case of a normal man to whom thyroid was given the gaseous exchange was greatly increased.

On the other hand, the administration of the gland has in some cases in man (Magnus-Levy) and in dogs (Underhill and Saiki and Rahel Hirsch¹⁸) been found to cause no alteration in metabolism. Similar results in the case of a normal man were obtained by Magnus-Levy¹⁹ who found no distinct increase of oxygen intake or carbon dioxid output while administration of thyroid to a patient with myxedema caused an increase in oxygen intake of 80 per cent. Underhill and Saiki found that thyroid fed to normal dogs effected a slight increase in urinary nitrogen. Small doses appear to have as pronounced an effect as larger ones. In the case of two patients, Scholz and Hirschloff observed with marked daily gain in weight not the slightest disturbance in nitrogen balance.

Unlike thyroid, thymus fed or injected into animals has appeared to have no effect on nitrogen metabolism. Extirpation experiments, however, indicate some connection between the thymus and growth of the skeleton, that is, calcium metabolism.

Carbone²⁰ appears to have found on thymectomized dogs and rabbits a slight increase in nitrogen in both urine and feces. Mikulicz, Reinbach, and Cunningham²¹ report an effect on goiter by thymus, similar to that of thyroid. Magnus-Levy reports two cases in which feeding thymus in exophthalmic goiter for longer or shorter periods was found to have no effect on oxygen consumption. Basch²² on thymectomized animals in comparison with controls of the same litter

16. Cramer and Krause: *Proc. Roy. Med. and Chir. Soc., London*, 1913, lxxxvi, 550.

17. Thiele and Nehring: *Ztschr. f. klin. Med.*, 1896, xxx, 41. Stüve: *Festschr. der Stadtischen Krankenhauses im Frankfort-am-Main*, September, 1896.

18. Underhill and Saiki: *Jour. Biol. Chem.*, 1908, v, 225. Hirsch: *Oppenheimer's Handbuch der Biochemie*, Jena, 1910, iii, 271.

19. In Von Noorden: *Metabolism and Practical Medicine*, American edition, Chicago, 1907, iii.

20. Carbone: *Gior. d. r. Accad. di med. di Torino.*, 1897, ix, 7.

21. Mikulicz: *Berl. klin. Wchnschr.*, 1895, xxxii, 342. Reinbach: *Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1898, iii, 309. Cunningham: *Jour. Exper. Med.*, 1896, iii, 227.

22. Basch: *Ztschr. f. exper. Path. u. Therap.*, 1905, ii, 95.

obtained twice as great a calcium excretion. Roos²³ on a dog found that child's thyroid, with an iodine content of 0.025 per cent., given in doses of 5 gm. of dried substance caused no effect, while gland containing 0.18 per cent. in like amount produced increased nitrogen excretion.

Age affects the results obtained in an artificially produced condition of hyperthyroidism. Vermehren²⁴ states that patients of over 50 years of age show a greater increase of protein metabolism than children, while Georgiewsky¹² found that in dogs the reverse was the case, young animals reacting more readily than adults.

Perhan²⁵ studying the influence of thyroid principle on calcium metabolism in rabbits, showed that the ingestion of thyroid caused a loss of calcium from the tissues, which ran parallel to the amount of thyroid ingested. Falta, Bolaffio, and Tedesco²⁶ after parathyroidectomy found that thyro-iodine brought about increased excretion of calcium in the feces.

Schäfer,¹³ feeding thyroid to white rats, observed an increased calcium and magnesium excretion. His average variations are considerable and so render the results somewhat doubtful. In a case of myasthenia gravis, which may be an intoxication, Diller and Rosenbloom²⁷ have shown that a marked loss of calcium from the tissues obtains by way of the urine. In a period of eight days they found that 5.7 gm. of calcium oxide, out of a total excretion of 6.3 gm., was eliminated by this channel. Pemberton²⁸ also obtained in myasthenia gravis a similar loss of calcium from the tissues. Scholz found an increased excretion of alkaline earth elements in three cretins. He made complete mineral balances and concluded as a result of his extensive experiments that the metabolism in cretins is sluggish. Basch²⁹ found that injections of soluble calcium salts brought back the irritability to normal in the case of thymectomized dogs with changed psychical nature. Attempts³⁰ have been made to explain the influence on calcification by ascribing to the thymus a detoxicating action in building up acids circulating in the blood into nucleoprotein of the thymus. This suggestion has not been supported by sufficient experi-

23. Roos: *Ztschr. f. physiol. Chem.*, 1899, xxviii, 40.

24. Vermehren: *Deutsch. med. Wchnschr.*, 1893, xix, 255, 1037.

25. Perhan: *Compt. rend Soc. de biol.*, 1913, lxxii, 620.

26. Falta, Bertelli, Bolaffio, Tedesco, and Rudinger: *Verhandl. d. Cong. f. inn. Med.*, 1909, xxvi, 138.

27. Diller and Rosenbloom: *Am. Jour. Med. Sc.*, 1914, cxlviii, 65.

28. Pemberton: *Am. Jour. Med. Sc.*, 1910, cxxxix, 816.

29. Basch: *Jahrb. f. Kinderh.*, 1906, lxiv, 285; *Wien. klin. Wchnschr.*, 1903, xxxi, 893; *Deutsch. med. Wchnschr.*, 1913, xxxix, 1456.

30. Dmitricwski: *Jahresb. ü. d. Fortschr. d. Thierchem.*, 1900, xxx, 778.

mental evidence. Towles³¹ found no disturbance in the metabolism of calcium in exophthalmic goiter.

The older investigators on phosphorus metabolism during thyroid feeding determined phosphorus in the urine alone; they failed to consider fecal elimination. In thyroid feeding to normal men or animals or after thyroidectomy in both, the phosphorus may be excreted in increased amount either in the urine or feces. The amount depends on the size of the dose given. Phosphorus excretion may follow the nitrogen elimination or there may be a retention of phosphorus. Scholz found in a metabolism study of exophthalmic goiter (in a woman) that without thyroid treatment there was a loss of 2.09 gm. per day. In the case of a normal man ingesting thyroid the phosphorus pentoxid loss increased from 2.996 to 3.831 gm. per day.

There was no great increase of phosphorus in the urine with either subject, but in the feces the phosphorus elimination of the patient with goiter was increased to ten times the amount and that of the normal subject about 25 per cent. Since there was no such increase of nitrogen as of phosphorus outgo, Scholz believed that the latter was due to phosphate rather than nuclein metabolism. Richter¹² and Schiff³² confirmed these results. Anderson and Bergmann and Burger³³ found that with thyroid ingestion in the nonmyxedematous total phosphorus excretion was marked, amounting in the urine alone to 1 gm. above the amount ingested. Senator³⁴ confirmed these results. Burger's researches showed that the amount of ingested thyroid quantitatively governed the nitrogen and phosphorus pentoxid excretion. Roos in experiments on healthy dogs found that the administration of thyroid gland substance in large doses caused an increased phosphorus as well as sodium chlorid and nitrogen excretion. The increased phosphorus excretion continued longer than that of sodium chlorid. In a thyroidectomized dog, feeding of thyroid did not increase the phosphorus excretion to a greater degree than in the normal dog, but it remained considerably below normal. Roos noted evidence sustaining the idea that phosphorus as well as nitrogen assimilation requires the assistance of the secretory product of the thyroid.

Ord and White,³⁵ studying thyroid treatment in myxedema, noted a slight total increase in phosphorus metabolism. Richter found that the phosphorus excretion exceeded that of nitrogen. Schafer showed on white rats that the extent of increase of phosphorus excretion depended on the quantity of thyroid ingested, which had to be increased

31. Towles: *Am. Jour. Med. Sc.*, 1910, cxl, 100.

32. Schiff: *Ztschr. f. klin. Med.*, 1897, xxxiii (supplementary number), 284.

33. Burger: *Inaug. Diss.*, Halle, 1895.

34. Senator: *Berl. klin. Wchnschr.*, 1897, xxxiv, 109.

35. Ord. and White: *Brit. Med. Jour.*, 1893, ii, 216.

beyond a certain point before any results were obtained. However, Scholz in his studies on the three cretins above referred to concluded that the phosphorus retention is considerable on small intake, and does not increase in proportion to intake.

The results with thyroid feeding following thyroparathyroidectomy or thyroidectomy alone, may vary even more. There may be a sub-normal elimination of phosphorus, a retention, or a return to normal metabolism or an increased phosphorus elimination. Underhill and Saiki¹⁸ observed a low output of phosphorus and a high output of purin nitrogen after the continued administration of large doses of thyroid tissue to dogs. Saccone³⁶ observed that the urinary phosphorus rose to three times the previous amount after removal from a dog of both the thyroids and parathyroids. The feeding of thyroiodin in addition to the normal diet reduced the excretion of phosphorus to the original low level. Roos showed that the administration of thyroid substance to a thyroidectomized dog did not increase the phosphorus elimination. After performing thyroidectomy in dogs, Ushenko³⁷ stated that the relation of the percentage of phosphorus to nitrogen in the urine first increased and later diminished. Similar results were obtained for ammonia. He concluded that the metabolism of phosphorus and nitrogen was acutely disturbed and that the synthetic processes were the ones mainly affected.

