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evident that the series will outstrip in duration, by far, all previous series of cases that have come under my observation. But the significance of this record is disclosed by a study of the fatalities.

Although one of the living patients has had the disease 24.3 years, not one of the patients who died succumbed during the first year of the disease. There were nine deaths from coma, but only two of these occurred in the hospital. Seven of these coma deaths were needless—they were the result of ignorance and inexperience or deliberate neglect of treatment, even to the extent of giving up insulin. In preinsulin days, a diabetic patient who broke diet might live for some time, but *facile descensus averno* is the pathway of that diabetic patient who has already outlived the usual expectation of his disease and, on insulin wings, soars high in diet. Of the remaining fourteen deaths, septicemia, meningitis, erysipelas, tuberculosis, multiple abscesses, and intestinal obstruction in a woman over 80 years of age, each accounted for one, while cardio-renal disease and penumonia each accounted for four deaths.

Ninety three of the 127 patients are still taking insulin, and the average dose is 21.4 units. Ten patients are alive and not using insulin.

The average gain in weight of the patients is 13.5 pounds (6 kg.), or 14.4 per cent. One patient, B. A., a girl, has gained 23.2 pounds (10.5 kg.), or 81 per cent., and another, 44.2 pounds (20 kg.) or 58 per cent.

EVOLUTION OF TREATMENT

The evolution of the treatment of diabetes epitomizes the trend of medicine. Thirty years ago, everybody prescribed for the diabetes. Then came a period when chemical inventions were novel and complex, and their intricacies demanded specialists for their execution and interpretation. Now we are reverting to the earlier epoch when the diabetic patient required the assistance of the general practitioner at his best. This is plainly apparent from the cases one now has to treat. Of the complaints of the diabetic patients today, one fourth are surgical, one fourth related to the circulation, and one fourth of a general nature, with practically the whole of the remaining fourth dependent on acidosis—the intimate complication of the disease. To meet all these demands, the physician who treats diabetic patients must practice medicine with eyes alert to all angles of the art; but, above all, he must be one hundred per cent. efficient in his endeavor to prevent the development of future cases.

Five Hundred Fatal Cases of Diabetes.—Coincident with the increasing use of insulin, the death rate from diabetes has been declining for a year and half. There is no proof as yet that these two phenomena are connected. To determine whether fatal cases of diabetes had received insulin, and if so, for how long, the Metropolitan Life Insurance Company analyzed data submitted by physicians who had certified the death certificates in 500 recent cases of diabetes. It found that less than one-half of these fatal cases received insulin at any time, and that 62 per cent. of those which did, received insulin for a period of less than one month. In 31 per cent. of the cases analyzed, insulin had been administered for a period of less than one week before death. Coma was the most frequent complication in these fatal cases. Arteriosclerosis was a complication in 24.8 per cent.; chronic nephritis in 23.4 per cent., and gangrene in 23.4. It was also shown by this study that insulin was much more commonly used in hospitalized cases than in the cases treated at home and that it is more extensively used in the larger cities than in rural areas or small towns.

HYPERINSULINISM AND DYSINSULINISM*

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Diabetes, of which hyperglycemia is a manifestation, is essentially a condition due to a deficient secretion of insulin by the islands of Langerhans; and, according to modern medical nomenclature, should be called hypo-insulinism. Diabetes, or hypo-insulinism, therefore, bears the same relation to the internal secretion of the pancreas that myxedema, or cretinism (hypothyroidism) has to that of the thyroid gland.

We know that hypothyroidism is not the only dysfunction of the thyroid gland and that there is a hypersecretion of that important organ, hyperthyroidism, in which there are certain characteristic symptoms; i. e., the syndrome called hyperthyroidism. It has been observed that hyperthyroidism sometimes precedes hypothyroidism.[1] It seems probable that there are other dysfunctions of the islands of Langerhans, besides hypo-insulinism, and that an excessive formation of insulin may occur. Hyperinsulinism should produce definite results, i. e., a reduction in blood sugar, which, when below a certain limit, about 0.070, brings on characteristic symptoms, now known as the insulin reaction. It also seems probable that a deficiency of the secretion of insulin may follow prolonged excessive work of the islands of Langerhans; just as in other glands, or organs, hypertrophy and hyperactivity may be followed by degeneration, atrophy and loss of function.

