A STUDY OF BLOOD SUGAR CURVES BEFORE AND AFTER THYROIDECTOMY

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The purpose of this paper is to present some interesting blood sugar curves taken before and after thyroidectomy and to study the changes in metabolism incident to surgery, particularly in respect to their bearing on the etiology of diabetes. During the past six years it has been our privilege to study the glycosuria and hyperglycemia occurring in a large number of patients presenting themselves for treatment because of symptoms of hyperthyroidism. In addition we have studied a smaller number of patients who came to us because of symptoms of diabetes but who also presented evidence of hyperthyroidism. In the first group a diagnosis of diabetes was made in a few instances and it is chiefly with these that we are concerned in this paper.

Space will not permit a review of the voluminous literature relative to the combined problem of diabetes and hyperthyroidism. Furthermore, a very complete review was made by John (1) in 1927 and by Lahey and Joslin (2) in 1928. Two previous reviews, one by Fitz (3) in 1921, and later, one by Wilder (4) are also outstanding.

Considerable variance in opinion apparently exists as to what constitutes true diabetes in the presence of hyperthyroidism. Both Fitz and Wilder were extremely cautious not to include any cases in their series wherein there was any doubt as to the presence of diabetes. Joslin and Lahey discarded from their report eleven cases ordinarily classified as diabetes and omitted nine more which they classified as potential diabetes. Their basis for doing so they clearly state: "For the present, therefore, and to avoid premature diabetic cures, we have raised the standard for the diagnosis of diabetes in hyperthyroidism to a blood sugar of 150 mgm. fasting or 200 mgm. or more after meals in addition to glycosuria." They felt that Wilder and Fitz must have used the same diagnostic standards, although this the latter did not specifically state.

Joslin and Lahey consider that hyperthyroidism alone is the factor in disease of the thyroid which leads to glycosuria and is distinctly more important than the accompanying increased metabolism, whereas Wilder states his position as follows: "The phenomena exhibited by patients with true diabetes combined with states of hyperthyroidism or hypothyroidism appear to be related to the general metabolic rate and are therefore susceptible of explanation without recourse to speculation as to a specific

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interdependence of the thyroid and pancreas.'' John, on the other hand, states that the hyperglycemia and glycosuria associated with hyperthyroidism must be regarded as a functional diabetes with a definite disturbance of the insulogenic apparatus and presents evidence from which he concludes that the degree of hyperglycemia bears no relation to the severity of the hyperthyroidism or to the height of the basal rate.

A fundamental piece of work by Sanger (5) in 1922, in which he studied the respiratory quotient in patients with hyperthyroidism and in controls, led him to conclude that the increase in the respiratory quotient after giving glucose proves that individuals with a thyrotoxicosis burn carbohydrates more readily than normal individuals and inasmuch as their blood sugars remain elevated they obviously cannot be storing it. Thyroid fed animals after a certain period of time have very little liver glycogen even though they are fed on high carbohydrate diets.

We have, therefore, in hyperthyroidism, a liver poor in glycogen because of the insistent calls of the muscles for more glycogen because of the increased metabolism. A similar condition exists in diabetes mellitus, a liver low in glycogen, but for another reason, insufficient insulin to enable the liver and muscles to store it. Macleod (6), commenting on the work of Porges and Salomon, in which they determined the respiratory quotient in dogs in which the pancreas had been removed two days previous to the tying of the vessels of the liver, and found quotients ranging from 0.859 to 1.19, remarks that the chief interest of these results is to show that similar changes in R. Q. occur in completely diabetic animals as in normal ones, and when the influence of the abdominal viscera is removed, thus indicating, contrary to the belief of many, that the muscles in diabetes have not lost their power to oxidize carbohydrate. Joslin (7) states that it is becoming more and more evident that it is not so much the lack of the diabetic to utilize carbohydrate as lack of carbohydrate to utilize.

