

THE BASAL METABOLISM IN EXOPHTHALMIC GOITER *

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BOSTON

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INTRODUCTION

Four and one half years ago a study of the basal metabolism in exophthalmic goiter was started at the Massachusetts General Hospital. Preliminary reports on this work appeared in June, 1916,¹ and in July, 1917.² It was impossible for us at the latter date, because of the imminence of mobilization, to present more than the barest outline of our work, together with the conclusions drawn to that time.

The original program of the research was to follow the metabolism and clinical condition of a series of cases of exophthalmic goiter over a period of several years, during which time the patients would be undergoing therapy of one sort or another. This was carried out to

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1. Means, J. H.: Studies of the Basal Metabolism in Disease, Boston M. & S. J. **174**:864 (June 15) 1916.

2. Means, J. H., and Aub, J. C.: Study of Exophthalmic Goiter from Point of View of the Basal Metabolism, J. A. M. A. **69**:33 (July 7) 1917.

the end of April, 1917. Then, during the two years of the war, the patients, for the most part, disappeared from observation, although nine were seen once during that time.³ Since our discharge from the service in March, 1919, we have made every effort to locate these patients and to get them to the hospital for further observations. Of the total cases of toxic goiter, fifty-five in number, which comprised the original series, nine patients are known to be dead, twenty-four have recently had basal metabolism determinations, ten more have been seen or heard from, and twelve are lost.

The purpose of the present paper, then, is twofold: in the first place, we wish to present in full the data that we outlined in previous papers, and secondly, to present and discuss the data recently secured. Our discussion is based on 345 metabolism observations on 130 patients.

HISTORICAL

For the purposes of this paper, an exhaustive résumé of the literature is not necessary.

On the subject of the gas exchange in thyroid disease, the German literature, beginning with Magnus-Levy,⁴ is voluminous; the American literature is scanty. DuBois⁵ unquestionably is the pioneer in this country, and in his paper a review of the German literature will be found. Following DuBois we,^{1, 2} also Boothby,⁶ and very recently McCaskey,⁷ have emphasized the importance of basal metabolism determinations as an index of toxicity in hyperthyroidism.

We believe that our own work is the first in this country in which the metabolism of patients with exophthalmic goiter has been followed before treatment, and for periods of two or more years after treatment.

It would obviously be out of place to discuss the vast literature of the surgery or of the roentgen-ray treatment of the thyroid. An account of the early work in roentgen-ray treatment of exophthalmic goiter at the Massachusetts General Hospital has been published by Seymour.⁸

3. These observations were kindly made for us by Dr. Harry Linenthal, assisted by Miss Catherine Thacher.

4. Magnus-Levy, A.: *Gaswechsel bei Thyroidea*, Berl. klin. Wchnschr. **32**: 650, 1895.

5. DuBois, E. F.: *Metabolism in Exophthalmic Goiter*, Arch. Int. Med. **17**: 915 (June) 1916.

6. Boothby, W. M.: *Clinical Value of Metabolic Studies in Thyroid Cases*, Boston M. & S. J. **175**:564 (Oct. 19) 1916.

7. McCaskey, G. W.: *The Basal Metabolism and Hyperglycemic Tests of Hyperthyroidism with Special Reference to Mild and Latent Cases*, J. A. M. A. **73**:243 (July 26) 1919.

8. Seymour, M.: *Treatment of Graves' Disease by the Roentgen Rays*, Boston M. & S. J. **175**:568 (Oct. 19) 1916.

The whole subject of the relation of the thymus gland to exophthalmic goiter has been set forth by Halsted in a Harvey Lecture.⁹ Halsted predicts that for roentgen-ray and radium treatment there is a great future, particularly because of the important rôle of the thymus in the causation of exophthalmic goiter, and the profound effect of irradiation on that gland. Other writers, Boggs¹⁰ for example, have reported good results with the roentgen ray, especially when the thymus gland is exposed as well as the thyroid.

METHODS

The methods used will merely be mentioned, having been described and discussed in previous papers.^{1, 11, 12}

The gas exchange of normal individuals resting, and in the post-absorptive condition, has, with certain recognized variations due to age and sex, been found to be very constant if expressed in terms of their body surface.^{13, 14} The gas exchange of patients with hyperthyroidism, on the other hand, is elevated above the normal. We have used the degree of elevation as a measurement of the degree of thyroid intoxication.

The basal gas exchange was determined with the Benedict universal respiration apparatus, and the heat production was calculated therefrom. Through April, 1917, we used the calorific value of oxygen for the respiratory quotient obtained; in those calculations after that time we determined oxygen only and assumed an R. Q. of 0.82.

The body surface was determined from DuBois' height weight chart,¹⁵ except in a few instances early in the work, where the linear formula¹⁶ was used.

9. Halsted, W. S.: Significance of the Thymus Gland in Graves' Disease, Harvey Lectures, 1913-14, p. 224.

10. Boggs, R. H.: Treatment of Goiter by Roentgen Rays, Interstate M. J. **24**:362 (April) 1917.

11. Palmer, W. W.; Means, J. H., and Gamble, J. L.: Basal Metabolism and Creatinin Elimination, J. Biol. Chem. **19**:239, 1914.

12. Means, J. H.: Studies of Basal Metabolism in Obesity and Pituitary Disease, J. M. Research **32**:121, 1915.

13. Means, J. H.: Basal Metabolism and Body Surface, J. Biol. Chem. **21**:263, 1915.

14. Gephart, F. C., and DuBois, E. F.: Basal Metabolism of Normal Adults with Special Reference to their Surface Area, Arch. Int. Med. **17**:902 (June) 1916.

15. DuBois, D., and DuBois, E. F.: Formula to Estimate Approximate Surface Area, Arch. Int. Med. **17**:863 (June) 1916.

16. DuBois, D., and DuBois, E. F.: The Measurement of the Surface Area of Man, Arch. Int. Med. **15**:868 (June) 1915.

The roentgen-ray treatments were given at the Massachusetts General Hospital by Drs. G. W. Holmes and A. S. Merrill and we understand that they will publish an account of the work from the point of view of the roentgenologist with full particulars as to methods. The thyroid and thymus glands were both exposed at each treatment to nearly the maximum dose the skin would stand. The treatments were given from three to four weeks apart, as a rule, though sometimes a longer gap would occur.

The surgical operations, unless otherwise stated in the tables, were performed by Dr. C. A. Porter at the Massachusetts General Hospital. Almost without exception, the operations consisted in either ligation of the superior vessels or in partial thyroidectomy. The word lobectomy as we have used it in the tables indicates a partial thyroidectomy.

CLINICAL AND METABOLISM DATA

Our work is set forth in a series of tables. These, though voluminous, have been purged of all but essential data.

In the matter of figures, we have endeavored to give as few as possible. In case two figures are derivable, one from another, but one has been shown. Thus, the patient's age, sex, height and weight are given, but his surface area is not. If anyone wishes the area he has but to turn to DuBois' chart.¹⁵ The oxygen absorption not being interesting per se is omitted, but the calories per square meter per hour, which are derived from it, are shown. The carbon dioxid and respiratory quotient are not given, because they do not enter directly into the present problem. They may be published later. In all periods used the quotients were within normal limits.

To determine the variation from the normal metabolism we have used the standards, which have been adopted by the Russell Sage Institute,¹⁷ which take into account the variations due to age and sex. Our figure for the variation of the metabolism from the normal is the percentile variation above or below (expressed by + or —) the appropriate one of these standards. The really essential figures for purposes of discussion are the percentile variation from the normal metabolism, the pulse rate and the body weight.

We will now proceed with a running account of the material contained in the several tables, adding such clinical notes as the occasion seems to demand and later we shall analyze the data contained therein.¹⁸

17. Aub, J. C., and DuBois, E. F.: Basal Metabolism of Old Men, *Arch. Int. Med.* **19**:823 (June) 1917.

18. In the text and in the tables all patients are referred to by our laboratory numbers. They were referred to by the same numbers in our earlier paper, and will be in future papers, hence can readily be identified.

Controls.—Normal controls have appeared in earlier papers. A certain number of pathologic controls have likewise been obtained. In Table 1 are collected the data on twenty-two such cases, together with that of three normals (Nos. 7, 43 and 44). We do not pretend, of course, that alterations in the metabolism are confined to thyroid disease. It is a well known fact that they occur in other ductless gland disturbances and in blood diseases, also in acidosis and fever. Table 1 is interesting, however, in that it shows a variety of abnormalities in which there is little, if any, variation from the normal. Two cases of neurasthenia (Nos. 1 and 119) and one of a psychoneurosis (No. 109) all vary less than 10 per cent. from the normal. The same is true in such conditions as myasthenia gravis (No. 4), Raynaud's disease (No. 8), elephantiasis (No. 11), acroparesthesia (No. 14), Addison's disease (No. 20), and metrorrhagia (No. 69). A case of pernicious anemia (No. 17) and one of secondary anemia (No. 108) were also within normal limits. A rise is often found in pernicious anemia,^{19, 20} but in our case, just mentioned, it will be noted that there was not a very severe degree of anemia at the time the observation was made. Two cases of tachycardia of unknown origin (Nos. 19 and 50) varied only 5 and 11 per cent., respectively, above the standard. A case of irritable heart (No. 158) was quite within normal limits. A case of paroxysmal tachycardia (No. 67) showed a definite elevation, and it is interesting to note that the elevation is greater during an interval than during a paroxysm. Two cases of obesity (Nos. 47 and 58) were quite within normal limits. This is additional evidence in favor of the view expressed by one of us (J. H. M.) in an earlier paper²¹ that there is no fundamental change in the basal metabolism in obesity. An inactive acromegalic (No. 122) was also normal. Of two diabetics, one (No. 55) showed a normal figure, the other (No. 56) a slight reduction. This last patient, however, had been starving for over four days, so this reduction was quite what we should expect. A case of psoriasis in an elderly woman (No. 94) showed a rise of 12 per cent., and a case of pelvic inflammation and phlebitis (No. 124) showed a rise of 8 per cent., which is within the range of normal variation.

19. Meyer, A. L., and DuBois, E. F.: Basal Metabolism in Pernicious Anemia, *Arch. Int. Med.* **17**:965 (June) 1916.

20. Tompkins, E. H.; Brittingham, H. H., and Drinker, C. K.: Basal Metabolism in Anemia, *Arch. Int. Med.* **23**:441 (April) 1919.

