REPORT OF A CASE OF HYPERTHYROIDISM

which was associated with obesity, arteriosclerotic and hyperthyroid heart disease, severe diabetes mellitus, a febrile response to iodine, and possible undulant fever, and in which the diabetes was completely controlled without insulin following thyroidectomy.

E. J. RYAN, M.D.

A sixty-one year old white woman presented herself at the Clinic in July, 1939, complaining of "heart trouble." For the preceding eight or nine years she had had attacks of rather rapid and irregular heart action, the patient herself being conscious of the irregularity. At first these had occurred at rare intervals of once or twice a year, but as time passed, they were noted with increasing frequency. During the preceding year she had had four or five such episodes, the most recent of which had lasted for six weeks. Effort dyspnea, orthopnea, vertigo and tinnitus were denied. Slight swelling of the left ankle had been noted for only a few days. Moderate pain in the left side of the chest was considered to be muscular in origin.

Enlargement of the anterior neck had been present for four or five years, and nervous tension had gradually increased during the preceding year. Obesity had been present for a long period of time and there had been no recent weight loss. Appetite alteration, hyperhidrosis and heat intolerance were denied.

In the light of subsequent developments, it is also interesting to note that no history of glycosuria, polydipsia, polyuria or fever was elicited.

The patient was restless, apprehensive and uncooperative. The height was sixty-four inches and the weight on admission was 237 pounds. The temperature was 98.2° F. The thyroid gland was moderately enlarged and nodular. A fine tremor was present. The right breast had been removed thirty years previously. Auricular fibrillation was present with an apical heart rate of 168 beats per minute and a radial pulse rate of 128. The left border of cardiac dullness was 12 cm. to the left of the midsternal line. A systolic murmur was audible at the pulmonic area. The blood pressure was 174 systolic and 88 diastolic. There was definite peripheral vascular thickening. Slight pretibial edema was noted. The lungs were clear and the abdominal examination was negative.

Urinalyses and blood counts were normal. The serologic reactions of the blood were negative. The blood sugar four hours postprandial was 142 mg. per 100 cc. The basal metabolic rate was plus 18 per cent. A roentgenogram of the chest revealed cardiac enlargement with fibrous infiltration at the hilum of each lung, and extension into the peripheral zone. An electrocardiogram confirmed the auricular fibrillation noted clinically, and an occasional ventricular premature contraction was present.

The patient was seen initially in the Department of Cardiology, where diagnoses were made of (1) nodular goiter with hyperthyroidism, (2) hyperthyroid-arteriosclerotic heart disease, functional capacity class 2, with enlargement of the heart, auricular fibrillation, and early congestive heart failure, and (3) obesity. She was seen in consultation by a member of the Surgical Division, who concurred in the diagnosis of low-grade hyperthyroidism, but with the reservation that further studies should be carried out after rest and digitalization. Determination of the diabetic status was deferred temporarily.

She returned three weeks later after digitalization and rest. Subjectively there had been very little change. Auricular fibrillation still was present, but the apical rate had fallen to 134 and the radial rate to 84. The basal metabolic rate was plus 37 per cent, and the fasting blood cholesterol was 134 mg. per 100 cc. The administration of digitalis was maintained in dosages of one and one-half

grains of the dried leaf daily; fifteen minims of Lugol's solution three times a day were prescribed, but it is very doubtful that the patient followed this recommendation. In another three weeks, she was admitted to the hospital for thyroidectomy.

In the hospital the usual preoperative routine of sedation, rest, and fifteen minims of Lugol's solution three times a day were prescribed. The temperature was normal on admission, but gradually rose and reached 101.8° F. (Chart 1) on the fifth hospital day. At that time, she noted nausea, generalized aching, and coryza. The latter condition was considered causative at first, but when it subsided and the fever continued, an undulant fever skin test was done. This was strongly positive. The undulant fever agglutination was negative, and the opsonocytophagic index revealed no phagocytosis. A course of sulfanilamide therapy was carried out without benefit to the patient. The pulse rate increased in spite of therapy.