Hyperglycemia is characteristic of diabetes, whereas by no means is it always present in states of hyperthyroidism, as many patients with severe forms of thyrotoxicosis and high metabolic rates exhibit normal blood sugar curves. In patients, therefore, with hyperthyroidism in which hyperglycemia is present, it must be assumed, in order to explain the anomaly, that some disturbance of the insulogenic apparatus must be taking place. Neither Wilder's explanation, that in hyperthyroidism insulin is more rapidly destroyed, nor Sanger's, that toxic changes in the liver cells prevent storage, is satisfactory, else the hyperglycemia would bear a quantitative relationship to the hyperthyroidism.

Let us now consider the opinions of various authorities concerning the diabetic Anlage according to Naunyn's conception. Joslin (1) raises the question as to whether true diabetes ever occurs in hyperthyroidism unless this factor is present and says that one can hardly fail to reach the conclusion that if the diabetic Anlage were present to only a slight degree in

a patient, hyperthyroidism would bring it to the fore. John (8) quotes Naunyn as follows: ''I consider it justifiable to draw the conclusion that the thyroid causes glycosuria only when there exists a predisposition to diabetes.'' And Von Noorden: ''Pure hyperthyroidism in the presence of a fully normal chromaffin system will seldom produce an alimentary and spontaneous transitory glycosuria.'' Wilder (4) expresses himself in this way: ''Patients with no diabetes and consequently with large supplies of insulin, reveal no lack of tolerance for carbohydrates, even when their metabolism is stimulated by extreme grades of hyperthyroidism because their supply of insulin is more than adequate.'' From this statement it might be implied that an abnormal blood sugar curve in the presence of hyperthyroidism suggests a potential diabetes. According to Joslin's statistics, an hereditary history of diabetes can be obtained in only about 25 per cent of diabetic patients. In his cases of hyperthyroidism and diabetes it was 20 per cent. Statistics are always open to question, despite the care with which they are taken, and are notably unreliable. Moreover, as pointed out by Joslin, the diabetic age zone is around 50 years. It is certainly possible that many potential diabetics may well die of other causes before reaching this age, or, having attained this age, an exciting cause of sufficient force may never have presented itself.

The efficiency of a blood sugar curve as a means of detecting a very mild potential diabetes, it has seemed to us, is open to question from the following point of view. May it not be that a diabetic Anlage of such a mild form may be present as to evade detection by our ordinary methods and be brought out into the open only by the development of hyperthyroidism in the patient? The blood sugar curves of two patients with mild diabetes uncomplicated by hyperthyroidism lends support to this contention (Charts 8 and 9).

In our group of true diabetes and hyperthyroidism there are twenty-four patients who were operated upon. Ten of these were of the parenchymatous and fourteen the adenomatous hyperplastic type. There was one death. Following operation, increase in tolerance was rapid and in some cases, remarkable in degree. We have included two patients (Charts 1 and 2) in this group who possibly should be placed in the potential diabetic group. Their histories will be discussed later.

Blood sugar curves before and after operation were determined on a series of twenty selected patients who showed glycosuria in addition to hyperthyroidism. Sections of the thyroid showed eight with parenchymatous and nine with adenomatous hyperplasia, and three with cystic colloid goiters. The blood sugar curves of only five showed failure to go below 150 mgm. at the end of the second hour. There was apparently no relationship between the type of thyroid disturbance in the toxic goiters and the curve.

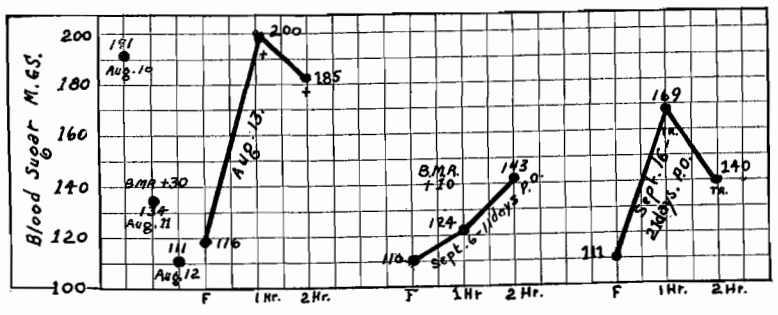
Using the diagnostic standards of Joslin and Lahey for the identification of diabetes associated with hyperthyroidism, we have included two

patients in our series of true diabetes, as stated above, who have shown, following thyroidectomy, return to approximately normal curves.