It was this line of reasoning that caused me to think that there may be such a condition as hyperinsulinism, and when I saw the insulin reaction in diabetic patients, I realized that I had seen many nondiabetic patients who had complained of the same symptoms; i. e., hunger, weakness and the anxiety neuroses. I mentioned this to Dr. Banting while on a visit to the diabetes clinic in the Toronto General Hospital in March, 1923, and asked him whether he or others had observed an excessive secretion of insulin in laboratory animals or human beings. He said that they had done nothing on that line and that he had seen nothing in medical literature on the subject, and we have not been able to find any reference to hyperinsulinism in any medical publication.

Knowing the amount of food ingested at a given time, by means of blood sugar determinatons we are able to estimate with some accuracy the degree of insulin secretion, particularly since we know that by the administration of insulin, hypodermically, the amount of sugar in the blood may be reduced to any level, depending on the number of units administered and on the amounts of glucose-forming food ingested. It therefore seemed probable that, since hypoglycemia is the result of hyperinsulinemia, a study of the blood sugar in patients who have symptoms of hyperinsulinism should show readings of below 0.070 (70 mg. per hundred cubic centimeters of blood).

HYPOGLYCEMIC REACTIONS IN NONDIABETIC PATIENTS

The first patient, a physician, who presented symptoms of hyperinsulinism, consulted us, March 19, 1923,

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* Read before the Section on Practice of Medicine at the Seventy-Fifth Annual Session of the American Medical Association, Chicago, June, 1924.

1. Barker, Hoskins and Mosenthal: Endocrinology and Metabolism, New York, D. Appleton & Co. **1**: 66, 300, 302, 1922.

saying that every day about one hour before his noon meal he felt weak, nervous and so hungry that he could not work. He had found that he would get relief from taking candy or a soft drink or from drinking milk, eating fruit, or from eating anything. It was then about an hour before his time for luncheon, and a specimen of blood was obtained for the determination of its sugar content. It was found to be 0.065 (or 65 milligrams per hundred cubic centimeters of blood). On another occasion, May 15, 1923, the same hour, the blood sugar was 0.070. This patient has no other symptoms, except that he had been overweight and had lost about 25 pounds (11.3 kg.). His blood pressure was low, systolic 95, diastolic 60. A well balanced diet was given him, with instructions to take food of some kind every three hours. A year later, this physician told me that he had been feeling well since he had been taking food five times a day.

Oct. 4, 1923, a patient, who had been under observation at times for various digestive troubles for seven years, complained in these words: "I get so hungry and weak every day about an hour before meals that I feel as though I will die if I do not eat something. I believe that I would die if I had to go two or three hours past meal time without anything to eat. Eating anything always relieves me, and I am comfortable for three or four hours after meals." He was told to wait in the office to let us see him at a time when he was having the symptoms of which he complained. His blood sugar

Blood Sugar Readings and Urinary Findings

Time	Blood Sugar	Urine Test
12:15 p. m.	0.098	No sugar
12:45 p. m.	0.116	No sugar
1:15 p. m.	0.167	Trace of sugar
2:30 p. m.	0.135	No sugar
3:30 p. m.	0.067	Trace of sugar

was 0.065 at noon. He was told to eat a full meal and come back two hours later. The blood sugar was then 0.130. A glucose tolerance test (100 gm. of glucose) was given him, with the blood sugar readings and urinary findings given in the accompanying table.