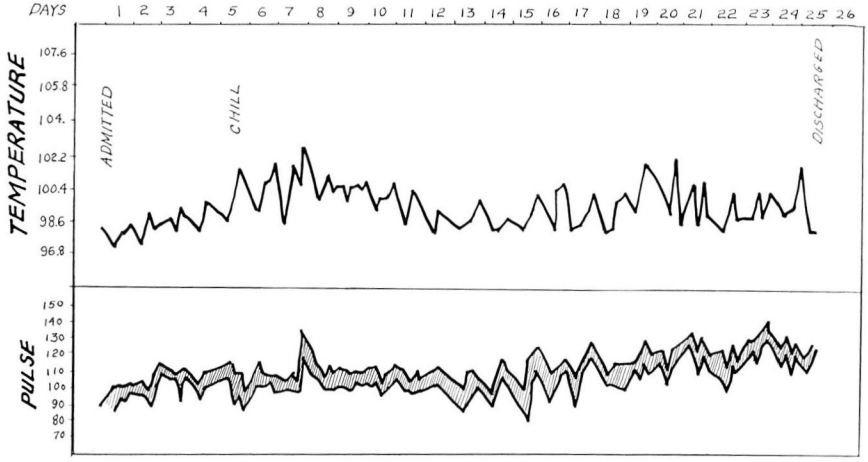

CHART 1: Temperature and pulse curves during hospital stay from August 22 to September 17, 1939.

Her diabetic progress during this period in the hospital is interesting. Because of the obesity, the diet was established and maintained at 1,140 calories daily. Initial blood sugars, fasting or four hours postprandial, ranged from 160 mg. per 100 cc. to 300 mg. per 100 cc. Standard (amorphous) insulin was started in small dosages and was rapidly increased to a total of 90 units in twenty-four hours. In spite of this, moderate hyperglycemia persisted, although glycosuria, which was never conspicuous, disappeared as a result of a relatively high renal threshold. Two days before dismissal, with a total twenty-four hour dosage of 85 units of protamine-zinc insulin and 20 units of standard insulin, blood sugars four hours postprandial ranged from 153 mg. per 100 cc. to 186 mg. per 100 cc. She was asked to continue a careful adherence to a weighed diet of the above caloric value, and to take 95 units of protamine-zinc insulin each morning.

Because the general condition of the patient afforded a contraindication to operation, and because of the possibility of undulant fever, the patient was dismissed on September 16, 1939, to continue therapy at home. Therapeutic recommendations included bed rest, maintenance doses of digitalis, five minims of Lugol's solution daily, and diet and insulin as outlined above. The adminis-

tration of roentgen therapy to the thyroid was to be considered at a later date. The prognosis was not considered good.

Within a few days after returning home, the temperature became normal and subjective improvement occurred. A course of undulant fever vaccine therapy was initiated soon thereafter by her local physician. Improvement in strength progressed and no symptoms of cardiac decompensation were observed. Auricular fibrillation continued. The diabetes remained under satisfactory control in spite of moderate excess over the prescribed diet, and the insulin dosages averaged 75 to 100 units of protamine-zinc daily. The weight fell gradually and in March was 166 pounds, representing a loss of seventy-one pounds in eight months.

The patient was not seen from September, 1939, to March, 1940, progress being reported by members of the family. On the latter date, when again studied, it was clear that the hyperthyroidism still was present, and thyroidectomy was advised. She entered the hospital for operation in June, 1940.

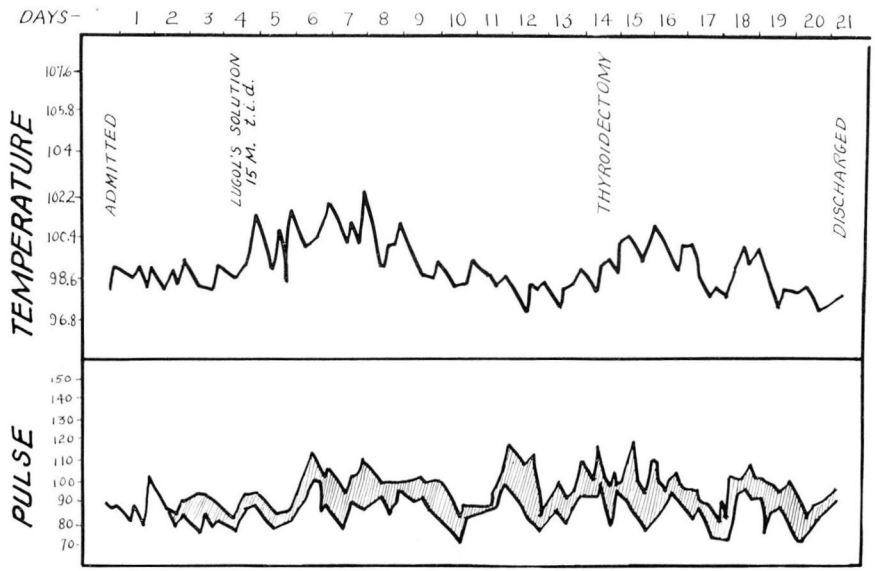

CHART 2: Temperature and pulse curves during hospital stay from June 4 to June 25, 1940.