21. Means, J. H.: Basal Metabolism in Obesity, *Arch. Int. Med.* **17**:704 (May) 1916.

TABLE 1.—METABOLISM DATA. CONTROL CASES

No.	Date	Sex	Age	Weight, Kg.	Height, Cm.	Pulse	Calories per Square Meter per Hour	Percentile Variation from Standard	Remarks
1	6/10/14	♂	22	63.2	185.5	88	41.2	+ 4	Neurasthenia
4	6/11/14	♂	22	63.2	185.5	79	39.3	0	
7	10/19/14	♂	22	38.3	75	36.5	- 1	Myasthenia gravis
8	12/ 3/14	♂	60	69.3	67	31.5	- 7	Normal
11	2/18/15	♂	40	56.7	165.0	74	35.5	- 1	Raynaud's disease
14	5/24/15	♂	18	55.0	157.5	84	36.4	- 4	Elephantiasis -
14	4/ 6/15	♂	60	65.0	150.0	67	35.1	+ 3	Acroparesthesia
17	4/20/15	♂	41	51.7	162.0	78	37.1	- 4	Pernicious anemia, Hg 70%, R. C. 2.9 ml.
19	4/26/15	♂	55	70.0	98	39.3	+ 5	Tachycardia of unknown origin
20	5/ 6/15	♂	31	62.0	62	42.0	+ 6	Addison's disease
43	11/18/15	♂	19	71.3	175.0	60	44.0	+ 7	Normal
44	11/19/15	♂	23	62.1	156.0	78	42.6	+15	Normal
47	12/18/15	♂	25	77.5	160.0	65	38.3	+ 3	Obesity
50	1/12/16	♂	32	54.0	172.5	105	43.8	+11	Tachycardia of unknown origin
55	2/18/16	♀	47	55.0	161.8	80	35.3	- 2	Diabetes not sugar-free, alveolar CO ₂ 33.3 mm.
56	2/19/16	♀	36	49.5	162.0	59	31.2	-14	Diabetes sugar-free, 5th day of fast; alveolar CO ₂ 29.4 mm.
58	4/ 1/16	♀	38	109.0	159.0	80	37.8	+ 4	Obesity and hypertrophic arthritis
67	9/11/16	♀	50	59.4	166.8	176	42.0	+20	Paroxysmal tachycardia during paroxysm
67	9/11/16	♀	50	59.4	166.8	85	45.3	+29	Paroxysmal tachycardia during interval
69	9/14/16	♀	18	56.3	161.0	87	37.2	- 2	Metrorrhagia
108	11/16/16	♀	46	56.8	164.0	101	38.5	+ 7	Secondary anemia
109	11/17/16	♀	32	46.0	158.2	93	38.6	+ 6	Psychoneurosis
119	12/ 5/16	♀	22	62.3	165.5	96	40.5	+ 9	Neurasthenia
122	12/10/16	♀	31	75.5	175.0	82	39.0	+ 7	Acromegaly, inactive
124	12/19/16	♀	40	67.5	168.0	91	38.9	+ 8	Phlebitis, pelvic inflammatory (subacute), glycosuria
158	3/14/17	♀	20	45.0	163.5	77	38.8	+ 5	Irritable heart
94	10/28/16	♀	78	69.0	163.4	68	36.9	+12	Psoriasis

A more interesting collection of controls is shown in Table 2. This comprises cases with thyroid enlargement, but with no clear cut clinical evidence of thyrotoxicosis. The size and character of the goiter are indicated in the table, and under "Remarks," a statement of the general nature of the case is given. Of these seventeen cases, only two varied more than 10 per cent. from the standard (Nos. 91 and 92). Both these patients had tachycardia, and although very atypical, these may yet have been cases of mild exophthalmic goiter. In our first paper² we showed diagrammatically that the elevation in metabolism in thyrotoxicosis runs essentially parallel to the clinical evidence of intoxication. This table shows the corollary that patients with thyroid tumors, but with no definite clinical evidence of hyperthyroidism have no increase in their metabolism. In these seventeen

cases we have been able to secure follow-up data in only seven, but none of these seven have clinically developed any indication of exophthalmic goiter.

Differential Diagnosis.—Soon after the work on our series of exophthalmic goiter cases was started, we began to receive requests from clinicians for basal metabolism determinations for purposes of differential diagnosis in cases presenting suggestive symptoms. Such a group of cases is shown in Table 3. It will be worth while to spend a little time examining these.

Thirty-three cases are included in this table. Of these, twelve (Nos. 35, 46, 73, 74, 75, 80, 81, 103, 118, 146, 155 and 127) showed a variation of not more than 10 per cent. from the standard. Seven of these twelve patients have been seen or heard from this year, and none of them has developed exophthalmic goiter.

One case (No. 65) in which it was thought that prolonged irradiation might have produced hypothyroidism, showed a result 13 per cent. below the standard. This figure is somewhat suggestive of hypothyroidism, no doubt, but the patient, when seen this year, presented no clinical evidence of that condition.

Only three cases of this group showed a rise of more than 40 per cent. One of these (No. 159) was one of recurrent thyroid carcinoma. The metabolism result is interesting inasmuch as the only other thyroid carcinoma we have studied showed a reduction from the normal.²² The next highest metabolism in this group is that of Case 147. This patient had a colloid goiter with suggestive symptoms. Unfortunately, in neither of these patients were we able to secure follow-up data. Case 112 is quite striking, for when first seen, no goiter or eye signs were present, but he had suggestive symptoms and the metabolism was 44 per cent. above normal. His later history shows that subsequently he developed true exophthalmic goiter.

Of the remaining seventeen cases showing a rise of anywhere between 10 and 40 per cent. above normal, eight have been lost. Four have subsequently developed exophthalmic goiter (Nos. 26, 84, 136 and 152). Two patients are now in good health (Nos. 116 and 153); one case (No. 78) seems to be rather of the effort syndrome class and two cases still remain in the doubtful class (Nos. 27 and 149).

We believe that our Tables 2 and 3 illustrate clearly the importance of metabolism determinations for purposes of differential diagnosis in cases of obscure thyroid disease. Table 2 shows that for the

22. Means, J. H., and Aub, J. C.: Basal Metabolism in Hypothyroidism Arch. Int. Med. **24**:404 (Oct.) 1919.

TABLE 2.—METABOLISM DATA. PATIENTS WITH ENLARGED THYROID GLANDS BUT WITHOUT CLINICAL EVIDENCE OF HYPERTHYROIDISM

No.	Date	Sex	Age	Weight, Kg.	Height, Cm.	Pulse	Calories per Met. Hour and Stand.	Percent Variation from Standard	Thyroid			Duration of Goiter	Remarks	Patient's Condition in Spring of 1919
									Degree of Enlargement	Character	Brit			
13	3/27/15	♀	30	56.0	158.0	82	40.0	+10	++	Soft, smooth, symmetrical	0	10 years	Symptoms of toxemia at onset; perfectly well for several years	Remained in good health; has married and had twins
15	4/ 9/15	♀	14	37.5	150.0	81	44.5	+ 3	+	Soft, smooth, symmetrical	0	2 years	In good health	No information
	9/28/16		15	41.0	154.0	88	43.3	+ 1	+	Soft, smooth, symmetrical	0	In good health	
	1/13/17		16	42.5	155.8	87	44.5	+ 3	0	0	In good health	
24	6/ 2/15	♀	25	52.0	169.0	90	38.2	+ 3	+	Soft, smooth, symmetrical	0	3½ years	Well but easily fatigued	About the same
61	6/14/16	♀	31	64.0	155.4	67	36.6	0	..	Asymmetrical, irregular goiter, probably multiple cysts	0	1 year	Symptoms of toxemia at onset; none now after course of roentgen ray	No information
70	9/16/16	♀	20	49.8	158.2	82	36.5	- 1	+	Soft, smooth, symmetrical	0	2 years	Slightly nervous; eyes somewhat prominent	Appears neurotic rather than thyrotoxic
76	9/25/16	♀	43	68.0	167.5	87	33.3	- 7	++	Firm, smooth, asymmetrical	0	2 years	Marked psychoneurosis	No information
82	10/ 4/16	♀	30	67.0	172.0	77	39.7	+ 9	++	Soft, smooth, symmetrical	0	6 years	Slight toxemia in past, well now following course of roentgen ray	No information
85	10/12/16	♀	35	47.3	160.0	76	37.6	+ 3	+++	Soft, smooth, symmetrical	0	10 years	Well but easily fatigued	No information
90	10/18/16	♀	22	54.7	158.0	76	38.8	+ 5	++	Soft, smooth, symmetrical	+	6 months	Toxemia in past, clearing up on course of roentgen ray	No information
91	10/20/16	♀	34	57.5	163.0	106	42.6	+17	++	Soft, smooth, symmetrical	0	34 years?	Marked neurasthenia, nystagmus	No information
92	10/21/16	♀	20	46.6	157.0	94	41.3	+12	++	Soft, smooth, symmetrical	0	2 years	Debility	No information
98	11/ 3/16	♀	47	60.0	157.5	79	38.2	+ 6	++	Soft, smooth, symmetrical	0	2 years	Nervous in past, clearing up on course of roentgen ray	Better; no evidence of Graves' disease
132	1/18/17	♀	30	63.0	176.0	64	35.1	- 4	++	Soft, smooth, symmetrical	0	2 years	Some nervousness in past; none now	Goiter the same; no signs of toxemia
133	1/18/17	♀	24	45.5	158.0	83	36.5	- 1	+	Soft, smooth, symmetrical	0	24 years?	Somewhat nervous; history of increased sweating	No information
140	2/10/17	♀	22	63.0	163.5	87	40.1	+ 8	+	Soft, smooth, symmetrical	0	15 years	Occasionally nervous; slight tremor	Goiter the same; no signs of toxemia
145	2/20/17	♀	41	57.0	175.0	101	39.6	+10	..	Round, smooth mass in lobe of pigeon's egg; probably cyst	0	15 years	In good health	Goiter just as before; no signs of toxemia
150	3/ 4/17	♀	15	51.5	160.0	85	38.5	-10	..	Hard, round mass in isthmus size of a grape	0	15 years	Slight suggestion of myxedema	No information

TABLE 3.—METABOLISM DATA. BORDERLINE CASES

No.	Date	Sex	Age	Weight, kg.	Height, Cm.	Pulse	Calories per Square Meter and Hour	Per- cent- tile Vari- ation from Standard	Remarks	Patient's Condition in Spring of 1919
9	3/13/15	♀	51	58.2	169.0	123	47.2	+35	Tachycardia of unknown origin.	No information
26	6/22/15	♀	33	60.0	158.0	97	44.9	+23	Mitral disease plus suggestive symptoms.	Definitely
27	4/9/19	♀	37	59.5	151.0	107	55.5	+52	Slight but definite signs of thyrotoxicosis.	Slightly thyrotoxic
27	7/8/15	♀	30	50.3	151.0	69	42.6	+17	Full thyroid; slightly suggestive symptoms.	Not much evidence of Graves' disease; asthma her chief trouble
35	1/20/17	♀	31	51.5	158.8	81	44.6	+22	Slight eye signs; no thyroid enlargement or toxic symptoms	No information
35	10/21/15	♀	34	43.0	158.8	99	38.0	-1	Tachycardia of unknown origin.	No definite evidence of Graves' disease
46	12/14/15	♂	18	56.0	173.0	99	45.0	+10	Prolonged irradiation; ? of hypothyroidism.	No evidence of thyroid disease
65	8/28/16	♀	46	67.0	165.0	87	31.3	-13	Very slight fullness of thyroid, eye signs and toxic symptoms	No information
73	9/20/16	♀	37	63.0	164.0	89	38.7	+6	Postoperative Graves'; slight recurrence of symptoms	Essentially normal
74	9/21/16	♀	36	37.5	155.5	84	34.9	-4	Improved; slight tremor; slight nervousness, otherwise no evidence of thyrotoxicosis.	Normal
75	4/22/16	♀	29	61.5	162.5	90	38.7	+5	Slight fullness of thyroid; very mild symptoms.	Seems to fall best in class of "effort syndrome"
78	4/27/16	♀	22	55.4	171.0	89	51.1	+29	Prolonged irradiation; atypical symptoms now.	In good health
80	4/29/16	♀	22	55.4	149.0	113	38.6	+14	Full thyroid; slight symptoms.	No information
80	10/3/16	♀	21	38.9	171.0	100	43.5	+20	Slight enlargement of thyroid, and somewhat atypical symptoms	Picture of very mild Graves' disease
81	10/3/16	♀	23	60.2	161.3	88	44.3	+18	Slight fullness of thyroid; suggestive symptoms.	No evidence of Graves' disease; moderately neurotic
84	10/10/16	♀	24	49.2	156.5	86	43.6	0	Intrathoracic goiter	No information
103	2/12/17	♀	15	41.0	161.8	126	43.1	+15	No eye signs of goiter but very suggestive symptoms	Subsequently developed true Graves' disease
104	11/11/16	♀	53	69.0	161.8	83	40.1	+15	Incipient phthisis	No information
112	2/8/17	♀	53	66.5	169.5	79	37.9	+8	Colloid goiter; ? hyperthyroidism.	No information
112	11/21/16	♀	50	54.3	169.5	104	54.1	+44	Full thyroid and suggestive symptoms.	No information
115	11/24/16	♀	26	58.4	169.0	88	41.3	+12	Enlarged thyroid and atypical symptoms.	No information
116	11/25/16	♀	65	42.0	156.0	133	44.6	+31	Chronic alcoholism with suggestive symptoms.	No information
118	12/1/16	♀	36	51.6	167.0	88	39.0	+7	Enlarged thyroid; suggestive symptoms.	Probably had Graves' disease in interim
105	11/12/16	♀	43	55.5	157.0	89	43.9	+22	Improved; five roentgen ray treatments; no evidence of hyperthyroidism now	No information
134	1/19/17	♀	36	59.0	170.0	103	46.9	+19	Enlarged thyroid; suggestive symptoms.	No information
136	1/29/17	♀	30	55.5	156.0	104	45.9	+29	Colloid goiter and suggestive symptoms.	Symptoms about as before
146	4/12/19	♀	32	58.0	156.0	88	45.9	+29	Suggestive symptoms; no eye signs or goiter.	Developed true Graves' disease; better now
146	2/21/17	♀	34	60.3	171.0	89	36.8	+1	Full thyroid; no symptoms	No information
147	2/22/17	♀	51	41.3	162.0	89	54.3	+55	Postoperative Graves'; disease.	Exophthalmos persists; no other signs of Graves' disease
149	2/24/17	♀	51	41.3	162.5	98	53.8	+54	Marked exophthalmos; no goiter or symptoms.	No information
152	3/7/17	♀	44	50.5	162.5	106	49.3	+37	Full thyroid; no symptoms.	No information
152	3/7/17	♀	39	70.5	179.0	99	51.4	+30	Recurrent carcinoma of thyroid.	No information
153	3/9/17	♀	21	55.0	172.0	93	43.9	+19	Tachycardia of unknown origin.	About the same
154	3/10/17	♀	58	58.3	159.0	94	40.0	+14	Neurasthenia	
155	3/10/17	♀	49	70.0	166.0	89	41.9	+9		
157	3/13/17	♀	20	56.9	169.0	104	49.5	+34		
159	3/15/17	♀	66	66	167.5	102	57.1	+56		
162	4/7/17	♀	53	46.5	162.5	89	38.8	+11		
127	1/11/17	♀	31	55.0	178.0	105	38.3	+4		