The first patient, case C. A. D. (Chart 1), age 56, housewife, came complaining of tachycardia, dyspnoea on exertion for two weeks, tremor of the hands for three months and weakness, sweating and loss of about ten pounds in a month. She stated that she had been eating considerable candy for three

CHART I

CASE—C. A. D. PATHOLOGICAL DIAGNOSIS—PARENCHYMATOUS AND ADENOMATOUS HYPERPLASIA

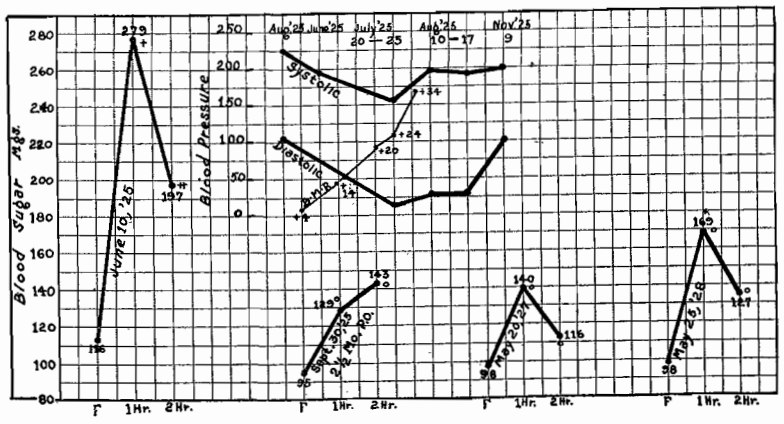


weeks. Sugar was found on routine urinalysis and the following morning her fasting blood sugar was 191 mgm. Reference to the chart will disclose the rapid return to a normal fasting level on a quantitative diabetic diet. The blood sugar curve the following day was certainly in the diabetic range. The basal rate at the same time was +32 per cent. Following removal of the thyroid, and on an unrestricted diet the two curves taken perhaps a little too early can certainly not be called diabetic, nor are they entirely normal. Subsequent curves six months or a year later might have been entirely normal. That this has been our experience in other cases, the charts will show.

The second patient, case H. T. (Chart 2), housewife, age 53, was first seen in September, 1923, because of symptoms referable to hypertension and mod-

CHART II

CASE—MRS. H. T. PATHOLOGICAL DIAGNOSIS—PARENCHYMATOUS HYPERPLASIA



crate obesity. No sugar in the urine was discovered at that time and the fasting blood sugar was 90 mgm. Reference to Chart 2 will show the blood sugar curves on her second admission two years later when she presented symptoms of nervousness, weakness, thirst and polyuria of two months' standing. No