Magnus-Levy,¹⁹ discussing the metabolism of sulphur in exophthalmic goiter, says that nothing is known about its excretion either as to amount or its balance. The catabolism of sulphur, however, as shown by Daddi and Marchetti³⁸ varies as little from the normal as do the constituents of the nitrogen partition in protein metabolism. The excretion of sulphur after thyroid feeding of the nonmyxedematous frequently rises (Pfeiffer and Scholz³⁹ and Georgiewsky¹⁹), according to Burger,¹⁹ as high as 60 per cent., or much higher than the rise in nitrogen, though this result is not constant. Pfeiffer and Scholz found that the sulphur excretion rose to about the same extent as that of nitrogen, after thyroid feeding.

Sulphur excretion may parallel that of nitrogen or rise above it. Hirschstein⁴⁰ recently reported conclusions only of metabolism studies during long-continued thyroid medication, in which in a certain type of hypothyroidism, designated the asthenic, readily leading to great emaciation, there was a high excretion of sulphur, nitrogen, and phos-

36. Saccone: *Ann. di med. navale*, 1907, 13, i, 573.

37. Ushenko: *Russk. Vrach.*, 1913, 1751; *Chem. Abstr.*, 1913, vii, 3150.

38. Daddi and Marchetti: *La Clinica Moderna*, No. 1; *Biochem. Centralbl.*, 1904, ii, 752.

39. Pfeiffer and Scholz: *Oppenheimer's Handbuch der Biochemie der Menschen und der Tiere*, 1910, iii, Part 1, 294.

40. Hirschstein: *Med. Klin.*, 1914, x, 1569.

phorus, the sulphur excretion being especially high. Another type, designated plethoric hypothyroidism, is recognized by a high body resistance, the tissues showing no tendency to disintegration. Hirschstein determines by a preliminary trial which type predominates by thyroid feeding, or first by a high potassium diet, which he claims will cause a similar high excretion of sulphur, phosphorus, and nitrogen in the asthenic type, just as thyroid feeding does. He states that thyroid treatment in such patients is not advisable. The question arose whether these excreted end-products of protein metabolism were the results of tissue destruction or the washing out of residues stored in the body. The high sulphur and phosphorus excretion in some patients of the asthenic type, with great bodily wasting and susceptibility to intercurrent disease (tuberculosis), led him to believe that protein catabolism was the main factor. This author believes, however, that both forms are possible.

This study was carried out on a patient in the Jefferson Hospital, in the service of Dr. McCrae, to whom we are indebted for permission to study the case and for the clinical history, which is here given in part:

Clinical History.—Mrs. G. D., aged 28, white, was admitted to the Jefferson Hospital Aug. 6, 1913. Her general health had always been good. Menstruation was established at the age of 11 and was apparently normal in every respect until two years previous to her entrance it began to lessen in amount and duration. The previous year and one-half there had been amenorrhea. She had never been nervous until the onset of the present trouble. Her appetite always had been good, but for the previous four weeks it had been almost insatiable. The craving was mostly for bread and pastry. The bowels were regular. The present trouble began two years before. She noticed that her disposition had changed from an agreeable one to one markedly less so, that her temper flared up and she became irritated on the slightest provocation. These were the only symptoms apparent except for the beginning change in menstrual periods. Shortly afterward she noted a tremor of the hands, which had increased very little up to that time. In the previous year she noted that her eyes were becoming more prominent and in the previous three months she had noticed an increased size of her neck. On noticing this last symptom she consulted a physician, who treated her medically over a period of five weeks, with but slight improvement. During the medical treatment the patient received on three occasions hypodermic injections of pituitary extract and eight or nine days after each injection she became unconscious for periods of from twenty-four to seventy-two hours. She had headaches frequently and edema of ankles at times. She complained of dyspnea on slight exertion, but there was no dysphagia. In the previous six months the patient had gained considerable in body weight. Alopecia was noted of the hairy portions of the body. The patient was well nourished, with a most noticeable exophthalmos. The pulse was 110, the temperature 98.

Physical examination showed that on the neck there was an asymmetric enlargement of thyroid gland, more marked on the right than the left side. The enlargement began in the right side glands. There was no palpable thrill. The enlargement moves up on swallowing. The greatest circumference over the gland was $14\frac{3}{4}$ inches. The chest, lungs and heart sounds were normal. The

extremities were negative. The abdominal wall contained excessive amounts of fat.

The urinary examination was negative.

Blood examination on Aug. 15, 1913, showed hemoglobin 60 per cent., white cells 8,200, red cells 4,150,000, and color index 0.7 plus; the polymorphonuclears were 48 per cent., small lymphocytes 42 per cent., large lymphocytes 8 per cent., eosinophils 2 per cent. There was no reduced tolerance for glucose or fructose noted.

August 23 we began giving three lutein tablets daily to the patient. Bulimia continued. Examination of feces August 25 was negative. Wassermann examination resulted in positive three plus on September 5. On September 10, after mixed treatment, the patient showed a gain of 10 pounds the previous week. On the 11th she was given Roentgen-ray and thyroid treatment. On the 13th she was given pituitary treatment. On the 15th she was given 0.6 gm. salvarsan intravenously with no ill effects. On the 16th the weight indicated a loss of 6 pounds in the previous week. The patient stated that after the intravenous injection of salvarsan she felt a great deal more active mentally.

Blood examination, October 12, showed hemoglobin 91 per cent., red cells 5,950,000, color index 0.8, white cells 12,600.

An eye report of Aug. 11, 1913, showed vision of right eye 20/100, of left eye 20/200. The pupil diameter was 3.5 mm. The reactions to light, accommodation and convergence were normal. The muscle balance was normal, ocular movements were unimpaired, and the tension was normal. The eyeballs had undergone a proptosis of about 4 mm. in advance of the superior margin of the orbits. There was marked exophthalmos, so that the palpebral fissure could not be closed. Von Graefe's sign was present, as was also Stellwag's sign. Moebius' sign was absent. The right eye disk margins were clear and the vessels normal. There were no hemorrhages, and the fundus was negative. There was myopia of one-third diopter. The left eye mediums were clear, the disk margins were hazy on the nasal side, the cup was filled in, and the vessels were normal. The disk was slightly pale on the temporal side, and there was low myopia. The poor vision was due to the myopic condition of the eyes.

Roentgen examination on Aug. 13, 1913, showed the sella turcica and accessory sinuses normal. There was a calcareous deposit in the pineal gland.

The provisional diagnosis was goiter and pluriglandular disturbance.

PLAN AND METHOD OF STUDY

The patient was kept in a room in the Jefferson Hospital and under charge of a special nurse throughout the period of study. The purpose was to study the metabolism of the patient on a constant moderately high calcium diet, 1 gm., and to determine also the effect of the administration of both the thyroid and thymus gland substance. Both income and outgo of nitrogen, phosphorus, sulphur, calcium and magnesium were determined. The uniform diet and the amounts of each food given were based on the patient's choice during a preliminary day. The patient in all periods was placed on this uniform diet, which consisted of the foods given in Table 1, in addition 1 gm. of pure salt and 15 gm. of granulated sugar. There were also given each day bananas (scraped), 100 gm.; peaches (no juice), 100 gm.; tomatoes, 100 gm.; corn, 100 gm.; grape nuts, 50 gm.; potatoes (chips), 50 gm.; coffee, 200 c.c. and tea, 400 c.c.; both sampled daily. In order to reduce errors of sampling to a minimum, these foods were selected because of

the fact that they were low in calcium and nitrogen and yet gave variety to the diet. The details of food preparation and collection of excreta were carried out with the careful cooperation of the patient and of the hospital staff. The meat was prepared previous to the experiment, thoroughly mixed, boiled, and again thoroughly mixed, placed in glass jars, sterilized and kept in a frozen condition until used. Aliquot portions were taken for analysis.

