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Clinical calorimetry: fourteenth paper metabolism in exophthalmic goiter

Eugene F. Du Bois

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CLINICAL CALORIMETRY

FOURTEENTH PAPER

METABOLISM IN EXOPHTHALMIC GOITER*

EUGENE F. DU BOIS, M.D.
NEW YORK

TABLE OF CONTENTS

To those who are accustomed to think in terms of the energy requirement, exophthalmic goiter stands out *par excellence* as the disease of increased metabolism, and the increased metabolism stands out as the chief symptom of hyperthyroidism. The determination of the heat production seems to afford the best index of the severity and course of the disease. There is great need of some purely objective test in hyperthyroidism to indicate the effect of treatment, since psychotherapy can modify profoundly all subjective symptoms. At present the scientific status of the treatment of exophthalmic goiter is about at the point where we would be with diabetes if there were no laboratory tests for glucose and the acetone bodies.

No one of the simpler objective tests taken alone gives an accurate idea of the course of the disease; but when a number are taken together and added to the clinical impression of the observer, they afford a rough measure of the severity of the case. The rapidity of the heart action is perhaps the best guide, but the heart is often affected by other conditions, and damage to the heart may outlast the other symptoms. Rise in temperature is so irregular as to preclude its use as a reliable

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* From the Russell Sage Institute of Pathology, in Affiliation with the Second Medical Division of Bellevue Hospital.

index. Changes in the size of the gland do not parallel the course of the disease. Changes in weight, warmth of skin and sweating are but consequences of the increase in heat production. Eye symptoms, tremor, nervous irritability, weakness, diarrhea are all too variable to be of reliance and are too difficult to measure accurately. The blood pressure is of some use as a guide, but it is affected by age and the condition of the cardiovascular system. The sugar tolerance depends on other ductless glands as well as the thyroid, and even in health has wide limits. The mononucleosis which has been considered characteristic by Kocher, Halsted and others is found in other diseases, and does not seem significant enough to be our main reliance.

In contrast to the above mentioned symptoms, an increased basal metabolism is found with great regularity in exophthalmic goiter, and in severe cases reaches a level found in no other condition. On the other hand, in cretinism and myxedema the metabolism is lower than in any other disease. The administration of thyroid extract, particularly in myxedema, raises the heat production. All other diseases in which metabolism is increased are easily distinguishable from exophthalmic goiter, and they never approach the extremes found in this condition. The basal metabolism is higher than normal in youth, in fever, in lymphatic leukemia and pernicious anemia, in severe cardiac disease, and in some cases of severe diabetes and cancer. It is lower than normal in old age, in some wasting diseases and perhaps in some cases of obesity. Diseases of the ductless glands other than thyroid show in some cases an increase, in some a decrease; but these are comparatively small.

The theories of exophthalmic goiter at present are in a somewhat chaotic state. The suprarenals, thymus and most of the other ductless glands are thought by many to be involved, and the symptoms have lately been divided into sympatheticotonic and vagotonic groups. Even in regard to the thyroid itself some advance the theory of dysthyroidism in addition to or in place of hyperthyroidism. Such confusion is natural when we have few objective tests and many bizarre symptoms which can be ascribed at will to various ductless glands whose functions are obscure. It would seem as if we needed more laboratory work for those who hold no brief for any particular kind of therapy. Even the most extreme advocates of the new theories ascribe the chief rôle to an overactivity of the thyroid gland. For the purpose of simplicity in this paper one may consider the symptoms of exophthalmic goiter to be caused by too much thyroid secretion, and allow the reader to select for himself those cases in which he believes other glands to be involved.

PREVIOUS STUDIES OF THE RESPIRATORY EXCHANGES

The question of the metabolism in exophthalmic goiter has been reviewed by Magnus-Levy,[1] Hirsch,[2], and Falta;[3] Scholz[4] has given a large number of references on the subject of cretinism.

Friedrich Müller,[5] in 1893, first pointed out the increase in metabolism in exophthalmic goiter by showing that a patient lost weight and nitrogenous substances on a diet that was more than sufficient to cover the needs of a normal person. Magnus-Levy[6] two years later was the first to demonstrate the increase in the respiratory metabolism in hyperthyroidism and the decrease in myxedema. Since then he has studied many cases of both diseases and has used the respiratory metabolism as an index of the effects of treatment, thus demonstrating the increase in heat production following the administration of thyroid extract. He found that in myxedema the rise in heat production began in the first week of the administration of the extract and increased gradually till the fourth or fifth week. The effect was most pronounced in severe cases, causing a rise of from 50 to 70 per cent. In the mild cases the increase was slight, never going above 20 per cent., and in five of the nine normal controls there was no rise at all. Stüve,[7] who worked with Magnus-Levy, found that thymus extract had no effect on the heat production. Magnus-Levy and Stüve found the metabolism greatly increased in exophthalmic goiter, and their results, together with those of the others who have studied this subject, are recorded in Table 1. Thiele and Nehring,[8] and Anderson and Bergman[9] studied the influence of thyroid extract, the former finding an increase in the metabolism of obesity patients after its use and the latter no increase with two normal men.

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1. Magnus-Levy: Von Noorden's Handbuch der Pathologie des Stoffwechsels, Berlin, 1906.

2. Hirsch, Rahel: Oppenheimer's Handbuch der Biochemie, iv, 2, 165.

3. Falta: Die Erkrankungen der Blutdrüsen, Berlin, 1913.

4. Sholz: Klinische und Anatomische. Untersuchungen über den Cretinismus, Berlin, 1906.

5. Müller, Friedrich: Beiträge zur Kenntniss der Basedowische Krankheit, Deutsch. Arch. f. klin. Med., 1893, li, 335.

6. Magnus-Levy: Gaswechsel bei Thyroidea, Berl. klin. Wchnschr., 1895, xxxii, 650; Untersuchungen zur Schilddrüsenfrage, Ztschr. f. klin. Med., 1897, xxxiii, 269; Ueber Myxoedem, ibid, 1904, lii, 201.

7. Stüve: Respiratorische Gaswechsel bei Schilddrüsenfutterung Morbus Basedowii u. s.w., Fest. Stadt. Krankenh., Frankfurt a. M., Mahlau, 1896.

8. Thiele and Nehring: Untersuchungen des respiratorischen Gaswechsel unter dem Einflusse von Thyreoideapraparaten und bei anaemischen Zustanden des menschen, Ztschr. f. klin. Med., xxx, 41.

9. Anderson and Bergmann: Einfluss der Schilddrüsenfutterung auf den Stoffwechsel des gesunden Menschen, Skand. Arch. f. Physiol., 1898, viii, 326.

TABLE 1.—Goiter Cases in the Literature Arranged—

Observer	Patient	Sex*	Age, Years	Duration of Disease, Years	Clinical Classification
Hirschlaff	Louise B.	♀	..	9	Very severe last ten days of life
Author	Case 6 (Anna K.)	♀	26	10	Severe
Author	Case 3 (James McE.)	♂	29	9(?) ½(?)	Severe
					100% above average for women
Salomon	R. H.	♂	40	11	Five months before death
Hirschlaff	Louise B.	♀	21	9	Severe first two months in hospital
Magnus-Levy	Frl. E. B.	♀	20	..	Severe; acute
Salomon	Fall I	♂	23	5	
Magnus-Levy	Fr. Kr.	..	26	26	Very severe; pregnant six months
Undeutsch	Ja.	♀	24	½	"Ziemlich Schwer"
Author	Case 1 (Max W.)	♂	40	1⅓	Severe
Magnus-Levy	Hr. G.	♂	25	..	Severe
Undeutsch	K.	♀	23	4	(Mod. severe?)
Magnus-Levy	Frau Schr.	♀	42	..	Very severe
Pribram and Porges	E. Tesch.	♀	23	2	(Mod. severe?)
Author	Case 2 (Edwin T.)	♂	20	½	Acute; mod. severe
Pribram and Porges	M. S.	..	25	½	(Acute; mod. severe ?)
Salomon	M. J.	♀	25	1½	(Mod. severe?)
Magnus-Levy	Frl. E. T.	♀	22	..	Severe
Magnus-Levy and Stüve	Fr. R. B.	♀	26	..	Severe
Author	Case 4 (Dr. G. S. L.)	♂	52	3-4	Severe
Salomon	Fall II	♀	19	½	
					50% above average for women
Magnus-Levy	Hr. J.	♂	20	..	Severe
Falta	J. H.	..	22	..	(Mild?)
Falta	R. Fl.	♀	3½	3	(Severe?)
Author	Case 9 (Marion B.)	♀	22	3	Mild; operated
Author	Case 8 (Sarah M.)	♀	29	8	Mild; operated
Magnus-Levy	Frl. Ung.	♀	55	..	Severe
Author	Case 7 (Anna R.)	♀	29	5	Moderately severe
Author	Case 10 (Margaret L.)	♀	51	1	Atypical cardiac
Magnus-Levy	M. P.	♂	11½	..	Small struma, otherwise normal
Magnus-Levy	Fr. O.	♀	54	..	Simple goiter
Stüve and Magnus-Levy	Frl. G. W.	♀	24	..	Severe

—According to the Level of the Respiratory Metabolism

Calories per Sq. M. per Hr. Meeh	Pulse Rate	Blood Pressure, Syst.	Enlargement of Heart to Left, Cm.	Enlargement of Thyroid	Exophthalmos	Von Graefe Sign	Mental Irritability	Tremor	Warmth of Skin	Emaciation	Remarks
72.1											
66.1	122	.....	0	+	+	±	++	+	++	+	After ligation of 2 arteries
65.6	100-124	130-146	3.5	++	+	+	++	+	++	++	Alcoholic
64.6											
61.7	110-120	.....	0	+	—	—	+	....	.....	++	
61.7	100-130	.....	±	+	++	++	++	+	++	+	
60.0	120										
58.0	++	.....	+	+	++	++	+	+	+	++	
57.2	142										
56.6	++	.....	+	+	+	—	++	++	+	+	
55.4	100-136	130-150	2.5	++	++	±	+++	+	++	±	
54.4	112										
53.7	92-122	.....	+	+	++	....	....	+			
53.1	130-150										
53.0	++	.....	+	..	....	....	+	+			
50.6	92-112	140-150	0	+	+	±	++	+	++	±	
50.2	++	.....	+	+	+	+	....	+			
49.7	90-100	.....	±	+	—	—	+	+	+	±	
49.6	100										
49.3											
49.2	97-101	148	2	++	+	+	+	++	++	+	After ligation of 4 arteries
48.7	90-124	.....	+	+	+	+	....	....	.....	±	
48.5											
46.1	122										
44.8	.....	.....	..	..	—	—	....	+	+		
44.5	80-150	130	..	+	+	++	++	+	++		
44.1	.....	.....	..	..	+	....	+	....	+	—	Par. thyroidect. 2 and 1 yrs. ago
43.8	.....	.....	0	+	—	—	+	+	±	....	Partial thyroidectomy 8 yrs. ago
43.5	120										
43.4	84-92	.....	0	+	+	+	+	+	+	+	
42.0	68-88 Fibril	170	2-3	++	+	+	+	....	++	+	
40.6	.....	.....	—	±	—	—	....	—	.....	—	
40.6	94										
39.9	100-120										

TABLE 1.—

Observer	Patient	Sex*	Age, Years	Duration of Disease, Years	Clinical Classification
Magnus-Levy	Frl. M. Kr.	♀	20	..	Mild
Falta	Ad. K.	♂	33	6	(Severe?)
Undeutsch	Wit.	♀	24	14?	"Forme fruste"
Magnus-Levy	Hr. Be.	♂	20	..	Mild
Magnus-Levy	Frl. E. W.	♀	21	..	Severe
Magnus-Levy	Fr. B.	♀	52	..	Half way between Kropf and forme fruste
Author	Case 5 (Peter N.)	♂	23	5	Atypical; operated
					Upper normal limit for women
Magnus-Levy	Hr. R. B.	♂	20	..	Mild
					Average for normal men
Magnus-Levy	Frl. U.	♀	55	..	Typical; mild
Author	Case 11 (Miss B. H.)	♀	31	4	Atypical; operated
Magnus-Levy	Frl. E. D.	♀	25	..	Simple goiter
Magnus-Levy	Frl. Sch. M.	♀	28	..	Mild
Magnus-Levy	Frl. M. Kl.	♀	17	..	Simple goiter
					Average for normal women
Magnus-Levy	Frl. Rh.	♀	36	..	Half way between Kropf and forme fruste; simple goiter

* In this column, ♂ denotes male and ♀ female.

Hirschlaff[10] made one of the most valuable contributions to the subject by studying in great detail over a long period a very severe case of hyperthyroidism which eventually came to necropsy. The oxygen consumption of this patient was about 77 per cent. above normal, rising to 105 per cent. above normal in the last week of life. Magnus-Levy considers that some of the high results on this patient were due to restlessness, but some were obtained while she was under the influence of morphin. This careful laboratory work on one patient is of more value to science than the clinical observation of a hundred patients. Jaquet and Svenson[11] found no constant rise in metabolism when they treated cases of obesity with thyroid extract. They also studied the specific dynamic action of food on these patients, and concluded that it was less than normal before treatment with thyroid

10. Hirschlaff, W.: Zur Pathologie und Klinik der Morbus Basedowii, Ztschr. f. klin. Med., 1899, xxxvi, 200.

11. Jaquet and Svenson: Zur Kentniss des Stoffwechsel fettsuchtigen Individuen, Ztschr. f. klin. Med., 1900, xli, 375.

—(*Continued*)

Calories per Sq. M. per Hr. Meeh	Pulse Rate	Blood Pressure, Syst.	Enlargement of Heart to Left, Cm.	Enlargement of Thyroid	Exophthalmos	Von Graefe Sign	Mental irritability	Tremor	Warmth of Skin	Emaciation	Remarks
39.7	80										
39.7	120-140	140	2	++	—	—	+	++	++	+	
37.7	100+	125	0	+	—	—	++	++	+	±	
37.0	78										
36.5	128										
35.7	96	.....	±	+	—	—	....	±			
35.5	72-94	.....	1	±	—	—	+	++	—	+	Four arteries ligated 1 yr. ago
35.5											
34.7											
34.7											
34.7	88-90										
34.6	72-96	112-120	0	—	±	—	++	+	—	+	Par. thyroidect. 2 mos. ago
34.6	86										
34.1	80										
3.30											
32.3											
29.4	72-92	.....	0	±	±	+	....	±	.....	....	Hysterical temperament

extract but greater than normal after treatment. Salomon[12] considered the increase in metabolism to be the most important objective symptom of hyperthyroidism, and followed it during treatment with "Radogen" and the serum of a thyroidectomized horse. Neither of the remedies caused a fall in the metabolism. Steyrer[13] studied the effects of thyroid tablets on one exophthalmic goiter and one myxedema patient, using a Pettenkofer-Voit respiration chamber. Pribram and Porges,[14] working under Salomon, studied the "nüchtern" or basal metabolism from fifteen to seventeen hours after the last meal of diets containing various amounts of nitrogen. They found the heat production from 4 to 8 per cent higher the morning after a diet containing from 31 to 42

12. Salomon, H.: Gaswechseluntersuchungen bei Morbus Basedowii und Akromegalie, Berl. klin. Wchnschr., 1904, xxiv, 635.

13. Steyrer, A.: Ueber die Stoff und Energieumsatz bei Fieber, Myxoedem und Morbus Basedowii, Ztschr. f. exper. Path. u. Therap., 1907, iv, 720.

14. Pribram and Porges: Ueber den Einfluss verschiedenartiger Diätformen auf den Grundumsatz bei Morbus Basedowii, Wien. klin. Wchnschr., 1908, xxi, 1584.

gm. of nitrogen than after mixed diets rich in carbohydrate. They do not consider that this differs from what would be found in normal persons after such excessive protein feeding, and believe that the basal metabolism is not much influenced by protein or meal abstinence. In one patient two treatments with the Roentgen ray did not cause any drop in the oxidative processes. More recently Undeutsch,[15] using the Rolly-Rosiewicz modification of the Benedict universal respiration apparatus, compared the rise in metabolism following the administration of various forms of protein to patients with exophthalmic goiter. He found that 40 gm. of Aleuronat increased the metabolism more than 35 gm. Roborat, and that both had greater action than 200 gm. chopped beef. Two normal controls gave the same results. He concludes that animal protein has a lower specific dynamic action than vegetable. Undeutsch also made observations on three of his patients from one to two weeks after a partial thyroidectomy. One patient showed a drop of more than 10 per cent. in the heat production, one a drop of 20 per cent. and a third with "forme fruste" and colloid goiter only a slight reduction.

Von Bergman[16] studied several myxedema patients, finding the metabolism moderately decreased. He observed a rise of 25 per cent. in the heat production in an obesity patient after the administration of thyroid extract. Falta[3] reports respiration experiments on three of his exophthalmic goiter patients made by Dr. Bernstein. Means,[17] studying several obesity patients and making a large number of respiration experiments on one marked case, found a marked rise in metabolism after thyroid administration.

The literature on the treatment of exophthalmic goiter is too enormous to be reviewed in this paper, and only those remedial measures used on the patients here described will be discussed. A partial thyroidectomy has been and perhaps always will be the standard method of treatment. Recently many surgeons have been ligating one or more of the thyroid arteries under local anesthesia as a preliminary to the more radical operation or in place of it. Medical treatment gives slower results which are often very satisfactory. Mental and physical rest over long periods of time, combined with abundant food, almost invariably improves the patient's condition, and in many cases there is a tendency toward recovery without any treatment. Beebe and

15. Undeutsch, W.: Experimentelle Gaswechseluntersuchungen bei Morbus Basedowii; Grundumsatz und Umsatz nach Aufnahme von animalischem und vegetabilischem Eiweiss, Inaug. Dessert., Leipzig, 1913.

16. Von Bergman: Der Stoff und Energieumsatz beim infantilem Myxoedem und beim Adipositas universalis mit einem Beitrage zur Schilddrüsenwirkung, Ztschr. f. exper. Path. u. Therap., 1909, v, 646.

17. Means: Studies of the Basal Metabolism in Obesity and Pituitary Disease, Jour. Med. Research, 1915, xxxii (New Series, xxvii), 121.