This patient lived in a suburb, about an hour's ride by trolley, and after the glucose tolerance test went home without eating anything. He said that before he reached the end of his trolley ride he was so weak that he could hardly walk, and that it was with great effort that he was able to get home. He said that he thought he would die before his wife could get him something to eat, and felt so faint that he could hardly eat; but that he felt all right after eating. Since his last blood sugar reading at 3:30, two hours before he had food, was 0.067, it was probably much lower when he had the severe hypoglycemic reaction. In this case, the glucose seemed to have stimulated the secretion of insulin, which continued after the glucose had been disposed of. There also seems to be a lowered glucose tolerance in this case, probably a dysinsulinism, in a patient who is potentially diabetic.

Jan. 23, 1924, a married woman, aged 39, with a history of a transient glycosuria on two occasions in the previous eighteen months, presented marked symptoms of hypoglycemia without having had insulin. She had been overweight, having weighed 220 pounds (99.7 kg.), when a trace of sugar was first found in the urine, in the summer of 1922. She was then placed on a low fat, low carbohydrate diet and reduced to 160 pounds (72.6 kg.), but her health had become impaired during that time. She complained of one striking symptom in these words: "I awaken at from 12 to 2 at night with a nervous rigor, or quivering, very weak, disturbed feeling, cold extremities, and am hungry. Eating an orange relieves me." She also complained of the "nervous rigors" when her stomach was empty during the day. A blood sugar reading was ordered taken during one of these nervous rigors, and it was found to be 0.047 (the lethal low blood sugar point in rabbits is 0.040). Two hours after having had 25 gm. of glucose, the blood sugar was 0.130. This patient presented symptoms of both hyperinsulinism and hypoinsulinism, apparently a dysinsulinism analogous to patients showing evidences of both hyperthyroidism and myxedema. This patient had no sugar in the urine at any time during a six weeks' stay in the infirmary, though, since her family physician is a careful, well prepared physician, I do not question her having had glycosuria when she weighed 220 pounds (99.7 kg.) and was no doubt eating an excess of glucose forming foods. A detailed report of these three cases will be given with the complete histories of other patients that we believe had hyperinsulinism.

The foregoing three cases showed symptoms of hyperinsulinism, and, with blood sugar findings below 0.070, stimulated us to undertake further studies of the blood sugar at the fasting period in nondiabetic patients. Since that time blood sugars have been made a routine in the examination of all patients.

It should be remembered that all our patients come to us for treatment of some gastro-intestinal or nutritional disturbance, and all in this series were ambulatory, though some of them were sent to the infirmary for rest, diet and general observation. Blood sugar determinations were made in 253 patients, ninety-two of whom were diabetic patients who showed varying degrees of hyperglycemia. Of the 169 cases, twelve patients had blood sugar readings of below 0.070 in specimens obtained during the fasting period; and all of these, with two or three exceptions, had symptoms that could result from hypoglycemia. The blood sugar determinations were made by Dr. W. S. Geddes, or under his direction. The Folin-Wu method was used.

BLOOD SUGAR READINGS IN STARVATION

The question as to whether these low blood sugar readings were due to a lack of food or to a hyperinsulinemia was considered. If due to a lack of food, the starving patient should show a low blood sugar. We chanced to have four patients who were literally starving to death. Three were cases of carcinoma, with almost complete occlusion of the esophagus. All three patients were very much emaciated, and had been almost unable to take any food for several days or weeks before they came to us. None of them gave a history of symptoms of hypoglycemia. The blood sugar readings on these three patients were 0.090, 0.084 and 0.090.

We also had a patient who had almost complete stenosis of the pylorus, due to tumor, ulcer or carcinoma of the pyloric end of the stomach. The roentgen-ray examination showed 90 per cent. retention of the barium meal in six hours, and 75 per cent. retention in twenty-four hours. This patient had vomited practically everything she had eaten for weeks and was in a state of marked emaciation. The blood sugar was 0.079.

