

EFFECT OF HYPERTHYROIDISM UPON DIABETES MELLITUS

STRIKING IMPROVEMENT IN DIABETES MELLITUS FROM THYROIDECTOMY

BY FREDERICK A. COLLER, M.D.

AND

C. B. HUGGINS, M.D.

OF ANN ARBOR, MICH.

FROM THE DEPARTMENT OF SURGERY, MICHIGAN UNIVERSITY HOSPITAL

WE WISH to emphasize the remarkable improvement in carbohydrate tolerance following subtotal thyroidectomy in diabetes mellitus complicated by hyperthyroidism, and to discuss important factors in the management of this problem, more particularly from a surgical viewpoint. This specific syndrome has in the past been attended with a high mortality which has now been almost eliminated since both conditions can be improved to a point where operative removal of portions of the thyroid can be done without undue risk.

Diabetes mellitus is a condition in which less than the normal amount of glucose can be oxidized in a unit of time. When the fat burned is more than four times the glucose burned acidosis occurs. If the diet does not supply the total calories, the extra calories of the metabolism are derived from body fat. In hyperthyroidism with its high metabolic rate, the total metabolism may be twice that of the ordinary diabetic patient, accordingly, when these two conditions exist together the usual diabetic diet may supply half or less of the calories consumed and the remainder will come from the patient's body fat. The entrance of this very large amount of fat into the metabolic mixture, combined with the inability to oxidize a sufficient amount of glucose (because of the diabetic state), results in acidosis. The use of insulin in amounts sufficient to cause the combustion of the proper amount of glucose on one hand, and the lowering of the metabolic rate by iodine on the other hand, work together to bring the patient to a safe condition for operation.

The literature bearing upon the subject has been reviewed recently from a clinical metabolic standpoint by Wilder¹ and from an experimental viewpoint by Allen.² The surgical aspects of this problem have not been comprehensively dealt with, although occasional case reports have appeared. The surgical attack on the thyroid has been carried out on (a) normal glands, (b) adenoma with and without hyperthyroidism and (c) exophthalmic goitre.

O'Day,³ encouraged by the improvement in sugar tolerance by thyroidectomy in four diabetic patients with exophthalmic goitre, operated upon the thyroid of two young patients with diabetes but with "no goitre symptoms" and reported restoration of normal carbohydrate tolerance in one, and nine ounces of carbohydrate a day in the other. Crile,⁴ in a fascinating article on the "kinetic drive," described a series of operations on a patient with severe diabetes consisting of section of both cervical sympathetic

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trunks, left suprarenalectomy and partial thyroidectomy with some improvement in sugar tolerance of a patient without evident thyroid disease. Fitz⁵ was not particularly encouraged by the results of operation in this group of cases, although his observation led him to believe that "occasionally an operation may not only prolong life but be of greater benefit." He describes five patients with non-toxic goitre on whom thyroidectomy was done without mortality or benefit to the diabetes; six patients with exophthalmic goitre with one operative death, and six with adenomatous goitre with hyperthyroidism with one death. The diabetes was greatly benefited in one case of exophthalmic goitre and in three cases of adenomatous goitre. The results reported by Fitz and our own which confirm his findings in cases of diabetes mellitus and adenomatous goitre without hyperthyroidism as well as the experimental work of Allen lead us to the conclusion that the removal of a normal thyroid or a goitre without hyperthyroidism will not benefit the associated diabetes mellitus. Wilder¹ analyzes 15 cases of exophthalmic goitre and 23 cases of adenomatous goitre with hyperthyroidism associated with diabetes mellitus. Thirty-three of these cases were operated upon without a death and he concludes that thyroidectomy is almost always followed by a considerable gain in sugar tolerance. He finds that diabetes mellitus complicating hyperthyroidism does not exceed 1.1 per cent. being more frequent in the adenomatous group, 2 per cent., than in the exophthalmic group 0.6 per cent.

Rohdenburg⁶ reports thyroidectomy in two cases of exophthalmic goitre with diabetes with improvement in the latter condition.

Dyas⁷ reports three cases of exophthalmic goitre with glycosuria and probable diabetes treated by thyroidectomy without death. All cases remained sugar free following operation on unrestricted diet during a period of observation of several weeks. Unfortunately no blood sugar studies are given.

Buchanan⁸ reports a case of diabetes mellitus complicated by hyperthyroidism with thyroidectomy and great improvement in carbohydrate tolerance.