most part patients with goiters, but without clinical signs of thyrotoxicosis, have a normal metabolism, and that, furthermore, such cases do not subsequently become toxic. The metabolism determination, therefore, seems to be an excellent means of differentiating toxic and nontoxic goiters. Table 3 indicates that in cases with suggestive symptoms those patients with a normal metabolism do not subsequently develop exophthalmic goiter, while those with an elevation often-times do. In this class of cases, therefore, the metabolism determination appears to differentiate between true hyperthyroidism and simple neurasthenia, and makes possible a far earlier diagnosis of exophthalmic goiter than would the clinical picture alone.

Exophthalmic Goiter.—The data of our exophthalmic goiter series are presented in Tables 4, 5 and 6. It will be well to give short histories of these cases, fifty-five in number. The physical findings in each case at the time our first observation was made are indicated by plus marks, one meaning slight, two moderate, three marked. The statement as to the toxicity at the head of each history is based on the clinical impressions, not on the metabolism findings. For all dates the reader is referred to the several tables.

Table 4 shows the results obtained in fifteen cases in which the patients received essentially no treatment except with the roentgen ray, either alone or combined with rest. This table includes:

CASE 10.—Mrs. M. J. M. (E. M. 200812, X-Ray 306). Duration, six months. Very toxic. Eye signs + +. Tremor + +. Thyroid moderately enlarged, hard; loud bruit.

After ten roentgen-ray treatments she showed no improvement, objectively, in her metabolism, or in her pulse rate. She thought she felt better, but she gained no weight. She died (Oct. 3, 1917) sixteen months after her last metabolism determination, presumably of exophthalmic goiter.

CASE 12.—Mrs. T. W. (E. M. 200595, X-Ray 703). Duration eight years. Slightly toxic. Eye signs, none. Tremor +. Thyroid moderately enlarged, hard; faint bruit; definite myocarditis.

A somewhat atypical case of long standing goiter which, according to the history, had only recently become toxic; for some reason when first seen had been receiving a course of thyroid extract. She presented the picture of mild hyperthyroidism, but the metabolism was elevated 71 per cent. After cessation of thyroid and the administration of quinin hydrobromid, it dropped to 49 per cent., while her pulse dropped from 104 to 80. After six roentgen-ray treatments there was essentially no change in the metabolism and a slight rise in pulse and weight. She was seen this year and did not appear toxic, although the goiter persists. Myocardial insufficiency seemed the chief trouble. A metabolism determination was not obtained.

CASE 21.—Miss J. D. (E. M. 201753, X-Ray 519). Duration, two months. Moderately toxic. Eye signs +. Tremor + + +. Thyroid moderately enlarged; loud bruit.

After five roentgen ray treatments she showed a very striking improvement, fall in metabolism and pulse and gain in weight. She died December, 1917. The cause of death could not be learned.

CASE 25.—Mrs. A. L. (E. M. 202294, X-Ray 278). Duration, four months. Moderately toxic. Eye signs, none. Tremor +. Thyroid slightly enlarged, soft; bruit very loud. She showed a fall in metabolism and pulse rate and a gain in weight after four treatments, but no immediate further improvement after three additional treatments. When seen this year she did not appear to be toxic and her symptoms seemed referable to myocarditis. There was no longer any thyroid enlargement, and no eye sign or tremor.

CASE 33.—Mr. B. S. (E. M. 204683, X-Ray 591). Duration, two years. Moderately toxic. Eye signs +. Tremor + +. Thyroid moderately enlarged, soft; bruit + +.

He recovered completely after no other treatment than six roentgen-ray exposures, and he has remained well for over two years doing full work. His last metabolism figure was 14 per cent. below normal, but he presented no clinical signs of myxedema.

CASE 48.—Mrs. E. N. (E. M. 205776, X-Ray 693). Duration, four and one half years. Very toxic. Eye signs + + +. Tremor + +. Thyroid moderately and asymmetrically enlarged. Loud bruit.

After thirteen roentgen-ray treatments she has shown a marked improvement, fall in metabolism and pulse. When seen this year she showed slight exophthalmos, but no sign of intoxication. She had become very obese.

CASE 53.—Mr. R. S. (E. M. 206770, X-Ray 729). Duration, three weeks. Moderately toxic. Eye signs + + +. Tremor + + +. Thyroid slightly and symmetrically enlarged, soft. Loud bruit.

He showed essentially no change after seven treatments, but a year later, without further treatment, he showed a marked improvement, fall in metabolism and pulse rate, and gain in weight. He has not been seen this year, but writes that he was accepted for the U. S. Army, went overseas with his organization and has now been discharged and is working in a shipyard.

CASE 66.—Miss E. C. C. (O. P. D. 306686, X-Ray 888). Duration, two years. Moderately toxic. Eye sign +. Tremor +. Thyroid slightly and symmetrically enlarged, rather hard. Moderate bruit.

She had only roentgen-ray treatment. After eleven exposures she had recovered completely. When seen this year she presented no evidence of intoxication and had a normal metabolism. She was working to full capacity.

CASE 107.—Mrs. R. M. (O. P. D. 255857, roentgen ray 964). Duration, three years. Slightly toxic. Eye signs +. Tremor +. Thyroid slight; hard, enlargement of the right lobe. Slight bruit. This patient had had a hemithyroidectomy two years before our first observation, with recurrence of symptoms recently.

She grew distinctly worse after four roentgen-ray treatments. Her present condition has not been learned.

CASE 110.—Miss E. M. (E. M. 211726, X-Ray 1011). Duration, five months. Slightly toxic. Eye signs +. Tremors +. Thyroid slight, soft, symmetrical enlargement. Moderate bruit.

She showed no fall in metabolism on rest alone and then recovered after six roentgen-ray treatments. When seen this year she showed very slight tremor and slightest fullness of the thyroid. Her metabolism was just above normal and she was working to full capacity.

CASE 111.—Mrs. S. S. (E. M. 211757, X-Ray 1012). Duration, two months. Very toxic. Eye signs negative. Tremor + + +. Thyroid moderate soft, symmetrical enlargement. Loud bruit.

After thirteen roentgen-ray treatments she has had a marked fall in metabolism and pulse rate, and a good gain in weight. When seen this year she was clinically improved. She was still toxic, but all signs and symptoms were less marked. She was doing her own housework.

TABLE 4.—METABOLISM DATA. EXOPHTHALMIC GOITER. ROENTGEN-RAY SERIES

Number Age Height, Cm.	Date	Weight, Kg.	Pulse	Calories per Square Meter Hour	Percentile Variation from Standard	Roentgen Ray Treat- ments No.	Progress Judged Clinically		Activity: A. Complete Rest in Ward B. Complete Rest Outside C. Partial Rest D. Usual Life	Remarks
							Subjec- tively	Objec- tively		
No. 10 Mrs. M. J. M. 50 years 157 Cm.	3/14/15	63.5	127	59.0	+68	0	A 2 days	On course of opium since last observation On quinin hydrobromid since last observation Doing considerable house work for year; appearance unchanged
	3/20/15	119	58.7	+68	0	A	
	5/12/15	57.2	108	53.1	+52	1	Improved	Worse	A	
	5/18/16	57.2	127	65.7	+88	9	Improved	Same	C	
No. 12 Mrs. T. W. 41 years 154.5 Cm.	3/26/15	40.0	104	61.5	+71	0	D	Had been taking thyroid extract; discontinued On quinin hydrobromid since last observation; dis- continued Goiter smaller
	4/17/15	80	53.7	+49	0	D	
	12/14/16	43.9	96	52.6	+46	6	Improved	Same	D	
No. 21 Miss J. D. 37 years 164 Cm.	5/19/15	45.0	77	54.9	+50	0	A 2 weeks	Goiter smaller; much less nervous Working for over a year
	6/3/15	81	53.8	+53	1	Improved	Improved	A	
	6/26/15	85	54.9	+56	2	Improved	Improved	A	
	1/31/17	63.2	67	41.3	+13	2	Almost well	Almost well	D	
No. 25 Mrs. A. L. 34 years 153 Cm.	6/8/15	50.5	117	66.8	+83	0	A 3 days	Feels and looks much better than last year
	12/12/16	56.6	106	58.7	+61	4	Improved	Improved	D	
No. 33 Mr. B. S. 24 years 169.5 Cm.	5/2/17	53.2	113	59.5	+63	3	A 1 day	Better; tremor most troublesome symptom, inter- feres with work; barber Practically well; tremor nearly gone Perfectly well; working Working since last observation
	10/12/15	50.0	103	70.3	+78	0	C	
	6/5/16	52.7	96	59.6	+51	4	D	
	11/23/16	57.0	65	45.2	+14	2	Improved	Well	D	
No. 48 Mrs. E. N. 30 years 168 Cm.	2/1/17	60.0	73	39.8	+1	0	Well	Well	D	Less tremor; less exophthalmos Signs of thyrotoxicosis much less marked; some myo- cardial damage Leading normal life for 2 years
	5/5/19	59.0	56	34.1	-14	0	Well	Well	D	
	1/1/16	52.0	137	66.3	+82	0	A 2 weeks	
	1/21/16	53.3	123	58.8	+61	1	Improved	Improved	A	
	2/2/16	53.5	118	59.0	+62	1	Same	Same	A	
	6/9/16	60.0	102	58.9	+61	0	Same	Same	D	
	10/16/16	69.5	120	59.5	+63	4	Same	Improved	D	
	1/8/17	68.0	96	56.1	+54	4	Same	Improved	D	
No. 53 Mr. R. S. 21 years 171.5 Cm.	4/26/17	74.3	93	46.0	+26	3	Improved	Well	D	Eye signs less marked than a year ago; not objec- tively nervous now
	4/14/19	90.0	97	46.3	+27	3	Well	Well	D	
	5/13/19	87.0	88	45.8	+25	0	Well	Well	D	
	2/16/16	64.5	100	58.5	+48	0	A 2 days	
	5/17/16	61.0	98	62.1	+57	5	Same	Same	C	
	11/20/16	65.5	96	63.1	+60	2	Improved	Same	C	
	2/13/17	63.0	92	59.0	+49	0	Well	Well	C	
	12/12/17	66.0	70	44.6	+13	0	D	