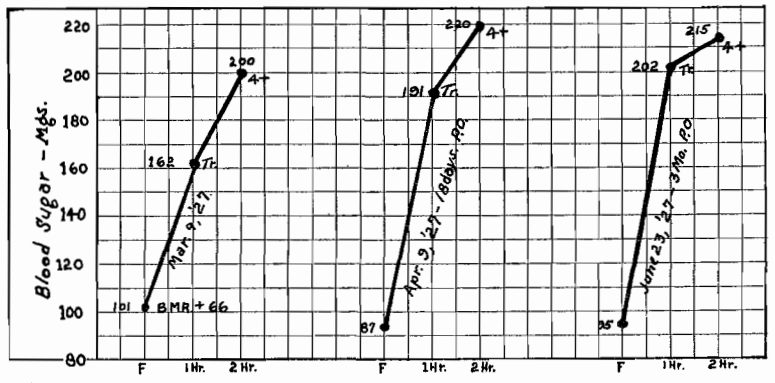
thyroid enlargement could be palpated and her symptoms were thought to be due to hypertension and a mild diabetes. A quantitative diabetic diet low in salt was started and the urine became sugar free immediately. Reference to the chart shows the falling diastolic blood pressure. Coincident with this a capillary pulse was first noticed and an increasing metabolic rate. Further search for a goiter was made and on stereoscopic chest films a substernal enlargement was seen which at operation proved to be a parenchymatous hyperplastic goiter. Two and a half months afterward on a diet unrestricted as to carbohydrate the blood sugar curve returned approximately to normal. Two years later it was entirely normal and a year later it was such as might be considered as representing a latent diabetes.

Wilder (4) mentions that there are a number of case reports in the literature which show return to normal tolerance following thyroidectomy. None of these, however, included blood sugar estimations after glucose meals. Gray (9) in 1923 reported a series of abnormal curves before and normal curves after removal of the thyroid. In Wilder's own case the patient had a fasting blood sugar of 271 mgm. and 60 gm. of sugar in the urine. One year following removal of 15 gm. of hyperplastic thyroid tissue, the curve was 110 mgm. fasting, 168 mgm. at one hour and 160 mgm. at two hours. He believes that on the basis of this evidence this patient had a latent diabetes.

Failure of the curve to return to normal following thyroidectomy is illustrated by case A. McL. (Chart 3). This patient, age 40, housewife,

CHART III

CASE—MRS. A. MCL. PATHOLOGICAL DIAGNOSIS—DIFFUSE PARENCHYMATOUS HYPERPLASIA

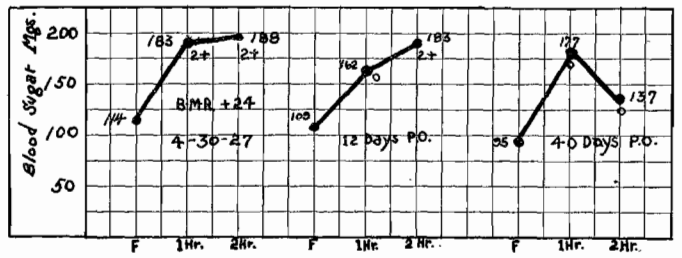


complained of nervousness, loss of weight and tachycardia for six months. No especial thirst or polyuria had been present. Both routine urines contained abundant sugar. Three months after removal of a parenchymatous hyperplastic goiter the curve showed even a higher second hour level than before operation. On the basis of experience in other cases one might have predicted a return to normal tolerance following operation. The results in this patient, however, demonstrate conclusively that one can not always predict the outcome.

A similar type of curve of lesser height is illustrated by case C. M. (Chart 4). This patient, a housewife, age 42, came with symptoms of

CHART IV

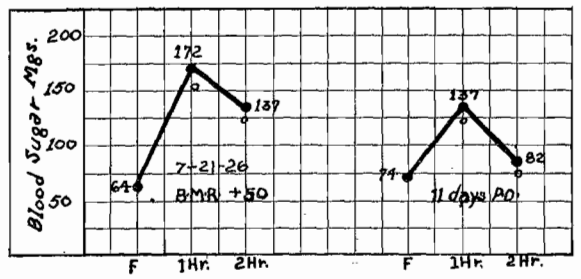
CASE—MRS. C. M. PATHOLOGICAL DIAGNOSIS—DIFFUSE ADENOMATOUS HYPERPLASIA WITH ADENOMATOSIS



nervousness and palpitation of ten months' duration without any of the classical symptoms of diabetes. Although the basal rate was only plus 24 per cent, the curve before operation is that of a potential diabetes. Forty days later it was in the borderline group quite similar to the final curve in case C. A. D. and the initial curve of case W. H. J. (Chart 5). The tendency for the second hour level to drop toward normal would seem to