Rogers,[18] and more recently Beebe[19] alone, have used a cytotoxic serum prepared by injecting sheep with an extract of human thyroid tissue. This serum has never come into general use. Some patients cannot take the serum on account of violent local and constitutional reactions, and others who can take it show little improvement, as is the case with all other forms of treatment. Rogers[20] uses partial thyroidectomy in some cases, and serum in a few others, but places his chief reliance on ligation of two or more of the thyroid arteries as giving the best results in the long run. He has used thyroid extract in some cases for a few days after the ligation, and in other asthenic patients has given a thyroid preparation called "X Thyroidin," or thyroid "residue." Forcheimer[21] is very enthusiastic about the quinin-ergotin treatment which he devised several years ago. He gives quinin hydrobromate, 5 grains, and ergotin, 1 grain in gelatin coated pills four times a day. All of the foregoing clinicians insist on rest from work and mental relaxation as part of the treatment.

Plummer[22] has recently abstracted the histories of the unusually large number of cases treated at the Mayo Clinic, and on the basis of averages has arranged the symptoms in the order of their onset as follows: (1) cerebral stimulation; (2) vasomotor disturbances of the skin; (3) tremor; (4) mental irritability; (5) tachycardia; (6) loss of strength; (7) cardiac insufficiency; (8) exophthalmos; (9) diarrhea; (10) vomiting; (11) mental depression; (12) jaundice; (13) death. Of especial interest is the work of Rudinger[23] on the nitrogen minimum in hyperthyroidism. He places his patients on Landergren's low nitrogen diet, and found the nitrogen output to be so much greater than in normal persons that he considers there is a 100 per cent. increase in the destruction of body nitrogen on the fourth day of the diet. In regard to the discussion as to whether we are dealing with a hypersecretion or abnormal secretion of the thyroid, it may be well to call attention to the statement of Magnus-Levy, "The quantitative relations

18. Rogers, John, and Beebe, S. P.: The Treatment of Hyperthyroidism by a Specific Cytotoxic Serum, THE ARCHIVES INT. MED., 1908, ii, 297.

19. Beebe, S. P.: The Serum Treatment of Hyperthyroidism, Jour. Am. Med. Assn., 1915, lxiv, 413.

20. Rogers, John: The Course of Acquired Disease of the Thyroid Gland and the Principles which Seem to Control Its Progress, Ann. Surg., 1914, p. 281; Exophthalmic Goiter and Its Treatment, New York State Jour. Med., 1915, xv. 4; Am. Jour. Physiol, 1915, xxxvi, 113; ibid., 1915, xxxvii, 121, 453; ibrid., 1915, xxxix, 154; ibid., 1916, xxxix, 345.

21. Forcheimer, F.: Exophthalmic Goiter, in Therapeusis of Internal Diseases, 1913, iii, 895.

22. Plummer, H. S.: The Clinical and Pathologic Relationships of Hyperplastic and Nonhyperplastic Goiter, Jour. Am. Med. Assn., 1913, lxi, 650.

23. Rudinger: Ueber den Eiweissumsatz bei Morbus Basedowii, Wien. klin. Wchnschr., 1908, xxi, 1581.

of thyroid secretion are almost totally unknown, and are much too complicated to allow our following out a theory of hyperthyreosis in all its details; much less . . . does it enable us to argue a theory of dysthyreosis." Falta, Newburgh and Nobel,[24] on the basis of experiments with various organ extracts, believe in "Ueberfunction" rather than "Dysfunction" in exophthalmic goiter, and consider that the difference in symptoms is due to differences in the constitution of the patient.

METHODS OF EXPERIMENT

Most of the patients studied over considerable periods of time remained in the metabolism ward described in Paper 3 of this series. They were placed in the respiration calorimeter in the morning hours, either without breakfast or after special meals, if the tests were being made to determine the specific dynamic action of food. Each patient was put in the calorimeter for half an hour or so a day or two before the first experiment, in order to let him become accustomed to the interior of the apparatus. No patient objected, since all realized that their treatment was being controlled by the results of the observations. Some of the patients had marked tremors when they moved, but inside the calorimeter they were lying quietly on a comfortable bed, and they moved but seldom. The work-adder was of great service in giving an accurate idea of the relative activity of the subject in each period. In the severe cases with moist skin, the work-adder was even more sensitive than usual, since any movement on the part of the patient liberated an abnormal amount of moisture from the bedding and clothing, expanding the air of the box to a marked degree. This accounts for some of the high readings of this instrument; but some of the patients with severe cases were distinctly restless, particularly toward the end of an observation. It was for this reason that short experiments were used by preference.

The female patients were taken directly from the general medical or surgical wards. A few of both sexes came to the calorimeter room from their homes in the neighborhood, lying down for at least two hours before the observation began. Great care was taken to avoid fatigue or excitement, since it was apparent that the metabolism of these thyroid patients showed great lability.

CASE HISTORIES

CASE 1.—*History.*—Max W., aged 40, storekeeper, born in Roumania, Hebrew, admitted Feb. 11, 1914. Had typhoid fever when 18 years old. Two years ago he was operated on for inguinal hernia. About this time he was refused life insurance because he weighed 190 pounds. He drinks little, but smokes from fifteen to twenty cigarets a day.

24. Falta, Newburgh and Nobel: Ztschr. f. klin. Med., 1911, p. 72.

Present Illness.—In January, 1913, he received news of the violent death of his brother, and was much excited for a week. The next month he suffered from a severe unproductive cough, was nervous and lost weight. He was sent to the mountains with a diagnosis of tuberculosis, but did not improve. The Wassermann reaction was found to be strongly positive, and he was treated with mercury, still without improvement. October 13, he went to Mount Sinai Hospital, where a diagnosis of exophthalmic goiter was made and medical treatment tried. Shortly afterward he went to the Presbyterian Hospital, where his protein and carbohydrate metabolism was studied by Dr. Geyelin.[25] It was found that the blood sugar was 109 mg. per hundred c.c., the phenolsulphonephthalein output 85 per cent., the leukocytes 11,250, polymorphonuclears 68 per cent., lymphocytes 24 per cent., large mononuclears 5 per cent., and eosinophils 3 per cent. The urine showed traces of sugar, and the Wassermann test was strongly positive.

Physical Examination.—Feb. 11, 1914, the patient is 173.7 cm. tall, of rather large frame with small hands and tapering fingers. The skin is dark, flushed, warm and slightly cyanotic. The beard is thick, the pubic hair normal but the hair on the chest scant and the breasts fatter than the rest of the body. The face is broad and flat, the expression angry and the eyes staring with slight protrusion. The upper lid covers about 2 mm. of the cornea, but does not follow the cornea when the patient looks down. There is some weakness of convergence; he winks but seldom, and the forehead wrinkles but slightly.

There is moderate soft enlargement of the thyroid, especially the right lobe. The neck measures 37 cm. in circumference. The apex of the heart is in the fifth space 11 cm. to the left of the midline, and the limit of dulness 12.5 cm. to the left. The action is rapid and shows a marked irregularity, apparently respiratory in type, with long pauses at the end of expiration. There is a soft systolic murmur at the apex. Carotid pulse is large, radial small. The hands show red areas on the thenar and hypothenar eminences, and there is a tremor when he is excited. There is a scar of an old left inguinal hernia operation, and the left testis is very small and soft; the right testis is large, but of normal consistency. His disposition is nervous, he is excitable, quick in thought and action, and he takes malicious pleasure in teasing his fellow patients, a cretin and a pituitary patient, both somewhat slow mentally.

Treatment and Course.—The data concerning the food and urine are given in Table 2. In February and March the temperature was between 98.4 and 100, the pulse 110-140, the respirations from 26 to 28. March 18, the patient had an acute follicular tonsillitis with a transient rise in temperature to 103.2. Two days later it was normal. During April the temperature was below 99.6, the pulse 104-124, respirations from 20 to 22. Blood pressure, February 15, systolic, 150, diastolic, 70; March 7, 130-60; April 6, 132-82; April 23, 148-74. Beebe's serum was begun, March 5, and the doses slightly increased from time to time. The patient received twenty-three doses up to April 30, and after this the serum was given by Dr. Beebe, himself, at fairly regular intervals. With the serum he was given 1 grain of potassium iodid twice a day. The local reaction from the injection was at times quite marked, but the patient felt so much better that he cheerfully submitted to the discomfort and was enthusiastic about the treatment.

During his stay in the hospital he averaged about three stools a day. He improved distinctly even before he received any treatment other than rest in bed and good food. The diarrhea stopped, as did the sweating, and he was not so nervous. There was slight glycosuria after 100 gm. of glucose. A note, April 15, says he weighed more than on admission, that he was eating more and was feeling stronger each day. It was noticed that he had a polyuria,

25. Geyelin, H. R.: The Carbohydrate Metabolism in Hyperthyroidism as Determined by Examination of Blood and Urine, THE ARCHIVES INT. MED., 1915, xvi, 975.

TABLE 2.—Clinical Data in Case 1

Date	Temperature		Total Calories Food	Carb., Gm.	Fat, Gm.	Food N.	Urine N.	Body Weight	Urine, Volume, c.c.
	Max.	Min.							
2/13/14	99.6	98.6	2,974	176.0	179.0	15.7	14.88	.....	2,735
2/14/14	99.6	98.6	3,675	232.0	234.0	21.3	13.87	62.24	2,500
2/15/14	99.6	98.6	4,091	256.0	252.0	21.5	14.58	62.00	2,450
2/16/14	99.4	98.2	3,662	230.0	238.0	19.7	12.69	61.76	2,525
2/17/14	99.0	98.6	4,324	289.0	273.0	23.3	18.15	61.89	3,150
2/18/14	100.0	98.6	3,971	313.0	228.0	18.0	15.75	62.02	3,720
2/19/14	99.6	98.6	3,970	273.0	259.0	21.8	19.25	61.81	2,720
2/20/14	99.6	98.6	3,620	299.0	201.0	20.0	17.17	61.60	3,240
2/21/14	99.0	98.6	3,801	367.0	198.0	17.6	15.58	62.26	3,045
2/22/14	99.8	98.8	3,758	289.0	216.0	21.6	18.16	62.27	3,830
2/23/14	99.6	99.0	3,874	292.0	226.0	22.6	16.19	62.28	3,240
2/24/14	99.6	99.0	3,628	274.0	212.0	21.0	17.46	61.77	3,200
2/25/14	99.8	99.2	2,411	187.0	119.0	20.9	19.91	61.17	2,890
2/26/14	99.4	98.6	4,246	310.0	232.0	22.7	17.73	61.03	2,360
2/77/14	100.0	98.6	2,533	263.0	121.0	13.0	17.36	60.90	2,990
2/28/14	99.2	98.4	3,520	271.0	205.0	19.8	14.37	60.71	2,610
3/ 1/14	99.2	98.8	3,399	284.0	184.9	20.0	15.60	60.71	3,320
3/ 2/14	99.6	98.4	2,809	199.0	157.0	20.0	18.21*	60.52	3,240
3/ 3/14	99.8	98.6	3,739	290.0	215.0	21.4	18.21*	60.29	3,150
4/ 4/14	99.8	99.0	2,842	211.0	169.0	15.7	14.59*	60.06	2,375
3/ 5/14	99.8	98.6	3,396	255.0	199.0	19.6	17.15*	60.10	2,930
3/ 6/14	99.6	99.0	3,796	273.0	207.0	20.2	12.61*	60.10	2,000
3/ 7/14	99.8	98.8	.....	.....	.....	....	.....	60.14	.....
3/22/14	99.0	98.0	.....	.....	.....	....	.....	.....	.....
3/23/14	99.4	98.8	2,328	193.0	121.0	16.0	12.16	59.25	3,136
3/24/14	99.0	98.2	3,366	252.0	198.0	19.2	10.59	.....	1.940
3/25/14	99.2	98.4	3,475	301.1	187.0	19.5	11.39	.....	3,200
3/26/14	98.4	98.4	3,408	264.0	196.0	19.6	11.27	60.01	2,890
3/27/14	99.2	98.0	3,494	305.0	187.0	19.1	11.10	60.06	2,490
3/28/14	98.4	98.4	3,640	294.0	206.0	20.0	12.36	60.12	2,960
3/29/14	98.8	98.2	3,891	333.0	214.0	20.9	11.54	60.56	3,365
3/30/14	98.8	98.4	3,560	368.0	164.0	20.4	11.32	61.00	3,460
3/31/14	99.2	98.6	3,976	393.0	195.0	21.5	13.04	61.18	2,500
4/ 1/14	99.6	98.6	4,294	437.0	213.0	20.2	12.11	61.37	2,390
4/ 2/14	98.6	98.0	4,216	422.0	212.0	20.0	12.19	61.88	2,600
4/ 3/14	98.8	98.6	4,232	419.0	215.0	20.2	11.60	61.88	2,900
4/ 4/14	99.6	98.4	4,205	405.0	217.0	20.6	11.85	61.91	2,320
4/ 5/14	99.4	98.4	4,444	435.0	225.0	21.8	12.53	62.26	2,970

* Average feces N. per day March 2 to 6, 3.67 gm.

TABLE 2.—(*Continued*)

Date	Temperature		Total Calories	Carb., Gm.	Fat, Gm.	Food N.	Urine, N.	Body Weight	Urine, Volume, c.c.
	Max.	Min.							
4/ 6/14	99.2	98.4	3,316	379.0	144.0	16.3	13.10	62.26	2,790
4/ 7/14	98.4	98.4	4,529	425.0	214.0	20.3	13.09	62.26	3,060
4/ 8/14	99.0	98.4	4,506	433.0	237.0	20.0	12.62	62.62	2,660
4/ 9/14	98.8	98.4	4,345	444.0	214.0	20.7	12.17	62.90	3,190
4/10/14	98.8	98.4	4,538	424.0	242.0	20.2	13.17	63.19	3,200
4/11/14	99.6	98.2	4,062	372.0	216.0	20.0	13.28	63.32	2,500
4/12/14	99.8	98.2	4,568	401.0	253.0	21.6	11.85	63.45	2,330
4/13/14	98.8	98.6	4,801	550.0	213.0	22.0	17.54	63.01	3,770
4/14/14	98.4	98.4	4,103	408.0	213.0	20.9	12.55	62.58	1,420
4/15/14	98.4	98.4	4,282	406.0	219.0	20.6	15.58	62.92	1,390
4/16/14	99.6	98.4	4,136	388.0	217.0	20.0	15.64	63.26	1,500
4/17/14	99.6	98.8	4.164	343.0	241.0	20.1	15.02	63.58	1,330
4/18/14	99.2	98.4	4,319	355.0	249.0	21.1	15.36	63.58	1,660
4/19/14	99.4	98.8	4,108	380.0	217.0	20.8	14.85	63.58	1,580
4/20/14	99.0	98.8	3,981	350.0	217.0	20.6	15.69	63.90	1,860
4/21/14	99.2	98.4	3,817	319.0	214.0	20.2	14.18	63.81	1,600
4/22/14	99.6	98.6	4,041	369.0	214.0	20.8	17.23	63.73	1,800
4/23/14	98.8	98.4	4,353	399.0	230.0	22.6	17.85	.....	1,980
4/24/14	98.6	98.0	2,943	280.0	151.0	15.1	14.27	63.29	1,889
4/25/14	99.0	98.6	4,064	375.0	214.0	20.7	14.40	.....	1,620
4/26/14	99.4	98.2	4,071	369.0	217.0	20.9	15.52	.....	1,840
4/27/14	99.2	98.2	4,107	361.0	215.0	20.9	15.19	64.56	1,850
4/28/14	98.8	98.2	3,997	360.0	214.0	20.6	14.55	.....	2,360

and the salt in the diet was cut down to from 3 to 4 gm. a day. Two days after this change the urine volume rose to 3,900 c.c., with 22 gm. sodium chlorid in twenty-four hours. After this the volume dropped markedly. By April 24 he was able to be up and about most of the day without fatigue. When he left the hospital the thyroid gland and the eyes were as on admission, but the heart action was regular most of the time.

A year later, April 22, 1915, he spent another day in the metabolism ward and went into the calorimeter again. He had done very well under Dr. Beebe's treatment, gaining 22 pounds in weight. He was able to work in his store eight or ten hours a day, and a few weeks ago walked 5 miles. He seldom has palpitation, but does not try to walk upstairs. He is not so excitable as a year ago. He is able to wear a collar one size smaller than last year. He looks much fatter and stronger, but the eye symptoms are unchanged and the skin is still moist and warm. The apex of the heart is maximum in the fifth space 13.3 cm. to the left of the midline, and the action is so markedly irregular as to suggest auricular fibrillation, a diagnosis which is confirmed by the electrocardiogram.

CASE 2.—*History.*—Edwin T., aged 20 years, student, admitted Feb. 24, 1915, discharged May 1. At the age of 10 had an attack of acute rheumatic fever, and since then has had many sore throats. Three years ago he worked

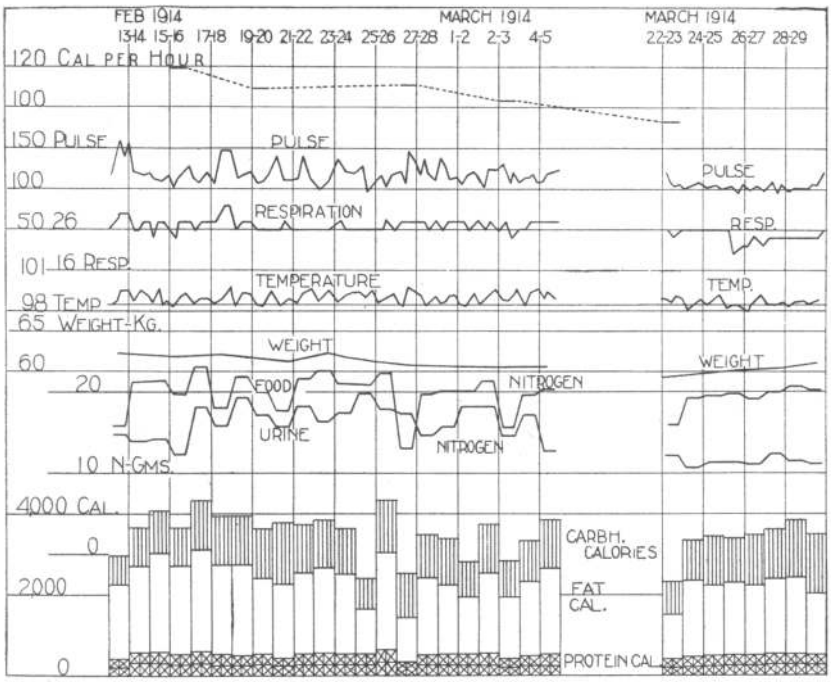

Fig. 1.—Chart in Case 1. Max W.