Hubbell⁹ briefly mentions a case operated upon with improvement in diabetes.

Falta¹⁰ reports irradiation of the thyroid in six cases of exophthalmic goitre with diabetes and apparent improvement in the carbohydrate tolerance in four of them.

Glycosuria of a mild and transient nature occurring with hyperthyroidism has been described frequently in the literature and was encountered often in our experience. Fasting hyperglycæmia is a rare occurrence; although a high normal value is frequently seen. Alimentary hyperglycæmia following a test meal is frequent. There is no close relationship between the severity of the hyperthyroidism as determined by the basal metabolic rate and the hyperglycæmia. The curve obtained following sugar ingestion is that of the emotional type. In the University Hospital is a large diabetic clinic and all cases with hyperglycæmia are carefully studied there. The cases described in this report were referred to us from this group as cases of diabetes mellitus.

Since June, 1924, there have been 1150 cases of diabetes mellitus treated in this clinic. Of this number 12 cases were complicated by hyperthyroidism. All were treated by operation with one death. Eleven of these cases were adenomatous goitre with hyperthyroidism and one was a case of exophthalmic goitre. Many facts can be demonstrated by the report of a typical case:

CASE I.—(No. 160,668) *admitted in diabetic coma: insulin with prompt improvement, continuation of medical treatment for several weeks. Subtotal thyroidectomy. Apparent cure of diabetes.*

Mrs. S., housewife, age thirty-one, had increased thirst and polyuria for two months

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with loss of 15 pounds in weight associated with a moderate degree of nervousness and palpitation. One week before entrance she felt drowsy, became irrational and was brought to the hospital for treatment. Examination showed confused mental state, Kussmaul hyperpnœa, sweating, a small goitre and tachycardia. She was considered to be in extremis. The urine contained large quantities of sugar and the acetone bodies. The plasma CO₂ combining power was 24 volume per cent. The blood sugar 267 mgm. per 100 c.c. She was treated with the usual anti-coma methods with considerable improvement for several days. It was then more clearly seen that there was a definite nervousness, tachycardia and sweating and hyperkinesis. A basal metabolic rate was

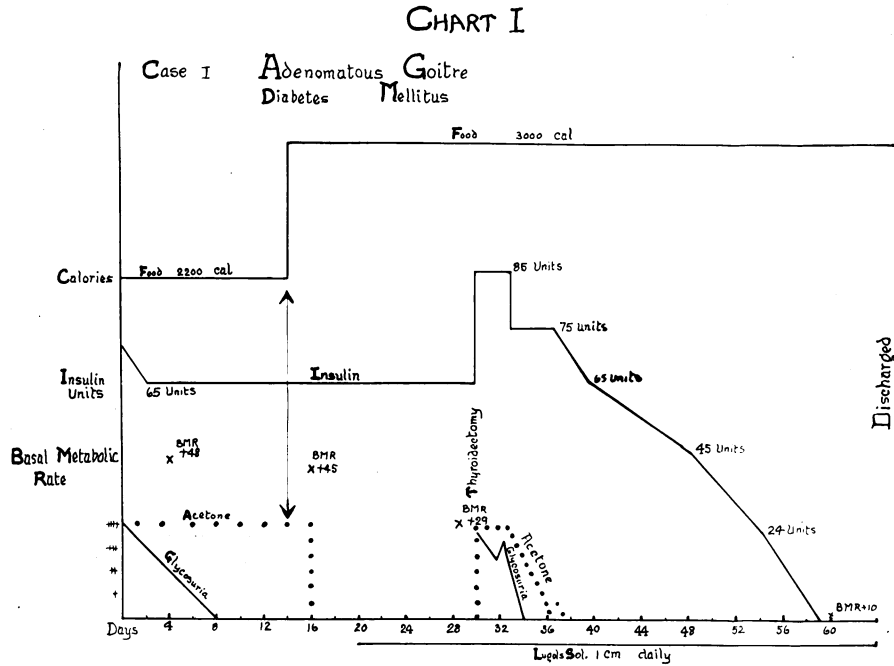


CHART I.—This chart illustrates the effect of diet on acidosis; and of operation on carbohydrate tolerance, basal metabolism, insulin requirements, and acidosis.