No. 86 Miss E. C. C. 27 years 174.5 Cm.	8/29/16 12/ 2/16 2/24/17 4/ 7/17 4/12/19	43.2 49.6 50.0 49.0 49.0	118 118 104 104 80	52.6 49.2 41.8 47.3 34.6	+42 +33 +13 +28 - 6	0 4 2 1 4 Improved Improved Same Well D Improved Improved Same Well D	Teaching school; almost no tremor Thyroid smaller; less bruit No eye signs; no tremor; no thyroid enlargement
No. 107 Mrs. R. M. 51 years 156 Cm.	11/16/16 1/27/17 4/ 5/17	45.0 45.5 49.0	... 81 106	49.3 42.5 53.8	+41 +21 +54	0 3 1 Well Worse D Well Worse D	Leading normal life; appears and feels well Recurrence of symptoms following overwork
No. 110 Miss E. M. 39 years 157.5 Cm.	11/19/16 11/24/16 12/ 3/16 12/18/16 1/30/17 3/ 8/17 4/ 9/17 5/ 7/19	56.8 56.6 54.7 56.8 61.0 64.7 65.5 66.5	96 112 108 119 105 91 84 78	49.0 51.7 49.1 51.7 48.9 42.8 36.3 41.3	+34 +42 +35 +42 +34 +17 - 1 +15	0 0 1 0 2 1 2 0 Same Same Improved Same Improved Almost well Well A 4 days A A A C C D D	Quinin hydrobromid for last ten days Thinks she is much better; still looks toxic Appears less toxic Been back at work for six weeks	
No. 111 Mrs. S. S. 55 years 151.2 Cm.	11/19/16 11/26/16 12/ 5/16 1/10/17 3/ 8/17 4/15/19	39.0 38.5 37.1 40.0 41.0 48.5	131 129 114 140 141 100	65.4 64.1 55.0 65.6 64.7 44.0	+87 +83 +57 +87 +85 +26	0 0 1 1 2 9 Same Improved Improved Same Same Improved A 2 days A A C C D	Extreme nervousness Less nervous Very slight tremor; thyroid barely perceptible	
No. 113 Mrs. B. M. T. 23 years 155.8 Cm.	11/22/16 1/25/17 3/12/17 4/29/17	58.0 55.0 54.5 55.2	153 116 110 133	65.6 54.6 51.6 54.3	+77 +48 +39 +47	0 2 2 0 Same Same Same D D A 1 week A 1 week Improved Improved Same D D A 1 week A 1 week	Acute infection for last two weeks Had diphtheria between this and preceding observation
No. 120 Mrs. L. K. 45 years 160 Cm.	12/ 7/16 12/22/16 1/31/17 3/29/17	53.6 49.5 50.5 53.5	128 130 112 114	60.2 61.6 56.2 53.4	+67 +71 +55 +48	0 0 2 2 Same Improved Improved D C D D Same Same Same Improved D C D D	Exophthalmos increasing Seems less toxic but eye signs are increasing and thyroid enlarging
No. 123 Mrs. C. M. 29 years 152.5 Cm.	12/14/16 12/20/16 1/ 9/17 1/13/17 1/21/17 2/ 1/17 3/ 8/17 4/24/17 4/26/18 5/ 7/19	48.0 49.0 42.3 43.6 45.9 43.9 45.5 51.0 56.0 55.0	157 133 112 118 127 122 128 125 122 111	70.0 64.2 49.7 51.9 57.5 58.6 64.4 63.9 80.5 50.6	+89 +74 +34 +40 +55 +68 +74 +73 +66 +39	0 0 1 0 0 1 3 3 0 Same Improved Improved Worse Same Improved Same D D A 1 day A A A A C D Same Improved Improved Worse Same Improved Same D D A 1 day A A A A C D	Much better; looking after husband and two children
No. 135 Mrs. V. M. D. 39 years 164.5 Cm.	1/28/17 2/ 7/17 2/15/17 3/ 9/17 4/ 5/17 1/30/18 5/10/19	53.2 53.7 53.9 57.5 58.1 56.0 65.5	122 106 108 119 108 116 104	50.6 44.4 46.9 53.5 46.5 45.1 37.5	+39 +22 +28 +47 +25 + 4	0 0 0 1 6 0 Improved Improved Same Same Well A 11 days A C C D Improved Improved Same Same Well A 11 days A C C D	Quinin hydrobromid for six months Less exophthalmos Doing light housework Has had a healthy child since last observation

CASE 113.—Mrs. B. M. T. (E. M. 213651, X-Ray 1015). Duration, three years. Moderately toxic. Eye signs +. Tremor + +. Thyroid moderate, soft, symmetrical enlargement. Faint bruit.

She improved somewhat after four roentgen-ray treatments but died later, the date and cause of death being unknown to us.

CASE 120.—Mrs. I. K. (O. P. D. 315898, X-Ray 1029). Duration, one year. Moderately toxic. Eye signs + + +. Tremor + + +. No visible enlargement of thyroid.

She showed some improvement after four roentgen-ray treatments. Subsequently she has remained in fairly good health, but both eyes have had to be enucleated because of extreme exophthalmos.

CASE 123.—Mrs. C. M. (E. M. 212328, X-Ray 1020). Duration, eight years. Very toxic. Eye signs + + +. Tremor + + +. Thyroid marked, soft, symmetrical enlargement. Loud bruit.

After six roentgen-ray treatments she showed a definite improvement; fall in metabolism and pulse and gain in weight. When seen this year she was clinically improved. The exophthalmos persists. Slight tremor was present. The goiter was smaller. She was still somewhat toxic but was working to usual capacity.

CASE 135.—Mrs. V. M. D. (W. M. 212958, X-Ray 872). Duration, one year. Slightly toxic. Eye signs + + +. Tremor +. Thyroid slight, soft symmetrical enlargement. Faint bruit.

She recovered after seven treatments. When seen this year, except for slight exophthalmos and a persistent tachycardia she showed no signs or symptoms of exophthalmic goiter. Her metabolism was normal, and she was caring for her family and nursing her baby.

In Table 5 are collected the data obtained in sixteen cases before and after partial thyroidectomy.

CASE 3.—Mrs. L. S. (W. M. and W. S. 197641). Duration, four years. Very toxic. Eye signs + +. Tremor + +. Thyroid moderate, soft symmetrical enlargement. Loud bruit.

One year and one half after lobectomy she showed a fall in metabolism and a gain in weight. No change occurred in her pulse rate. Her condition this year could not be learned.

CASE 16.—Mr. S. T. (W. M. and W. S. 201372). Duration, one year. Moderately toxic. Eye signs + +. Tremor + + +. Thyroid, moderate, soft symmetrical enlargement.

Two years after operation he showed a higher metabolism than he did before. Essentially, no change in pulse rate and a slight gain in weight. His condition this year could not be learned.

CASE 51.—Mr. W. W. H. Duration, eight months. Slightly toxic. Eye signs +. Tremor +. Thyroid, slight fullness; faint bruit. He gave a history of no improvement after six roentgen-ray treatments. After lobectomy at the Mayo clinic he gained weight, had a normal metabolism and a slower pulse. Later he had a slight return of toxemia. He has not been seen this year, but writes that he is quite well.

CASE 71.—Mrs. H. R. (E. M. and W. S. 210587, X-Ray 794). Duration eighteen months. Moderately toxic. Eye signs +. Tremor +. Thyroid, moderate, soft symmetrical enlargement.

She gave a history of no improvement after eight roentgen-ray treatments. This was before coming under our observation. She showed a striking fall in metabolism and pulse rate immediately after operation and later a rise. This year her metabolism is still 22 per cent. above normal, but she has gained weight, has no tachycardia and appears to be well. There is still slight exophthalmos. She is following her usual occupation.

CASE 83.—Mr. W. H. (W. M. and W. S. 210852). Duration, one year. Very toxic. Eye signs + + +. Tremor +. Thyroid, moderately enlarged. Faint bruit.

When first seen he was still toxic in spite of a ligation done at the Mayo Clinic. He showed a striking improvement after lobectomy and had a normal metabolism and pulse rate one month after operation. His condition this year was not learned.

CASE 88.—Miss C. P. (E. M. and W. S. 211054, X-Ray 879). Duration, one year. Very toxic. Eye signs + + +. Tremor + +. Marked, soft symmetrical enlargement of thyroid. Loud bruit.

She gave a history of no improvement after four roentgen-ray treatments, but showed a marked improvement after ligation and then grew worse again after lobectomy. This year, however, she is looking and feeling well, and her metabolism is only + 15 per cent. She has been working for two years; a slight exophthalmos remains.

CASE 99.—Miss M. T. P. (W. M. and W. S. 211454, X-Ray 1094). Duration, eleven years. Very toxic. Eye signs + + +. Tremor + + +. Thyroid, marked asymmetric enlargement. Loud bruit.

This patient also reported no improvement after eight roentgen-ray treatments. She showed an increase in toxemia following lobectomy, but later a gradual improvement under roentgen-ray treatment. When seen this year she still had a slight exophthalmos, slight fullness of the left lobe of the thyroid, with bruit, but other signs and symptoms of thyrotoxicosis were practically absent. Her metabolism was decreased and she had been working to full capacity for one year and one half.

CASE 106.—Mrs. N. M. (E. M. and W. S. 211553). Duration, two years. Slightly toxic. Eye signs, none. Tremor +. Thyroid, moderate, hard, asymmetrical enlargement. No bruit.

She apparently became entirely normal within four months after lobectomy. This year she was clinically well, but her metabolism was + 24 per cent.

CASE 117.—Miss V. R. (W. M. and W. S. 211801). Duration, two years. Slightly toxic. Eye signs +. Tremor + +. Thyroid, slight soft symmetrical enlargement. Faint bruit.

After operation she showed an immediate decrease followed by an increase in toxemia. However, she writes this year that she is in excellent health. She has been married and is doing her own housework.

CASE 125.—Miss M. D. (E. M. and W. S. 212305). Duration, one and one half years. Very toxic. Eye signs, +. Tremors, + + +. Thyroid, moderate, hard, symmetrical enlargement. Loud bruit.

She had had a ligation before coming under our observation. She showed a marked fall in pulse rate and metabolism on rest in bed, and a continued gradual improvement after a ligation and lobectomy. When seen this year she had a slight exophthalmos and a hard mass in the isthmus of the thyroid, the size of a pigeon's egg; no bruit. There was no evidence of thyrotoxicosis. Metabolism was decreased and she had been working for two years as a domestic.

CASE 126.—Mrs. M. L. (W. M. and W. S. 212598). Duration, eighteen months. Slightly toxic. Eye signs, +. Tremor, +. Thyroid, slight soft symmetrical enlargement. Faint bruit.

She had had nine roentgen-ray treatments before coming under our observation. She showed a return of the metabolism to normal, a normal pulse rate and a gain in weight after lobectomy. She died subsequently. We have been unable to learn the date and cause of death.

CASE 129.—Mr. W. E. R. (W. M. and W. S. 212711). Duration, one year. Slightly toxic. Eye signs, none. Tremor + +. Thyroid, slight fullness. No bruit.