TABLE 1.—ANALYSIS OF FOODS†

Sample	Daily Food Intake	Sample No.	N	P ₂ O ₅	MgO	CaO	S
Milk.....	100 c.c.	1	0.568		0.023	0.15	
Milk.....	100 c.c.	2	0.568	Comp.	0.023	0.159	
Milk.....	100 c.c.	3	0.568	0.219	0.024	0.157	Comp.
Milk.....	100 c.c.	4	0.583		0.025	0.162	0.025
Milk.....	100 c.c.	5	0.589		0.025	0.163	
Cheese.....	50 gm.	1	2.054		0.033	0.504	Comp.
Cheese.....	50 gm.	2	2.136	Comp.	0.033	0.529	
Cheese.....	50 gm.	3	2.272	0.621	0.03	0.486	Comp.
Cheese.....	50 gm.	4	2.3		0.03	0.463	0.081
Cheese.....	50 gm.	5	2.44		0.027	0.479	
Butter....	50 gm.	2	3.546	0.509	0.081	0.129	0.07
Bread.....	200 gm.						
Composite†.....		5	2.584	0.903	0.288	0.188	0.585
Meat (a).....	100 gm.	3a	1.266	0.521	0.037	0.022	Comp.
Meat (b).....	26 gm.	3b	1.803	0.475	0.037	0.026	0.102
City water.....	2,600 c.c.	...			0.04	0.035	0.029

* The milk and cheese were sampled and aliquot parts taken daily for period composites. Aliquot parts were again taken of these milk and cheese samples and composited into one sample each for both phosphorus and sulphur determinations. Aliquot parts of bread and butter were taken, which were composited into one sample. Patient began using meat 3b on Sept. 17, 1915. Proportionate aliquot parts of 3a and 3b were taken for sulphur, and for phosphorus in period 3.

† The daily intake consisted of (a) bananas (scrapped), 100 gm.; peaches (no juice), 100 gm.; tomatoes, 100 gm.; corn, 100 gm.; (b) grape nuts, 50 gm.; potato chips, 50 gm.; (c) coffee, 200 c.c.; tea, 400 c.c. (tea and coffee sampled daily and aliquots taken). Portions (a) and (c) were evaporated to dryness and composited with (b) comprising Composite 5.

‡ The quantities given are the total daily intake in grams.

The investigation extended over twenty-six days and consisted of five periods of five days' duration, except Period 1, which consisted of six days.

Urine was collected in exact twenty-four hour samples and kept in a refrigerator. Thymol was used as a preservative. The feces were separated by the use of carmin and kept in thymolized friction-top cans in a frozen condition until the end of the period, when they were thoroughly mixed for analysis.

All of the calcium except that in the urine was determined gravimetrically by McCrudden's methods.⁴¹ Urinary calcium was determined volumetrically by the same method. Nitrogen in the urine was estimated by the Kjeldahl-Gunning method. Phosphorus was determined by Neumann's method, gravimetrically. Sulphur in the urine was estimated by Benedict's method; in the food and feces, by a modification of Wolf and Osterberg's method.³² The analytical data of foods, urine and feces are given in Tables 1, 2 and 3.

The periods into which the experiment was divided were: 1, a fore-period, without any treatment; 2, a thyroid period, in which 6 grains of thyroid (Armour) were given daily, being increased to 9 grains each for the last two days, amounting to 36 grains in all; Period 3, a middle or after-period, in which no treatment was given; a thymus period

TABLE 2.—ANALYSIS OF FECES *

Period Number	Feces	N	P ₂ O ₅	MgO	CaO	S	Data
Foreperiod 1.....	443.5	9.49	4.981	1.393	5.034	0.583	Calculated to 5 day basis
Thyroid period 2.....	475.6	10.02	4.442	1.341	4.304	0.594	
Middle period 3.....	508.6	8.93	3.976	1.284	3.772	0.822	
Thymus period 4.....	521.1	9.64	4.328	1.345	3.871	0.745	
After period 5.....	544.5	9.16	4.116	1.242	3.91	0.808	Feces 5 of more liquid consistency

* The quantities given are the totals in grams for the respective periods.

(Period 4), in which 15 grains of thymus (Armour) were given daily, making a total of 75 grains, and an after-period (5), in which no treatment was given.

COMMENT

Some outstanding facts with regard to the metabolism in each of the periods of treatment will be outlined before going into a general discussion and comparison of the findings with regard to the individual elements concerned.

The point to be observed in Period 1, Table 4, with the patient receiving no treatment, is the loss of nitrogen, phosphorus, and magnesium, while calcium and sulphur are practically at a balance. The high daily loss of nitrogen amounts to 3.8 gm., or 37.03 per cent. of the intake. There is considerable loss of phosphorus, 0.399 gm., or 14.4 per cent. of the intake, while the loss of magnesium amounts to 0.025 gm., or 4.92 per cent.

41. McCrudden: Jour. Biol. Chem., 1910, vii, 83.

42. Wolf and Osterberg: Biochem. Ztschr., 1910, xxix, 429.

The calcium oxid and sulphur retentions announced to 0.01 and 0.023 gm., respectively. In this patient there was a loss of nitrogen somewhat over half as great as the gain Scholz¹ found in the case of his patient with goiter, who stored 7.437 gm. nitrogen daily without

TABLE 3.—ANALYSIS OF URINE *

Urine Number	Date	Vol., C.c.	N	P ₂ O ₅	MgO	CaO	S
Foreperiod 1 (no treatment)							
1.....	9/ 3	910	8.1	1.448	0.171	0.017	0.581
2.....	9/ 4	2,265	15.08	3.02	0.313	0.016	0.957
3.....	9/ 5	2,210	9.98	1.659	0.228	0.009	0.544
4.....	9/ 6	Lost					
5.....	9/ 7	2,137	10.25	2.14	0.271	0.024	0.675
6.....	9/ 8	3,374	15.58	2.614	0.295	0.013	0.983
Period 2, thyroid treatment							
7.....	9/ 9	2,980	13.2	2.319	0.26	0.024	0.77
8.....	9/10	2,131	7.82	1.323	0.152	0.016	0.472
9.....	9/11	2,825	9.81	1.91	0.189	0.017	0.696
10.....	9/12	2,521	13.1	2.468	0.269	0.023	0.828
11.....	9/13	1,895	7.64	1.318	0.139	0.016	0.476
Period 3 (no treatment)							
12.....	9/14	2,200	6.8	1.393	0.127	0.006	0.675
13.....	9/15	1,615	6.42	1.142	0.101	0.018	0.466
14.....	9/16	1,800	7.9	1.37	0.139	0.018	0.52
15.....	9/17	1,948	10.76	1.715	0.218	0.024	0.742
16.....	9/18	1,535	8.16	1.044	0.159	0.023	0.715
Period 4, thymus treatment							
17.....	9/19	885	6.6	0.868	0.147	0.015	0.609
18.....	9/20	1,860	8.53	1.16	0.168	0.018	0.79
19.....	9/21	1,210	6.14	0.95	0.119	0.007	0.434
20.....	9/22	1,030	7.22	1.27	0.154	0.01	0.562
21.....	9/23	1,212	10.28	1.609	0.214	0.013	0.748
Period 5 (no treatment)							
22.....	9/24	1,610	8.06	1.456	0.181	0.018	0.565
23.....	9/25	1,975	7.7	1.132	0.174	0.016	0.633
24.....	9/26	1,735	6.82	0.906	0.14	0.015	0.455
25.....	9/27	2,168	7.53	1.065	0.186	0.029	0.498
26.....	9/28	1,310	6.53	0.982	0.144	0.013	0.43

* The quantities given are the totals in grams for each day.

treatment. The opposite condition obtains here. That sulphur is not lost with such a high daily excretion of nitrogen is unusual Ver-mehren²⁴ observed in myxedema a loss of 20 per cent. of nitrogen by

the feces, and Anderson⁴³ observed defective absorption as regards nitrogen and fat. In such cases the absorption improves with thyroid treatment.¹⁹ Improved absorption from the intestine was observed in Period 2 (Table 5) after thyroid administration. The urinary calcium excretion is unusually low, 15.9 mg. in twenty-four hours, or 1.54 per

TABLE 4.—PERIOD 1; BALANCE OF NITROGEN, PHOSPHORUS, MAGNESIUM, CALCIUM AND SULPHUR *

	N	P ₂ O ₅	MgO	CaO	S
Excretion, urine.....	11.8	2.176	0.256	0.016	0.752
Excretion, feces.....	2.28	0.996	0.279	1.006	0.117
Excretion, total.....	14.08	3.172	0.534	1.023	0.869
Ingestion, total.....	10.27	2.773	0.509	1.032	0.892
Retention or loss.....	-3.8	-0.399	-0.025	+0.01	+0.023
Per cent. of retention or loss.....	-37.03	-14.40	-4.92	+0.94	+2.57

* The quantities given are daily averages in grams.

cent., while the calcium in the feces is high, 97.8 per cent. of the total intake. Nitrogen in the feces was approximately three times the normal, being 22.2 per cent., indicating poor absorption. The condition of metabolism here, with high urinary losses, is such that there was a considerable amount of work for the kidneys to perform. The metabolism was below normal. The patient's weight remained constant at

TABLE 5.—PERIOD 2, THYROID TREATMENT; BALANCE OF NITROGEN, PHOSPHORUS, MAGNESIUM, CALCIUM AND SULPHUR *

	N	P ₂ O ₅	MgO	CaO	S
Excretion, urine.....	10.31	1.868	0.201	0.019	0.652
Excretion, feces.....	2	0.889	0.268	0.861	0.119
Excretion, total.....	12.32	2.756	0.57	0.88	0.771
Ingestion, total.....	10.1	2.773	0.502	1.062	0.892
Retention or loss.....	-2.22	0.017	0.032	0.182	0.121
Per cent. of retention or loss.....	-21.96	0.61	6.36	17.1	13.56

* The quantities given are daily averages in grams.