45 per cent. plus. She was treated with a diet of protein 55, fat 170, carbohydrates 45, supplying 2200 calories and 65 units of insulin were required daily. She immediately became sugar free except for a faint trace. Diacetic acid remained in the urine in large amounts. The diet was changed to protein 60, fat 275, carbohydrate 75, supplying 3000 calories and the urine became acetone free. After seventeen days of study and treatment she was given compound solution of iodine, one c.c. daily for nine days with a resulting drop in the basal metabolic rate to 29 plus. Subtotal thyroidectomy was done and followed by an uneventful convalescence except for a glycosuria and acetonuria for four days. The insulin dosage was gradually reduced so that on the twenty-third post-operative day she remained sugar free for the first time without insulin on a diet of 3000 calories. She was discharged on this diet and has gained steadily in weight and strength. She has an occasional transient glycosuria. The glucose tolerance curve, typical of diabetes mellitus before operation did not vary essentially following it.

This case illustrates well the possibility of the restoration to an approximately normal condition of a moribund patient with diabetes mellitus. The progress of the case is shown graphically in Chart I. The chief factor, leading to permanent improvement by operation, after the abolition of the acute

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acidosis was the recognition of the presence of hyperthyroidism. This was not at once apparent since the goitre was very small and the symptoms of tachycardia and nervousness were attributed to the acidosis. Its recognition also gave an important aid in the dietary treatment, as it can be seen in Chart I that a high grade of acetonuria persisted for days after glycosuria had ceased. It could be predicted after the determination of the metabolic rate that the acidosis would disappear by raising the total number of calories, since the original diet was based on a normal metabolic rate and neglected

TABLE I.
Demonstrating the Great Improvement in Hyperthyroidism and Carbohydrate Tolerance Effected by Thyroidectomy.

Case No.	Admission weight	Weight loss in pounds	Time in months	Initial basal metabolism	Pre-operative basal metabolism	Post-operative basal metabolism	Days of iodine	Pre-operative insulin daily in units	Pre-operative diet in calories	Post-operative insulin discontinued	Post-operative diet
1	136	35	8	55	40	16	8	None	2400	3 days	2400
2	125	45	?	49	33	3	12	U.13	2400	25 days	2400
3	115	40	?	54	36	2	21	U.45	2400	18 days	3010
4	114	15	2	48	29	10	9	U.65	3000	22 days	3000
5	113	34	6	49	25	13	20	U.36	2500	7 mos.	2500
6	100	55	11	29	29	6	—	None	House Diet	16 days	2400
7	90	42	3	75	57	—	41	U.90	3000	—	
8	105	64	18	33	8	2	—	None	2330	5 days	2400
9	108	57	10	22	14	2	—	None	2400	7 days	2400
10	125	20	5	72	57	12	13	U.40	3000	15 days	2400
11	106	30	6	45	38	4	19	U.108	3000	29 days	
12	90	17	3	63	33	7	22	U.50	3000	16 days	2400

the 50 per cent. increase in the basal rate that was present. She was living on her body tissues and the calories provided by her fats were insufficiently covered by glucose to be completely burned. As soon as her quantitative caloric requirement was met, the acidosis disappeared. It is especially noteworthy that in the adequate diet the high fat ratio of the diet was maintained. Thus in the diabetic patient an increase of the general metabolism must be met by an adequate diet for the caloric requirements of the body.

Following thyroidectomy there occurs an immediate but brief increase in the metabolism. With all cases there was a mild or moderate glycosuria and acidosis lasting from four to seven days following operation. This indicates the need for more calories in the form of glucose and an increase

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in the amount of insulin at this time. After operation, when the basal metabolic rate has dropped to normal, there is a marked increase in the carbohydrate tolerance. In all cases in the series, insulin, if needed before operation could eventually be dispensed with even with a high caloric diet. This was possible within one month after operation with the exception of Case V, in which the insulin though much reduced could not be entirely dispensed with for seven months. This patient was pregnant in addition to having diabetes mellitus and hyperthyroidism. This improvement in function is well shown in Table I. It must be emphasized that the diabetic state is not cured by thyroidectomy but is improved to such an extent as to simulate a cure. The glucose tolerance tests following the post-operative improvement of function in our series were of the diabetic type. In many of the cases careful dieting had to be followed after operation for an indefinite period.

It will be seen from Table I that two patients were in coma at the time of entrance to the hospital. These cases offer no unusual difficulties either in diagnosis or treatment. Of greater interest to the surgeon is the onset of diabetic coma following thyroidectomy in a supposedly non-diabetic patient. As already stated the entire carbohydrate metabolism is upset by hyperthyroidism and especially by the severe but transitory exacerbation following operation, so that a mild or unrecognized diabetic may have a dangerous and stormy post-operative course. This is illustrated by Case II.