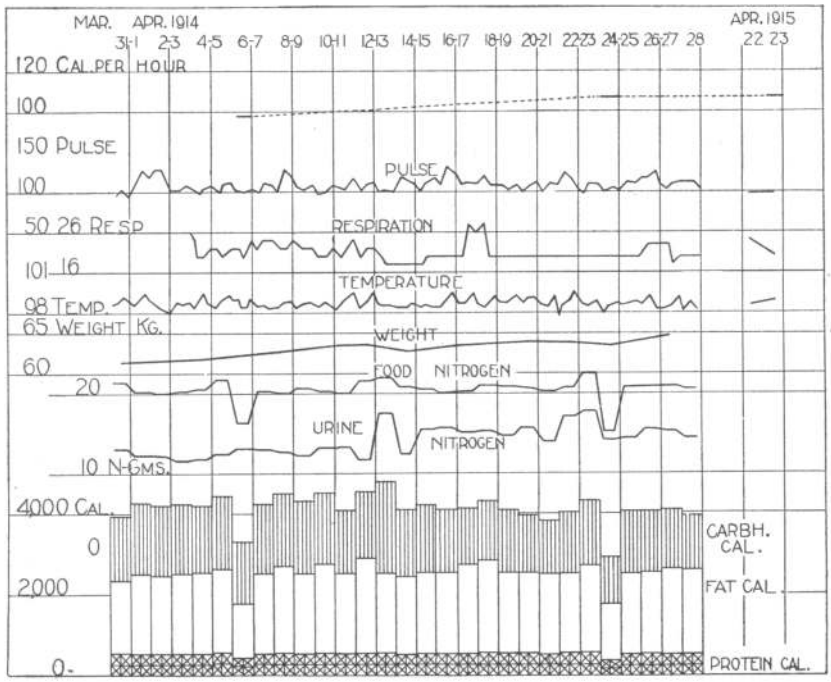

Fig. 2.—Chart in Case 1. Marx W. (continued).

very hard in school. At this time he was able to participate in track athletics. He has been accustomed to taking about six cups of strong tea every day, and has always been nervous. About six months ago he became excitable and restless and a little later was obliged to stop work. About three months ago his friends began to speak of a change in his facial expression. He grew steadily worse until three weeks ago, when a diagnosis of hyperthyroidism was made by Dr. R. J. Shea, and proper treatment started. He lost 13 pounds in weight, but regained most of it under Dr. Shea's care.

Physical Examination.—The patient is 168 cm. tall, moderately thin, the bones are slender, and the distribution of hair is normal for his age. The facies is neurotic in type and the expression angry with slight protrusio bulbi. The tonsils are large and succulent with deep crypts. The thyroid is soft and enlarged, measuring 12 cm. broad, 3 cm. in the vertical direction at the isthmus and 4 cm. at each lobe. The heart is not enlarged, but the first sound is of poor quality, short and sharp, and there is a murmur over the pulmonic area which resembles a hemic or extracardiac murmur. The heart action is forcible, but the radial pulse small. The skin is flushed, warm and moist, often breaking out into sweat. There is a tremor when he is excited.

Treatment and Course.—The first month in the hospital he was given no medication but kept quiet in bed. He became less and less excitable, the skin became cooler and drier and he was happy and helpful in the ward. About March 10 he began to be homesick and at times excitable. March 23, Beebe's serum was started in 5 minim doses almost every day. March 29, there was a severe local reaction accompanied by nausea. After this the serum was given in smaller doses every three days until April 14.

The patient felt a little better after the first few doses of serum, but later grew steadily worse, becoming more depressed, discouraged and at times very nervous. Between April 7 and 21 he was much excited over some personal matters, and was hard to manage. April 21, he was removed to the surgical ward, and the right inferior thyroid artery tied under novocain anesthesia by Dr. Rogers. April 23 and 29, the other three arteries were tied, the patient experiencing no pain, and scarcely ever showing a pulse rate above 100. He felt better and was up and about the ward the day after each operation.

May 10, he was readmitted for a calorimeter observation after ten days in the country. He has felt better and has slept well. The wounds are healing well and his general condition seems improved, but the physical examination is much the same as when first admitted to the hospital. For clinical data see Table 3.

CASE 3.—*History.*—James McE., aged 29, factory worker, admitted March 1, 1915, on the service of Dr. Lockwood, with the diagnosis of exophthalmic goiter and alcoholism; at the age of 22 had an attack of appendicitis. He is a heavy smoker, drinks much tea and has periodic attacks of drunkenness lasting about a week. He has been thin, nervous and in rather poor health for the last nine years, and has been very excitable for two or three years. Seven months ago he became very nervous. Five months ago he noticed swelling of the neck, palpitation and dyspnea. At this time he had severe pains in his face not relieved by the extraction of a tooth. Two weeks ago he began to have night sweats, cough, pain in the bones, hoarseness and he lost weight rapidly.

Physical Examination.—The patient is 166 cm. tall, emaciated, restless, expression staring, skin flushed, warm and sweating, pubic and axillary hair scant. Exophthalmos moderate, von Graefe's and Moebius' signs positive. The teeth show much caries and pyorrhea. There is a marked bilateral enlargement of the thyroid gland. Thorax is poorly formed, heart apex 13 cm. to left of midline, regular but markedly overacting, with a rough systolic murmur, loudest to the left of the sternum. Pulse is Corrigan in type. There is a fine tremor of fingers and tongue, and a distinct odor of acetone on the breath.

TABLE 3.—CLINICAL DATA IN CASE 2

Date, 1915	Food					Urine					
	Total Calories	Protein, Gm.	Fat, Gm.	Carbohyd., Gm.	Food N	Urine N	Excreta N, Gm. †	N Balance, Gm.	Urine Glucose, Gm.	Urine Vol., c.c.	Body Weight, Kg.
Feb. 25-26	3,107	98.7	166.7	280.9	15.79	.....	.....	.....	.....	.....	50.18
Feb. 26-27	2,330*	61.7	134.0	202.7	9.87	15.69	16.68	—6.81	.....	830	49.78
Feb. 27-28	2,882	92.9	139.9	292.6	14.86	16.70	18.18	—3.32	.....	990	.....
Feb. 28- 1	2,723	87.0	142.3	254.7	13.92	17.71	19.10	—5.18	.....	1,030	49.88
Mar. 1- 2	3,704*	101.0	211.6	322.4	16.16	18.44	20.05	—3.89	.....	1,040	.....
Mar. 2- 3	3,462	98.6	184.3	327.9	15.78	16.98	18.56	—2.78	.....	990	.....
Mar. 3- 4	364.1	104.6	188.6	355.6	16.73	17.50	19.17	—2.54	.....	1,065	49.78
Mar. 4- 5	3,221	93.2	172.9	279.3	14.91	16.42	17.91	—3.00	10.64	1,050	49.40
Mar. 5- 6	2,897	132.1	125.9	288.9	22.16	19.51	21.73	+0.43	14.71	1,602	50.42
Mar. 6- 7	2,763	85.5	141.1	268.3	13.68	18.15	19.52	—5.84	15.15	1,595	50.04
Mar. 7- 8	3,760	111.0	210.2	331.6	17.76	15.55	17.33	+0.43	5.31	1,035	50.37
Mar. 8- 9	2,999	155.9	172.9	183.3	24.94	21.22	23.71	+1.23	7.92	1,627	50.06
Mar. 9-10	3,517	105.8	194.6	311.2	16.92	6.87	8.56	+8.36	0	900	50.36
Mar. 10-11	2,419	69.1	124.6	238.9	11.06	13.59	14.70	—3.64	18.06	1,018	49.32
Mar. 11-12	3,549	100.1	203.8	302.5	16.01	15.13	16.73	—0.71	7.20	1.320	.....
Mar. 12-13	3,525	97.1	204.1	299.8	15.53	11.35	12.90	+2.63	7.41	1,075	50.05
Mar. 13-14	3,728	99.5	221.8	306.7	15.92	14.68	16.27	—0.35	9.54	1,160	50.18
Mar. 14-15	3,638	97.6	199.1	338.4	15.61	15.24	16.80	—1.19	7.80	1,260	50.10
Mar. 15-16	2,075	66.9	194.5	242.3	10.70	11.80	12.87	—2.17	5.57	880	50.11
Mar. 16-17	3,180	66.5	205.3	243.4	10.64	13.28	14.34	—3.70	6.87	1,170	49.76
Mar. 17-18	3,159	67.9	202.3	243.6	10.86	8.88	9.97	+0.90	4.62	800	50.01
Mar. 18-19	3,200	70.7	203.3	248.3	11.34	12.53	13.66	—2.32	9.37	1,040	.....
Mar. 19-20	3,550	69.8	218.0	301.8	11.16	11.49	12.60	—1.44	11.87	1,090	50.28
Mar. 20-21	3,631	64.9	253.1	246.9	10.38	10.23	11.27	—0.89	8.24	980	50.28
Mar. 21-22	3,467	72.9	209.3	298.7	11.66	12.61	13.78	—2.12	8.96	1,230	50.27
Mar. 22-23	3,281	65.0	226.1	222.2	10.40	12.75	13.79	—3.39	14.52?	946	49.22
Mar. 23-24	3,305	66.1	203.4	278.5	10.58	10.09	11.15	—0.57	8.88	815	49.98
Mar. 24-25	3,466	65.8	225.0	268.9	10.52	9.47	10.52	0.00	6.87	720	50.18
Mar. 25-26	3,591	66.8	227.0	294.1	10.68	9.47	10.54	—0.14	8.00	920	50.24
Mar. 26-27	3,836	66.0	256.2	288.0	10.56	10.03	11.09	—0.53	9.24	880	50.17
Mar. 27-28	3,639	65.6	247.0	261.8	10.50	9.58	10.63	—0.13	3.08	710	49.94
Mar. 28-29	4,194	71.3	269.2	341.0	11.40	10.65	11.79	—0.39	8.13	820	50.00
Mar. 29-30	3,681	81.6	219.1	314.2	13.05	9.72	11.03	+2.02	14.50	930	50.00
Mar. 30-31	3,602	70.2	118.8	302.1	11.23	10.93	12.05	—0.82	24.51	1,040	50.30
Mar. 31- 1	2,922	74.1	162.7	269.6	11.86	11.57	12.76	—0.90	15.90	780	50.30
Apr. 1- 2	3,874	96.1	214.0	363.3	15.38	13.03	14.57	+0.81	11.42	1,100	50.35
Apr. 2- 3	3,866	96.9	200.0	392.5	15.50	12.50	14.05	+1.45	8.20	1,250	50.63

† Urine N plus 10 per cent. of food N.

TABLE 3.—(*Continued*)

Date, 1915	Food					Urine					
	Total Calories	Protein, Gm.	Fat, Gm.	Carbohyd., Gm.	Food N	Urine N	Excreta N, Gm.	N Balance, Gm.	Urine Glucose, Gm.	Urine Vol., c.c.	Body Weight, Kg.
Apr. 5- 6	3,549	89.9	192.4	350.2	14.38	10.73	12.17	+2.21	11.30	970	.....
Apr. 6- 7	3,871	94.2	195.0	407.5	15.07	10.37	11.88	+3.19	8.61	800	50.90
Apr. 7- 8	3,758	98.9	197.5	369.9	15.82	11.71	13.29	+2.53	7.53	910	50.75
Apr. 8- 9	3,908	99.4	193.6	414.7	15.90	11.49	13.08	+2.82	17.22	960	51.15
Apr. 9-10	3,532	99.2	211.0	283.6	15.87	12.05	13.64	+2.23	9.77	1,260	51.38
Apr. 10-11	3,874	98.6	215.4	357.7	14.79	?	.....	.....	?	?	51.16
Apr. 14-15	4,109	105.2	195.5	453.6	16.83	11.21	12.89	+3.94	15.65	1,120	51.48
Apr. 15-16	3,303	83.5	195.6	278.6	13.36	11.04	12.38	+0.98	17.0	1,160	.....
Apr. 16-17	3,863	88.4	221.4	351.7	14.14	11.66	13.07	+1.07	14.9	1,390	51.49
Apr. 17-18	3,392	99.6	163.2	157.6	15.94	11.77	13.36	+2.58	.....	1,185	.....
Apr. 18-19	3,623	98.5	179.5	378.1	15.76	11.43	13.01	+2.75	.....	960	51.50
Apr. 19-20	3,494	88.5	166.2	386.5	14.16	12.33	13.75	+0.41	16.4	1,040	51.40
Apr. 20-21	3,769	98.0	181.8	408.8	15.68	12.55	14.12	+1.56	.....	1,050	51.38

* Food approximate on these two days.

Treatment and Course.—For the first twelve days in the hospital he was kept in bed without medication and improved slowly. March 14, after the first observation in the calorimeter, the Forcheimer ergotin and quinin hydrobromate treatment was begun. He continued to improve slowly in general condition, and gained 6 pounds in weight. The blood pressure was 130-65 and 146-66 mm. Hg. The Wassermann reaction was weakly positive; the urine contained a trace of albumin and a few casts. Temperature 99-100, pulse 108-124 up to March 15, then 82-100.

April 8, he was transferred to the surgical wards, and one superior thyroid artery was ligated under local anesthesia. May 2, one inferior thyroid artery was exposed, but the pulse became so rapid and feeble that the wound was hastily sutured without an attempt being made to ligate the vessel. The patient continued to improve slowly. May 14, the left limit of cardiac dulness was 11 cm. to the left of the midline; the murmur was unchanged. The general condition was better than a month before. For clinical data see Table 4.

Notice of his death in February, 1916, has just been received.

CASE 4.—*History.*—Dr. G. S. L., aged 52, physician, had typhoid fever twenty-five years ago. He smoked from six to nine cigars a day. His eyes have always been prominent. Three or four years ago when his weight was about 215 pounds, he noticed a slight tremor of the hands and slight dyspnea and palpitation on exertion. About one year ago the neck increased in size. The four thyroid arteries were ligated in January, 1914, (three months ago), but he was nearly exsanguinated by a secondary hemorrhage from the superior thyroid artery. He was given quinin hydrobromate for a month, but developed cinchonism. Thyroidectin in September made him worse. For the last week he has had no treatment.

Physical Examination.—April 9, the patient is 180 cm. in height, tall and large framed. The expression is staring, the skin flushed, warm, moist, smooth, and slightly darkened. Dermatographia is present. There is no hair on the chest. There is moderate protrusio bulbi, slight von Graefe's sign, convergence

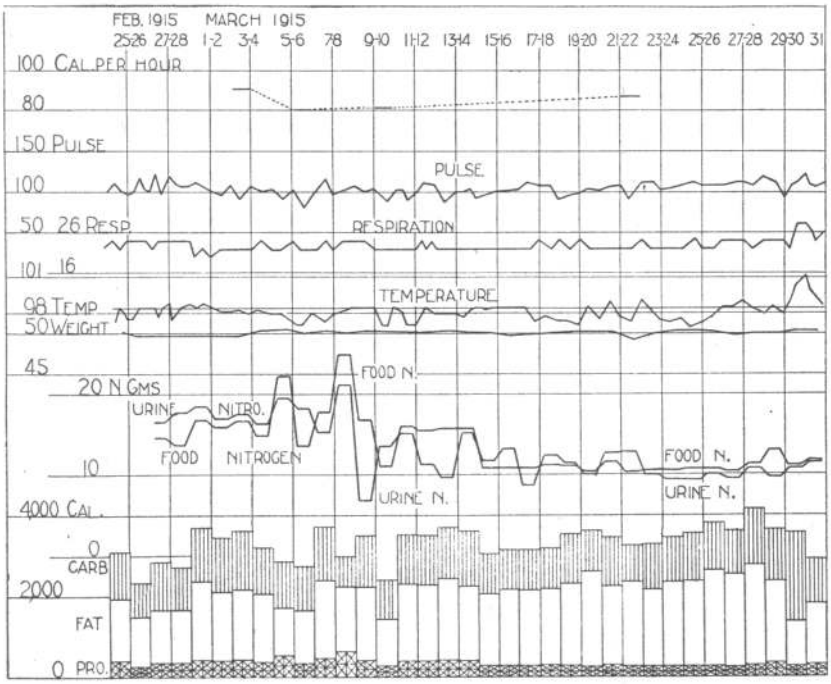

Fig. 3.—Chart in Case 2. Edwin T.

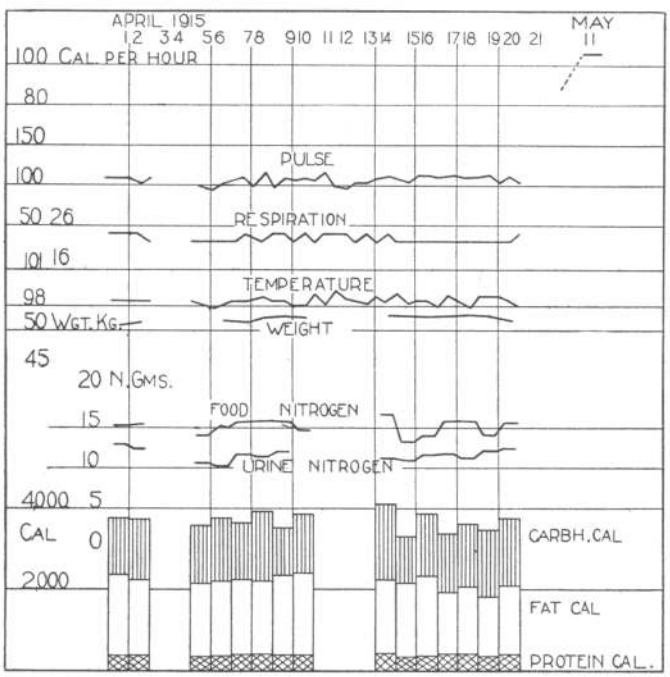

Fig. 4.—Chart in Case 2. Edwin T. (continued)

weak, thyroid lobes and isthmus enlarged. Heart apex impulse is 16 cm. from midline, action regular and heaving. There is a soft systolic murmur maximum in the pulmonic region. Pulse is 100, of large size. Blood pressure is 148 mm. There is a marked tremor of the hands and tongue and also of the legs when standing.