TABLE 5.—METABOLISM DATA. EXOPHTHALMIC GOITER. SURGICAL SERIES

Number Age Height, Cm.	Date	Weight, kg.	Pulse	Calories per Square Meter and Hour	Per- cent- ile Varia- tion from Stan- dard	Progress Judged Clinically		Activity: A. Complete Rest in Ward B. Complete Rest Outside C. Partial Rest D. Usual Life	Remarks
						Subjec- tively	Objec- tively		
No. 3 Mrs. L. S. 35 years 157 Cm.	10/ 8/14	42.0	104	65.6	+80	A 3 weeks	Three roentgen ray treatments before coming under observation One roentgen ray treatment Lobectomy Oct. 16, 1914 Much better; all signs and symptoms greatly dimin- ished; working
	10/10/14	42.0	102	63.1	+73	Same	Same	A	
	11/ 6/14	39.2	104	59.0	+62	Improved	Improved	A	
	6/ 6/16	53.0	108	54.5	+49	Improved	Improved	D	
No. 16 Mr. S. T. 33 years 168 Cm.	4/19/15	62.7	100	51.4	+30	A 1 day	Lobectomy April 20, 1915
	3/31/17	67.0	96	57.1	+45	Same	Improved	D	
No. 51 Mr. W. W. H. 33 years 174.5 Cm.	2/ 8/16	54.6	108	55.2	+40	C	Six roentgen ray treatments before coming under observation Lobectomy May 19, 1916, at Mayo Clinic Back at work in banking business
	6/20/16	58.0	80	40.4	+2	Improved	Well	C	
No. 71 Mrs. H. R. 37 years 166.5 Cm.	12/22/16	61.5	96	47.0	+19	Worse	Worse	D	Had eight roentgen ray treatments before coming under observation, without improvement Lobectomy Sept. 25, 1916
	9/19/16	68.0	113	49.6	+36	A 1 day	
	9/23/16	67.6	101	51.1	+40	A	
	10/ 2/16	65.9	88	42.1	+15	Improved	Improved	A	
	10/31/16	69.5	122	49.8	+36	Improved	Improved	C	
	11/14/16	70.5	113	49.4	+35	Improved	Improved	D	
	12/12/16	70.9	101	46.1	+26	Worse	Same	D	
	2/ 3/17	72.5	104	45.5	+25	Same	Improved	D	
	4/11/17	73.5	98	43.8	+20	Well	Improved	D	
	4/ 1/19	77.5	88	44.8	+23	Well	Well	D	
No. 83 Mr. W. H. 22 years 160 Cm.	4/29/19	76.0	80	44.5	+22	Well	Well	D	Ligation at Mayo Clinic July, 1916, superior arteries Lobectomy Oct. 16, 1916
	10/ 5/16	49.9	127	61.7	+56	A 3 days	
	10/ 9/16	52.0	96	53.7	+36	A	
	10/27/16	45.5	97	51.5	+30	Improved	Improved	A	
	11/18/16	43.6	81	42.8	+ 8	Improved	Improved	C	

No. 88 Miss C. P. 22 years 161 Cm.	10/14/16	54.7	144	64.1	+73	A 3 days	Had four roentgen ray treatments before coming under observation, without improvement Ligation Nov. 2, 1916 Lobectomy Nov. 17, 1916 All signs and symptoms less marked Exophthalmos nearly gone; no tremor; no thyroid palpable
	10/18/16	54.7	141	57.1	+54	A	
	10/26/16	51.8	143	56.1	+52	A	
	11/11/16	51.0	124	44.3	+20	A	
	11/29/16	52.3	129	47.3	+28	A	
No. 89 Miss M. T. P. 36 years 170.6 Cm.	12/11/16	51.1	127	47.8	+29	A	Had eight roentgen ray treatments before coming under observation, without improvement Quinin hydrobromid since last note Lobectomy Nov. 23, 1916 Four roentgen ray treatments One roentgen ray treatment
	12/11/16	51.1	127	47.8	+29	A	
	12/11/16	51.1	127	47.8	+29	A	
	12/11/16	51.1	127	47.8	+29	A	
	12/11/16	51.1	127	47.8	+29	A	
No. 106 Mrs. N. M. 41 years 153.5 Cm.	12/11/16	51.1	127	47.8	+29	A	Lobectomy Nov. 24, 1916 Some slight suggestion of myxedema
	12/11/16	51.1	127	47.8	+29	A	
	12/11/16	51.1	127	47.8	+29	A	
	12/11/16	51.1	127	47.8	+29	A	
	12/11/16	51.1	127	47.8	+29	A	
No. 117 Miss V. R. 22 years 168.2 Cm.	12/11/16	51.1	127	47.8	+29	A	Lobectomy Jan 6, 1917 Ligation at St. Lukes Hospital, New Bedford, May, 1916 One roentgen ray treatment since last observation Ligation Jan. 19, 1917 Lobectomy Jan. 30, 1917 Working for nearly two years
	12/11/16	51.1	127	47.8	+29	A	
	12/11/16	51.1	127	47.8	+29	A	
	12/11/16	51.1	127	47.8	+29	A	
	12/11/16	51.1	127	47.8	+29	A	
No. 125 Miss M. D. 27 years 166.8 Cm.	12/11/16	51.1	127	47.8	+29	A	Working for nearly two years
	12/11/16	51.1	127	47.8	+29	A	
	12/11/16	51.1	127	47.8	+29	A	
	12/11/16	51.1	127	47.8	+29	A	
	12/11/16	51.1	127	47.8	+29	A	

TABLE 5.—METABOLISM DATA. EXOPHTHALMIC GOITER. SURGICAL SERIES—Continued

Number Age Height, Cm.	Date	Weight, Kg.	Pulse	Calories Per Square Meter and Hour	Percent- tile Varia- tion from Stand- ard	Progress Judged Clinically		Activity: A. Complete Rest in Ward B. Complete Rest Outside C. Partial D. Usual Life	Remarks
						Subjec- tively	Obiec- tively		
No. 126 Mrs. M. L. 34 years 160 Cm.	1/7/17	49.3	122	53.5	+47	A 2 days	Had nine roentgen ray treatments before coming under observation Lobectomy Jan. 23, 1917
	1/20/17	50.3	105	52.6	+44	A	
	2/4/17	49.9	96	41.6	+14	A	
	2/11/17	49.3	105	43.4	+19	A	
	3/27/17	51.0	100	43.8	+20	A	
	10/29/17	56.5	76	37.4	+2	Almost well	Almost well	C	
No. 129 Mr. W. E. R. 39 years 169.5 Cm.	1/14/17	47.7	145	58.9	+49	A 3 days	Lobectomy Jan. 20, 1917, at private hospital
	5/7/19	52.5	96	39.8	+3	Well	Well	D	
No. 137 Mr. E. T. B. 35 years 166.2 Cm.	2/3/17	58.0	112	67.5	+71	A 1 day	Had an acute throat infection since last note and developed auricular fibrillation Lobectomy March 5, 1917 Three roentgen ray treatments, spring of 1917
	2/16/17	55.0	119	63.5	+61	A	
	2/25/17	50.9	96	66.9	+69	A	
	3/2/17	51.6	102	61.6	+56	A	
	3/14/17	49.5	87	52.8	+34	A	
	4/7/17	58.2	121	65.9	+67	C	
	3/29/19	68.0	64	40.9	+4	Well	Well	D	
No. 143 Miss M. E. H. 36 years 156 Cm.	2/15/17	54.1	104	46.3	+27	A 3 days	Had seven roentgen ray treatments before coming under observation Lobectomy Feb. 24, 1917 Lobectomy June 30, 1917
	2/18/17	54.1	105	48.1	+32	A	
	3/4/17	53.0	107	43.3	+19	A	
	3/15/17	55.0	100	41.3	+13	A	
	4/20/17	53.6	92	46.6	+28	C	
	4/9/19	54.5	64	32.3	-11	Well	Well	D	
No. 148 Miss B. H. 26 years 161 Cm.	2/23/17	47.0	110	56.2	+52	D	One roentgen treatment Lobectomy June 28, 1917
	6/25/17	46.0	94	54.1	+46	A	
	5/1/19	56.5	60	40.9	+10	Well	Well	D	
No. 151 Mrs. M. E. T. 46 years 158 Cm.	3/6/17	52.2	117	64.6	+79	A 1 day	Lobectomy March 27, 1917
	3/13/17	52.3	111	59.1	+64	A	
	3/19/17	51.4	102	56.6	+57	A	
	4/1/17	49.0	100	48.5	+35	A	
	5/9/19	49.0	117	50.3	+40	D	

Two years after lobectomy he had a normal metabolism and clinically was well. He was working to full capacity.

CASE 137.—Mr. E. T. B. (E. M. and W. S. 213101). Duration, six years. Moderately toxic. Eye signs +. Tremor + +. Thyroid, moderate soft, symmetrical enlargement. Faint bruit.

He showed little consistent improvement immediately after lobectomy. When seen two years later, he was well, but he had had three roentgen-ray treatments in that time. Slight exophthalmos persisted, but his metabolism was normal and he had been working for nearly two years.

CASE 143.—Miss M. E. H. (W. M. and W. S. 213273). Duration, ten months. Slightly toxic. Eye signs, none. Tremor + +. Thyroid, moderate, soft, symmetrical enlargement. Moderate bruit.

She had had seven roentgen-ray treatments before coming under our observation. She apparently was cured by two successive lobectomies. When seen this year she had no signs or symptoms of exophthalmic goiter. She had a normal metabolism, and had been working for more than one year.

CASE 148.—Miss B. H. (E. M. and W. S. 215081). Duration, two months. Very toxic. Eye signs +. Tremor +. Thyroid moderate, soft symmetrical enlargement. Faint bruit.

When seen this year, two years after operation, she had no signs or symptoms of exophthalmic goiter, except a slight exophthalmos. She had a normal metabolism, and had been working one year.

CASE 151.—Mrs. M. E. T. (W. M. and W. S. 213639). Duration, eight months. Moderately toxic. Eye signs +. Tremor + +. Thyroid, moderate, soft, symmetrical enlargement. Loud bruit.

When seen two years after lobectomy she still had an elevated metabolism and signs and symptoms of a slight thyrotoxicosis. She was doing light housework.

In Table 6 are collected a somewhat miscellaneous group, some in which the series of observations is incomplete, and some that were followed both during the roentgen-ray and the surgical treatments.

CASE 18.—Miss M. A. W. (E. M. 201409). Duration, six years. Slightly toxic. Eye signs +. Tremor, none. Slight thyroid enlargement.

She gave a history of having had a more severe exophthalmic goiter in the past, from which she had recovered. She improved rapidly on a short rest and quinin hydrobromid. She has remained well. She is working at her profession of nursing.

CASE 22.—Miss H. Duration, seven years. Moderately toxic. Eye signs + +. Tremor +. Thyroid, right lobe enlarged. Bruit present.

One observation only was made on this patient. She had a thyrotoxicosis recurring after a lobectomy done seven years before. She also showed an elevation of 43 per cent. in the basal metabolism. Her present condition is not known.

CASE 23.—Mrs. F. G. (E. M. and W. S. 201801, X-Ray 511). Duration, eight years. Very toxic. Eye signs + + +. Tremor + +. Thyroid, marked, hard enlargement. Loud bruit.

She died two days after ligation of the right superior thyroid vessels. The vessels on the left side had been ligated eleven days before.

CASE 32.—Mrs. E. J. S. (E. M. 204549). Duration, three years. Slightly toxic. Eye signs +. Tremor +. Thyroid, slightly and asymmetrically enlarged. No bruit.