It seems that, in cases of starvation, the amount of sugar in the blood is kept within the normal range by endogenous catabolism. There is some evidence to

show that patients with carcinoma have reduced carbohydrate tolerance; but even so, in these cases the amount of glucose derived probably from the protein of the patient's own tissues was sufficient to keep the blood sugar above the point at which hypoglycemic reactions occur. Since, in the starvation cases, the blood sugars were within the low normal range, and none of the four patients had symptoms of hypoglycemia, and the patients having blood sugars below 0.070 with few exceptions had symptoms of an overdose of insulin, it surely seems that there is such a condition as hyperinsulinism.

CONCLUSIONS

1. Hyperinsulinism is a condition, perhaps a disease entity, with definite symptoms; i. e., those described as being due to hypoglycemia.

2. It seems probable that one of the causes of hyperinsulinism is the excessive ingestion of glucose-forming foods and that, as the result of overactivity induced by overeating, the islands of Langerhans become exhausted and hypo-insulinism (diabetes) follows. It is possible that the hunger incident to hyperinsulinism may be a cause of overeating, and, therefore, the obesity that so often precedes diabetes.

3. It seems probable that dysinsulinism, either an increase or a decrease in the secretion of insulin, may follow infection or trauma of the pancreas.

4. Since excessive hunger is a symptom of hypoglycemia, it may be that normal hunger is the call for glucose and that it may be in part or wholly of pancreatic origin and not entirely an expression of an empty stomach. It is also possible that, associated with ulcer of the stomach or duodenum, there may be a coexisting disorder of the pancreas, and that the frequent feedings which give relief in ulcer may do so by supplying the glucose to meet the needs of overfunctioning islands of Langerhans. In one case of ulcer, we found a low blood sugar.

5. Since blood pressure readings have been low in all except two of the nondiabetic patients who have had symptoms of hypoglycemia, it seems possible that hypo-adrenalinism may be associated with hyperinsulinism. It also seems probable that secretory disorders of the islands of Langerhans may be associated with dysfunctions of the thyroid, the pituitary bodies and other organs of internal secretion.

6. Fractional tests of gastric secretions after the Ewald meal have been made in several nondiabetic patients having symptoms of hyperinsulinism, with variable results, so that these is no apparent relation of secretory disorders of the stomach to pancreatic dysfunction.

7. No studies of the external secretion of the pancreas were made in these cases. It seems probable, however, that since a chronic pancreatitis is probably a cause of dysinsulinism, the glands secreting trypsin, amylopsin and steapsin are often involved, with either increased or decreased function.

REPORT OF CASES OF HYPERINSULINISM

CASE 1.—*History.*—A physician, J. G. P., aged 62, a white man, married and having six children, all living, March 19, 1923, complained of an uncomfortable sensation in the stomach when empty; a weak and nervous feeling before dinner and supper, but said he got relief from taking a soft drink, fruit, or from eating a meal. He slept well for three or four hours after retiring and then remained awake the remainder of the night. He tired easily, but had no dyspnea on exertion. He was irritable, and worried unnecessarily over business and professional matters. The blood pressure had been low at times, the systolic ranging from 110 to 85.

The family history was not important.

He had had the usual diseases of childhood, without sequelae. During adult life he had been strong, robust and active in professional and civic affairs. He had typhoid fever in 1895; pneumonia in 1902 and again in 1919; influenza, three times, and cystitis in 1910. He said he had no venereal infection. He had had digestive disturbances at times for the past six years, a heavy aching sensation in the epigastrium, sour stomach, etc.

He was a small eater now, though formerly he ate immoderately. He drank one cup of coffee for breakfast. He had been overworked for years. He smoked excessively and had been a moderate drinker at times since early manhood.

During the past five or six weeks he had worked very hard, and began having discomfort in the stomach about meal time, usually before dinner and supper when the stomach was empty, associated with a depressed, weak feeling and nervousness. Relief would be obtained by eating his usual meal, fruits, or even taking a soft drink. Often after sleeping three or four hours at night he would remain awake the rest of the night. There was frequently during the day a feeling of weakness, and he became fatigued easily from moderate exercise.