Treatment and Course.—After the calorimeter observation, April 9, the patient was given Dr. Rogers' thyroid "residue," 1 c.c., twice a day until April 16, when he returned for another test, his condition being unchanged except that the heart action was perhaps a little quieter.

In October, 1914, a thyroidectomy was performed. The day after the operation the temperature rose to 101, the pulse to 150, and the respirations to 70 per minute. He died a week later.

TABLE 4.—CLINICAL DATA IN CASE 3

Date, 1915	Food					Urine					
	Total Calories	Protein, Gm.	Fat, Gm.	Carbohyd., Gm.	Food N	Urine N	Excreta N, Gm. †	N Balance, Gm.	Urine Glucose, Gm.	Urine Vol., c.c.	Body Weight, Kg.
Mar. 9-10	3,322	100.7	183.0	294.5	16.11	11.94	13.55	+2.56	0	1,470	41.39
Mar. 10-11	3,315	94.1	178.7	309.1	15.06	13.51	15.02	+0.04	0	1,380	41.84
Mar. 11-12	3,189	93.7	182.5	270.3	15.00	14.18	15.68	−0.68	0	1,695	41.26
Mar. 12-13	2,558	86.2	145.9	206.9	12.79	15.09	16.47	−2.68	0	1,390	41.16

† Urine N plus 10 per cent. of food N.

CASE 5.—*History.*—Peter N., aged 23, with atypical exophthalmic goiter (?), mechanic, admitted April 9, 1915, discharged April 25. His father is 6 feet 4 inches tall (193 cm.). The patient has had sore throat several times. He grew very fast between the ages of 15 and 18. At the age of 18 he became weak and nervous, losing his temper easily. He suffered from severe headaches two or three times a week and his hands grew so tremulous that he has been unable to work for the last year. About a year ago he was in the Massachusetts General Hospital, where his respiratory metabolism was studied by Dr. Means and found to be within normal limits. The superior thyroid arteries were tied, and since then the headaches have been less frequent and the hands drier. He is not much stronger, and he sleeps only two or three hours a night.

Physical Examination.—April 25, 1915, the patient's height is 6 feet 2 inches (187.7 cm.). He is tall and thin with no suggestion of acromegaly. The hands are tapering. The expression is anxious; there are no eye symptoms. The thyroids are soft and slightly enlarged. The hands and feet are sweating, dermatographia marked. Cardiac dulness extends 12 cm. to the left of the midline. Electrocardiograms show a slight respiratory arrhythmia. There is a marked tremor of the right hand and slight tremor of the left. Roentgenoscopy reveals a normal sella turcica. There is a trace of glucose in the urine. During his short stay in the hospital there was no change in his condition. For clinical data see Table 5.

CASE 6.—*History.*—Anna K., aged 26, single, born in Ireland, nurse, admitted April 27, 1914, whose mother, one brother and one sister are nervous, had acute rheumatic fever at 16 and has had one attack of severe tonsillitis. For the last ten years she has been high-strung and easily frightened. For several years she has had dyspnea and palpitation on exertion. About December, 1913, all of these symptoms grew worse, and she began to have severe headaches, scanty menses, marked sweating and polyphagia and polydipsia. In February, 1914, she was badly frightened in a runaway, and the symptoms increased in severity. She has lost 15 pounds in weight.

For the last two months she has been given thyroid "residue" by Dr. Rogers. April 4, both superior arteries were ligated by Dr. Rogers in Bellevue Hospital.

Physical Examination.—The patient is very thin, frame small, expression tired and neurotic, speech jerky and agitated, voice weak. Skin moist. Exophthalmos slight, eyelids puffy, no von Graefe's sign, tongue and hands tremulous. Thyroid moderately enlarged, especially on the right. Cardiac impulse diffuse, maximum in the fifth space 8.5 cm. to the left of the midline. Action rapid and regular.

Treatment and Course.—After the first calorimeter observation, the two inferior thyroid arteries were ligated, April 29. May 13, the patient returned to the calorimeter room for the day feeling less nervous and more ambitious than before. June 22, she reported to Dr. Rogers weighing 112 pounds, pulse 90, general condition much improved.

TABLE 5.—CLINICAL DATA IN CASE 5

Date, 1915	Food					Urine					
	Total Calories	Protein, Gm.	Fat, Gm.	Carbohyd., Gm.	Food N	Urine N	Excreta N, Gm. †	N Balance, Gm.	Urine Glucose, Gm.	Urine Vol., c.c.	Body Weight, Kg.
Apr. 10-11	3,362	85.3	205.4	268.8	13.64	.....	.....	.....	.....	.....	63.95
Apr. 14-15	2,330	66.2	137.4	190.5	10.69	12.17	13.23	−2.64	Slight trace	747	63.44
Apr. 15-16	2,893	69.5	170.2	250.1	11.12	12.16	13.27	−2.15	Trace	840	64.00
Apr. 17-18	2,942	87.3	160.6	265.8	13.97	13.34	14.74	−0.87	.....	1,100	.....
Apr. 18-19	2,757	73.2	143.1	274.6	11.71	11.94	13.11	−1.40	.....	1,240	65.18
Apr. 19-20	2,808	72.7	130.5	316.1	11.63	11.94	12.65	−1.02	Trace	1,080	64.64
Apr. 20-21	3,023	74.7	171.6	273.4	11.95	11.49	12.69	−0.74	.....	1,460	65.28
Apr. 21-22	2,714	83.3	149.5	239.6	13.32	11.82	13.13	+0.19	Trace	1,420	64.65
Apr. 22-23	2,465	84.9	137.8	203.7	13.58	12.95	14.31	−0.73	Trace	1,300	64.32
Apr. 23-24	3,006	85.6	189.3	218.1	13.70	12.81	14.18	−1.37	Heavy trace	1,000	64.20
Apr. 24-25	2,847	87.3	174.6	210.9	13.97	12.61	14.01	−0.04	5.21	1,300	64.45

† Urine N plus 10 per cent. of food N.

CASE 7.—*History.*—Anna R., aged 29, unmarried, cook and saleswoman, born in Ireland, admitted May 8, 1913, discharged June 5, five years ago had typhoid fever and shortly afterward noticed swelling of her throat. A year or so later her tonsils were removed by a doctor who told her she had a goiter. Since the attack of typhoid she has had at times tremor, palpitation, restlessness and loss of weight. She thinks she has improved during the last two years. A year or so ago her friends noticed that her eyes were staring. She has been able to work up to the time of admission.

Physical Examination.—The patient is tall and thin, exophthalmos present, von Graefe's and Stellwag's signs present. There is slight tremor of hands and tongue. The heart is slightly enlarged, first sound of poor quality. The thyroid is moderately enlarged.

Treatment and Course.—May 8 to 11 temperature is normal, pulse from 84 to 88, respiration from 20 to 22. The first calorimeter observation was on May 10. On the 12th under local anesthesia Dr. Rogers ligated the left superior and right inferior thyroid arteries and removed the tip of the left upper pole. May 16, the two other vessels were ligated and the tip of the right pole removed. After the first operation the temperature was 99 to 100, pulse 100-112, respiration 24 to 26. After the second operation she was given half a grain of the

Loomis Laboratory special thyroid extract every four hours until May 18. She menstruated from May 16 to May 19. For three days after the operation the temperature was 99 to 102, pulse 96-130, respiration 24 to 32. By May 20, at the time of the second calorimeter observation, the temperature was almost normal. By May 25 she was up and about the ward.

After leaving the hospital she spent two months in the country and gained weight up to 117 pounds. Since then she has been at work and has lost 2 pounds, but has not felt nervous except when she works hard. May 14, 1914, she returned for a calorimeter observation. The scars of the operation were well healed, the left lobe and isthmus of the gland were moderately enlarged and the right lobe considerably enlarged. She was still thin and nervous, and the voice weak and husky, but she looked a little better than a year ago.

A week or so after the last calorimeter observation she was married, and did well until her husband lost his job on account of the war. She started work in the store again, and her weight dropped to 104 pounds and all the symptoms returned. In March, 1915, she reported at the ward very thin, very nervous, hands very tremulous, skin moist, pulse very rapid and small.

CASE 8.—*History.*—Sarah M., aged 29, chambermaid, unmarried, born in Ireland, admitted April 29, 1914, discharged May 4, nine years ago came to America, and eight years ago began to suffer from loss of weight, nervousness, weakness, tremor and enlargement of the neck. Three months later she was operated on, and apparently part of the thyroid gland removed. She recovered quickly, and for the next six years enjoyed good health. One year ago she began to have a return of the weakness, nervousness and loss of weight. She became excitable, sweated easily, and slept poorly. At times she had palpitation. She thinks the neck has swollen again.

Physical Examination.—April 29, the patient is tall, fairly well nourished, and does not look sick. The eyes are a little brighter than normal, but there is no exophthalmos, no von Graefe's sign and only slight weakness of convergence. The left lobe of the thymus is absent, the right lobe moderately enlarged. There is slight tremor of the tongue and hands on excitement. The heart is not enlarged and is not overacting; pulse from 86 to 97. The skin is a little moist and not flushed.

Treatment and Course.—The afternoon of the calorimeter observation a partial thyroidectomy was performed by Dr. Rogers. She made a rapid recovery, and when she reported in February, 1915, she had no subjective or objective symptoms.

CASE 9.—*History.*—Marion B., aged 22, unmarried, admitted Feb. 4, 1915, discharged February 5, was sent down from the Presbyterian Hospital, where her case was studied in detail by Dr. Geyelin. In 1912 the heart began to beat fast, she sweated easily and began to notice swelling of the neck. Four operations were performed at the Presbyterian Hospital. In July, 1913, two arteries were ligated. Two months later the right lobe of the gland was removed. In February, 1914, an appendectomy was necessary. In July, 1914, part of the left lobe of the thyroid was removed, and she felt better until September, 1914, when her nervousness returned. At the time of her admission she had been menstruating four days.

Physical Examination.—The patient is short and rather stout; excitable. She has a nervous, staring, angry expression. The exophthalmos is marked, the pupils are dilated, the skin moist, the pulse small and soft.

CASE 10.—*History.*—Margaret L., aged 51, married, with atypical exophthalmic goiter, auricular fibrillation and mitral insufficiency, admitted March 25, 1914, died May 19, 1914. She had three children in good health. A year ago she began to feel nervous, and lost appetite and weight. She noticed a rapidly growing swelling on the right side of the neck. This was removed by operation in July, 1913. Since then she has been worse and has violent palpitation of the

heart all the time. A month ago she began to have huskiness of the voice, swollen arms and legs and much dyspnea.

Physical Examination.—The patient is well developed and well nourished, dull mentally, slow of speech, the voice husky but not brassy. Skin thick, hard, dry, feels myxedematous. Slight exophthalmos, no von Graefe or Stellwagon sign.

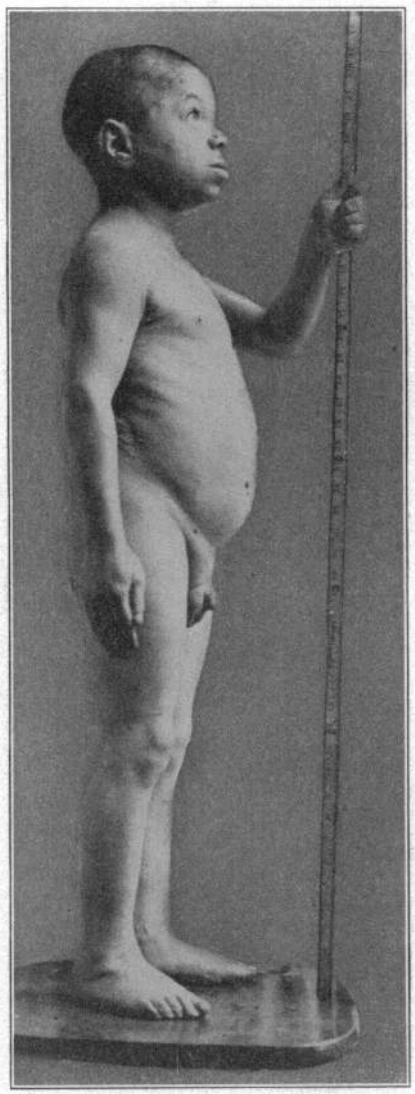

Fig. 5 (Case 12).—Benny L. Cretin holding ruler marked in inches.

Right lobe of thyroid absent, left lobe slightly enlarged. Heart much enlarged with an irregularity shown by tracings to be due to fibrillation. There is a systolic murmur at the apex. There is some fluid in the right pleural cavity. She is dyspneic and looks seriously ill.

Treatment and Course.—At first she was given thyroid "residue," but for three weeks before the calorimeter observation received no medication except codein and ammonium carbonate to control the cough. May 5, a small thymus gland was removed. Histologic examination showed "fatty infiltration of the thymus, thymic tissue appears normal." After the operation she developed fever, rapid pulse, grew weaker and died. There was no necropsy.

Case 11.—*History.*—Miss B. H., aged 31, trained nurse, admitted April 4, discharged April 20, 1914. In childhood had pertussis, scarlet fever, measles, varioloid, mumps, bronchitis, typhoid fever at 15 years, appendicitis and peritonitis at 20, many attacks of tonsillitis and finally tonsillectomy at 22, and diphtheria at 29. For the last two or three years she has worked very hard as a nurse on difficult cases.

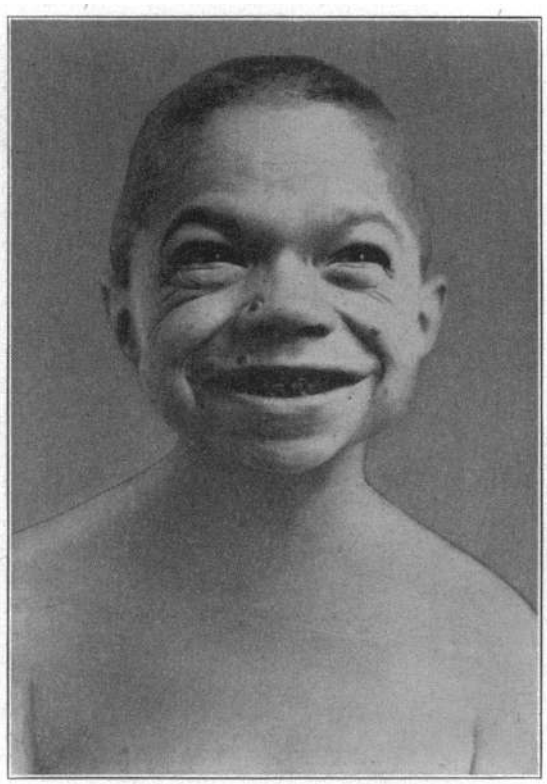

Fig. 6 (Case 12).—Benny L. Cretin, 36 years old (continued).

In 1910 she noticed that the thyroid was enlarged. In August, 1913, while nursing a typhoid patient she began to have severe diarrhea with eighteen movements a day. She vomited continually, the pulse was very rapid, and she was excitable and weak. After prolonged rest these symptoms would clear up enough to allow her to work once more. In January, 1914, the right side of the thyroid became enlarged and painful, nervousness increased and she lost 20 pounds. In February, 1914, the right lobe of the gland was removed. Two days later the voice, which had been clear, dropped to a whisper, and did not return to normal for a year or so. After the thyroidectomy the pulse rate dropped from an average of 140 to 72, and she has had but little palpitation and no sensation of undue

warmth. The nervousness has begun just as bad, and she has diarrhea whenever she takes fats. At the time of admission to Bellevue she was much depressed over the loss of her voice, which she feared was to be permanent.

Physical Examination.—April 4, 1914, the patient is of moderate height (159.2 cm.), thin, looks tired and nervous, at times excitable, but always anxious to cooperate in treatment or observations. There is a very slight exophthalmos, slight widening of the palpebral fissure, eyes bright, no von Graefe's sign. There is no enlargement of the isthmus or remaining lobe. The heart is normal and not rapid. There is no dermatographia but at times there is tremor.

Fig. 7 (Case 12).—Benny L. Roentgenogram of hand.

Treatment and Course.—While in the hospital she was very nervous, slept poorly, and at times vomited. The temperature was normal, pulse 72 to 92, respiration 22 to 26. Until the completion of the second calorimeter observation, April 13, she received no medicine, then thyroid "residue," 1 c.c. hypodermically twice a day until the third test. While in the hospital on a low diet containing about 4 gm. of nitrogen the urinary nitrogen was from 3 to 4 gm. a day.

After leaving the hospital she went to the country, and her appetite improved and she gained strength and did well except for a sudden severe stomatitis which loosened her teeth. In March, 1915, she reported looking thin but almost well. She is able to do light work nursing if she rests between cases. Her physician now attributes many of her symptoms during the past year to hysteria.

CASE 12.—*History.*—Benny L., aged 36 (?), with cretinism, Hebrew, admitted April 8, 1914, discharged May 2, was taken to the Children's Hospital on Ran-

dall's Island sixteen years ago, and during that time has had no visitors, so that his previous history is unknown. He has not changed since his admission, and he is very happy playing with the boys and going to school, where he learns practically nothing. He can write his name, dress and feed himself and he corresponds to a child of about 7 years in the Binet test. In 1906 an attempt was made to transplant sheep's thyroid into the pelvis of the left kidney and later into the abdomen. There were no favorable results. He has had numerous courses of treatment with Parke, Davis & Co. thyroid extract, but on doses as small as from one-half to 1 grain three times a day develops tachycardia, weakness and often faints.

TABLE 6.—CLINICAL DATA IN CASE 12 (BENNY L.)