183 pounds, when not under medication. On August 24 her weight was 181 pounds, and on September 7 it was 183, indicating a gain of two pounds with metabolism below normal.

In Period 2, Table 5, 36 grains of thyroid gland, ingested in five

43. Anderson: *Hygiea*, 1898, ix, 68; *Jahresb. ü. d. Fortschr. d. Thierchem.*, 1899, xxix, 427.

days, produced a marked effect on metabolism, causing a distinct increased retention over Period 1 of 15.07 per cent. nitrogen, 15.01 per cent. phosphorus pentoxid, 10.78 per cent. magnesium oxid, 16.16 per cent. calcium oxid and 10.99 per cent. sulphur. Nitrogen alone of all these elements remains negative at 21.96 per cent., or a daily loss of 2.22 gm. This agrees with Magnus-Levy's¹⁹ finding in myxedema.

Sulphur metabolism need not always parallel that of nitrogen. Magnus-Levy found the losses were greater during the beginning of the treatment. The nitrogen losses during the first nine days of his investigation were, respectively, 1.1, 0.3, 1, 2.7, 1.8, 3.3, 2.9, 1.6, and 2.9 gm., averaging 1.96 gm. The great daily variation in nitrogen losses is noticeable in the present instance. Phosphorus retention is 0.017 gm., or 0.61 per cent., being almost a balance. In case of calcium and sulphur there was a decided retention, amounting to 0.182 gm. and 0.121 gm., respectively, indicating for calcium, at least, a better absorption from the intestine. The same fact holds for nitrogen and calcium in the feces, which are 19.8 and 81.27 per cent., compared to 22.2 and 97.8 per cent., respectively, in Period 1. There was practically no change in calcium oxid excreted through the kidneys. The body weight now decreased to 177 pounds on September 17, which represented a considerable loss (at least six pounds) after the experiment began. While the volume of urine excreted in Period 1 was high, there now was an average increase of 293 c.c. (diuresis) (Table 3). This will be discussed more fully later. Incomplete data indicate that thyroid also increased the sodium chlorid excretion.

TABLE 6.—PERIOD 3, POSTTHYROID PERIOD; BALANCE OF NITROGEN, PHOSPHORUS, MAGNESIUM, CALCIUM AND SULPHUR *

	N	P ₂ O ₅	MgO	CaO	S
Excretion, urine.....	8.01	1.333	0.149	0.018	0.629
Excretion, feces.....	1.79	0.795	0.257	0.754	0.164
Excretion, total.....	9.80	2.128	0.406	0.773	0.793
Ingestion, total.....	10.25	2.770	0.5	1.021	0.892
Retention or loss.....	0.45	0.642	0.094	0.248	0.099
Per cent. of retention or loss.....	4.39	23.17	18.77	24.33	11.06

* The quantities given are daily averages in grams.

The nitrogen balance in Period 3 shows a retention of 0.48 gm., or 4.39 per cent. This indicates an increased retention of 26.35 per cent. over the preceding period. The stimulating effect of thyroid on metabolism continues and is greater in this than in the thyroid period. This is also true of phosphorus, in which the retention reached 23.7

per cent. The magnesium retention increased over the preceding period to 18.77 per cent.

The increase of calcium and sulphur was less in this period than in the preceding. However, magnesium and calcium in this period reach the maximum retention of 18.77 and 24.83 per cent., respectively, or 0.098 and 0.248 gm. This leaves 73.7 per cent. calcium oxid excreted through the feces, which in Period 1 contained 97.8 per cent. Urinary calcium does not vary any more than 0.55 per cent., or a mean of 7 mg. per day throughout the investigation. In this period, five to ten days following thyroid treatment, it is seen that the thyroid exerts its greatest effect on the metabolism of calcium and magnesium, which reaches its maximum quicker than metabolism of the other elements. The sulphur retention of 11.06 per cent. showed a slight decrease. Fifteen grains of thymus were administered daily, or a total of 75 grains for a period of five days.

TABLE 7.—PERIOD 4; EFFECT OF THYMUS TREATMENT ON NITROGEN, PHOSPHORUS, MAGNESIUM, CALCIUM AND SULPHUR RETENTION *

	N	P ₂ O ₅	MgO	CaO	S
Excretion, urine.....	7.75	1.171	0.161	0.013	0.619
Excretion, feces.....	1.93	0.866	0.269	0.776	0.149
Excretion, total.....	9.68	2.037	0.43	0.789	0.768
Ingestion, total.....	10.32	2.727	0.502	1.002	0.892
Retention or loss.....	0.63	0.69	0.072	0.216	0.124
Per cent. of retention or loss.....	6.15	25.3	14.31	21.5	13.85

* The quantities given are daily averages in grams.

The metabolism in Period 3 shows a retention of all elements, nitrogen being the lowest, 4.39 per cent. On administration of thymus gland (Period 4) the retention of nitrogen increases slightly, 1.76 per cent., or to 0.634 gm.; there was also a slightly increased retention of phosphorus and sulphur. However, magnesium oxid and calcium oxid retention decreased by 4.46 per cent. and 2.83 per cent., or the retention was 14.31 and 21.50 gm., respectively. The continuing effect of thyroid is not apparent in the magnesium and calcium metabolism; but this effect is shown in the slight increases in the metabolism of nitrogen, phosphorus and sulphur. That this is the lagging effect of thyroid stimulation, rather than the effect of thymus, appears probable. Blondel, as well as Tarrulli and Curatulo⁴⁴ claim that feeding of thymus causes increased nitrogen and phosphorus excretion.

44. Blondel, Tarulli and Curatulo: Biedl's Innere Sekretion, 1913, Part 1, 303.

In general, the results with thymus feeding have been negative. The urine excretion during this period decreased markedly to a daily mean of 1,239 c.c. The body weight of the patient also decreased 8 pounds from September 17 to the 24th, even though there was retention of all the elements, which is greatest relatively for phosphorus and calcium, being 25.30 and 21.50 per cent. respectively.

TABLE 8.—PERIOD 5; BALANCE OF NITROGEN, PHOSPHORUS, SULPHUR, CALCIUM AND MAGNESIUM IN THE POSTTHYMUS PERIOD

	N	P ₂ O ₅	MgO	CaO	S
Excretion, urine.....	7.33	1.108	0.165	0.018	0.520
Excretion, feces.....	1.83	0.823	0.248	0.782	0.162
Excretion, total.....	9.16	1.931	0.414	0.8	0.682
Ingestion, total.....	10.46	2.727	0.498	1.019	0.892
Retention or loss.....	1.3	0.796	0.085	0.219	0.21
Per cent. of retention or loss.....	12.45	29.19	16.96	21.47	23.56

* The quantities given are daily averages in grams.

TABLE 9.—RETENTION OR LOSS, PERCENTAGE

	1	2	3	4	5
N.....	-37.03	-21.96	4.39	6.15	12.45
P ₂ O ₅	-14.4	0.61	23.17	25.3	29.19
MgO.....	-4.92	6.36	16.77	14.31	16.96
CaO.....	0.94	17.1	24.33	21.5	21.47
S.....	2.57	13.56	11.06	13.85	23.56

TABLE 10.—RETENTION, OR LOSS, ABSOLUTE, IN GRAMS

	1	2	3	4	5
N.....	-3.80	-2.22	0.45	0.63	1.3
P ₂ O ₅	-0.399	0.017	0.642	0.69	0.796
MgO.....	-0.025	0.032	0.004	0.072	0.085
CaO.....	0.01	0.182	0.248	0.216	0.219
S.....	0.023	0.121	0.099	0.124	0.21

In the postthymus period (Period 5) the retentions of the elements remained high, being at a maximum for the elements nitrogen, phosphorus and sulphur.

Tables 9 and 10 give the absolute and percentage retentions for all periods. It will be seen that the great increases in retention occurred

toward the left of the table, that is during the thyroid period (Period 2) or in the postthyroid period (Period 3). The increases in retention after Period 3 are gradual for all elements.

On the whole the retentions, both relative and absolute, are at their maximum in the postthymus period, sulphur 23.56 per cent., phosphorus 29.19 per cent., calcium 21.47 per cent., magnesium 16.96 per cent. (calcium and magnesium were highest in Period 3, 24.33 per cent. and 18.77 per cent., respectively), nitrogen 12.45 per cent. The absolute retentions occurred in the following order: nitrogen 1.3 gm., calcium 0.219 gm., sulphur 0.21 gm., phosphorus 0.796 gm., magnesium 0.085 gm. The percentage of retentions show there is a certain parallelism in metabolism for nitrogen and the mineral elements. Towles,⁴⁵ studying metabolism in exophthalmic goiter, has pointed out that there is often a parallelism between the nitrogen and calcium in health and disease, unless the calcium intake is very high. McCrudden and Fales⁴⁶ point out that this has been found for other elements, and that it holds for the retention of nitrogen and of the mineral elements in a normal body. Hoffström,⁴⁷ who studied the metabolism of a pregnant woman over a long period, also showed a similar retention of nitrogen and the other elements.