This patient appeared clinically to be only slightly toxic, but she had a very high metabolism. When seen five and one half months later, having followed

TABLE 6.—METABOLISM DATA. EXOPHTHALMIC GOITER. MISCELLANEOUS

Number Age Height, Cm.	Date	Weight, Kg.	Pulse	Calories per Square Meter and Hour	Percent- tile Vari- ation from Stand- ard	Roent- gen Ray Treat- ments No.	Progress Judged Clinically		Activity: A. Complete Rest in Ward B. Complete Rest Outside C. Partial D. Usual Life	Remarks
							Subjec- tively	Objec- tively		
No. 18 Miss M. A. W. 31 years 164 Cm.	4/22/15	71	39.9	+9	0	A 1 week	On quinin hydrobromid
	10/23/16	48.0	86	41.5	+14	0	Improved	Improved	C	
	4/ 2/17	49.5	90	39.4	+8	0	Improved	Improved	D	
No. 22 Miss H. 35 years	5/23/15	65.5	105	52.1	+43	0	D	Lobectomy in 1908
No. 23 Mrs. F. G. 29 years	5/24/15	33.7	121	67.0	+81	1	A 12 days	June 11, 1915, Ligation left superior vessels; June 22, 1916, ligation right superior vessels
No. 32 Mrs. E. J. S. 38 years 163.5 Cm.	10/ 7/15 3/28/17	58.0 55.0	111 120	63.1 68.4	+73 +87	0 1 Improved Improved	A 5 days D	Goiter smaller
No. 40 Mrs. D. K. N. 27 years 163 Cm.	11/ 9/15	55.8	103	47.4	+23	0	A 1 week	
No. 52 Miss C. M. 22 years 170 Cm.	2/10/16	50.0	130	65.3	+76	0	A 6 days	Ligations, November and December, 1913; lobectomy March 2, 1916
No. 59 Miss A. M. B. 40 years 157 Cm.	6/ 5/16	47.5	132	49.1	+36	0	A 4 days	
No. 62 Mrs. M. A. H. 40 years 155.3 Cm.	6/16/16 11/23/16 3/29/17 8/ 7/19	61.0 61.5 60.0 57.0	117 112 106 94	49.1 48.0 47.7 48.6	+36 +33 +32 +35	4 5 2 0 Improved Improved Same Same Improved	C C C D	

No. 68 Mrs. J. B. 35 years 153.2 Cm.	9/12/16 12/13/16 2/17/17 2/26/17 4/ 8/19	50.5 53.0 54.5 52.4 49.5	88 90 81 80 82	50.6 46.1 49.9 47.7 49.9	+39 +26 +37 +31 +37	9 2 3 0 8 Improved Worse Same Improved Improved	D D A Same D	
No. 72 Miss E. P. 18 years 161 Cm.	9/19/16 11/28/16	51.1 53.5	111 106	49.4 49.5	+30 +30	5 0 Improved	D D	
No. 77 Mrs. S. I. R. 29 years 154.5 Cm.	9/26/16 10/ 7/16 10/21/16	53.4 50.0 49.1	151 133 124	54.6 54.5 58.5	+48 +47 +58	0 0 0 Same Improved	A 3 days A A	Lobectomy Nov. 3, 1916
No. 89 Miss M. S. 23 years 162.5 Cm.	10/14/16 12/ 4/16 2/ 9/17 3/26/17	61.0 64.0 63.0 61.0	112 101 110 103	57.1 50.1 54.0 54.1	+54 +46 +46 +46	5 2 3 3 Same Improved Same	D D D D	Working in shoe factory right along; has done so ever since onset
No. 93 Mrs. A. B. 33 years 163 Cm.	10/27/16 1/ 7/17 1/22/17 2/13/17 2/24/17 3/ 8/17 3/28/17 2/ 4/18 4/ 1/19	55.2 51.9 53.5 56.7 55.5 57.2 58.0 59.0 59.0	131 133 129 125 103 99 102 93 88	51.0 49.9 50.3 49.8 38.4 39.2 38.1 36.6 33.7	+40 +37 +38 +37 +5 +7 +4 0 - 8	0 2 1 1 0 0 0 0 0 Same Same Same Improved Well Weak Same Well	C A 6 days A A A A A D D	Just recovered from acute tonsillitis Lobectomy Feb. 14, 1917 Doing housework
No. 100 Miss E. McH. 41 years 147 Cm.	11/ 4/16 11/ 7/16	51.1 51.5	149 140	50.6 50.2	+41 +39	15 0 Same	A 3 days A .	
No. 114 Miss O. S. 41 years 164.8 Cm.	11/23/16 1/10/17 5/ 3/17 7/ 2/19	55.0 65.5 63.0 60.5	107 76 74 68	53.0 34.9 38.0 34.5	+47 - 3 + 6 - 4	1 2 1 0 Well Well Well	C D D D	
No. 121 Miss M. M. 21 years 152.5 Cm.	12/ 9/16 12/16/16 12/23/16 1/ 6/17 1/12/17 1/22/17 1/31/17 2/12/17 3/ 5/17 3/27/17 4/13/17 4/29/17 4/10/19	59.5 57.0 56.3 55.5 55.0 52.3 52.3 53.2 56.0 58.7 58.1 60.5	126 131 117 116 112 108 122 117 141 114 79 59	80.5 77.4 67.9 67.9 63.5 66.7 64.2 64.2 75.1 66.2 58.5 43.7 41.1	+118 +109 +84 +84 +72 +78 +74 +74 +103 +79 +58 +15 +11	0 0 0 1 1 0 0 0 1 1 1 0 3 Improved Improved Improved Same Same Improved Same Same Same Improved Well	D A 1 day A A A A A A A B A A 2 days A D	Lobectomy April 16, 1917

TABLE 6.—METABOLISM DATA. EXOPHTHALMIC GOITER. MISCELLANEOUS—(Continued)

Number Age Height, Cm.	Date	Weight, Kg.	Pulse	Calories per Square Meter and Hour	Per- cent- tile Varia- tion from Stand- ard	Roent- gen Ray Treat- ments No.	Progress Judged Clinically		Activity: A. Complete Rest in Ward B. Complete Rest Outside C. Partial D. Usual Life	Remarks
							Subjec- tively	Objec- tively		
No. 130 Miss K. L. 17 years 167.7 Cm.	1/16/17	50.5	125	58.5	+46	0	A 1 day	
	1/17/17	50.2	120	54.1	+35	0	A	
	1/22/17	50.3	112	52.0	+30	0	Improved	Improved	A	
	1/30/17	49.5	103	52.5	+31	0	Same	Same	A	
	2/1/17	50.0	109	50.4	+26	0	Improved	Same	A	
	2/13/17	51.0	107	48.8	+29	0	A	
No. 131 Mrs. S. J. G. 33 years 176 Cm.	4/28/17	56.0	99	51.3	+28	0	Improved	C	Lobectomy Feb. 24, 1917, at Melrose Hospital
	1/16/17	59.0	99	51.9	+42	0	A 3 days	
	1/22/17	59.5	81	48.6	+33	0	Improved	Improved	A	
	2/4/17	57.5	97	47.7	+31	0	Improved	Same	A	
	3/22/17	55.3	96	48.1	+32	1	Same	A	Just been through a bronchopneumonia and after that an acute frontal sinusitis
	4/26/19	61.5	77	44.5	+22	0	Improved	Well	D	Never has had any consistent treatment
No. 133 Mr. C. J. 33 years 186 Cm.	2/ 5/17	64.5	104	53.7	+26	0	D	Quinin hydrobromid for one week
	2/19/17	67.5	102	55.8	+41	0	Same	D	
	4/ 8/17	67.7	101	56.3	+43	0	Improved	Improved	D	
No. 139 Mrs. R. K. 23 years 161.5 Cm.	2/ 6/17	58.0	108	55.6	+50	1	D	
	4/12/17	55.0	107	54.6	+48	2	Improved	D	
No. 144 Mrs. H. 37 years 163.7 Cm.	2/17/17	74.3	113	53.8	+47	0	A 3 days	Lobectomy July, 1914, Peter B. Brigham Hospital
	3/ 7/17	76.0	82	46.4	+27	0	A	
No. 156 Theodore D. 11 years 147.5 Cm.	3/19/17	38.8	124	65.6	+29	0	A 3 days	
	8/ 2/19	39.0	102	52.7	+15	4	Improved	Improved	D	
No. 160 Mrs. K. 57 years 170 Cm.	3/26/17	57.8	119	62.3	+78	0	A 2 days	Lobectomy April 13, 1917
	4/10/17	47.5	130	66.5	+99	1	Worse	Worse	A	
No. 161 Mrs. C. M. 26 years 165 Cm.	3/29/17	46.4	123	68.1	+84	0	A 12 days	Lobectomy Oct. 10, 1917
	4/ 6/17	45.3	128	61.6	+67	0	Same	A	
	10/ 8/17	61.0	118	61.1	+65	0		

no treatment in the interim, she appeared and felt better, but had a still higher metabolism and pulse rate, and she had lost weight. Her present condition could not be learned.

CASE 40.—Mrs. D. K. N. (W. M. 205075). Duration, eighteen months. Moderately toxic. Eye signs +. Tremor +. Thyroid, slight fullness.

This patient was observed only once and has never been located since.

CASE 52.—Miss C. M. (E. M. 192096, W. S. 194108). Duration, three years. Very toxic. Eye signs + + +. Tremor + +. Thyroid, moderate, soft, symmetrical enlargement. Faint bruit.

She had had two ligations done two years before our observation. She died of acute pericarditis eleven days after lobectomy.

CASE 59.—Miss A. M. B. (W. S. 208734). Duration, eighteen years. Moderately toxic. Eye signs +. Tremor +. Thyroid, slight fullness. Slight bruit.

This patient was observed only once. We have not been able to locate her since.

CASE 62.—Mrs. M. A. H. (O. P. D. 289505, X-Ray 706). Duration, four and one half years. Slightly toxic. Eye signs + +. Tremor + + +. Thyroid, slight symmetrical enlargement.

She had had four roentgen-ray treatments before we started our observations. When seen this year she had had seven more. She was clinically better but her metabolism was unchanged. There still was slight exophthalmos. She had been working for two years.

CASE 68.—Mrs. J. B. (E. M. 213374, X-Ray 524). Duration, seven years. Moderately toxic. Eye signs + +. Tremor +. Thyroid moderate soft, symmetrical enlargement.

She has had prolonged roentgen-ray treatment. Our observations cover the last half of this course only. No change occurred in metabolism, pulse rate or weight during this time, though clinically she appeared to be a little better.

CASE 72.—Miss E. P. (O. P. D. 286790, X-Ray 676). Duration, one month. Slightly toxic. Eye signs +. Tremor +. Thyroid, slight symmetrical enlargement. Faint bruit.

She was observed only twice. This year she writes that she is in good health.

CASE 77.—Mrs. S. I. R. (W. M. and W. S. 210686). Duration, two and one-half years. Very toxic. Eye signs +. Tremor + +. Thyroid, moderate soft symmetrical enlargement. Loud bruit.

She died following a lobectomy.

CASE 89.—Miss M. S. (O. P. D. 300446, X-Ray 817). Duration, eighteen months. Slightly toxic. Eye signs + +. Tremor +. Thyroid, moderate soft symmetrical enlargement. Loud bruit.

She was observed during roentgen-ray treatment, under which she showed no definite improvement. Her present condition could not be learned.

CASE 93.—Mrs. A. B. (W. M. and W. S. 212531, X-Ray 968). Duration, two months. Slightly toxic. Eye signs +. Tremor +. Thyroid, slight soft symmetrical enlargement. Moderate bruit.

She was observed through a course of roentgen-ray treatment which had no apparent effect. She was operated on later, recovered promptly, and has remained well for two years. When seen this year she had no signs or symptoms of exophthalmic goiter. Her metabolism was normal and she was doing housework for a family of four.

CASE 100.—Miss McH. (W. M. 211450). Duration, seventeen months. Slightly toxic. Eye signs +. Tremor +. Thyroid, right lobe palpable. No bruit.

She had had fifteen roentgen-ray treatments before we saw her. She has not been seen this year, but her doctor writes that she has recovered.

CASE 114.—Miss O. S. (O. P. D. 314339, X-Ray 962). Duration, three years. Moderately toxic. Eye signs + + +. Tremor +. Thyroid, marked soft symmetrical enlargement. Bruit present.

She was observed during a course of roentgen-ray treatments. She recovered promptly. When seen this year she presented moderate exophthalmos, but no other signs of exophthalmic goiter. Her metabolism was normal and she was working to full capacity.