Date	Temperature		Total Calories	Carb., Gm.	Fat, Gm.	Food N.	Urine, N.	Body Weight	Urine, Volume, c.c.
	Min.	Max.							
4/ 8/14	....	99.2	.....	.....	.....	....	....	.....	.....
9/ 9/14	98.4	98.6	2,381	229.0	120.0	12.5	7.90	.....	1,200
4/10/14	98.4	98.4	1,118	112.0	53.0	6.6	5.95	23.19	965
4/11/14	98.2	98.2	1,227	125.0	56.0	7.7	6.19	.....	920
4/12/14	98.2	98.2	1,396	140.0	65.0	8.4	6.66	.....	1,000
4/13/14	98.2	98.2	1,496	152.0	70.0	8.7	6.89	.....	1,070
4/14/14	98.6	99.4	1,129	162.0	37.0	4.8	4.67	23.34	795
4/15/14	98.2	98.4	1,360	137.0	63.0	8.2	3.53	.....	710
4/16/14	98.4	99.0	1,229	130.0	55.0	7.3	6.36	.....	950
4/17/14	97.6	98.2	1,034	100.0	51.0	5.9	5.83	24.21	935
4/18/14	97.8	98.0	1,128	109.0	55.0	6.8	5.16	.....	800
4/19/14	98.0	98.6	974	94.0	47.0	5.8	7.01	.....	1,195
4/20/14	98.0	98.2	1,196	117.0	57.0	6.9	6.11	.....	1,195
4/21/14	98.0	98.8	643	66.0	23.0	6.1	5.39	24.06	970
4/22/14	98.0	98.6	1,187	119.0	54.0	7.8	6.19	.....	900
4/23/14	98.0	98.2	704	57.0	38.0	4.4	4.82	24.30	770
4/24/14	97.6	98.0	1,050	103.0	50.0	6.5	5.05	.....	815
4/25/14	97.8	98.6	1,187	135.0	50.0	6.4	5.60	.....	1,040
4/26/14	98.6	98.6	963	103.0	44.0	5.0	4.61	.....	820
4/27/14	98.0	98.6	839	128.0	25.0	3.2	4.13	23.61	672
4/28/14	98.0	98.6	728	68.0	36.0	4.5	4.04	.....	700
4/29/14	98.6	100.0	618	59.0	31.0	3.5	5.32	.....	1,350
4/30/14	99.6	100.2	1,061	99.0	53.0	6.3	6.11	.....	1,400
5/ 1/14	100.2	101.0	356	37.0	17.0	...	....	23.06	.....

Physical Examination.—The patient (Figs. 5-7) is short, 110.3 cm. tall (3 feet 7½ inches), stout, with prominent abdomen, short, trick extremities and short pudgy hands, the face is broad, wrinkled, with thick lips, broad nose, baggy eyelids, teeth widely spaced, in poor condition with much gingivitis and pyorrhea. The thyroid is not palpable, heart normal, abdomen shows slight umbilical hernia. Scars over right kidney, skin very dry, harsh, inelastic with fine branny desquamation. There are pads of fat on each side of the neck, and others just anterior to axillae. External genitals resemble those of a boy of 7; there are no male secondary sexual characteristics. Blood pressure is 125 mm., Wasser-

mann test strongly positive; the urine contains much sterile pus, evidently due to large calculi shown by roentgenoscopy to be in the pelves of the kidneys. The temperature was slightly subnormal most of the time, pulse 64-80, respiration 18.

The patient was always in good humor. He had a good sense of fun and was a natural clown, his voice was hoarse and childish but he differed from the normal child in being able to sit quiet for hours at a time. He grew tired rather easily, his appetite was very small, his bowels constipated. April 27, in the afternoon, the administration of thyroid extract was begun, 1 grain three times a day; the temperature rose to the level of 100 F, pulse 100, respiration 18, blood pressure 115. He felt limp, and looked sick so that the drug had to be discontinued. For clinical data see Table 6.

Discussion of Results

THE BASAL METABOLISM IN EXOPHTHALMIC GOITER

The determination of the basal metabolism in exophthalmic goiter is a matter of technical difficulty. The patients are excitable, restless and easily tired. For this reason great care must be used when nose or mouthpieces or face masks are employed, since these may prove uncomfortable toward the end of an experiment or series of experiments. The respiration calorimeter, although perfectly comfortable for a normal person for five hours, often tires a goiter patient after three hours. Fortunately the apparatus is so delicate and accurate that the measurement of the heat production by the method of indirect calorimetry is satisfactory after a preliminary period of three-fourths hour. Experiments one hour long could be employed, but two hour observations are more satisfactory since the method of direct calorimetry is not as accurate as could be wished in the first experimental hour. This will be discussed later.

There is a distinct tendency for the patients to become more restless as the observation progresses, and it will be noted that the metabolism in the fasting experiments is usually higher in the second hour than in the first. There is also a tendency on the part of patients as well as normal controls to show a slightly higher metabolism the first time they are the subject of a real experiment, although they are all trained by a short "dummy experiment" a day or so previously. Goiter patients on some days are distinctly more disquieted than usual, and one gets the impression that on such days the increase in metabolism is due partly to the restlessness and partly to an exacerbation of the disease which causes both restlessness and increased heat production.

It has long been realized that tremor and involuntary activity on the part of goiter patients might be responsible for a considerable portion of the increase in metabolism. Magnus-Levy discussed these factors, and found that the increase in metabolism is almost as marked when the patient is sleeping or under the effect of opium. He found also that the tremor of paralysis agitans increased the oxygen consumption only from 20 to 30 per cent. A careful scrutiny of the

results reported in the present work shows that restlessness, tremor and mental irritability contribute only a small percentage of the increase in most of the cases. The activity of the patients was checked by the delicate work-adder and by careful observation. All of the patients

TABLE 7.—THE INFLUENCE OF SLEEP, RESTLESSNESS, ETC., ON METABOLISM IN HOURLY PERIODS

Subject and Date	Calories per Hour Ind.	Per Cent. above Lowest Figure	Work-Adder Cm.	Behavior of Patient
Case 1 (Max W.)				
Feb. 16	114.6	..	31	A little restless; involuntary tremor at end of period
	124.1	9	14	A little restless
Feb. 20	104.9	..	16	Calm and quiet
	114.2	9	22	Calm; slightly excited by visitor for ten minutes
Feb. 21	120.8	3	26	After dextrose; quiet
	117.2	..	55	After dextrose; very restless
Mar. 4	101.1	..	15	Asleep the whole hour
	106.2	5	58	Awake, pulse rapid last half hour
April 6	92.2	..	25	Quiet; asleep 50 minutes
	99.4	8	55	Very restless
	101.4	10	51+	Very restless; uncomfortable
April 23, 1915	102.8	..	21	Fairly quiet; asleep 30 minutes
	111.0	8	33	Fairly quiet; asleep 5 minutes
Case 2 (Edwin T.)				
Mar. 3	93.6	5	23	Quiet, reading 45 minutes
	89.2	..	30	Asleep 50 minutes in 90-minute period
Mar. 6	80.2	0	6	Reading whole hour; very quiet
	80.2	..	19	Asleep 55 minutes; fairly quiet
Mar. 10	75.4	..	16	Sleeping; slightly restless
	87.3	16	18	Reading 55 minutes
Mar. 22	79.8	..	?	Sleeping; very quiet
	88.0	11	10	Reading 55 minutes; quiet
	94.8	20	30	Asleep
May 11	96.2	..	15	Restless; stretched arms
	115.1	20	34	Restless; vomited shortly after exp.
Case 3 (James McE.)				
Mar. 12	95.8	..	14	Reading quietly 50 minutes
	98.6	3	23	Reading quietly 36 minutes
	101.7	6	30	Not reading; fairly quiet
Mar. 31	88.6	..	10	Reading 60 minutes; quiet
	95.6	8	26	Reading 32 minutes; restless
Case 4 (Dr. G. S. L.)				
April 16	104.8	..	29	Fairly quiet
	109.3	4	58	Slightly restless
Case 6 (Anna K.)				
April 28	102.6	1	36	Restless
	101.5	..	38	Quieter

were as quiet as the normal controls for at least some of the periods of observation. Most of them slept quietly during a considerable portion of some periods. When we compare the sleeping and quiet periods with those in which the patient was awake or excited or restless, we find no constant and striking increase large enough to change our inter-

TABLE 8.—Summary of Results of Respiration Experiments

Subject and Date	Character of Experiment	Average Pulse Rate	Average R. Q.	Per Cent. Divergence of Direct from Indirect Calorimetry	Indirect Calorimetry Average Calories per Hour					Per Cent. Rise above Patient's Own Basal Metabolism	Day of Basal Determination Used for Comparison	Remarks
					Per Kg.	Per Sq. M. Meeh	Per Cent. Rise above Average Normal Basal 34.7 Meeh	Per Sq. M. Linear	Per Cent. Rise above Average Normal Basal 39.7 Linear			
Case 1 (Max W.)												
2/16/14	Basal.....	137	0.76	— 4	1.93	62.0	+79	69.4	+75	....	.....	Slightly restless
2/18/14	¾ to 3¾ hrs. after 100 dextrose	124	0.90	— 1	1.79	57.7	....	64.7	....	+ 2	Av. Feb. 20, 27, Mar. 4	Slightly restless
2/20/14	Basal.....	111	0.77	— 4	1.78	57.0	+64	63.7	+60	....	.....	Quiet
2/21/14	¾ to 2¾ hrs. after 100 dextrose	105	0.94	— 5	1.91	61.5	....	68.8	....	+ 9	Av. Feb. 20, 27, Mar. 4	Restless 1 hour
2/25/14	1½ to 3½ hrs. after 8.9 N as casein	138	0.83	— 3	2.02	64.7	....	71.9	....	+14	Av. Feb. 20, 27, Mar. 4	Quiet
2/27/14	Basal.....	136	0.77	— 2	1.83	58.4	+68	65.4	+65	....	.....	Restless 1 hour
3/ 2/14	1½ to 3½ hrs. after 9.0 N as meat	101	0.82	+ 3	1.87	59.6	....	66.5	....	+ 5	Av. Feb. 20, 27, Mar. 4	Quiet
3/ 4/14	Basal.....	108	0.77	— 2	1.73	54.9	+58	61.0	+54	....	.....	Asleep 1 hour; restless 1 hour
3/23/14	Basal.....	87	0.77	+ 4	1.57	49.7	+43	55.3	+39	....	.....	Quiet; dozed
4/ 6/14	Basal.....	95	0.79	+ 1	1.59	51.0	+47	57.1	+44	....	.....	Restless
4/24/14	Basal.....	120	0.78	+ 1	1.69	54.4	+57	60.9	+53	....	.....	Restless
4/23/15	Basal 1 yr. later.....	99	0.77	— 4	1.46	49.6	+43	57.7	+45	....	.....	Quiet; dozed
Case 2 (Edwin T.)												
3/ 3/15	Basal.....	99	0.78	— 4	1.84	54.9	+58	61.7	+55	....	.....	Slightly restless
3/ 5/15	2 to 6 hrs. after 8.95 N as casein	88	0.86	— 4	1.78	53.4	+54	60.6	+53	+ 7	Av. Mar. 3, 6 and 10	Quiet
3/ 6/15	Basal.....	87	0.81	+ 4	1.60	47.9	+38	53.8	+37	....	.....	Quiet
3/ 8/15	2 to 5 hrs. after 10.19 N as meat	95	0.82	— 6	1.88	56.2	62	63.4	....	+11	Av. Mar. 3, 6 and 10	Quiet
3/10/15	Basal.....	92	0.80	—12	1.65	49.1	+42	55.3	+39	....	.....	Quiet
3/22/15	Basal.....	107	0.79	— 3	1.71	52.8	+52	59.4	+50	....	.....	Quiet
5/11/15	Basal 2 to 3 weeks after ligation	134	0.76	— 4	2.10	63.0	+82	71.2	+79	....	.....	Slightly restless

Case 3 (James McE.) 3/12/15	Basal.....	109	0.78	— 6	2.40	67.2	+94	74.4	+87	....	.....	Quiet
3/31/15	Basal after quinin and ergotin	97	0.82	— 4	2.30	64.0	+84	70.7	+78	....	.....	Fairly quiet
5/14/15	Basal after ligation...	115	0.75	— 8	2.30	68.1	+97	76.1	+92	....	.....	Fairly quiet
Case 4 (Dr. G. S. L.) 4/ 9/14	Basal.....	100	0.77	— 0	1.45	46.9	+42	55.0	+38	....	.....	Quiet
4/16/14	Basal after thyroid "residue"	99	0.76	— 4	1.54	51.5	+50	57.6	+45	....	.....	Slightly restless
Case 5 (Peter N.) 4/14/15	Basal.....	71	0.83	+ 8	1.10	35.5	+ 2	38.8	— 2	....	.....	Very quiet
Case 6 (Anna K.) 4/28/14	Basal after ligation of 2 arteries	121	0.75	— 5	2.30	66.1	+104	....	....	....	.....	Fairly quiet
5/13/14	Basal after ligation of 2 more arteries	100	0.81	— 8	1.90	55.1	+71	....	....	....	.....	Very quiet
Case 7 (Anna R.) 5/10/13	Basal.....	119	0.79	— 8	1.45	43.4	+34					
5/20/13	Basal after ligation...	...	0.76	— 7	1.79	49.9	+55	....	....	....	.....	Quiet
5/28/13	Basal.....	...	0.77	— 5	1.64	49.2	+52					
5/14/14	Basal 1 yr. later.....	97	0.80	— 4	1.48	43.6	+35	....	....	....	.....	Very quiet
Case 8 (Sarah M.) 4/29/14	Basal*.....	92	0.78	— 4	1.41	43.8	+36	....	....	....	.....	Fairly quiet
Case 9 (Marion B.) 2/5/15	Basal.....	127	0.77	— 1	1.40	44.1	36	....	....	....	.....	Restless
Case 10 (Mrs. L.) 4/20/14	Basal.....	85	0.76	— 1	1.30	42.0	30					
Case 11 (Miss B. H.) 4/ 8/14	Basal.....	60	0.83	+ 4	1.21	35.4	+10	40.0	+ 8	....	.....	Quiet
4/13/14	Basal.....	74	0.81	— 1	1.19	35.1	+ 9	39.9	+ 8	....	.....	Very quiet
4/18/14	Basal after thyroid "residue"	94	0.84	— 2	1.15	33.4	+ 3	37.8	+ 2	....	.....	Very quiet
Case 12 (Benny L.) 4/10/14	Basal.....	84	0.92	+ 8	1.21	27.6	—20	33.0	—17	....	.....	Very quiet
4/14/14	1 to 4 hrs. after 100 dextrose	88	1.00	— 1	1.34	31.4	....	37.9	....	+15	April 10	Very quiet
4/21/14	1½ to 5½ hrs. after 3.6 N casein	82	0.93	+ 6	1.23	28.9	....	34.9	....	+13	April 23	Quiet
4/23/14	Basal.....	78	0.87	— 0	1.09	25.6	—26	31.0	—22	....	.....	Quiet
4/27/14	1 to 4 hrs. after 70 dextrose	79	0.95	+ 0	1.19	27.7	....	33.3	....	+ 7	April 23	Very quiet
5/ 1/14	After thyroid extract	95	0.79	— 6	1.44	33.2	— 4	39.8	+ 0	+28	April 23	Very quiet

* After very small breakfast.

pretation of the results. All of the experiments which show significant differences between the various periods either in the heat-production, work-adder reading or activity of the patient as noted in the protocol have been grouped in Table 7. Some of the patients were allowed to read while in the calorimeter, since it was found that they were quieter if their minds were pleasantly occupied. It will be seen that the metabolism was about the same during the reading periods as during the periods of slightly restless slumber characteristic of this disease. Edwin T. (Case 2) was the only subject who showed an increase of more than 10 per cent. on account of movement. On March 10, reading seemed to increase the calories 16 per cent. March 22, the reading metabolism is about half way between that of two widely varying sleeping periods, and May 11 it rose on account of nausea in the last period.

The results of all the respiration experiments are summarized in Table 8, and the average metabolism on the days of the basal determinations compared to the normal averages discussed in the thirteenth paper of this series. It will be noted that in all the thin patients the rise above the normal is less marked when the measurements are made according to the linear formula than if Meeh's formula for the determination of the surface area be employed. If we confine our attention for the time being to the basal metabolism during the first week that the patients were in the hospital, we can compare the cases here reported with those already described in the literature. In all there is a total of forty-five patients whose respiratory metabolism has been studied, fasting and as quiet as the circumstances would permit. It has seemed best to group these in Table 1 arranging them according to the calories per square meters of surface area as calculated from Meeh's formula. The calculation of the calories has been made from the tables of Magnus-Levy,[26] using the oxygen consumption and respiratory quotient, assuming that protein furnished about 15 per cent. of the calories. This gives a more accurate basis of comparison than the mere statement of cubic centimeters of oxygen or carbon dioxid per kilogram and minute. Still better comparisons might be made if we could use the linear formula or its modification; but this is impossible because many of the authors do not give the heights of the patients. We are similarly handicapped in the tabulation of other symptoms, since many of the clinical reports are very brief. Still it is possible to make a fairly complete chart which allows us to see which symptoms accompany the cases with high metabolism. The plus marks are necessarily my own interpretation of the author's statements.

26. Magnus-Levy: Von Noorden's Handbuch der Pathologie des Stoffwechsels, Ed. 2, 1906, i, 207.

At the head of the list comes Hirschlaff's patient Louise B. shortly before her death with the most extreme symptoms of hyperthyroidism. There are eight other subjects whose metabolism is greater than 56.5 calories per square meter per hour, a figure 75 per cent. above the average for women. Of these all are classified as severe or very severe, except one designated "ziemlich schwer." All show a very rapid pulse, thyroid enlargement, exophthalmos, mental irritability, warmth of skin, tremor and emaciation. Eleven more patients are above the figure which represents a 50 per cent. increase in metabolism. Of these, one is classified as very severe, five are classified as severe, and five as moderately severe. With most of these the pulse rate averages over 100 and there are signs of cardiac enlargement. Goiter, mental irritability, tremor and warmth of skin are present in all. Exophthalmos is absent in one, and the emaciation is slight as a rule.