CASE II.—(No. 124,843.) *Adenomatous goitre; mild glycosuria on one occasion before operation. Subtotal thyroidectomy followed by diabetic coma on second post-operative day. Medical treatment. Cure.*

Mrs. B., a housewife of fifty-eight, entered the surgical ward for treatment of goitre and nervousness of three years' standing. She was overiodized before entrance by use of a patent medicine with accentuation of all symptoms during the previous four months. Loss of fifty-eight pounds in ten months. Increased thirst for one year. Examination showed an emaciated elderly woman with an adenomatous goitre of moderate size, arteriosclerosis, pulmonary emphysema, cardiac enlargement and compensated myocardial disease. Basal metabolic rate plus 29 per cent. She was treated with bed rest and a high caloric diet for two weeks. On one occasion there was a moderate glycosuria but on three other examinations the urine was sugar free. The glycosuria was regarded as of the transitory type seen in simple hyperthyroidism and the carbohydrate metabolism was not studied. Subtotal thyroidectomy was done unaware of the presence of diabetes. On the day following the operation she became comatose, developed deep respirations, an acetone breath and a severe glycosuria, acetonuria and hyperglycæmia were demonstrated. She was treated with large doses of insulin and glucose given intravenously with restoration to a satisfactory state. After this 45 units daily of insulin were required for one week. On the eighteenth post-operative day insulin was discontinued and she tolerated a house diet of 2500 calories without glycosuria.

This case demonstrated the need for a careful investigation of the carbohydrate metabolism in all patients with hyperthyroidism and glycosuria. We believe it important in these cases to make a quantitative determination of the excreted sugar on a known diet and of the blood sugar with the standard glucose tolerance test in these cases.

Another complication which arose in the treatment of one of these cases was the confusion of diabetic acidosis with its exaggerated hyperpnœa, cya-

nosis and mental obfuscation with tracheal obstruction. This is illustrated by Case III.

CASE III.—(No. 16,518.) *Severe diabetes and hyperthyroidism. Diabetic coma on two previous occasions. Difficulties in dietary management. Subtotal thyroidectomy. Diabetic coma resembling tracheal stenosis; tracheotomy, broncho-pneumonia, death.*

Mrs. E., a housewife of forty-four, had noticed thyroid enlargement for eleven years with thyroidism for the past twelve months. Two months before entrance she had polydipsia and polyhagia. Diabetic coma occurred with treatment by local physicians who were later unable to control diabetes. She had lost forty-two pounds in four months. Examination showed an emaciated, very nervous woman with hyperpigmentation of the skin and a large solitary adenoma of the thyroid. Basal metabolic rate plus 90 per cent. Typical diabetic glucose tolerance curve. CO₂ combining power of plasma 30 volumes per cent. Intense glycosuria and acetonuria. She was placed on a diet of 2600 calories with 100 units of insulin daily. There was considerable nausea, vomiting, diarrhoea, epigastric pain with attacks of dyspnoea and precordial distress. The urine could not be kept consistently free of acetone or glucose. She developed broncho-pneumonia which added to the difficulties of treatment but which cleared up in twelve days. Eventually she began to gain weight on a diet of 3000 to 5000 calories with large doses of insulin. The compound solution of iodine was given, one c.c. daily for forty days. The basal metabolism then had fallen to plus 57 per cent. and she was less nervous. A subtotal thyroidectomy was done easily and rapidly under ethylene anaesthesia. On the evening of the operation the respirations became labored and she became cyanotic and comatose. An emergency tracheotomy was done by the house surgeon without relief of symptoms. The subsequent administration of glucose and insulin restored the breathing to a normal state. Bronchopneumonia again developed and she died in four days. Autopsy showed a chronic atrophic interstitial pancreatitis; broncho-pneumonia; diphtheritic infection of wound; mediastinitis.

This experience, occurring as it did in this series, is recorded with no great feeling of pride to demonstrate the need of wise judgment to prevent confusion between two superficially similar conditions each demanding immediate action. More careful and discriminating clinical observation would undoubtedly disclose the true situation. The important distinction between the two types of respiratory difficulty is the presence of stridor with laryngeal narrowing in the obstructive respiratory condition.