It will be noted that the maximum retentions of nitrogen, phosphorus and sulphur occurred in the final period, while the highest retentions for calcium and magnesium occurred in the postthyroid period; that is, with calcium and magnesium the maximum effects were reached earlier.

With regard to the influence of thymus administration, it will be noted that when this treatment was discontinued, there is a rise in retention in the case of all elements. Furthermore, in the cases in which the rise in retention is continuous, the retention increased to a greater extent when thymus was withdrawn than it had in the preceding period. That is, the thymus treatment apparently produced an effect distinguishable from and opposed to the continuing effect of the thyroid treatment. It appears to have exerted a depressing effect on the thyroid stimulation of metabolism. In view of the lack of data with regard to the effect of thymus administration on metabolism, the interpretation of these findings offers many difficulties. Falta,⁴⁸ on the basis of indirect evidence, suggests that probably the thymus gland belongs to the anabolic (retardative) group of ductless glands, as contrasted with the thyroid as a member of the catabolic or dissimilatory group.

45. Towles: *Am. Jour. Med. Sc.*, 1910, cxi, 100.

46. McCrudden and Fales: *THE ARCHIVES INT. MED.*, 1912, ix, 273.

47. Hoffström: *Skand. Arch. f. Physiol.*, 1910, xxiii, 326.

48. Falta, Bolaffio, and Tedesco: Cited by Biedl (65) Part 1, p. 164. Falta and Meyers: *The Ductless Glandular Diseases*, Philadelphia, 1915, p. 80.

Through the pioneer work of Hertoghe it has been shown clinically how frequently hypothyroidism occurs, causing various slight infiltrations now clinically recognized and relieved by thyroid medication.

Our knowledge of the purpose of the thymus gland in metabolism is obscure. However, in the last few years the observations of surgeons have added considerably to our knowledge. Swale Vincent⁴⁹ observes that the conception that the thymus is not altogether a lymph organ is gaining ground. A nutritive rôle has also been suggested for the thymus, it being a glandular organ rich in nucleoprotein.

Weil,⁵⁰ Hart and Nordmann,⁵¹ state that on the whole the verdict appears to be that the organ is not essential to life, even in quite young animals. It has long been thought that the human thymus reaches its greatest development at about the second year, and then begins to degenerate. But it was shown in the year 1890 by Waldeyer⁵² that even in advanced age a considerable amount of thymus tissue persists and probably maintains its function as does the thyroid. Zoja⁵³ had previously shown that the thymus persists till the age of puberty. Recently Hammar⁵⁴ has insisted that the organ continues to grow up to the period of puberty, and reaches its greatest development between the fourteenth and sixteenth years. Microscopic evidence shows that it functions still later, though losing in weight. A true atrophy of the parenchyma, with elimination of function, comes on at about 50 or 60 years of age. At this period the thyroid function also decreases (Hertoghe). It seems, then, that we must regard the thymus as an organ regularly present, and probably in an active functional condition up to the age of puberty, if not up to the menopause.

Gare and Capelle hold there is a reciprocal relation between the thyroid and thymus glands. The association between the thyroid and thymus glands⁵⁵ may be of importance in hyperthyroidism, in which a hyperplasia of the thymus has been reported to occur. Indeed, the degree of the latter has been directly related to the severity of exophthalmic goiter manifestations.⁵⁶ H. Matti reports that research and study of the literature show thymus with thyroid are directly concerned with the production of exophthalmic goiter. Thymus changes are directly coordinate with and parallel to changes in the thyroid.⁵⁷

49. Vincent: *Internal Secretion and the Ductless Glands*, London, 1912.

50. Weil: *Lyon Med.*, 1910, cxv, 847.

51. Hart and Nordmann: *Berl. klin. Wchnschr.*, 1910, xlv, 814.

52. Waldeyer: *Verhandl. des 10 Internat. Med. Cong.*, Berlin, 1891, p. 15; cited by Vincent (Footnote 49) p. 357.

53. Zoja: Cited by Vincent (Footnote 49), p. 358.

54. Hammar: *Verhandl. d. Anat. Gesellsch. a. d. 19te Versammlung*, Geneva, 1905.

55. Hoskins: *Am. Jour. Med. Sc.*, 1911, cxli, 1349.

56. Gebele: *Beitr. z. klin. Chir.*, 1910, lxx, 20.

57. Matti: *Berl. klin. Wchnschr.*, 1914, li, 1365.

Tatum found that the thymus of rabbits atrophied after excision of the thyroid. A. Kocher⁵⁸ states that a tendency to tardy hyperplasia or tardy involution of the thymus is evident in nearly 50 per cent. of all cases of exophthalmic goiter. Halsted⁵⁹ in exophthalmic goiter twice found the thymus enlarged, with typical thymus symptoms predominating, and also found that 82 per cent. of the postmortem examinations showed thymus enlargement, while in those deaths due to heart failure after operation 95 per cent. showed thymus enlargement.⁶⁰ Gebele⁶¹ describes persistent thymus in exophthalmic goiter. The castration experiments of Marassini and Gellin⁶² point out that this operation gives rise to an enlargement of the thymus, and Squandrini⁶³ believes that castration interferes with the normal involution of the gland. These experiments further point to some kind of internal secretion which ministers to the economy of the organism before the reproductive organs are fully developed. They believe that normally this internal secretion is provided by the testes or ovary after puberty, but if castration is perfected the thymus maintains its original structure and function.

Defective nutrition is caused in young dogs by extirpation of the thymus, the animals usually living about a year. Again, dilatation of the heart in such animals suggested that the thymus has an antagonistic action to the suprarenals.⁴⁹ The fatal effects of thymectomy in rats, as found by Klose and Marquini, could not be confirmed by Pappenheimer,⁶³ using controls of the same litter.

Soli⁶⁴ found changes in the development of bone in animals deprived of their thymus (supposedly deranged metabolism). Rabbits, if deprived of their thymus at a sufficiently early stage in their development, fail to develop their bony skeleton normally, while guinea-pigs and chickens respond less readily. Utterström,⁶⁵ after feeding thyroid to rabbits for weeks and months, concluded that two factors in hyperthyroidism affect the thymus: one is an indirect depressing effect, due to a disturbance in metabolism; the other is a direct stimulation, due to hyperthyroidism. Which predominates depends on the animal's constitution, conditions of the experiment and especially on the size of the thyroid dose.

58. Kocher: *Arch. f. klin. Chir.*, 1914, cv, 769, 832.

59. Halsted: *Bull. Johns Hopkins Hosp.*, 1914, xxv, 223.

60. Falta and Meyers in *The Ductless Glandular Diseases*, p. 45, say: "That long continued oversaturation of the body with the thyroid gland secretion may give rise to disturbances of the functions of the sexual glands is not at all remarkable, only the significance of the thymus hyperplasia is as yet unclear."

61. Gebele: *Beitr. z. klin. Chir.*, 1910, lxx, 20.

62. Marassini, Gellin and Squandrini: Cited by Vincent (Footnote 49), p. 365.

63. Pappenheimer: *Jour. Exper. Med.*, 1914, xix, 319.

64. Soli: *Arch. ital. biol.*, 1909, lii, 217; *Chem. Abstr.*, 1911, v, 2128.

65. Utterström: *Arch. de méd. exper. et d'anat. path.*, 1910, xxii, 550.

DIURESIS

A marked daily increase in urine volume (average volume 2,472 c.c.) occurred during thyroid treatment over that of the foreperiod (Period 1) (average volume 2,179 c.c.), which increase amounted to 293 c.c. The patient was on a constant water intake. The urine volume of Period 2 also exceeded that of the following period by 652 c.c. As shown by Rahel Hirsch (Table 13), in the work of Scholz,

TABLE 11.—DIURESIS DUE TO THYROID TREATMENT *

Period		Mean Temperature, F.	Mean Urine Volume, C.c.
No treatment.....	1	70.7	2,179
Thyroid.....	2	59.8	2,472
No treatment.....	3	67.0	1,820
Thymus.....	4	75.6	1,239
No treatment.....	5	61.2	1,759

* Period averages are given.