CHART V

CASE—MRS. W. H. J. PATHOLOGICAL DIAGNOSIS—DIFFUSE PARENCHYMATOUS AND MODERATE ADENOMATOUS HYPERPLASIA



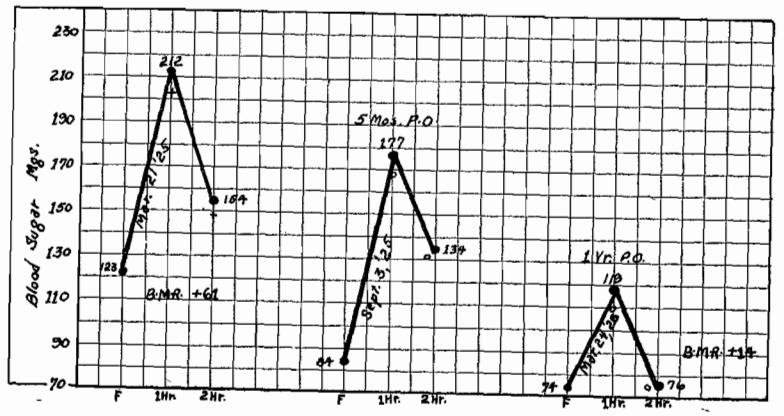
indicate that if a further curve had been taken six months or a year later it would have been entirely normal.

This contention is supported and illustrated quite clearly by the experience in case McC. (Chart 6) whose curve five months after operation is almost identical with that of case C. M. One year after operation it was entirely normal. This patient, age 40, a housewife, operated upon in 1921 for an adenomatous hyperplastic goiter, felt fine for a year; then her neck began to enlarge again and she lost weight. Her mother, age 60, has had diabetes for at least ten years. Here is our diabetic Anlage history clearly present in the mother, but the daughter with a hyperthyroidism in 1921 did not develop a diabetes, as the urines were sugar free at that time. The recurrent hyperthyroidism in 1925 had only a mild effect

on her tolerance despite the high metabolic rate of plus 61 per cent, and the final curve shows no evidence of a disturbed carbohydrate metabolism.

CHART VI

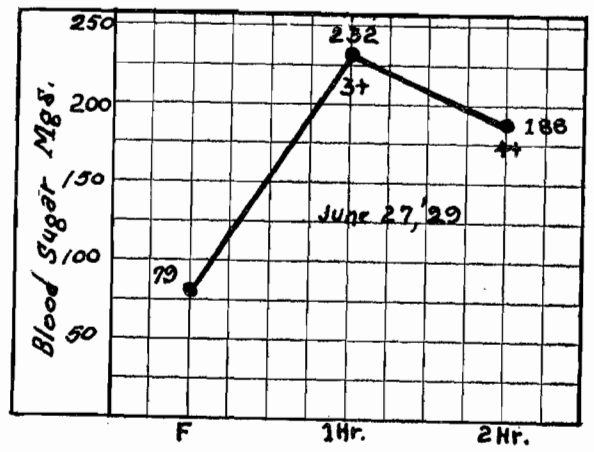
CASE—MRS. MCC. PATHOLOGICAL DIAGNOSIS—ADENOMATOUS HYPERPLASIA



A similar recurrent hyperthyroidism in case C. M. B. (Chart 7) is an illustration of disclosure of the diabetic Anlage in the father of a diabetic child who has been under our care for five years. This man, age 47, had a colloid adenoma removed in 1919, at which time no sugar was found in the urine. Again, in 1926, a double resection for a nodular adenomatous hyperplastic goiter was made. At this time the basal metabolism was

CHART VII

CASE—C. M. B. "COLLOID ADENOMA" REMOVED APR. 4, 1918.. NODULAR ADENOMATOUS HYPERPLASTIC COLLOID GOITER REMOVED DEC. 3, 1926. B. M. R. + 24