CASE 121.—Miss M. M. (E. M. 212253, W. S. 214295, X-Ray 1021). Duration, one year. Very toxic. Eye signs +. Tremor + +. Thyroid, moderate soft symmetrical enlargement. Moderate bruit.

This patient had the highest metabolism of any in the series. She has been studied very completely from the start to the present time. A course of roentgen-ray treatments, together with complete rest, brought her metabolism from +118 to +58 per cent., with only a slight fall in pulse rate, and no gain in weight. After lobectomy her metabolism promptly fell to +15 per cent., with a corresponding fall in pulse. This year she had a metabolism only 11 per cent. above normal and was apparently cured. She received three more roentgen-ray treatments after operation. She had a barely perceptible exophthalmos. She had been working for two years as a domestic.

CASE 130.—Miss K. L. (E. M. 212770). Duration, six weeks. Moderately toxic. Eye signs +. Tremor + + +. Thyroid, moderate soft symmetrical enlargement. Loud bruit.

She showed a definite improvement on rest alone. Later she was operated on in an outside hospital. This year she writes that she is not improved.

CASE 131.—Mrs. S. J. G. (E. M. 229863, X-Ray 1067). Duration, five months. Slightly toxic. Eye signs +. Tremor +. Thyroid, slight fullness. No bruit.

When seen this year, after two years of essentially no treatment, she showed a slight fall in metabolism and pulse rate, gain in weight and slight general improvement.

CASE 138.—Mr. C. J. (O. P. D. 320460). Duration, six years. Moderately toxic. Eye signs + + +. Tremor + +. Thyroid not enlarged.

He was observed for two months only, during which time he took essentially no treatment and showed no change. His present condition could not be learned.

CASE 139.—Mrs. R. K. (O. P. D. 195120, X-Ray 1051). Duration, four years. Slightly toxic. Eye signs + +. Tremor +. Thyroid, moderate soft symmetrical enlargement. Loud bruit.

She was observed twice during roentgen ray treatment. There was no great change in her condition. Her present condition could not be learned.

CASE 144.—Mrs. H. (W. M. 213327). Duration, two years. Slightly toxic. Eye signs +. Tremor +. She had a hemithyroidectomy at the Peter Bent Brigham Hospital in 1914. The remaining lobe of the thyroid was slightly enlarged.

Present condition unknown.

CASE 156.—Theodore D. (W. M. 213713, X-Ray 1060). Duration, five months. Moderately toxic. Eye signs + + +. Tremor + +. Thyroid, moderate soft symmetrical enlargement. Moderate bruit.

A boy with moderately severe exophthalmic goiter, had four roentgen-ray treatments and this year was much better. All signs and symptoms of thyrotoxicosis were less marked.

CASE 160.—Mr. K. (E. M. and W. S. 213989). Duration, two months. Moderately toxic. Eye signs + +. Tremor + +. Thyroid, moderate soft symmetrical enlargement. Moderate bruit.

She got more toxic in spite of complete rest in bed and died after lobectomy.

CASE 161.—Mrs. C. M. (E. M. 213880, W. S. 217740). Duration, eight months. Moderately toxic. Eye signs + +. Tremor +. Thyroid, moderate asymmetrical enlargement. Moderate bruit.

She showed a slight fall in metabolism on rest in bed and died later following a lobectomy.

INTERPRETATION OF DATA

To interpret the data set forth in the preceding tables properly is somewhat difficult. We have sought, by using the basal metabolism as an index of toxicity, to determine the exact effect of roentgen-ray therapy and partial thyroidectomy on the course of exophthalmic goiter. Confusing factors always arise, however. The factor of rest, for instance, or that of drugs, keeps coming in to complicate the picture, as does that of the tendency to spontaneous recovery. Having found that rest alone usually causes the metabolism to fall, we must take great care in attributing observed improvement entirely to surgery or to the roentgen ray. In experimental animals one could study a single factor at a time. This cannot be done with patients if we have proper regard for their welfare. Nevertheless, the present studies bring out a number of interesting points, which we will discuss in turn.

The data of the various cases differs in completeness. It would have been highly desirable if each case had been observed at definitely fixed intervals. This has not been possible. Some patients have been more than willing to come for observation whenever we wished. Others who do not live near Boston have sometimes been able to come only at long intervals. In order to draw conclusions as to the result of treatment, therefore, we have had to separate the cases into groups, each group illustrating some one point.

For purposes of interpretation we have constructed a diagram (Fig. 1). In this are shown, the effect of rest alone, that of rest plus quinin hydrobromid, that of surgery and that of roentgen-ray treatment. The diagram shows average results, represented as columns. To illustrate the effect of rest, for example, we have taken the figures for all cases where observations were secured before and after a period of rest in bed, and averaged the metabolism before and after. The columns represent these averages. The same thing has been done in regard to rest plus quinin hydrobromid. As a matter of fact, these two points are taken directly from Tables 1 and 2 of our first paper.²

The data concerning the effect of the roentgen ray has been handled as follows: First, the cases that had been observed before and after roentgen-ray treatment were tabulated, as in Table 3 of our first paper. We then made the following groupings: Group 1, observations secured after from one to two treatments; Group 2, after from three to five treatments; Group 3, after from six to seven

treatments; Group 4, after ten or more treatments, and Group 5, from two to three years after the fifth treatment. These groups were composed for the most part of observations on the same patients, but sometimes, for example, we had observations on a patient to include in Groups 1 and 3, but not in Groups 2 or 4. In a preliminary diagram we arranged five pairs of columns, the first of each pair representing the average metabolism of the group before treatment, the second after treatment. In the diagram actually shown there is but one "before" column which is the average of the five "before"

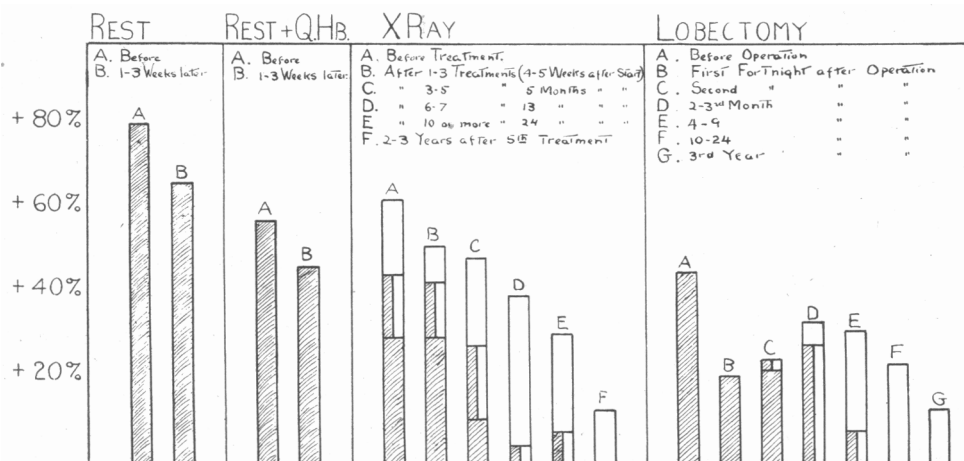


Fig. 1.—Diagram showing average metabolism levels and effect of various sorts of treatment thereon. The columns indicate the percentile increase above the standard. The cases composing each average are enumerated in the Appendix. The method of constructing the diagram is explained in the text. The shading indicates what proportion of the patients forming any average were receiving complete rest (full shading), partial rest (half shading), and what proportion were leading their usual lives (unshading).

columns of the five groups. The five "after" columns have been reduced to this average "before" column by a simple proportion:

$$B : A = B_2 : A_2$$

in which B = the actual "before" column of the group, B_2 the average "before" column, and A = the actual "after" column of each group, and A_2 = the reduced "after" column shown in the diagram.

This method, while somewhat cumbersome, was rendered necessary by discrepancies in the sequence of observations. However, it finally gives us a satisfactory curve of the effect of the roentgen ray on the largest group of cases available. We did not include in this curve those cases where our first observation was secured only after they had already had roentgen-ray treatment.

The surgical data has been handled in identically the same manner. A statement of exactly what cases were included in the formation of any of the columns in Figure 1 is given in the Appendix.

As we have mentioned before, the factor of rest continually comes in to obscure our deductions. In the diagram, therefore, we have indicated by shading what proportion of the cases were receiving complete or partial rest, and what proportion were leading their usual life.

Effect of Rest.—The first two columns in the diagram show that a group of cases observed at the beginning of a period of complete rest in bed had an average metabolism of + 81 per cent., and that after from one to three weeks the same group had an average of + 67 per cent. A study of the individual metabolism curves of the several cases shows that this drop is a very common, though not inevitable, occurrence. In a few of the more toxic cases, the curve rose in spite of complete rest. It will further be seen on such study that the fall is not progressive. After a time a level is usually reached, and rest alone will not cause a further drop. There is not a single patient in the series whose metabolism was brought to within normal limits by rest alone. These remarks apply to rest in bed over periods of weeks. They do not apply necessarily to rest extending for months or years. We have no observations on the effect of such prolonged rest.

Effect of Quinin Hydrobromid.—We have not studied the action of quinin hydrobromid thoroughly, nor over any long period. Its action when added to that of complete rest over periods of from one to three weeks is shown by the second pair of columns in the diagram. The average metabolism of this group before taking the drug was + 58 per cent. and after taking the drug it was + 47 per cent., a fall no greater than that accomplished by rest alone.

Effect of Roentgen Ray.—The series of roentgen-ray observations are distinctly interesting. The first column, that before treatment was begun, shows an average metabolism of + 63 per cent. At that time a little less than half the patients were getting complete rest, a little less than one-fourth were getting partial rest, and the remainder were following their normal mode of life. The second column, that after one or two treatments, shows a reduction to + 52 per cent. for the group, with relatively rather more of the patients getting complete rest than in the first. After from three to five treatments there is a slight drop, and after six or seven treatments there is a greater drop, with rest playing a lesser and lesser part. Finally, two or three years after the fifth treatment, the group average metabolism is only + 13 per cent. and all the patients are leading normal lives.

Under roentgen-ray treatment, then, the group, as a whole, showed a progressive improvement as measured in terms of the metabolism.

Effect of Surgery.—The group average before lobectomy was + 46 per cent. At that time all the patients were getting complete rest in bed. During the first fortnight after operation there is a very extraordinary fall to + 21 per cent. The next two columns, however, show a secondary rise up to the fourth month after operation. From then on there is a progressive fall, until in the third year the average is + 13 per cent. and all the patients are back leading normal lives. The marked fall in the metabolism immediately after lobectomy, followed by a secondary rise, is very common, though not, as will be seen by studying the individual curves, invariable. It may be due in part to the disturbance caused by the patients leaving the hospital and returning home, but this is not the sole cause, for some increase occurs while they are still in the wards.

Roentgen-Ray Therapy and Surgery Compared.—In the third year, after treatment was well established, the end results in the surgical and roentgen ray groups are identical, namely group averages of + 13 per cent. in each case, with all patients leading normal lives. With the roentgen ray group the improvement was gradual but progressive; with the surgical group there was a sudden marked improvement and a subsequent relapse. The factor of rest was distinctly greater in the surgical group than in the roentgen ray group, yet no more ultimate benefit was, apparently, secured. Moreover, before treatment was begun, the roentgen ray group had a much higher average toxicity than the surgical group, there being an increase in the metabolism of 63 per cent. in the former as against 46 per cent. in the latter. However, since all the surgical cases were resting before operation, while only a part of the roentgen ray cases were resting, the surgical group might be thought to be actually composed of more severe cases than the roentgen ray group. As a matter of fact, this is not true, however, for the highest metabolism observed in the former group, before the rest period had started, gives an average of only + 61 per cent., which is lower than that of the roentgen ray group before treatment.