Richter and Bürger, there is a marked increased excretion of urine by persons on thyroid administration, except in the case of Gluzinski and Lemberger, in which there was a decrease. Scholz obtained an increase of 886 c.c.; Richter 219 c.c.; Bürger 122 c.c.; while Gluzinski and Lemberger obtained a decrease of 206 c.c. In our experiments, during thymus treatment the volume went down to 1,239 c.c., or 1,233 c.c. less than with thyroid, a variation of almost 100 per cent. While

TABLE 12.—URINE VOLUME DOES NOT VARY WITH TEMPERATURE

Period	Temp., F.	Urine Vol., C.c.
2.....	59.8	2,472
5.....	61.2	1,759
3.....	67.0	1,820
1.....	70.7	2,179
4.....	75.6	1,239

the greatest and lowest volume of urine occurred when the temperature was lowest, 59.8 F., and the highest 75.6 F., respectively, yet a variation of 1,233 c.c. of urine is considerable in a hospital in which temperatures are more constant and normal. Rearranging the urine volumes according to increase in temperature (Table 12) shows that the volume varies independently of temperature. Pointing out one instance will suffice. During the second warmest period (Period 1) the urine volume was

2,179 c.c., while in the warmest period (Period 4) this was 1,239 c.c. Magnus-Levy found that the urine increased somewhat during thyroid treatment in myxedema (hypothyroidism) on constant water intake. This, he says, is supposedly due to the disappearance of watery myxedematous deposit and other substances, and that the same holds for thyroid extract administered to the nonmyxedematous.

TABLE 13.—URINE VOLUME, QUOTED FROM RAHEL HIRSCH (OPPENHEIMER) *

C.c. Urine, Foreperiod	Author	C.c. Urine, Treatment Period
2,396	Scholz.....	3,282
1,120	Richter.....	1,339
1,419	Gluzinski and Lemberger.....	1,213
1,044	Bürger.....	1,166

* Oppenheimer: *Handbuch der Biochemie*, 1910, iii, Part 1, 294.

Friedleben⁶⁶ noticed diminished urine volume, decrease in amount of urea, increased appetite and that the metabolism was altered in thymectomized animals. During the thymus period in the case under investigation the volume of urine decreased to 1,239 c.c., and in the following period again rose to 1,759 c.c. (Table 11). Whether this marked decrease in volume is due to thymus ingested or is a coincidence has not been definitely determined.

TABLE 14.—VARIATION IN BODY WEIGHT

Date	Period	Weight, Pounds	Change, Pounds
8/24/14.....	...	181	
9/ 7/14.....	1	183	Gain 2
9/17/14.....	3	177	Lost 6
9/24/14.....	4, end	185	Gain 8
10/ 2/14.....	End of Exp.	174	Lost 11
5/15/15.....	...	183	
	Before illness	185	
7/17/16.....	...	185.5	

Various results had been obtained with thymus extract prepared in different ways. Gouin and Audouard⁶⁷ report increased activity of the kidney by using subcutaneous injection of glycerol extracts of thymus glands.

66. Friedleben: Cited from Oppenheimer's *Handbuch der Biochemie*, 1910, iii, Part 1, 335.

67. Gouin and Audouard: *Biedl's Innere Sekretion*, 1913, Ed. 2, Part 1, 302.

An outstanding fact in this case is the marked variation in body weight. The weights during the present investigation for the periods given are as shown in Table 14.

From August 24 to September 7 the patient gained two pounds in weight. Previous to September 1 the patient had been on thymus treatment. The clinical data indicate a slight edema on September 1: "Areas of thickening in the subcutaneous tissues. With these thickened areas there appeared a sense of constriction over upper chest and fugitive pains generally distributed." The kidneys at this time were eliminating large quantities of nitrogen (3.8 gm.) in excess of ingestion and also large amounts of water. With imperfect elimination of nitrogenous end-products from the tissues, due to poor or decreased oxidation, it is easily conceivable that there could occur a slight edema or myxedema, with retention of some water, and hence a slight increase in weight.

Thyroid treatment, however, caused increased water excretion and with its stimulating effect on metabolism brought about retention of other constituents. The loss in weight (6 pounds) is perhaps due chiefly to water. We can approximately calculate this from nitrogen loss and water excretions from September 7 to 17 (Table 14). During this period there was a loss of 6 pounds in body weight. The total loss of nitrogen from September 7 to 14 amounted to 22.5 gm. This, calculated to the basis of tissue equivalent (6.25 and 4.7, protein and tissue factors), gives 1.5 pounds tissue loss. Diuresis of 293 c.c. daily for five days (excess in Period 2 over Period 1) causes a loss of 1,465 c.c. This amounts to 1,487 gm., or 3.3 pounds (specific gravity 1.015). The loss of 3.3 pounds water with 1.5 pounds tissue loss accounts for 4.8 pounds. The actual loss was 6 pounds.

In Period 4 there is a distinct retention of all the elements, especially nitrogen. Urine excretion decreases in volume and gain in weight occurs. In our case this amounted to 8 pounds. This continues through the thymus period. Thymus may also cause a retention of water. The above gain occurred from September 17 to 24.

This gain in weight due to retention of nitrogen and of water can approximately be calculated from the urine volumes. The nitrogen retention in Period 3 was 0.45 gm. daily; that is, 0.90 gm. of nitrogen was retained up to September 19. Retention of nitrogen for Period 4 was 0.634 gm. daily, or a total of 3.17 gm. The total nitrogen retention for September 17 to 24 was 4.07 gm., equivalent to 0.3 pound of tissue built up. The mean daily urine excreted is not so readily approximated, but averaging the volumes for Periods 3 and 5 gives 1,790 c.c., which can be taken as the average. For the thymus period there would be a retention of 551 c.c. a day, which totals 2,755 c.c., or 2,796 gm. This is equivalent to 6.2 pounds, and with the 0.3 pound

of tissue, gives 6.5 pounds gain for September 17 to 24. The actual gain was 8 pounds.

It has been held that the fat in this disorder is readily oxidizable and perhaps the loss of 11 pounds (from September 24 to October 2, Table 14) is due partly to such oxidation. Agreeing with this is the fact that little or no sulphur loss occurs during the periods of great nitrogen losses (Periods 1 and 2). Hirschstein⁴⁰ found the sulphur loss was extraordinarily high when great emaciation occurs in hypothyroidism.

The Chittenden low-protein diet allows 0.12 gm. nitrogen per kilogram of body weight, which Sivéu was able to reduce to 0.08 gm. per kilogram. In our case the metabolism of nitrogen, as shown by the urinary nitrogen figured on the basis of kilograms of body weight, is low, indicating a low state of metabolism. Results on this basis are perhaps partly due to the presence of inactive adipose tissue. Table 15 illustrates this fact.

TABLE 15.—NITROGEN METABOLISM

Period	Weight		Mean N in Urine, Gm.	N per Kg. Body Weight, Gm.
	Lbs.	Kg.		
	165	74	11.8	0.16
1.....	183	83	11.8	0.14
4.....	185	84	7.33	0.09

The daily intake of 2,058 calories, corresponding to 25 calories per kilogram body weight, with choice of diet, also indicates a low energy metabolism.

NITROGEN METABOLISM

Table 16 points out the gradual decrease of nitrogen, absolute as well as relative, in the feces. Vermehren²⁴ observed in myxedema a loss of 20 per cent. of nitrogen by way of the feces and Anderson⁴³ observed defective absorption of nitrogen and fat, but states that with thyroid treatment absorption improved. The best absorption in our patient showed an improvement of 4.7 per cent. over Period 1. This occurred in the postthyroid period. The nitrogen in the urine decreased from 114.8 per cent. of the intake to 70.2 per cent., a difference of 44.6 per cent. There were less of the nitrogenous end-products given off and more nitrogen retained. Large increases in nitrogen retention occurred in Periods 3 and 5, following the thyroid and thymus periods, being respectively 26.35 and 6.30 per cent. The nitrogen metabolism went from a daily loss of 3.8 gm. to a retention of 5.1 gm., within a period of twenty-six days. The variation in nitrogen balance thus reached a maximum of 49.48 per cent. This increase in

nitrogen metabolism is further substantiated by the fact that the sulphur retention increased 20.99 per cent., phosphorus 43.59 per cent., while the mineral elements, calcium and magnesium, were retained in about the same amount as that of sulphur.

In the foreperiod and the thyroid period the nitrogen balance was negative, with a loss of 3.8 and 2.2 gm., respectively. Thyroid feeding stimulated nitrogen retention by 15 per cent., which increased to 26 per cent. in the postthyroid period (Period 3). There was a drop in the urinary excretion of nitrogen of 24 per cent., or 2.3 gm. This indicated increased retention. The nitrogen loss of 2.2 gm. changed in Period 3 to 0.05 gm. retention. This marked effect of nitrogen metabolism continues through the remaining periods. An interesting point to note is that the relative absorption through the intestine in both posttreatment periods (Periods 3 and 5) was the same, the absolute values for nitrogen in the feces being respectively 1.79 and 1.83 gm., a difference of 45 mg., while there was a difference of 0.22 gm. in the nitrogen ingested. Hence in these posttreatment periods it will be observed that the absorptive power of the intestine for nitrogen was not changed to any extent. This appears to hold also for sulphur and phosphorus (Tables 16, 19 and 22).