The figure 38.2 represents the upper normal limit for men, and 35.5 that for women. Between these marks and that indicating a 50 per cent. increase there are sixteen patients, six severe, one moderately severe, four mild, and the others atypical, "forme fruste" or simple goiter. In them the tachycardia is not so marked, and exophthalmos and emaciation are inconstant. Goiter, mental irritability, tremor and warmth of skin are present. There are eight subjects within normal limits. Among these are four mild cases of exophthalmic goiter, two of simple goiter, and two cases in which operation had been performed, one of these being atypical from the start. One patient is below the normal limit. Magnus-Levy in one article classifies her case as half way between Kropf and "forme fruste," and in another article as simple goiter and refers to her as hysterical.

Age is a factor which changes our interpretation of some of the results. The boy M. P., aged 11½ years, with a small struma, is really a little below the average level for his age. Frau B. and Frl. U., aged 52 and 55, respectively, are at an age when the normal metabolism is from 5 to 10 per cent. lower than the average figure for younger women.

The patients whose metabolism is within or below the normal limits show but slight tachycardia, slight if any goiter or exophthalmos and no unusual warmth of skin. Two show mental irritability and tremor.

We must not forget that some of the symptoms of hyperthyroidism are due either wholly or in part to the increased metabolism. The sensation of unusual warmth, the hot, flushed skin and the sweating are caused by the fact that each square centimeter of skin must radiate more heat than in a normal person. These phenomena are found with an increased metabolism from almost any cause, although it is quite possible that in exophthalmic goiter they may be more marked for the same degree of increase. In like manner the loss of

weight is due to the fact that the increased heat production is not balanced by an increased caloric intake and absorption. The appetite of the goiter patient would keep the weight stationary or even cause an increase were the metabolism normal. For some reason the appetite and absorptive powers in hyperthyroidism are not quite sufficient to maintain weight, although laboring men with a much higher caloric requirement per day remain in nutritive equilibrium. This may be accounted for in part by the increased nitrogen metabolism, which is usually ascribed to a toxic destruction of protein. Part of the increase in pulse rate is also due directly to the increased metabolism which necessitates a greater blood flow. This, however, would not account for all of the increase, since muscular work, raising the metabolism from 50 to 100 per cent., seems to increase the pulse rate by only 10 to 30 beats per minute. Still we must remember in discussing the tachycardia and cardiac enlargement that the continued stimulation of metabolism in hyperthyroidism is very different from the stimulation due to muscular exercise which lasts for only a fraction of a day. If it were possible to stimulate the metabolism of a normal man twenty-four hours a day over the period of a year or more, we might perhaps reproduce the cardiac symptoms of hyperthyroidism as well as the warmth of skin and loss of weight.

The more we study the table, the more apparent it becomes that the increase in metabolism is proportional to the severity of the disease. The only exceptions in the group are found in doubtful or atypical cases, or those that have undergone operative treatment. Very severe cases show a metabolism 75 per cent. or more above the average, severe cases 50 per cent. or more, moderately severe and mild cases show an increase of less than 50 per cent., while a few mild and several atypical or cases in which operation has been performed are within normal limits. The degree of tachycardia, goiter, exophthalmos and mental irritability are roughly proportional to the increased heat production. Unfortunately we have not enough data to compare the level of metabolism with the degree of mononucleosis, the sugar tolerance, the drop in blood pressure from large vessels to the periphery, the eye sympoms and many others that are considered of prime importance by various authors.

THE RESPIRATORY QUOTIENTS

In the patients with high basal metabolism, the respiratory quotients are necessarily low after a fast of seventeen hours or more. Most of them are close to the figure of 0.77, which indicates that about 17 per cent. of the calories are derived from the combustion of carbohydrates. With normal men the quotient under similar conditions varies rather widely, but averages 0.82, showing that about 32 per

cent. of the calories are derived from carbohydrates. Therefore goiter patients who are kept in bed in the hospital evidently have less available glycogen after a fast of seventeen hours than normal men who have been up and about during the evening and morning before the experiment. This may be due either to the fact that the thyroid patients have insufficient appetites and start the evening with a smaller store of glycogen, or else that they use up the starch of the food and the stored glycogen more rapidly than the controls. The respiratory quotients here reported give no indication of any qualitative change in the metabolism. The lowest average basal quotient is 0.75, and this is exactly what might be expected in patients with exceedingly high metabolism. In Case 1 (Max W.) the quotients rose to 0.94 on one day and 0.98 on another after the ingestion of 100 gm. of dextrose. The latter figure shows that 89 per cent. of the calories was being derived from carbohydrate from two to three hours after the sugar was taken. The urine passed immediately afterward contained 3.9 gm. glucose, but it is evident that this glycosuria was not due to any impairment of the power to metabolize carbohydrates. The explanation must be sought in an abnormality of mobilization. Cramer and Krause[27] show that after the ingestion of thyroid substance the liver no longer retains glycogen as before.

DIRECT AND INDIRECT CALORIMETRY

One contribution to the science of metabolism which can be made only by a respiration calorimeter is a comparison of the direct and indirect calorimetry. The former method depends on the direct measurement of the heat of radiation, conduction and vaporization. The latter depends on the measurement of carbon dioxid and oxygen and the calculation of the foodstuffs metabolized each hour. It has been shown in the fourth paper of this series that the two methods agree within 0.17 per cent. when normal controls are studied in periods lasting three hours or more. In the seventh paper it was shown that the method of direct calorimetry gave a total which was 2.2 per cent. less than the indirect total in typhoid fever, and that the average divergence of the two methods in the individual experiments was 5 per cent. In the cases of hyperthyroidism here reported, the total number of calories measured is 8,052 according to the indirect method, and 7,823 according to the direct method, which is 2.9 per cent. lower. The individual experiments show that the average divergence is ± 4.1 per cent. With the cretin Benny L., the direct calorimetry was 1.5 per cent. higher than the indirect. When one considers the technical difficulty of making short respiration chamber experiments on sick patients, the close agreement of two absolutely independent methods is very

27. Cramer and Krause: Proc. Roy. Soc. London, 1913, B., lxxxvi, 550.

striking. The fact that the direct calorimetry is slightly lower can be ascribed to technical errors in the direct method, which have been discussed in previous papers. It may be due to an unmeasured loss of heat to the bed and bed clothing or to an error in the measurement of the average temperature change of the body. The effect of these errors is minimized in long experiments such as are used in normal controls, but it is necessary to use short experiments with patients. The slight disagreement does not point to any disturbance of the intermediary metabolism. The law of the conservation of energy holds good in exophthalmic goiter.

WATER ELIMINATION THROUGH SKIN AND LUNGS

In the thirteenth paper of this series it was shown that under the atmospheric conditions prevailing in the calorimeter experiments, normal men eliminated on an average 28.4 gm. of water an hour through skin and lungs. Of the total calories produced, the average percentage dissipated through vaporization of water was 23.9. Few of the experiments showed a deviation of more than 10 per cent. from this mean.

In hyperthyroidism the heat production and water vaporization are both increased, and in Table 9 we see that they are increased in almost equal proportion. The average water elimination of the severe and moderately severe cases is 39.9 gm. per hour. On an average, 25.7 per cent. of the heat is dissipated through vaporization, or almost the same as in the normal controls. The percentage rise in water elimination through skin and lungs would seem to be a valuable guide as to the extent of the rise in total metabolism.

SPECIFIC DYNAMIC ACTION OF PROTEIN AND DEXTROSE

Owing to the variations in the basal metabolism of goiter patients, the results of this part of the investigation are not as clear cut as might be desired. In Table 10 the figures obtained on Max W. (Case 1), Edwin T. (Case 2) and the little cretin, Benny L. (Case 12) are given. It is difficult to select the proper basis of comparison for these three groups. Should we use the same actual amount of food, the same amount per kilogram, per square meter of body surface or per calories metabolized per hour? Should we compare the results in terms of percentage increase in metabolism or in the terms of extra calories? In the two exophthalmic goiter cases the protein meals produced almost exactly the same percentage rise as in the normal controls. With Max W. (Case 1) the metabolism was higher after the meal containing the protein in the form of casein and egg albumin than after the same amount of protein as found in beef. Edwin T. (Case 2) showed just the opposite, but the meat contained more

TABLE 9.—Water Elimination of Goiter Patients: Basal Experiments

Subject and Date	Average Water, Gm. per Hour	Average Calories per Hour, Dir. Calor.	Per Cent. Calories Lost through Vaporization
Case 1 (Max W.)			
Feb. 16, 1914	45.33	114.40	29.16
Feb. 20, 1914	40.95	105.52	22.67
Feb. 27, 1914	41.48	109.34	22.16
Mar. 4, 1914	42.14	102.06	24.10
Mar. 23, 1914	35.76	96.41	21.66
Apr. 6, 1914	35.37	99.16	20.83
Apr. 24, 1914	37.22	107.22	20.28
Apr. 23, 1914	48.53	102.42	27.68
Average	40.85	.....	23.57
Case 2 (Edwin T.)			
Mar. 3, 1915	43.60	86.98	29.3
Mar. 6, 1915	35.30	83.81	24.6
Mar. 10, 1915	30.94	71.57	25.3
Mar. 22, 1915	37.76	84.82	26.0
May 11, 1915	54.06	101.30	31.2
Average	40.33	.....	27.3
Case 3 (J. McE.)			
Mar. 12, 1915	43.32	92.48	27.4
Mar. 31, 1915	31.59	88.55	20.17
May 14, 1915	57.31	95.75	34.9
Average	44.07	.....	27.49
Case 4 (Dr. G. S. L.)			
Apr. 9, 1914	30.24	103.73	17.03
Apr. 16, 1914	36.83	102.89	20.91
Average	33.54	.....	18.97
Case 5 (Peter N.), Apr. 14, 1915	28.31	74.80	12.37
Case 6 (Anna K.)			
Apr. 28, 1914	51.51	97.05	31.00
May 13, 1914	37.25	77.79	27.97
Average	44.38	.....	29.48
Case 7 (Anna R.)			
May 10, 1913	31.49	62.11	29.61
May 20, 1913	43.29	71.28	18.02
May 28, 1913	41.83	67.50	36.19
May 14, 1914	29.55	68.04	25.36
Average	36.45	.....	27.29
Case 8 (Sarah M.), Apr. 29, 1914	37.48	75.37	16.5
Case 9 (Marion B.), Feb. 5, 1915	35.77	80.16	26.06
Case 10 (Mrs. L.), Apr. 20, 1914	40.51	80.86	29.26
Case 11 (Bessie H.)			
Apr. 8, 1914	26.44	59.41	25.99
Apr. 13, 1914	21.06	56.81	21.65
Apr. 18, 1914	22.71	52.02	25.49
Case 12 (Benny L.)			
Apr. 10, 1914	10.48	29.61	20.67
Apr. 23, 1914	10.90	26.19	24.31
May 1, 1914	11.78	31.00	22.71
Averages Severe Cases—			
Case 1 (Max W.)	40.85	.....	23.57
Case 3 (James McE.)	44.07	.....	27.49
Case 4 (Dr. G. S. L.)	33.54	.....	18.97
Case 6 (Anna K.)	44.38	.....	29.48
Moderately Severe—			
Case 2 (Edwin T.)	40.33	.....	27.3
Case 7 (Anna R.)	36.45	.....	27.29
Average of six cases	39.94	.....	25.7

nitrogen than the casein meal. Max W. (Case 1) showed a somewhat smaller percentage rise in metabolism than the normal controls after 100 gm. dextrose. The findings on the small cretin Benny L. (Case 12) are difficult to interpret on account of his low calorific output, but he seems to show results not far from the normal.

It appears that the specific dynamic action of protein and dextrose is approximately the same as in health. There is certainly no marked increase such as some writers[28] have surmised, and there is no marked decrease such as is found in typhoid fever. There is little difference between protein in the form of meat and in the form of casein and egg albumin.

TABLE 10.—SPECIFIC DYNAMIC ACTION OF FOODS IN HYPERTHYROIDISM

Subjects	Food	No. of Experiments	Average Gm. N or Dext. in Food	Average Gm. N or Dext. per Kg. of Body Weight	Average Gm. N or Dext. per Cal. per Hour	Average Per Cent. Rise in Metabolism above Subject's Basal
Two normal men....	Protein meal.....	2	10.1	0.149	0.144	9.7
Case 1 (Max W.).....	Casein and meat...	2	8.9	0.146	0.082	9.5
Case 2 (Edw. T.).....	Casein and meat...	2	9.6	0.19	0.12	9.0
Case 12 (Benny L.)†	Protein meal.....	1	3.6	0.15	0.135	13.0
Three normal men...	Glucose*.....	3	100.0	1.37	1.36	9.7
Case 1 (Max W.).....	.....	2	100.0	1.64	0.92	5.5
Case 12 (Benny L.)†	.....	1	100.0	4.20	3.7	15.0
Case 12 (Benny L.)†	.....	1	70.0	2.94	2.6	7.0

* Subjects were given 115 gm. commercial glucose, which are equivalent to 100 gm. pure glucose.
† Cretin.

THE EFFECTS OF TREATMENT

Max W. (Case 1), after a stay of four months in various hospitals, was in the Bellevue metabolism ward for five days before the first determination of his basal metabolism. He received no treatment except good food, mental quiet and rest in bed with permission to get up and walk about for a few minutes at a time. In seventeen days the metabolism fell 12 per cent. After this he received the Beebe serum treatment with 1 grain of potassium iodid twice a day. In the next nineteen days the metabolism fell about 9.5 per cent., and the general condition improved correspondingly. Then while the treatment was being continued, the heat production rose almost to its level before the serum was begun. After one whole year of serum injections, during which time he was at home and at work, he returned

28. Von Noorden: New Aspects of Diabetes, New York, E. B. Treat & Co., 1912, p. 20.

to the hospital with a metabolism 5 per cent. lower than the day before treatment was begun. His mental irritability had lessened, his strength had increased, but his heart had developed fibrillation.

Edwin T. (Case 2) first took to bed when he was admitted to the metabolism ward. After a week of absolute rest in bed the first basal test was made. Three days later the metabolism was 13 per cent., and a week later 10 per cent. lower without medication. Subsequently it rose to within 4 per cent. of its original level under the influence of homesickness and some personal worries. He was given serum, but circumstances made it necessary to operate before a calorimeter test could be made. April 21, 23 and 29, all the thyroid arteries were ligated under painless local anesthesia. Twelve days after the last operation, his metabolism was 20 per cent. higher than before. He looked worse, but said he felt stronger.

James McE. (Case 3) was in the hospital twelve days before his first basal test. Immediately after this he was put on the Forcheimer ergotin and quinin hydrobromate treatment. In nineteen days the metabolism fell 5 per cent. April 10, one artery was tied; May 2, an operation was interrupted by collapse on the part of the patient. Twelve days after this the metabolism was 6 per cent. above the lowest point previously measured.

Anna K. (Case 6) was admitted to Bellevue April 27 and placed in the calorimeter the next day. On the 29th two thyroid arteries were ligated. Two weeks later the metabolism had fallen 17 per cent., which is about the decrease usually found during the first two weeks a patient is at rest in a hospital.

The basal metabolism of Anna R. (Case 7) was measured the third day she was in the hospital, May 12. On that afternoon, and May 16, the four thyroid arteries were tied. Four days later the metabolism was 15 per cent. above its original point, and eight days later it had changed but little. One year later it was at its original level.

The thyroid extract called thyroid "residue" had but slight effect on the metabolism. With Dr. G. S. L. (Case 4), a severe case, the metabolism rose slightly, with Miss B. H. (Case 11) it fell.

OBSERVATIONS ON A CRETIN

The basal metabolism of Benny L. (Case 12) averaged about 20 per cent. below the normal for adults according to his measured surface area. Children of his size average about 40 per cent. above the adult figure. This increase seems to be due chiefly to the process of growth which is lacking in the 36-year-old cretin. Although Benny's heat production is about half as great as that of a normal child of his size, we cannot consider him more than 20 per cent. below the normal for adults. The specific dynamic action of protein and carbohydrate, as we have said before, appears to be normal; but it is hard

TABLE 11.—CLINICAL—

Subject, Date, Weight, Surface Area, Linear Formula	Period	End of Period	Carbon Dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calorimetry, Cal.	Heat Eliminated, Cal.
Case 1 (Max W.).. 2/16/14	Prelim.	11:10	.....	.....	.....	.....	.....	.....	.....
61.76 Kg. 1.72 Sq. M.	1	12:10	36.19	34.79	0.757	44.62	0.515	114.64	108.09
	2	1:10	39.28	37.60	0.760	46.04	0.515	124.08	116.54
								238.72	
Max W..... 2/18/14	Prelim.	11:46	.....	.....	.....	.....	.....	.....	.....
62.02 Kg. 1.72 Sq. M.	1	12:46	41.81	33.14	0.917	42.53	0.658	113.45	111.71
	2	1:46	21.12	31.72	0.943	42.43	0.658	109.23	118.12
	3	2:46	38.26	33.13	0.840	42.25	0.658	111.22	114.40
								333.90	
Max W..... 2/20/14	Prelim.	11:36	.....	.....	.....	.....	.....	.....	.....
61.60 Kg. 1.73 Sq. M.	1	12:36	32.77	31.90	0.747	40.14	0.466	104.85	102.72
	2	1:36	37.19	34.38	0.787	41.75	0.466	114.24	105.67
								219.09	
Max W..... 2/21/14	Prelim.	10:45	.....	.....	.....	.....	.....	.....	.....
62.26 Kg. 1.73 Sq. M.	1	11:45	43.56	35.33	0.897	40.98	0.456	120.82	112.67
	2	12:45	45.07	33.52	0.978	41.85	0.456	117.20	116.41
								238.02	
Max W..... 2/25/14	Prelim.	11:32	.....	.....	.....	.....	.....	.....	.....
61.13 Kg. 1.71 Sq. M.	1	12:32	41.19	36.32	0.825	39.35	0.817	121.27	114.35
	2	1:32	43.37	37.60	0.839	41.29	0.817	126.06	123.58
								247.33	
Max W..... 2/27/14	Prelim.	11:18	.....	.....	.....	.....	.....	.....	.....
60.86 Kg. 1.70 Sq. M.	1	12:18	35.58	33.13	0.781	41.05	0.650	109.55	112.07
	2	1:18	35.94	34.25	0.763	41.90	0.650	112.78	112.12
								222.33	
Max W..... 3/2/14	Prelim.	11:50	.....	.....	.....	.....	.....	.....	.....
60.47 Kg. 1.70 Sq. M.	1	12:50	37.25	35.42	0.765	45.44	0.663	116.70	112.23
	2	1:50	38.75	32.28	0.873	46.48	0.663	109.25	112.08
								225.95	
Max W..... 3/4/14	Prelim.	10:52	.....	.....	.....	.....	.....	.....	.....
60.02 Kg. 1.70 Sq. M.	1	11:52	31.79	30.79	0.751	39.10	0.550	101.10	105.05
	2	12:52	34.55	32.04	0.784	45.17	0.550	106.19	111.50
								207.29	
Max W..... 3/23/14	Prelim.	11:06	.....	.....	.....	.....	.....	.....	.....
59.20 Kg. 1.68 Sq. M.	1	12:06	28.32	27.13	0.759	34.87	0.319	89.59	98.12
	2	1:06	29.31	27.63	0.771	34.44	0.319	91.46	97.22
	3	2:06	31.76	29.39	0.786	37.98	0.319	97.79	96.40
								278.84	