It would seem to us, from a study of these results, that the chance of cure in exophthalmic goiter is as good with roentgen-ray treatment as with surgery, in groups of cases of equal toxicity, and that being true, the former method is the preferable, for the danger of fatal outcome is less. Of the nine known deaths occurring in our original series of fifty-five cases, five were directly the result of surgery (Cases 23, 52, 77, 160 and 161). One patient (Case 10) after prolonged roentgen-ray treatment finally died apparently of exoph-

thalmic goiter. Three patients died of unknown causes; one of these (Case 126) after having apparently been cured by operation, one (Case 21) after having apparently been cured by the roentgen ray, and one after failure to improve materially under roentgen-ray therapy (Case 113).

We have given due consideration to the matter of the possible relationship of duration to the improvement in the roentgen ray and surgical groups. It must be admitted that there is a very definite tendency toward spontaneous recovery in exophthalmic goiter. To what extent the improvement in our two groups must be attributed to the natural course of the disease is an unanswerable question. The average duration of the roentgen-ray group in the spring of 1919 was about five and one-half years, while that of the surgical group was about three and one-quarter years. Whether the longer duration in the roentgen-ray group was an important factor in their progress, we cannot say. The lack of relation between duration and end result in individual cases makes it seem unlikely.

Relation of Metabolism to Other Factors.—Up to the present point our discussion has hinged almost entirely on the basal metabolism. The clinical progress, however, has been indicated in the tables. Before closing, it will be well to consider briefly the relation of metabolism to other factors, such as body weight and pulse rate. The respiratory quotients, the blood picture and pathologic findings we intend to study further, and if anything of interest is found it will be reported later.

We have already indicated in our earlier paper² that between the basal metabolism and the clinical picture there is a close parallelism. Subsequent observations have for the most part borne this out, although there are occasional exceptions.

To see what, if any, relationship there is between metabolism, weight and pulse, we have plotted these factors in all cases in which five or more observations have been secured. It is not worth while to encumber the present paper with these charts. It may be said, however, that in about 60 per cent. of the cases so charted, there is a close parallelism between pulse and metabolism, and in the remainder a certain amount of parallelism. This is what one would expect, and indicates that in any given case the resting pulse rate is a tolerably good index of the patient's progress. The pulse rate, however, gives comparative results only, for between the metabolism elevation and pulse elevation of different individuals there seems to be but little relationship. The pulse rate, therefore, is not an index of the absolute degree of intoxication in the patient seen for a single time, but it does furnish a relative index in a patient seen at different times.

One would also suppose that the curve of body weight would also bear a definite relationship to the metabolism curve, that when the metabolism fell the weight would increase, that, in other words, the curves would be reciprocal. In about 20 per cent. of the cases there is some evidence of such a reciprocal relationship, but in the rest there is not. Indeed, in some cases we find the exact opposite, the weight increasing with a rising metabolism and vice versa.

The matter of the relationship of metabolism elevation to blood sugar has been discussed by one of us (J. C. A.) in an earlier paper.²³ We have restudied these sugar curves in the light of the present end result data to see whether any information of value in prognosis could be got from the height of the hyperglycemia. No constant relationship of sugar curve to end result could be demonstrated.

Metabolism as a Guide to Treatment.—One may ask, what is to be learned from these studies in regard to the indications for treatment in exophthalmic goiter?

In the first place, as just stated, it seems clear that the majority of patients ultimately do as well with roentgen-ray therapy as with surgery, and that with less hardship to themselves. This being true and in view of the not infrequent fatal outcome of surgical operations on the thyroid, the roentgen-ray form of treatment would seem to be the method of choice. We do not mean by that that surgery is never indicated. Such cases as No. 93 and No. 121 that failed to improve under roentgen-ray therapy and promptly recovered after operation prove that surgery may be necessary. It will, however, be interesting to note in this connection that of a total of twenty-four patients who were operated on, nine had had more or less roentgen-ray treatment before surgery was done. In our diagram the group of columns illustrating the effect of the roentgen ray includes only those patients who received roentgen-ray treatment and rest alone; the group of columns showing the effect of surgery, on the other hand, includes patients who had had roentgen-ray treatment before operation. In this connection we should also like to call attention to the fact that none of the five patients who died following operation had received²⁴ roentgen-ray treatment beforehand. It is further interesting to note that in the ten postoperative cases in which we have from two to three year end result observations, the basal metabolism of five patients who had roentgen-ray treatments before operation (Cases 71, 88, 93, 121 and 143) averaged +6 per cent., while that of five patients who were operated on without previous roentgen-ray treatment²⁴ (Cases 106,

23. Denis, W., and Aub, J. C.: Blood Sugar in Hyperthyroidism, Arch. Int. Med. 20:964 (Dec.) 1917.

24. This statement is not absolutely true, for a few of these patients had received one roentgen-ray treatment before operation. A single treatment, however, is not of great moment and can be disregarded.

125, 129, 148 and 151) averaged +20 per cent. The metabolism of the former group of five averaged +44 per cent. before operation and that of the latter +50 per cent. While the two groups started about evenly, therefore, at the end of two years the group in which surgery was preceded by roentgen-ray treatment showed a far better result than the group in which surgery alone was done.

In view of all this, it seems clear that not only should the roentgen ray be tried first in the management of exophthalmic goiter, with the idea that it may be sufficient to cure the patient, but also because if not alone sufficient to cure, it may render subsequent operation safer, and more likely to be followed by good end results. Surgery, we believe, should be employed with conservatism, and usually only after the roentgen ray and other medical measures have failed. We also believe that after operation, if the metabolism remains elevated, the roentgen ray should again be employed. A case in point is that of (Case 99) Miss M. T. P. with whom no great fall in metabolism was secured by operation but who later definitely improved under roentgen-ray treatment.

In this connection we wish to state that we believe that the roentgen-ray treatment of the thymus is quite as important as that of the thyroid. In the cases that come to operation it seems possible that the safety imparted by previous roentgen-ray treatment is due in some measure to the effect on the former gland.

Numerous writers have felt that the sudden deaths following operations on the thyroid were of thymus origin. Kocher,²⁵ Halsted⁹ and others have performed thymectomies with favorable results. Klose²⁶ and others have shown that involution of the thymus follows irradiation. Treatment of the thymus by the roentgen ray, therefore, to our minds, should form a part of the pre-operative treatment of exophthalmic goiter. Exposure of the thyroid, we believe, should also be carried out. That roentgen-ray exposures of the thyroid render operations much more difficult through the production of adhesions between gland and capsule, is denied by Dr. C. A. Porter.²⁷

Can we now go a step further, and find in these metabolism studies anything that enables us to predict what patients probably will come to operation, and in which ones operation is contraindicated? We believe we can.

A study of the relation of pulse curve to metabolism curve in individual cases shows two fairly definite types: Type 1 in which

25. Kocher, T.: Die Behandlung der Basedowsche Krankh., München, med. Wchnschr. **13**:680, 1910.

26. Klose, H.: Beiträge zur Pathologie und Klinik der Thymusdrüse. Jahrb f. Kinderh. **78**:653, 1913.

27. Porter, C. A.: Personal Communication.

the pulse rate (when plotted in a uniform way with a base line of a pulse rate of fifty and a normal metabolism, and a top line of a pulse rate of 150 and metabolism \pm 100 per cent.) runs ten or more points above the metabolism curve, and Type 2 in which the pulse curve coincides with, or runs below, the metabolism curve.

Eppinger²⁸ gives an extreme tachycardia as one of the characteristics of the sympatheticotonic type, while a moderate tachycardia occurs in the vagotonic, and that latter type is presumably that in which there is most pronounced thymus involvement. Without entering into the discussion as to whether two such types actually exist, it occurred to us that it would be well to compare the end results in those of our cases that had an extreme tachycardia and a moderate metabolism elevation on the one hand (Type 1) with those that had an extreme metabolism elevation and a moderate tachycardia (Type 2) on the other hand. For this purpose, belonging to Type 1, we have Cases 66, 71, 88, 93, 110, 135, 143 and 129, and belonging to Type 2, Cases 33, 48, 121, 123, 125, 148 and 151. A study of the end results in these cases shows that the patients of Type 1 did about equally well with surgery or roentgen ray alone, or with surgery preceded by roentgen-ray treatment, while with Type 2 surgery alone gives poor results, the roentgen ray alone may cure, but the roentgen ray followed by surgery may be necessary in the more resistant cases.

Of the five patients who died following operation, four (Cases 23, 52, 160 and 161) belonged to Type 2, and only one (Case 77) belonged to Type 1. The chance of postoperative death, therefore, seems greater in Type 2, at least when roentgen-ray treatment has not been given beforehand.

An apparent contraindication to operation was found in a metabolism rising in spite of the fact that the patient was getting complete rest in bed at the time.

CONCLUSIONS

The conclusions drawn in our first paper are borne out by subsequent work. In addition, we should like to say that using the basal metabolism as an index of toxicity in exophthalmic goiter we have found that:

1. In the majority of cases the results after two or three years are equally good with roentgen-ray treatment as with surgery.
2. That after surgery the metabolism shows a rapid preliminary fall, a secondary rise followed by a final fall, that with roentgen-ray treatment there is a gradual progressive fall.

28. Eppinger, H., and Hess, L.: *Vagotonie, Sammlung Klinischen Abhandlungen über Pathologie und Therapie der Stoffwechsel von Noorden*, Nos. 9 and 10, Berlin, 1910.

3. That in securing the same end results with surgery or with the roentgen ray, a lesser rest factor is necessary with the roentgen ray. With the roentgen ray there is practically no mortality. With surgery there is a definite one.

4. That patients treated surgically do better, and the risk of operation is less, if they have previously had their thyroid and thymus glands irradiated.

5. That the risk of operation is greater and the need for pre-operative roentgen-ray treatment is greater in cases with a very high metabolism and moderate tachycardia than in those with an extreme tachycardia and moderate metabolism elevation.

6. That the safest program for the treatment of exophthalmic goiter, as a whole, is the routine irradiation of thyroid and thymus glands, in all cases, with surgery held in reserve for patients who do not then do well.

7. That surgery is contraindicated with patients whose metabolism is rising in spite of complete rest in bed, and also with patients of the type with moderate tachycardia and great metabolism increase, except when they have previously had thyroid and thymus glands treated by the roentgen ray.

8. Finally, we believe that in the management of exophthalmic goiter, periodic determination of the basal metabolism should be quite as much a routine as is the examination of the urine for sugar in diabetes mellitus. Further, that in borderline cases the basal metabolism furnishes very valuable aid in differential diagnosis.

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APPENDIX

The columns shown in Figure 1 are made up of observations on various cases as follows:

Rest Series: Cases 10, 88, 111, 121, 137, 151.

Quinin Hydrobromid Series: Cases 3, 77, 99, 117, 126, 130, 131, 135, 160, 161.

Roentgen-Ray Series:

From one to two treatments.—Cases 10, 21, 48, 93, 110, 111, 113, 120, 121, 123, 131, 135.

From three to five treatments.—Cases 21, 25, 33, 53, 66, 93, 107, 110, 111, 113, 120, 121, 123, 156.

From six to seven treatments.—Cases 12, 25, 33, 48, 53, 66, 110, 123, 135.

Ten or more treatments.—Cases 10, 48, 66, 111.

From two to three years after the fifth treatment.—Cases 33, 48, 66, 110, 111, 123, 135.

Surgical Series:

First fortnight.—Cases 71, 83, 88, 93, 117, 121, 125, 126, 137, 143.

Second fortnight.—Cases 3, 88, 93, 99, 106, 117, 125, 126, 143, 151.

Second and third months.—Cases 71, 83, 88, 93, 99, 106, 117, 125, 126, 130, 137, 143.

From fourth through ninth month.—Cases 71, 88, 99, 106.

From tenth through twenty-fourth month.—Cases 3, 16, 88, 93, 126.

Third year.—Cases 71, 88, 93, 106, 121, 125, 129, 143, 148, 151.