SUMMARY OF CASES *

CASE I.—A Jewish woman of fifty-four, complaining of headaches and hot flashes; symptoms of hyperthyroidism for five months and diabetic symptoms for two months. Examination showed nervousness, an adenoma of the thyroid, and oedema of the ankles. Blood pressure $\frac{170}{88}$. Urine showed a moderate glycosuria and acetonuria on entrance. Secondary polycythaemia. Typical diabetic response to glucose tolerance test before and after operation. Pathological report of thyroid: Multiple adenomas with abundant colloid.

CASE II.—An American woman of forty-six with latent syphilis, hyperthyroid symptoms of one year's duration, had had a moderate diabetes for eighteen months. Coma one week before entrance for forty-eight hours. Blood sugar on entrance 0.200 grams. Diabetic glucose tolerance curve. Diphtheria three weeks after operation. Thyroid pathology: Adenomatous goitre.

CASE III.—An American woman of fifty-five had a large goitre for thirty years with hyperthyroid symptoms of two months' duration. Glycosuria found on routine examina-

* These cases correspond by number with cases in Table I.

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tion. Myocarditis with auricular fibrillation. Lenticular opacities. Fasting blood sugar 0.217 grams. Typical diabetic glucose tolerance response. Pathological report: Adenomatous goitre with abundant colloid.

CASE IV.—See text, Case I.

CASE V.—An American woman of thirty-eight had a goitre for seventeen years, diabetes mellitus nine years; hyperthyroid symptoms one year. Hypertension. Two months' pregnancy at the time of operation. Glucose tolerance of the diabetic type. Excreted 26 grams of glucose on 2400 calorie diet without insulin. Pathological report: Multiple adenomas; localized patches of lymphoid hyperplasia. This patient needed insulin until after parturition to cover a high maintenance diet. This was then discontinued. She has gained 26 pounds in one year.

CASE VI.—See text, Case II.

CASE VII.—See text, Case III.

CASE VIII.—A Jewish housewife of fifty-two had a goitre for ten years with diabetic symptoms for eighteen months. Severe glycosuria on entrance with a moderate acetonuria. Auricular fibrillation and chronic myocarditis. Evidence of manic depressive psychosis while in the hospital. Fasting blood sugar 0.160 grams. Typical diabetic glucose tolerance response. Pathological report: Adenomatous colloid goitre.

CASE IX.—A male American paint sprayer of fifty-three had symptoms of diabetes for one year with nervousness. Onset was of rather severe hyperthyroidism five months ago. Neuroretinitis. Intense glycosuria on house diet. Fasting blood sugar 0.166 grams. Typical diabetic glucose tolerance curve both before and after operation. Pathological report: Graves' constitution adenomatous thyroid.

CASE X.—An American housewife of fifty-nine had a goitre for many years; nervousness, tachycardia, fatigue for three months. Examination showed an orange-sized adenoma of the left thyroid lobe, cardiac enlargement, signs of hyperthyroidism with marked tracheal compression. Typical diabetic glucose tolerance response. Intense glycosuria on a house diet. Pathological report: Colloid goitre with large degenerating adenomas. Auricular fibrillation for one week following thyroidectomy but an otherwise uneventful convalescence.

CASE XI.—An American housewife of forty-five complained of headache, loss of weight and slight œdema of the extremities. Mild hyperthyroidism for six months. Examination showed a large adenoma of the thyroid; neuroretinitis with arteriosclerotic changes. Typical diabetic glucose tolerance curve. Intense glycosuria and acetonuria on entrance. Pathological report: Adenomatous goitre.

CASE XII.—An American schoolgirl of sixteen had symptoms of diabetes for three months, with severe symptoms of hyperthyroidism in the same period following a severe emotional upset. Examination showed a chronic bilateral otitis media in addition to the classical picture of Graves' disease. Diabetic glucose tolerance curve. Marked glycosuria on entrance. Pathological examination of thyroid; exophthalmic goitre.

SUMMARY

1. Great improvement of carbohydrate function follows thyroidectomy in the syndrome of hyperthyroidism and diabetes mellitus. This is probably never a "cure" of the latter condition.
2. Thyroidectomy does not benefit carbohydrate tolerance in non-toxic thyroid states.
3. Glycosuria occurring in hyperthyroidism is an indication for study of the carbohydrate metabolism. Coma may result as a post-operative complication of thyroidectomy consequent upon an unrecognized coexistent diabetes mellitus.

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4. Care must be taken to rule out diabetic coma in cases of suspected tracheal obstruction.

5. Acidosis frequently results in hyperthyroidism with diabetes due to an insufficient number of calories provided in the diet.

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