For the first four days after admission the temperature remained normal. Lugol's solution then was given in dosages of fifteen minims three times a day. On the day after the administration of iodine was started, the temperature began to rise and fluctuated between 98.4° and 102.2° F. for five days (Chart 2). Lugol's solution was stopped on the fourth day of hyperpyrexia and large amounts of sodium chloride were given in an attempt to promote excretion of the iodine. The rise in temperature was considered to be the result of iodine medication. Subsequent small dosages of from five to ten minims of Lugol's solution once daily did not result in a recurrence of the elevation of the patient's temperature. The basal metabolic rate on the thirteenth hospital day was plus 24 per cent. Subtotal thyroidectomy was performed the following day. The convalescence was uneventful.

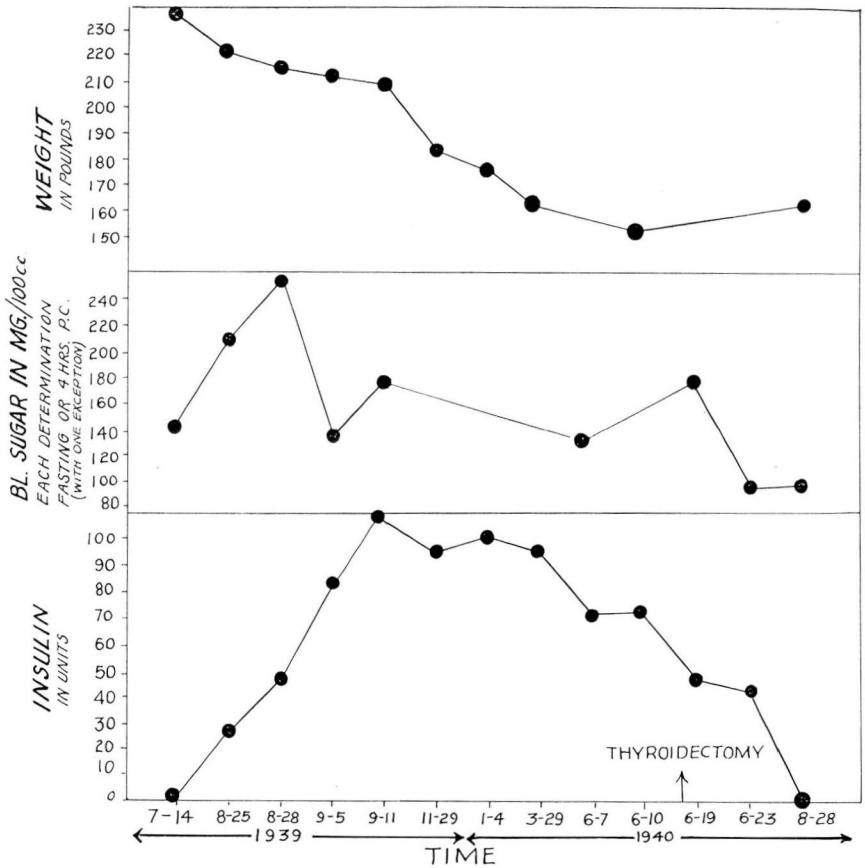

CHART 3: Representative readings showing weight, blood sugar, and insulin shifts from July, 1939, to August, 1940.

The patient continued to have auricular fibrillation during her stay in the hospital (Chart 2). Digitalis was maintained in dosages of one and one-half grains daily during the hospital stay, and after dismissal.

During the preoperative period the diabetes was well controlled on 75 units of protamine-zinc insulin daily, administered in one morning dose. Because of the more normal weight, the diet was increased first to 1,428 calories (carbohydrate content of 160 grams), and subsequently to 1,590 calories (carbohydrate content of 175 grams). Within a day or two postoperatively the insulin requirements fell to 50 units daily, and at the time of dismissal on June 25, 1940, had fallen further to only 40 units daily.