—Calorimetry in Goiter

Direct Calorimetry (Rectal Temp.), Cal.	Rectal Temp., C.	Average Pulse	Work-Adder, Cm.	Non-protein R. Q.	Per Cent. Calories from			Calories per Hour		Remarks
					Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M. (Meeh)	
.....	37.41	...	....	.....	..	..	..	....	.....	Basal
103.52	37.33	131	31.4	0.750	12	75	13	1.85	59.58	Restless
125.28	37.51	142	14.6	0.754	11	75	14	2.01	64.49	Restless
228.80										
.....	37.04	...	....	.....	..	..	..	....	.....	Dextrose in lemonade, 100 gm. at 10:55-11:00
103.40	36.89	127	20.0	0.940	15	17	68	1.83	58.78	
110.83	36.87	123	20.8	0.972	16	8	76	1.76	56.60	
115.92	36.84	123	31.2	0.847	16	44	40	1.80	57.63	
330.15										
.....	36.96	...	....	.....	..	..	..	....	.....	Basal
87.44	36.67	108	16.0	0.739	12	78	10	1.70	54.58	Quiet
123.60	37.03	114	21.5	0.784	11	65	24	1.85	59.47	Quiet
211.04										
.....	36.76	...	....	.....	..	..	..	....	.....	Dextrose in lemonade, 100 gm. at 9:55-9:57
108.59	36.69	103	25.7	0.908	10	28	62	1.94	62.47	Quiet
117.48	36.72	107	60.0	0.997	10	1	89	1.88	60.60	Restless
226.07										
.....	37.44	...	....	.....	..	..	..	....	.....	Protein meal; N = 8.9 gm. at 10 a. m.
111.31	37.39	139	19.6	0.829	18	48	34	1.98	63.46	Quieter
129.64	37.52	137	33.0	0.846	17	44	39	2.06	65.97	Quieter
240.95										
.....	37.12	...	....	.....	..	..	..	....	.....	Basal
105.53	37.00	137	47.6	0.776	16	64	20	1.80	57.51	Restless
113.14	37.01	135	56.0	0.755	15	71	14	1.85	59.20	Restless
218.67										
.....	37.08	...	....	.....	..	..	..	....	.....	Protein meal; N = 9.0 gm. at 10:04 a. m.
112.64	37.10	98	35.6	0.757	15	70	15	1.93	61.52	Asleep 15 min.
119.50	37.26	103	41.2	0.887	16	32	52	1.81	57.59	Quiet
282.14										
.....	37.12	...	....	.....	..	..	..	....	.....	Basal
93.60	36.90	99	15.3	0.741	14	76	10	1.68	53.55	Asleep all the hour
110 52	36.89	116	58.0	0.781	14	64	22	1.77	56.24	Awake
204.12										
.....	36.94	...	....	.....	..	..	..	....	.....	Basal
92.25	36.83	88	15.2	0.754	9	76	15	1.51	47.91	Asleep 45 min.
95.27	36.80	87	24.1	0.768	9	72	19	1.55	48.91	Asleep 24 min.
101.70	36.92	85	25.4	0.784	9	67	24	1.65	52.29	Fairly quiet
289.22										

TABLE 11.—

Subject, Date, Weight, Surface Area, Linear Formula	Period	End of Period	Carbon Dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calorimetry, Cal.	Heat Eliminated, Cal.
Max W.	Prelim.	11:15	.....	.....	.....	.....	.....	.....	.....
4/6/14									
61.32 Kg.	1	12:15	30.11	27.75	0.789	30.36	0.402	92.23	91.14
1.71 Sq. M.	2	1:15	32.13	29.98	0.779	35.74	0.402	99.44	99.65
	3	2:15	33.39	30.43	0.798	40.02	0.402	101.44	102.02
								293.11	
Max W.	Prelim.	11:13	.....	.....	.....	.....	.....	.....	.....
4/24/14									
63.35 Kg.	1	12:13	33.83	31.77	0.774	34.51	0.554	105.02	97.07
1.75 Sq. M.	2	1:13	35.04	32.60	0.782	39.93	0.554	108.00	106.82
								213.02	
Max W.	Prelim.	11:12	.....	.....	.....	.....	.....	.....	.....
4/23/15									
73.27 Kg.	1	12:12	32.82	31.30	0.763	45.09	0.669	102.84	103.95
1.854 Sq. M.	2	1:12	35.71	33.68	0.771	51.97	0.669	110.98	113.02
								213.82	
Case 2 (Edw. T.).	Prelim.	11:06	.....	.....	.....	.....	.....	.....	.....
3/3/15									
49.75 Kg.	1	12:06	29.78	.....	.....	40.78	0.506	.....	87.99
1.475 Sq. M.	2	1:06	30.48	28.26	0.785	43.55	0.506	93.59	94.69
	3	2:36	42.85	40.61	0.767	68.26	0.506	133.87	134.88
								227.46	
Edw. T.	Prelim.	11:00	.....	.....	.....	.....	.....	.....	.....
3/5/15									
50.39 Kg.	1	12:00	31.68	25.98	0.887	47.66	0.913	87.46	92.27
1.483 Sq. M.	2	1:00	33.04	27.48	0.874	46.16	0.913	92.31	96.99
	3	2:00	31.61	26.99	0.852	45.40	0.849	90.32	93.20
	4	3:00	29.97	26.74	0.815	45.94	0.849	88.62	95.06
								358.71	
Edw. T.	Prelim.	10.44	.....	.....	.....	.....	.....	.....	.....
3/6/15									
50.00 Kg.	1	11.44	27.56	23.99	0.836	36.38	0.583	80.18	84.34
1.478 Sq. M.	2	12:43	25.72	23.88	0.783	33.64	0.573	78.84	77.52
								159.02	
Edw. T.	Prelim.	11:02	.....	.....	.....	.....	.....	.....	.....
3/8/14									
49.69 Kg.	1	12:02	30.74	27.57	0.811	45.28	0.966	91.02	95.40
1.474 Sq. M.	2	1:02	32.81	29.73	0.803	43.97	1.006	98.11	98.78
	3	2:02	31.85	27.44	0.844	40.31	1.006	91.32	91.73
								280.45	
Edw. T.	Prelim.	10:56	.....	.....	.....	.....	.....	.....	.....
3/10/15									
49.32 Kg.	1	11:56	24.59	22.82	0.784	29.58	0.541	75.36	79.29
1.47 Sq. M.	2	12:56	29.05	26.22	0.806	32.30	0.541	87.29	88.84
								162.65	

—(*Continued*)

Direct Calorimetry (Rectal Temp.), Cal.	Rectal Temp., C.	Average Pulse	Work-Adder, Cm.	Non-protein R. Q.	Per Cent. Calories from			Calories per Hour		Remarks
					Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M. (Meeh)	
.....	36.68	...	....	.....	..	..	..	....	.....	Basal
86.09	36.59	93	25.4	0.787	12	64	24	1.51	48.16	Asleep 50 min.
103.27	36.67	90	55.0	0.776	11	68	21	1.62	51.93	Very restless
108.13	36.80	102	67.0	0.797	10	62	28	1.65	52.97	Very restless
297.47										
.....	36.68	...	....	.....	..	..	..	....	.....	Basal
100.23	36.75	125	40.5	0.769	14	68	18	1.66	53.66	
114.21	36.90	115	57.0	0.778	14	65	21	1.71	55.19	
214.44										
.....	37.04	...	....	.....	..	..	..	....	.....	Basal
93.62	36.87	101	21.0	0.753	17	70	13	1.40	47.70	Asleep 30 min.; quiet
111.22	36.85	97	33.0	0.764	16	69	15	1.52	51.48	Asleep 5 min.; quiet
204.84										
.....	37.72	...	....	.....	..	..	..	....	.....	Basal
85.15	37.66	99	35.0	.....	..	..	..	....	.....	Restless
88.14	37.51	98	23.0	0.781	14	64	22	1.88	56.21	Reading 45 min.
131.13	37.45	99	46.0	0.763	10	73	17	1.79	53.61	Asleep 50 min.
219.27										
.....	37.93	...	....	.....	..	..	..	....	.....	Protein meal*
77.14	37.58	90	6.0	0.922	28	20	52	1.74	52.06	Asleep 60 min.
80.52	37.20	87	14.0	0.902	26	25	49	1.83	54.95	Reading 52 min.
94.40	37.29	86	19.0	0.869	25	33	42	1.79	53.76	Quiet
93.40	37.32	88	15.0	0.819	25	46	29	1.76	52.75	Reading 30 min.; quiet 30 min.
345.46										
.....	37.25	...	....	.....	..	..	..	....	.....	Basal
81.35	37.19	85	6.0	0.844	19	44	37	1.60	47.93	Reading 60 min.; very quiet
84.89	37.38	88	18.0	0.778	19	60	21	1.58	47.11	Asleep 55 min.; fairly quiet
166.24										
.....	37.93	...	....	.....	..	..	..	....	.....	Meat; 10.19 gm. N at 8:55-9:04
88.69	37.78	93	19.0	0.814	28	46	26	1.83	54.70	Asleep 60 min.
85.37	37.47	95	5.0	0.802	26	50	24	1.97	58.96	Reading 60 min.
88.96	37.46	97	42.0	0.862	29	34	37	1.84	54.88	Awake, restless
263.02										
.....	37.87	...	....	.....	..	..	..	....	.....	Basal
69.79	37.65	89	16.0	0.789	16	60	24	1.53	45.51	Asleep, slightly restless
73.34	37.28	95	18.0	0.777	14	64	22	1.77	52.71	Reading 55 min.
143.13										

* Protein = 56.0 gm. (Nitro. = 8.95 gm.); Fat = 8.5 gm.; Carbh. = 47.1 gm.; 8:55 to 9:32 a. m.

TABLE 11.—

Subject, Date, Weight, Surface Area, Linear Formula	Period	End of Period	Carbon Dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calorimetry, Cal.	Heat Eliminated, Cal.
Edw. T.	Prelim.	11:07	.....	.....	.....	.....	.....	.....	.....
3/22/15									
49.17 Kg.	1	12:07	25.80	23.71	0.791	35.67	0.348	78.86	82.01
1.468 Sq. M.	2	1:07	29.12	26.38	0.803	35.17	0.348	88.01	87.01
	3	2:07	30.48	28.59	0.775	42.45	0.348	94.78	92.51
								261.65	
Edw. T.	Prelim.	11:33	.....	.....	.....	.....	.....	.....	.....
5/11/15									
50.37 Kg.	1	12:33	31.02	28.27	0.798	48.24	0.452	96.16	95.55
1.483 Sq. M.	2	1:33	33.75	34.47	0.712	59.87	0.452	115.11	107.61
								211.27	
Edw. T.	Prelim.	11:35	.....	.....	.....	.....	.....	.....	.....
11/1/15									
52.63 Kg.	1	12:35	31.77	29.39	0.786	53.39	0.358	97.73	95.07
1.508 Sq. M.	2	1:35	33.17	30.60	0.789	51.38	0.358	101.89	95.48
Case 3 (Jas. McE.)	Prelim.	11:16	.....	.....	.....	.....	.....	.....	.....
3/12/15									
41.16 Kg.	1	12:16	31.34	28.78	0.792	40.88	0.398	95.77	91.74
1.319 Sq. M.	2	1:16	30.92	29.96	0.751	45.31	0.398	98.57	96.66
	3	1:46	16.67	15.27	0.794	22.09	0.398	50.84	48.20
								245.18	
James McE.	Prelim.	11:00	.....	.....	.....	.....	.....	.....	.....
3/31/15									
39.98 Kg	1	12:00	30.55	26.24	0.846	29.79	0.316	88.61	80.65
1.303 Sq. M.	2	1:00	31.49	28.62	0.800	33.38	0.316	95.60	86.04
								184.21	
James McE.	Prelim.	11:12	.....	.....	.....	.....	.....	.....	.....
5/14/15									
45.29 Kg.	1	12:12	32.14	31.91	0.732	55.70	0.301	104.91	96.97
1.371 Sq. M.	2	1:12	33.34	31.25	0.776	58.92	0.301	103.73	101.66
								208.64	
Case 4 (Dr.G.S.L.)	Prelim.	11:08	.....	.....	.....	.....	.....	.....	.....
4/9/14									
71.78 Kg.	1	12:08	33.19	31.92	0.756	30.25	0.393	105.33	105.66
1.89 Sq. M.	2	1:08	33.30	30.88	0.784	30.23	0.393	102.62	102.22
								207.95	
Dr. G. S. L.	Prelim.	11:20	.....	.....	.....	.....	.....	.....	.....
4/16/14									
69.40 Kg.	1	12:20	32.58	31.94	0.742	35.50	0.460	104.83	106.58
1.86 Sq. M.	2	1:20	34.95	33.05	0.769	38.16	0.460	109.29	102.25
								214.12	
Case 5 (Peter N.)..	Prelim.	11:23	.....	.....	.....	.....	.....	.....	.....
4/14/15									
63.44 Kg.	1	12:23	22.85	20.32	0.818	28.42	0.375	67.89	77.85
1.795 Sq. M.	2	1:23	24.71	21.14	0.850	28.19	0.375	71.28	76.70
								139.17	

—(*Continued*)

Direct Calorimetry (Rectal Temp.), Cal.	Rectal Temp., C.	Average Pulse	Work-Adder, Cm.	Non-protein R. Q.	Per Cent. Calories from			Calories per Hour		Remarks
					Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M. (Meeh)	
.....	37.11	...	....	.....	..	..	..	....	.....	Basal
76.63	36.99	100	....	0.790	12	63	25	1.60	47.71	Sleeping, very quiet
80.53	36.83	108	10.0	0.803	10	61	29	1.79	54.48	Reading, quiet
97.31	36.97	112	30.0	0.772	10	70	20	1.72	57.34	Sleeping
254.47										
.....	37.23	...	....	.....	..	..	..	....	.....	Basal after ligation
95.83	37.25	131	15.0	0.772	12	69	19	1.91	57.31	Restless
106.76	37.24	137	34.0	0.683	10	90	0	2.29	68.60	Restless
202.59										
.....	37.16	...	....	.....	..	..	..	....	.....	Basal 6 mos. after ligation
90.04	37.06	96	18.0	0.786	10	66	24	1.86	56.5	Quiet; sleeping
100.06	37.18	107	14.0	0.789	9	65	26	1.94	58.9	Quiet; awake
.....	38.26	...	....	.....	..	..	..	....	.....	Basal
87.48	38.15	105	14.0	0.790	11	64	25	2.33	65.24	Quiet; reading
92.07	38.03	110	23.0	0.744	11	79	10	2.40	67.15	Quiet; reading
51.66	38.21	114	15.0	0.793	10	64	26	2.47	69.26	Fairly quiet
231.21										
.....	36.83	...	....	.....	..	..	..	....	.....	Basal after quinin and ergotin
82.62	36.90	95	10.0	0.851	9	46	45	2.22	61.54	Quiet; reading
94.47	37.21	99	26.0	0.800	9	62	29	2.39	66.39	Reading 32 min.; restless 28 min.
177.09										
.....	37.20	...	....	.....	..	..	..	....	.....	Basal after ligation
89.64	37.02	111	14.0	0.726	8	35	7	2.32	68.61	Fairly quiet
101.86	37.04	119	7.0	0.773	8	72	20	2.29	67.81	Fairly quiet
191.50										
.....	36.57	...	..	.....	..	..	..	....	.....	Basal
104.54	36.56	98	24	0.751	10	76	14	1.47	49.54	Quiet
102.91	36.58	101	16	0.782	10	67	23	1.43	48.27	Quiet
207.45										
.....	36.88	...	..	.....	..	..	..	....	.....	Basal; at 9:35-9:50 a. m. 1.0 c.c. thyroid "residue"
101.60	36.80	97	29	0.733						
104.17	36.84	101	58	.0764	12	80	8	1.51	50.42	Fairly quiet
205.77					11	71	18	1.57	52.57	Restless
.....	37.27	...	..	.....						
73.79	37.15	71	6	0.820	..	..	..	....	.....	Basal
75.80	37.13	71	2	0.858	15	52	33	1.07	34.66	Very quiet
149.59					14	41	45	1.12	36.39	Very quiet