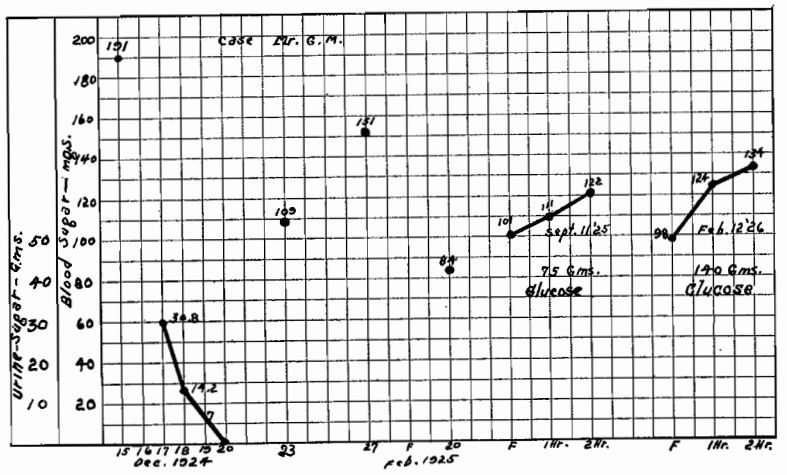


plus 24 per cent. Still no urinary sugar was present. In June, 1928, a trace of sugar was found, but none again until June, 1929, when a blood sugar curve gave the results shown on Chart 7. At that time no clinical

evidence of hyperthyroidism was present. The question arises as to whether this curve represents the residue of his old hyperthyroidism or evidence of a potential diabetes. Inasmuch as a hyperthyroidism ordinarily excites a latent diabetes and fans the flame, as it were, if this curve does represent a potential diabetes, why did not the two past instances of hyperthyroidism in his history precipitate it sufficiently to produce at least a glycosuria?

A third example of recurrent hyperthyroidism, not illustrated by a chart, bears a somewhat detailed report. A druggist, age 34, came in April, 1925, with symptoms of thirst and polyuria of a month's duration. A bilateral ligation for an exophthalmic goiter had been made elsewhere at age 22. He does not recall that anything was said about sugar in the urine at that time. Five years ago, at age 29, he was examined by a good internist who found sugar in the urine and obtained a blood sugar curve which the patient was told was normal and probably related to the goiter. Subsequent to this, in our records, the urine was negative for sugar. He had never been obese and there was no history of diabetes in the family. He

CHART VIII



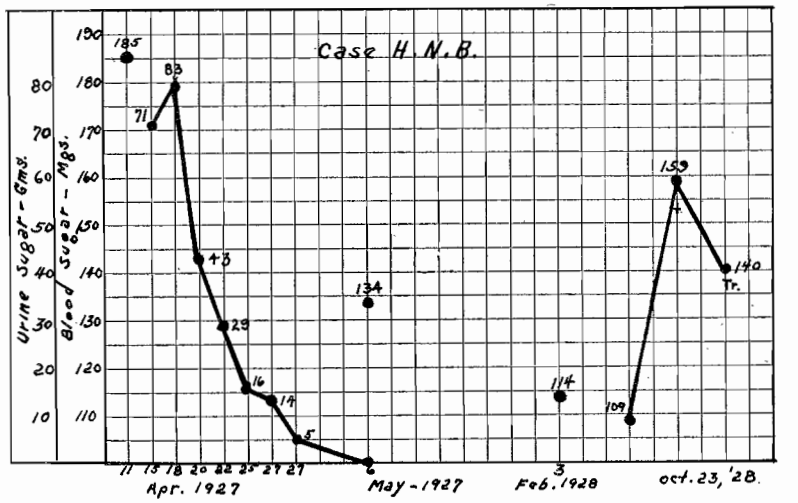
had, however, previous to the onset of the frank diabetes, eaten excessively of candy for four months, before this having been a heavy consumer of alcoholics. Examination revealed extreme emaciation, marked exophthalmos, tremor and sweating, and a toxic type of heart action. The basal rate was plus 36 per cent and the blood sugar 210 mgm. Seventy-five units of insulin daily was necessary to prepare him for operation. Subsequent to operation (pathological report: diffuse adenomatous and parenchymatous hyperplasia) his insulin dose was reduced to 40 units and his weight raised from 117 to 145 pounds.