She returned two months later. The only outstanding complaint was of recurrent smothering attacks, which were considered to be of vagotonic origin. Auricular fibrillation was present with a ventricular rate of 80, but there was no evidence of cardiac failure. The basal metabolic rate was minus 12 per cent. The dose of insulin had been reduced gradually and it had been discontinued two weeks before the patient's reentry. Dietary recommendations had been followed moderately well. The fasting blood sugar was 100 mg. per 100 cc., and two and one-half hours after a meal containing 31 grams of carbohydrate, 13

grams of protein, and 14 grams of fat, it was 86 mg. per 100 cc. The weight had increased from 152 pounds a few days postoperatively to 161 pounds. Chart 3 represents in graphic form the weight shift, a few representative blood sugar determinations of the many done, and the insulin requirements. With one exception, all blood sugar determinations were made while fasting, or four hours postprandial.

Sedation was prescribed, digitalis administration was maintained, and she was asked to continue the same dietary program.

Comments

Dr. E. J. Ryan: There are two factors in this case which could have contributed to a decrease in carbohydrate tolerance, and which justifiably raise the question of the presence of true diabetes mellitus. These are hyperthyroidism, and obesity of long standing. The absence of any significant degree of glycosuria likewise may be considered evidence against true diabetes. Because of the hyperthyroidism, hyperlipemia would not be expected and could not be considered of benefit in establishing the diagnosis. Degenerative changes, manifested particularly by rather marked peripheral arteriosclerosis and arteriosclerotic heart disease, favor a diagnosis of diabetes. However, there were no striking retinal changes. Glucose tolerance tests would have been helpful, but were not permitted by the patient.

Because of the relatively mild character of the hyperthyroidism, making the initial diagnosis difficult, and because of the relatively severe diabetes, probably hyperthyroidism occurred coincidentally with or was superimposed upon a true diabetes mellitus. If such were the case, the influence of hyperthyroidism upon the severity of diabetes, particularly as measured by insulin requirements, was strikingly demonstrated. The mechanism by which this action occurs is not understood clearly. Factors other than the thyroidectomy which probably contributed in some degree to the improved diabetic status are correction of the obesity, maintenance of reasonably good diabetic control, and the use of a diet of relatively high carbohydrate content.

Further observation of this patient from the diabetic standpoint is indicated, since it is not uncommon to observe a recurrence of hyperglycemia in such cases. This could be anticipated in this partiular instance should the patient become careless in her dietary regimen with resultant obesity, or should severe infection of any type develop.

At the time of the positive undulant fever skin test, it was felt that this disease was a contributing factor in her requirement for large quantities of insulin. In the light of subsequent developments, it is probable that the febrile course on that occasion was a result of iodine medication, just as it was shortly before operation.

The simultaneous occurrence of obesity and hyperthyroidism has not

been common in our experience. It is dependent, of course, upon a caloric intake which exceeds the individual's requirements, even when the metabolism is materially accelerated as a result of thyroid hyperactivity. Children with Grave's disease not uncommonly gain weight. Management of the obesity in this case differs in no significant respect from the program usually followed for correction of this condition.

Dr. George Crile, Jr.: This case is unusual because of the following features:

1. The patient's febrile response to the administration of iodine.

2. The rapid onset and severity of the diabetes and its complete control following thyroidectomy.

A febrile response to iodine rarely is seen in patients with hyperthyroidism. Barker and Wood[1] reported a group of seven cases which showed this reaction to iodine therapy, an incidence of 1.75 per cent in the 400 cases in their series. This is only the second case we have observed in which fever resulted from the administration of iodine, which disappeared following the withdrawal of the drug, and reappeared when iodine was given again. No explanation of this phenomenon has been made. It is important, however, to bear this reaction in mind when a patient with hyperthyroidism under treatment with iodine develops a fever. Small doses of iodine, such as 5 minims of Lugol's solution three times a day, usually are well tolerated, even when severe febrile reactions have been caused by the larger doses.

Reference

1. Barker, W. H., and Wood, W. B., Jr.: Severe febrile iodism during the treatment of hyperthyroidism, J.A.M.A., 114:1029-1037, (March 23) 1940.