TABLE 11.—

Subject, Date, Weight, Surface Area, Linear Formula	Period	End of Period	Carbon Dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calorimetry, Cal.	Heat Eliminated, Cal.
Case 6 (Anna K.).. 4/28/14 44.45 Kg.	Prelim.	11:12	.....	.....	.....	.....	.....	.....	.....
	1	12:12	31.73	31.25	0.738	49.35	0.407	102.57	97.70
	2	1:12	32.00	30.79	0.756	53.67	0.407	101.53	100.83
								204.10	
Anna K. ..... 5/13/14 44.50 Kg.	Prelim.	11:40	.....	.....	.....	.....	.....	.....	.....
	1	12:40	27.62	24.63	0.816	33.43	0.505	82.14	69.53
	2	1:40	28.40	26.01	0.794	41.06	0.505	86.31	81.27
								168.45	
Case 7 (Anna R.).. 5/10/13 46.71 Kg.	Prelim.	9:45	.....	.....	.....	.....	.....	.....	.....
	1	10:45	22.05	21.02	0.763	29.44	0.287	69.42	61.67
	2	11:45	21.67	17.95	0.878	29.64	0.287	60.98	60.15
	3	12:45	22.55	22.15	0.740	35.40	0.287	72.74	65.27
								203.14	
Anna R. ..... 5/20/13 42.91 Kg.	Prelim.	9:30	.....	.....	.....	.....	.....	.....	.....
	1	10:30	23.74	21.93	0.787	36.63	0.380	72.73	65.80
	2	11:30	24.72	23.55	0.763	43.42	0.380	77.68	72.33
	3	12:30	24.16	24.52	0.717	49.82	0.380	80.01	83.34
								230.41	
Anna R. ..... 5/28/13 43.29 Kg.	Prelim.	9:38	.....	.....	.....	.....	.....	.....	.....
	1	10:38	23.15	22.21	0.758	42.19	0.423	73.04	71.31
	2	11:38	22.13	21.01	0.766	38.89	0.423	69.19	67.88
	3	12:38	23.19	21.29	0.792	44.42	0.423	70.60	74.19
								212.83	
Anna R. ..... 5/14/14 48.20 Kg.	Prelim.	11:13	.....	.....	.....	.....	.....	.....	.....
	1	12:13	22.79	20.90	0.793	29.00	0.282	69.58	59.76
	2	1:13	23.55	21.86	0.784	30.09	0.282	72.63	65.43
								142.21	
Case 8 (Sarah M.) 4/29/14 55.96 Kg.	Prelim.	11:20	.....	.....	.....	.....	.....	.....	.....
	1	12:20	25.62	23.85	0.781	37.86	0.363	79.07	76.95
	2	1:20	25.28	23.79	0.773	37.09	0.363	78.70	79.67
								157.77	
Case 9 (Marion B.) 2/5/15 57.91 Kg.	Prelim	11:35	.....	.....	.....	.....	.....	.....	.....
	1	12:35	25.89	25.26	0.746	35.16	0.195	83.30	80.18
	2	1:35	25.80	23.59	0.796	35.15	0.195	78.91	79.99
	3	2:35	26.10	24.44	0.775	37.01	0.195	81.35	86.23
								243.56	
Case 10 (Mrs. L.).. 4/20/14 63.00 Kg.	Prelim.	11:18	.....	.....	.....	.....	.....	.....	.....
	1	12:18	25.45	25.30	0.732	40.91	0.382	82.79	85.12
	2	1:18	26.64	24.35	0.795	40.10	0.382	81.00	84.18
								163.79	

—(*Continued*)

Direct Calorimetry (Rectal Temp.), Cal.	Rectal Temp., C.	Average Pulse	Work-Adder, Cm.	Non-protein R. Q.	Per Cent. Calories from			Calories per Hour		Remarks
					Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M. (Meeh)	
.....	37.18	...	..	.....						
95.12	37.12	118	36	0.730	..	..	..	....	.....	Basal
98.98	37.08	123	38	0.750	11	82	7	2.31	66.39	Restless
194.10					11	76	13	2.28	65.71	Quiet
.....	37.04	...	..	.....						
71.74	37.11	95	10	0.818	..	..	..	....	.....	Basal
83.84	37.19	105	13	0.792	16	52	32	1.85	54.37	Very quiet
155.58					16	59	25	1.94	55.83	Very quiet
.....	37.39	119	..	.....						
59.36	37.34	...	30	0.758	..	..	..	....	.....	Basal
61.31	37.38	...	14	0.890	11	73	16	1.49	44.50	
65.65	37.40	...	36	0.733	12	33	55	1.31	39.09	
186.32					10	82	8	1.56	46.63	
.....	37.87	...	..	.....						
65.02	37.99	...	3	0.784	..	..	..	....	.....	Basal
67.81	37.98	...	12	0.757	14	63	23	1.69	48.23	Quiet
81.02	38.04	...	11	0.703	13	72	15	1.81	51.51	Quiet
213.85					13	87	0	1.86	53.06	Quiet
.....	37.16	...	..	.....						
66.87	37.16	...	..	0.749	..	..	..	....	.....	Basal
65.89	37.23	...	..	0.758	15	73	12	1.69	49.99	
69.74	37.23	...	..	0.789	16	69	15	1.60	47.36	
202.50					16	60	24	1.63	48.32	
.....	36.69	...	..	.....	..	..	..	....	.....	Basal 1 yr. later
67.01	36.88	97	9	0.791	11	63	26	1.44	42.69	Very quiet; dozed
69.07	36.98	97	10	0.781	10	67	23	1.51	44.56	Very quiet; dozed
136.08										
.....	37.33	...	..	.....	..	..	..	....	.....	Breakfast at 7 a. m.; toast 20 gm., milk 250 c.c.
73.30	37.26	97	24	0.778	12	66	22	1.41	43.90	Fairly quiet
77.44	37.22	86	33	0.768	12	69	19	1.40	43.70	Fairly quiet
150.74										
.....	37.00	...	..	.....	..	..	..	....	.....	Basal
73.61	36.87	114	46	0.742	6	83	11	1.44	45.20	Restless
82.04	36.92	132	31	0.795	7	63	30	1.36	42.82	Restless
84.82	36.91	136	36	0.773	6	73	21	1.41	44.14	Reading
240.47										
.....	38.18	...	..	.....	..	..	..	....	.....	Basal
81.05	38.11	81	26	0.721	12	84	4	1.31	42.46	Restless
80.67	38.05	88	36	0.794	12	62	26	1.29	41.54	Restless
161.72										

TABLE 11.—

Subject, Date, Weight, Surface Area, Linear Formula	Period	End of Period	Carbon Dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calorimetry, Cal.	Heat Eliminated, Cal.
Case 11 (Bessie H.)	Prelim.	11:40	.....	.....	.....	.....	.....	.....	.....
4/8/14									
47.06 Kg.	1	12:40	19.06	17.02	0.815	26.67	0.159	57.12	62.51
1.42 Sq. M.	2	1:40	19.41	16.68	0.846	26.21	0.159	56.44	61.34
								113.56	
Bessie H.	Prelim.	11:27	.....	.....	.....	.....	.....	.....	.....
4/13/14									
48.18 Kg.	1	12:27	18.42	16.22	0.826	20.31	0.125	54.63	56.23
1.43 Sq. M.	2	1:27	19.49	17.83	0.795	21.81	0.125	59.60	59.33
								114.23	
Bessie H.	Prelim.	11:05	.....	.....	.....	.....	.....	.....	.....
4/18/14									
46.62 Kg.	1	12:05	17.83	15.14	0.856	22.12	0.217	51.02	52.61
1.41 Sq. M.	2	1:05	18.57	16.57	0.815	23.29	0.217	55.49	54.87
								106.51	
Case 12 (Benny L.)	Prelim.	11:40	.....	.....	.....	.....	.....	.....	.....
4/10/14									
22.80 Kg.	1	12:40	10.28	7.67	0.974	10.45	0.363	26.10	31.38
0.829 Sq. M.	2	1:40	10.23	8.58	0.867	10.51	0.363	28.63	32.70
								54.73	
Benny L.	Prelim.	11.52	.....	.....	.....	.....	.....	.....	.....
4/14/14									
23.60 Kg.	1	12:52	13.13	9.40	1.016	12.54	0.293	32.58	32.32
0.84 Sq. M.	2	1:52	12.81	9.24	1.008	12.29	0.293	31.97	33.39
	3	2:52	12.05	8.99	0.975	11.69	0.293	30.91	33.82
								95.46	
Benny L.	Prelim.	11:10	.....	.....	.....	.....	.....	.....	.....
4/21/14									
24.04 Kg.	1	12:10	11.23	8 10	1.008	13.82	0.316	27.91	33.30
0.847 Sq. M.	2	1:10	11.02	8.90	0.899	13.47	0.316	30.13	32.12
	3	2:10	11.07	9.04	0.890	13.21	0.316	30.48	33.95
	4	3:10	11.15	8.79	0.923	12.94	0.316	29.86	33.30
								118.38	
Benny L.	Prelim.	11:10	.....	.....	.....	.....	.....	.....	.....
4/23/14									
23.97 Kg.	1	12:10	9.44	7.76	0.885	10.58	0.226	26.21	26.47
0.847 Sq. M.	2	1:10	9.20	7.83	0.855	11.21	0.226	26.25	28.57
								52.46	
Benny L.	Prelim.	11:20	.....	.....	.....	.....	.....	.....	.....
4/27/14									
23.86 Kg.	1	12:20	10.47	7.94	0.959	14.30	0.208	27.36	27.15
0.847 Sq. M.	2	1:20	10.75	8.33	0.939	13.79	0.208	28.58	29.55
	3	2:20	11.01	8.38	0.955	13.29	0.208	28.88	29.25
								84.82	
Benny L.	Prelim.	11:10	.....	.....	.....	.....	.....	.....	.....
5/1/14									
23.03 Kg.	1	12:10	10.86	10.05	0.785	11.67	0.236	33.22	31.09
0.833 Sq. M.	2	1:12	10.91	9.96	0.797	11.88	0.236	32.99	31.80
								66.21	

—(*Continued*)

Direct Calorimetry (Rectal Temp.), Cal.	Rectal Temp., C.	Average Pulse	Work-Adder, Cm.	Non-protein R. Q.	Per Cent. Calories from			Calories per Hour		Remarks
					Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M. (Meeh)	
.....	37.22	...	..	.....	..	..	..	....	.....	Basal
55.89	37.06	60	4	0.815	7	59	34	1.22	35.59	Quiet
62.93	37.11	59	3	0.850	7	47	46	1.20	35.17	Quiet
118.82										
.....	37.15	...	..	.....	..	..	..	....	.....	Basal
51.06	37.03	72	8	0.828	6	55	39	1.13	33.52	Very quiet
62.55	37.12	75	13	0.795	6	66	28	1.24	36.56	Very quiet
113.61										
.....	37.19	...	..	.....	..	..	..	....	.....	Basal; 1.0 c.c. thyroid "residue" at 9:30 a. m.
51.86	37.18	98	8	0.847	11	46	43	1.10	31.99	Very quiet
52.18	37.12	90	15	0.816	10	56	34	1.19	34.79	Very quiet
104.04										
.....	37.51	...	..	.....	..	..	..	....	.....	Basal
28.47	37.37	83	2	1.089	37	0	63	1.15	26.36	Very quiet
30.74	37.28	85	2	0.903	34	12	44	1.26	28.92	Very quiet
59.21										
.....	37.59	..	..	.....	..	..	..	....	.....	Lactose 100 gm.; water and lemon juice, 200 c.c.
30.10	37.49	89	2	1.092	24	0	76	1.38	32.16	Very quiet
32.56	37.46	89	2	1.083	24	0	76	1.35	31.56	Very quiet
31.62	37.36	87	2	1.040	25	0	75	1.31	30.51	Very quiet
94.28										
.....	37.41	..	..	.....	..	..	..	....	.....	Protein meal at 9:38-9:55 a. m.; N = 3.6 gm.
31.46	37.33	87	6	1.109	30	0	70	1.16	27.20	Very quiet
31.07	37.29	81	5	0.939	28	15	57	1.25	29.37	Very quiet
32.50	37.23	81	9	0.927	27	18	55	1.27	29.71	Quiet
31.46	37.15	78	10	0.974	28	6	66	1.24	29.10	Quiet
126.49										
.....	37.16	..	..	.....	..	..	..	....	.....	Basal
25.44	37.12	79	5	0.911	23	23	54	1.09	25.60	Very quiet
26.93	37.05	77	9	0.871	23	34	43	1.09	25.63	Quiet
52.37										
.....	37.34	..	..	.....	..	..	..	....	.....	Dextrose, 70 gm. at 10:20 - 10:22 a. m.
26.52	37.32	78	3	1.004	20	0	80	1.15	26.82	Very quiet
28.92	37.30	79	4	0.975	19	7	74	1.20	28.02	Very quiet
29.41	37.32	80	5	0.996	19	1	80	1.21	28.31	Very quiet
84.85										
.....	37.76	..	..	.....	..	..	..	....	.....	Thyroid extract
30.07	37.72	94	3	0.781	19	60	21	1.44	33.33	Very quiet
31.92	37.74	95	4	0.795	19	56	25	1.43	33.10	Very quiet
61.99										

to find the proper basis on which to compare it with results obtained on normal adults. The administration of thyroid extract raised the metabolism to normal in three and a half days, increased the pulse rate from about 80 to 95, and made the patient sick and miserable.

THERAPEUTIC APPLICATIONS

Mental and physical rest is the surest means of securing the drop in the metabolism which indicates a diminution in the pernicious activity of the thyroid. Psychotherapy is of some value, and this combined with rest may account entirely for the improvement following most of the so-called medical cures. Previous observers have found little or no reduction in the oxidative processes after treatment with "Radogen," the serum of thyroidectomized horses, and the Roentgen ray. To this list may be added from the present work thyroid "residue," the ergotin and quinin hydrobromate treatment, and Beebe's serum. These remedies, however, were tried on but one or two patients, and a more favorable report might have been justified if more cases had been tested. In the treatment of hyperthyroidism, calorimeters and other forms of respiratory apparatus seem to be therapeutic nihilists.

Some observers have found a prompt drop in the metabolism after a partial thyroidectomy. Ligation of the arteries usually causes a distinct rise in heat production which may last several weeks. This shows that following a ligation of the arteries the patients should be kept as quiet as possible and thyroid extract should on no account be given.

It is quite possible that the above mentioned therapeutic agents control some of the minor symptoms of the disease or render the major symptoms less apparent to the patient and his physician. We cannot consider the patient to be anywhere near a cure until the metabolism has approached the normal. We cannot consider a therapeutic agent to be curative unless it causes the metabolism to approach the normal more quickly than the tendency toward spontaneous improvement aided by mental and physical rest.

The need of large amounts of food by exophthalmic goiter patients is clearly shown. There is no indication against the use of fairly liberal amounts of protein, and there is no reason to prefer the proteins of vegetables and milk to those of meat. The number of calories required per day varies with the weight of the patient, the severity of the case and the degree of muscular activity. In general, it may be said that exophthalmic goiter patients need from one and one-half times to twice as much food as a normal person under similar conditions. Several of the patients studied produced over 100 calories an hour while at rest. Max W. (Case 1) and Edwin T. (Case 2) showed a slightly negative nitrogen balance when receiving 3,500 and

4,000 calories a day. Every effort should be made to give food of high caloric value in large amounts, or there will be losses of body fat and protein.

SUMMARY AND CONCLUSIONS

The metabolism in exopthalmic goiter has been studied for the first time in a respiration apparatus which is also a calorimeter. Thirty-seven observations were made on eleven patients with this disease, and six experiments were made on a cretin. With some of the patients the nitrogen balance was also studied.

The measurement of the heat production gives us the best index of the severity of the disease and of the effect of treatment. Very severe cases show an increase of 75 per cent. or more above the normal average, severe cases 50 per cent. or more, and moderately severe and mild cases less than 50 per cent., while a few mild and several atypical or cases in which operation has been performed may be within normal limits. In severe cases the warmth of skin and sweating can be accounted for entirely by the necessity for the increased elimination of heat. At least a part of the tachycardia is due to the increased metabolism, and perhaps it might be possible to reproduce the extreme tachycardia, the cardiac enlargement, emaciation and mental irritability if we were able to stimulate the metabolism of normal men for twenty-four hours a day over a period of months or years.

The specific dynamic action of protein and of glucose is within normal limits, and there is no consistent difference between the effects of protein in meat and an equal amount in milk and eggs. One patient was able to derive 89 per cent. of his calories from carbohydrate in an experiment when he was showing an alimentary glycosuria. There is evidently no interference with the oxidation of carbohydrates.

The methods of direct and indirect calorimetry agree very closely when one considers the technical difficulties. The method of direct calorimetry gave results which were slightly lower than the indirect, the total difference being 2.9 per cent., and the average difference in the individual experiments being $\pm$ 4.1 per cent. This and the absence of abnormal respiratory quotients shows that the law of the conservation of energy holds good in exophthalmic goiter, and that there is no profound disturbance of the intermediary metabolism.

The average water elimination through skin and lungs in the severe and moderately severe cases of hyperthyroidism is 39.9 gm. per hour. The increase above the normal is closely proportional to the increase in heat production; 25.7 per cent. of the calories are dissipated through vaporization in goiter patients, whereas the mean normal is almost the same, 23.9 per cent.

The level of the heat production was used as an index of the effect of medical treatment. Rest in bed for a week or more caused a drop of more than 10 per cent. The effects of treatment with Beebe's serum, thyroid "residue" ergotin and quinin hydrobromate was less marked each being tested on one patient. Ligation of the thyroid arteries with three out of the four patients studied caused a distinct rise in metabolism, the duration of which was uncertain. There is as yet no proof that any conservative form of treatment causes a greater reduction of metabolism than mental and physical rest.

One small cretin 36 years old produced about half the calories eliminated by children of his size. As estimated by the surface area, his metabolism was about 20 per cent. below the normal adult level. Three and a half days of treatment with thyroid extract raised his heat production to normal.

NOTE.—The work here reported was made possible by the cooperation of a number of associates who should receive credit for the major part of the work. The analyses of food, urine and feces were made by Mr. Frank C. Gephart, with the assistance of Mr. R. H. Harries and Mr. R. C. Stone. The electrical control of the calorimeter was in charge of Mr. G. F. Soderstrom, and the residual air analyses and calculations were made by Dr. A. L. Meyer and Mr. Harries. The results were checked and tabulated by Miss Grace Sims and Mr. Stone. Miss Estelle Magill and her assistants, Miss A. Honold, Miss M. M. Fauquier and others were responsible for the weighing and preparation of the food, the care of the patients and the collection of specimens.

I wish to express my thanks to Dr. John Rogers for providing most of the patients and for cooperating very actively in the work. I also wish to thank Dr. S. P. Beebe for supervising the serum treatment and Dr. G. R. Lockwood of the First Medical Division of Bellevue for permitting the use of material from his ward, and to Drs. W. H. Brundage, T. C. Janeway and R. J. Shea, who also sent patients for treatment and observation.