TABLE 16.—METABOLISM OF NITROGEN FOR ALL PERIODS
(RELATIVE AND ABSOLUTE) *

	Grams N, for All Periods					Percentage Based on Intake, for All Periods				
	1	2	3	4	5	1	2	3	4	5
Ingestion.....	10.27	10.1	10.25	10.32	10.46					
In feces.....	2.28	2	1.79	1.93	1.83	22.2	19.8	17.4	18.6	17.5
In urine.....	11.8	10.31	8.01	7.75	7.33	114.8	102.2	78.2	75	70.2
Retention.....	-3.8	-2.22	0.45	0.63	1.3	-37.03	-21.96	4.39	6.15	12.45

* Maximum increased retention 49.48 per cent. (Period 5).

Daddi and Marchetti³⁸ found the utilization of nitrogen good in thyroid treatment of exophthalmic goiter, even though the stools were somewhat soft. We confirmed this on feces Composite 5, which were more liquid in consistency. Our data on the administration of thyroid confirm the observations of Magnus-Levy¹⁹ that the gradual effect of thyroid action on the nitrogenous exchange, both in myxedematous and nonmyxedematous, and its persistence after the administration has been stopped, are very noticeable; that while there are differences in the degree of reaction of individuals, this reaction is no more noticeable for the obese than for other individuals. The loss of nitrogen in the feces remained high (from 22.2 to 17.4 per cent.), that is, the variation

in absorption was slight, 4.8 per cent. (Table 17). There is in general, however, a gradual decrease in fecal nitrogen, being 0.28 and 0.49 gm., respectively during the thyroid and postthyroid periods. Fecal nitrogen, in the thymus and postthymus periods, increased over Period 3 (forethymus period) by 0.14 and 0.24 gm., respectively.

Corresponding with the continued effect of thyroid on metabolism, the urinary nitrogen shows a gradual decreased elimination from 11.8 gm. (Period 1) to 7.33 gm. (Period 5), or a difference of 4.47 gm., amounting to 44.6 per cent. The nitrogen excretion during the thyroid and postthyroid periods was, respectively, 1.48 and 3.80 gm. less than in the foreperiod (Period 1); during the thymus and postthymus

TABLE 17.—GRADUAL DECREASE OF NITROGEN IN URINE AND FECES
(RELATIVE AND ABSOLUTE)

Period	N Intake, Gm.	N in Urine, Gm.	N in Urine, per Cent.	N in Feces, Gm.	N in Feces, per Cent.
1.....	10.27	11.8	114.8	2.28	22.2
2.....	10.1	10.31	102.2	2	19.8
3.....	10.25	8.01	78.2	1.79	17.4
4.....	10.32	7.75	75	1.93	18.6
5.....	10.46	7.33	70.2	1.83	17.5

TABLE 18.—MAXIMUM VARIATION IN ABSORPTION, EXCRETION AND RETENTION

	Absorption	Excretion, Urine	Retention	Period
N.....	4.8	44.6	49.48	5
P ₂ O ₅	7.3	37.9	43.59	5
MgO.....	5	20.6	23.69	3
S.....	5.3	26	20.99	5
CaO.....	24.1	0.57	23.39	3

periods, 4.05 and 4.47 gm. less than in Period 1, indicating that during both treatment with thyroid and thymus there was a more favorable nitrogen balance.

Table 18 is interesting because of several facts brought out. The variation in absorption from the intestine for all elements is fairly constant, approximating 5 per cent. Phosphorus runs slightly higher. Calcium, while constant in the urine, varies up to 24.1 per cent. in the feces and must be excreted by this channel. The retention of the other four constituents is indicated by the urine content. Table 18 shows that this exceeds 20 per cent. for all (except calcium being

greatest for nitrogen and phosphorus, respectively). It should be observed that the maximum increased retention was about the same for calcium and magnesium and occurred earlier (Period 3) than for the elements (nitrogen, phosphorus and sulphur) concerned in the metabolism of protein (Period 5), which was respectively 49.48, 43.59 and 20.99 per cent. Thus calcium and magnesium metabolism appear to be affected differently by thyroid stimulation than that of nitrogen, phosphorus and sulphur.

PHOSPHORUS METABOLISM

There was a fairly progressive decrease in the excretion of phosphorus by way of the intestines during and after thyroid treatment. The excretion of the feces during thymus feeding increased somewhat, as it also did for nitrogen. The lowest excretion in the feces occurred following thyroid action. In the next two periods, Periods 4 and 5,

TABLE 19.—METABOLISM OF PHOSPHORUS IN ALL PERIODS, RELATIVE AND ABSOLUTE AMOUNTS (PHOSPHORUS PENTOXID) *

	Phosphorus in All Periods, Gm.					Phosphorus in All Periods, per Cent.				
	1	2	3	4	5	1	2	3	4	5
Ingestion.....	2.773	2.773	2.770	2.727	2.727					
In feces.....	0.996	0.889	0.795	0.866	0.823	35.9	32.1	28.6	31.7	30.1
In urine.....	2.176	1.868	1.333	1.171	1.108	78.5	67.4	42.8	42.8	40.6
Loss or retention....	-0.399	0.017	0.642	0.69	0.796	-14.4	0.61	23.17	25.3	29.19

* Maximum retention 43.59 per cent. (Period 5).

there was a slight rise, but all variations were within the narrow limits of 7.3 per cent. Thus, it is seen that there was no marked increase in phosphorus metabolism with excretion through the bowel, such as Scholz¹⁹ observed in his case.

The progressive decrease of phosphorus excretion in the urine is noticeable, being from 2.18 to 1.11 gm., or a difference of 1.07 gm. (40.6 per cent.). Thyroid action caused a decreased excretion of 0.31 gm. and thymus 0.16 gm. over the preceding period in each case. This extended also into the postthyroid and postthymus periods, being 0.54 gm. and 0.06 gm., respectively. The maximum retention was 43.59 per cent. in Period 5.

MAGNESIUM METABOLISM

There was not over 5 per cent. variation in absorption of magnesium oxid from the intestine. A variation from 54.8 (Period 1) to 49.8 (Period 5), per cent. occurred. The absorption from the feces during thyroid and thymus action was practically the same, differing

only by 0.3 per cent. A marked effect of treatment on magnesium metabolism is seen from the urinary data. Excretion of magnesium oxid varied in Period 1 from 0.256 gm. to 0.149 gm. (Period 3), or from 50.4 to 29.8 per cent. The lowest excretion is caused by the continuing thyroid stimulation. The greatest retention occurs here (18.77 per cent.). The excretion rises slightly in Period 4 during thymus administration and also in Period 5 (33.06 per cent.). The maximum retention occurs in Period 5 (16.96 per cent.). This is an increased retention after the experiment began of 23.69 per cent. The absolute values for magnesium oxid retention in any period are small, being less than 100 mg.

TABLE 20.—METABOLISM OF MAGNESIUM IN ALL PERIODS
(RELATIVE AND ABSOLUTE) *

	As MgO, Gm.					As MgO, per Cent.				
	1	2	3	4	5	1	2	3	4	5
Ingestion.....	0.509	0.502	0.5	0.502	0.498					
In feces.....	0.279	0.268	0.257	0.269	0.248	54.8	53.4	51.4	53.7	49.8
In urine.....	0.256	0.202	0.149	0.161	0.165	50.4	40.3	29.8	32.04	33.06
Loss or retention...	-0.025	0.032	0.094	0.072	0.085	-4.92	6.36	18.77	14.31	16.96

* Maximum retention 23.69 per cent. (Period 3).

CALCIUM METABOLISM

In the first two periods there is apparently a condition of depressed metabolism with loss of magnesium, phosphorus and nitrogen, calcium and sulphur being at a balance. The kidneys functionated but slightly in calcium metabolism, excreting 0.420 gm. in twenty-five days (from 12 to 18 mg. daily). This is less than 2 per cent. of the ingested calcium. Secchi⁶⁸ found for a man 70 years old that the lowest urinary excretion was 9.4 per cent. on a high calcium diet (3.65 gm. per day). The calcium eliminated in the foreperiod by way of the intestines in our patient was 97.7 per cent. of the intake.

During thyroid treatment absorption improved. Calcium oxid in the feces decreased to 81.2 per cent., or 0.146 gm. The least calcium oxid eliminated by way of the feces (73.7 per cent. or 0.754 gm.) occurred in the postthyroid period (Period 3).