If a diabetic Anlage is a prerequisite in every case of diabetes, why did not his hyperthyroidism at age 22 precipitate it? Was his glycosuria eight years later really a benign type? Is it possible that the most recent

hyperthyroidism at age 34 was really a more severe form and did the excessive carbohydrate intake, as suggested by John, produce irreversible changes in the islands of Langerhans?

The blood sugar curves of two patients with true diabetes, but without hyperthyroidism, are shown on Charts 8 and 9. The first patient, a laborer, age 44, without a history of diabetes in the family, had been tired for six months and had had thirst and polyuria for two months. He had lost in weight from 234 to 213 pounds in two months. He was still excessively overweight, being 5 feet 9½ inches tall. No doubt that a true diabetes

CHART IX



was present can arise from inspection of the chart, showing the initial blood sugar and the gradually decreasing glycosuria. Use of a quantitative diet for ten months and reduction of his weight to normal apparently had the effect of restoring a practically normal tolerance, at least as far as a blood sugar curve is concerned. Comparison of this curve with the second curve on Chart 1 reveals the fact that they are practically identical. Furthermore, undoubtedly were this patient with a restored tolerance subjected again to excessive food intake, obesity, infection, or a hyperthyroidism, a return of his diabetes would occur.

The second patient, Chart 9, a druggist, age 32, was also overweight approximately 30 pounds previous to the onset of his diabetes. The onset, moreover, dated from a period of financial worry. An uncle had diabetes. Classical symptoms ushered in the diabetes. Reference to the chart shows a blood sugar of 185 mgm. and, after a quantitative diet was started, a glycosuria of 81 gm. Without insulin he was desugarized in a month's time, and ten months later, maintaining his weight and a normal blood sugar on a diet of C-235, P-91 and F-98, he asked that a blood sugar curve

be plotted. Compare the result of this with the final curves on Charts 1 and 2 and mark the similarity.

Return of the tolerance to normal after institution of proper treatment in diabetes is, of course, not rare, as many cases of such have been reported in the past. Details of the above cited cases were given simply as a means of comparing the curves of diabetic patients without hyperthyroidism with those complicated with thyrotoxicosis.

We definitely know that a diabetic Anlage is present in both of these last mentioned patients. Have we any right to say from the evidence presented that a diabetic Anlage of mild degree does not also exist in the first two patients discussed?

The blood sugar estimations in this work were all made by the Shaffer Hartman method as modified by Haskins and Holbrook (10). The urine tests for sugar were made using the Benedict's qualitative reagent. The amount of glucose given the patients was 1.7 gm. per kgm. of body weight.

From the evidence obtained from the study of this small group of selected cases it should be evident that no conclusions may be drawn except that the diagnosis of diabetes in the presence of hyperthyroidism is not an easy or a settled problem. It is our opinion, however, that following thyroidectomy failure of the curve to return to normal after a sufficiently long time is indicative of the presence of a mild diabetes. For the time being at least, and until more is understood regarding this question, these patients will be treated as borderline diabetics and their blood sugar curves studied at least once a year.

SUMMARY

1. The literature regarding the problem of combined diabetes and hyperthyroidism is discussed.

2. A brief resume is given of the results in 24 thyroidectomized diabetic patients in connection with the pathological diagnosis.

3. The blood sugar curves before and after thyroidectomy in 7 patients with potential diabetes are presented with charts.

4. The blood sugar curves following dietetic treatment of two diabetic patients without hyperthyroidism are compared with the post-operative curves of the previous group.

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