The calcium oxid elimination in the feces during twenty-five days varied in the forethyroid period (Period 1) from 97.8 to 73.7 (Period 3) and was 76.6 per cent. at the close of the experiment. Secchi, working on normal persons, found from 40 to 60 per cent. of the calcium eliminated in the feces. Thus in this patient there was appar-

68. Secchi: Biochem. Ztschr., 1914, lxxvi, 156.

ently a deficient elimination and poor absorption of calcium from the intestine. An improvement in absorption of 16.6 per cent. occurred during thyroid administration, which increased in the postthyroid period (Period 3) to 24.1 per cent. The metabolism continued at a slightly lower level (2.9 to 3.8 per cent.) during the thymus and post-thymus periods. That is, calcium metabolism remained practically the same in the last two periods. Bergeim, Stewart and Hawk⁶⁹ in studying the metabolism of a case after thyroparathyroidectomy, also found low calcium in the urine (1/121 of that in the feces). McCrudden and Fales⁷⁰ found in a normal boy a retention of 17.1 per cent. calcium oxid per day of 2.5 gm. ingested, while one fifth of the excreted calcium occurred by way of the urine. Sherman, Mettler and Sinclair⁷¹ in their experiments report that calcium in the urine varied from 3.9 per cent. to 23.7 per cent. Determann⁷² states that phos-

TABLE 21.—METABOLISM OF CALCIUM (CALCIUM OXID) IN ALL PERIODS
(RELATIVE AND ABSOLUTE) *

	Calcium Oxid, Gm.					Calcium Oxid, per Cent.				
	1	2	3	4	5	1	2	3	4	5
Ingestion.....	1.032	1.062	1.021	1.002	1.019					
In feces.....	1.007	0.861	0.754	0.776	0.782	97.8	81.2	73.7	77.5	76.6
In urine.....	0.016	0.019	0.018	0.013	0.018	1.54	1.81	1.79	1.24	1.78
Retention.....	0.01	0.182	0.248	0.216	0.219	0.94	17.1	24.33	21.5	21.47

* Maximum retention 23.39 per cent. (Period 3).

phorus and calcium excretion into the intestine is increased in exophthalmic goiter during thyroid treatment. Results obtained on the patient discussed above do not bear this out and do not confirm the results obtained by Falta, Tedesco and Bolaffio,⁴⁸ who found on thyroidectomized dogs no diminution in the metabolism of the mineral salts in the first days of hunger. There appeared, however, they report, to be a decreased excretion of sodium chlorid, also calcium, phosphorus and magnesium in the urine while on the administration of thyroid gland there was a rise in the calcium and phosphorus in the feces and of magnesium in the urine.

Further work⁶⁸ indicated that while in young children there is a retention of calcium in the normal adult there is a tendency for a calcium balance or equilibrium on varied diets containing from 0.4 to

69. Bergeim, Stewart, and Hawk: Jour. Exper. Med., 1914, xx, 225.

70. McCrudden and Fales: THE ARCHIVES INT. MED., 1912, ix, 287.

71. Sherman, Mettler and Sinclair: U. S. Dept. Agr. Bull. No. 227, 1910, O. E. S., p. 38.

72. Determann: Verdauung u. Stoffwechsel-Krankheiten, 1914, v, 60.

1.5 gm. calcium. Schabad,⁷³ among numerous calcium balance experiments in rickets, found an increased calcium excretion through the feces in the progressive stage of the disease; the calcium excretion through the urine was subnormal, but during convalescence above normal.

SULPHUR METABOLISM

The periods immediately following thyroid and thymus feeding, Periods 3 and 5, respectively, showed an increase within narrow limits in sulphur elimination through the feces (5.1 per cent., 0.048 gm., and 1.4 per cent., 0.045 gm.).

TABLE 22.—METABOLISM OF SULPHUR IN ALL PERIODS
(RELATIVE AND ABSOLUTE) *

	Sulphur, Gm.					Sulphur, per Cent.				
	1	2	3	4	5	1	2	3	4	5
Ingestion.....	0.892	0.892	0.892	0.892	0.892					
In feces.....	0.117	0.119	0.164	0.149	0.162	13.08	13.3	18.4	16.7	18.1
In urine.....	0.752	0.652	0.629	0.619	0.52	84.4	73	70.5	69.4	58.4
Retention.....	0.023	0.121	0.099	0.124	0.21	2.57	13.56	11.06	13.85	23.56

* Maximum retention 20.99 per cent. (Period 5).

The excretion of sulphur by way of the urine underwent a diminution during the posttreatment periods (Periods 3 and 5) of 2.5 per cent. and 11.0 per cent. Thyroid and thymus administration had slight effect on the excretion of sulphur in the feces, except that in the post-thyroid period (Period 3) sulphur excretion went up slightly, though less than 5 per cent., and remained near this level. In the urine there was a gradually decreasing excretion of sulphur from 84.4 per cent. (Period 1) to 58.4 per cent. (Period 5), a difference of 26 per cent. (0.232 gm. sulphur). The sulphur metabolism shows certain peculiarities. In the first place, in Period 1 there is no loss of sulphur such as occurred for phosphorus and nitrogen. The retention during the thyroid and thymus periods is approximately the same. There was only 26 mg. more sulphur metabolized during the thymus feeding. Decreased absorption occurred during the postthyroid period (Period 3), while in the postthymus period (Period 5) there was a considerable increase in metabolism, retention going from 0.124 gm. to 0.210 gm., or from 13.85 per cent. to 23.56 per cent. In the urine there was a gradual decrease from 0.752 to 0.520 gm., or a difference of 0.232 gm. from Period 1 to Period 5, amounting to 26 per cent. The administration of thyroid and thymus caused no rise of sulphur in the urine,

73. Schabad: Arch. f. Kinderheilk., 1910, liii, 380.

as occurred in feces. The retention was considerable in both treatment periods, 0.121 gm. in Period 2 and 0.124 gm. in Period 4, respectively, but greatest in Period 5, a total of 0.210 gm. (23.56 per cent.). Thus the sulphur excretion offers no suggestion of tissue disintegration.

Urinary Indican: The daily output of indican in the urine was determined by Jolle's colorimetric method. The average daily excretion of indican for each of the periods of study was as follows:

Period	Indican, Mg.
Foreperiod	25.2
Thyroid	12.6
Postthyroid	9.0
Thymus	10.0
Postthymus	4.4

It will be noticed that following thyroid treatment and coincident with improvement in nitrogen balance and in the condition of the patient there was a progressive decrease of urinary indican excretion. This may indicate decreased putrefaction, as it is associated with improved absorption of the food elements. The slight increase on thymus administration confirms certain work by Moraczewski, who found that the ingestion of thymus and certain other glandular tissues led to an increase in indican excretion.

SUMMARY AND CONCLUSIONS

A study was made of the metabolism of nitrogen, phosphorus, sulphur, calcium and magnesium on a patient with exophthalmic goiter, with apparently a slight hypothyroidism, and responding readily to treatment. The study was made in five periods of five days each, including periods of thyroid and thymus treatment.

In the preliminary period without treatment a marked disturbance of metabolism was noted, with pronounced losses of nitrogen, phosphorus, and magnesium and a practical balance of calcium and sulphur. The loss of nitrogen by the feces was much greater than that of an average normal person.

Thyroid treatment markedly stimulated the metabolism of all elements determined, this stimulation continuing long after treatment was stopped. Considerable retention of all elements was brought about, the maximum effect being reached sooner in the case of calcium and magnesium than in the case of nitrogen, sulphur and phosphorus. The retentions of the former reached their maximum in the third (postthyroid) period, while the latter showed a progressive increase in retention to the end of the experiment.

Slightly better intestinal absorption of nitrogen followed treatment, although the loss of nitrogen by the feces continued high. The intestinal absorption of other elements, with the exception of calcium,

varied but slightly. The urinary excretions of all elements except calcium markedly decreased after thyroid treatment, corresponding with the retention of these elements.

A retention of calcium was brought about, this reaching a maximum of 24.33 per cent. in the postthyroid period. The urinary calcium excretion was extremely low (2 per cent. of the intake) and continued so. The excretion of this element by the feces was markedly diminished, indicating better intestinal absorption.

The effect of thymus administration on the metabolism was less marked than that of the thyroid, but appeared to be distinct. In the thymus period the retention of all elements was depressed. When thymus administration ceased, the rate of retention for all elements immediately increased. Thus thymus treatment appeared to depress the stimulating effect of the thyroid on metabolism, which supports the view of a possible antagonistic action of these glands, such as has been suggested by others on the basis of indirect evidence.

The administration of thyroid caused diuresis immediately. Thymus treatment had the opposite effect, leading to a retention of water, with marked decrease in urine volumes (from 2,472 to 1,239 c.c.) on constant water ingestion.

The weight of the patient decreased on thyroid treatment and increased after withdrawal and on thymus administration. The variations (from 6 to 8 pounds) were apparently due in part to loss or gain of nitrogenous tissue constituents, but in the main to loss of water on thyroid treatment and retention on its discontinuance or on thymus treatment.

Following thyroid treatment there was a progressive decrease in urinary indican excretion. This may indicate lessened intestinal putrefaction.

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