Examination.—Nothing of importance was observed on physical examination. The teeth, tonsils, thyroid, heart, lungs and abdomen were apparently normal. The blood pressure was: systolic, 115; diastolic, 70; pulse, 45; and one month later: systolic, 95; diastolic, 60; pulse, 35. The weight was 163 pounds (74 kg.); height, 5 feet 11½ inches (181.6 cm.), the standard weight being 184 pounds (83.5 kg.).

Examination of the urine revealed: specific gravity, 1.026; albumin, 0; sugar, 0; indican, a trace; no cells or casts. Blood examination revealed: hemoglobin, 80; red cells, 4,360,000; white cells, 7,200; polymorphonuclears, 65 per cent.; small lymphocytes, 34 per cent.; large lymphocytes, 1.1 per cent.; no malaria. There was no occult blood in the feces, and there were no parasites. The Wassermann reaction was negative. The blood sugar, April 27, was 0.065; May 15, 0.070.

A fractional examination of the gastric contents after the Ewald test breakfast revealed:

Total acidity:	15	25	35	45	30
Free hydrochloric acid:	5	20	30	30	15

On roentgen-ray examination, the heart and the lungs were found normal; the gastro-intestinal tract was in a position level with the umbilicus; there were no filling defects; the twenty-four hour barium meal was in the cecum to the hepatic flexure.

The pathologic diagnosis was, no lesion found. The functional diagnosis was, hyperinsulinism, arterial hypotension, intestinal toxemia, 21 pounds (9.5 kg.) below the normal standard weight.

The etiologic factors were overwork and worry, with possible infection of the pancreas in an attack of influenza or pneumonia.

Treatment and Result.—The patient was instructed to eat three small meals a day, with a glass of milk or fruit three hours after meals. One year later the patient informed us that he had had no symptoms since he has been taking food five times a day.

CASE 2.—*History.*—H. J. R., aged 52, a miner, married, with one child living, Oct. 5, 1923, complained of hunger spells when his stomach was empty, preceding the time for his regular meals and often late in the afternoons. He became very nervous and weak when hungry, perspiring freely and often having to sit down to rest. He got so weak that he could hardly eat. At night he got cold and had sweats, aching all over.

The family history was not important.

He had the usual infectious diseases of childhood, without any complications. He had the grip in 1889, and the same year he had skin lesions suggesting syphilis, but two Wassermann tests were negative. He had symptoms of digestive disturbance for fifteen years, gas, pains in the stomach, constipation, mucus in the stools, and headaches. He had a bronchitis which was suggestive of tuberculosis, though no positive diagnosis was made.

He had been taking one cup of coffee daily, and smoked from eight to ten cigars each day. Formerly, he drank alco-

holic stimulants excessively. His diet had consisted largely of meats and carbohydrates.

At least fifteen years before, he began having constipation, gas in the stomach, and pains in the abdomen, and he passed mucus in the stools. He frequently had severe headaches, associated with constipation. In October, 1919, following an injury that crushed the left arm and necessitated amputation, the digestive symptoms became worse. For the past few months he had been almost incapacitated for work because of extreme hunger, weakness and nervousness for one or two hours before meals. He found that taking food relieved the symptoms.

Examination.—The teeth, tonsils, thyroid, lungs, heart and abdomen were normal. The left arm was amputated below the elbow. The weight was 175 pounds (79.4 kg.); height, 5 feet, 11 inches (180.3 cm.), the standard weight being 178 pounds (80.7 kg.).

The blood pressure was: systolic, 120; diastolic, 80; pulse, 40. Blood counts and differential were normal; there were no malarial parasites. The Wassermann reaction was negative. The blood sugar, October 4, was 0.065 (fasting); two hours after a meal, 0.130. The glucose tolerance test, Jan. 9, 1924, was 0.098; 0.116; 0.167; 0.135; 0.067, with a trace of sugar in the urine at 0.167. After the last blood reading, the patient went home and suffered considerable weakness, tremors, sweating and collapse, but eating relieved him. The urinalysis revealed: specific gravity, 1.025; albumin, 0; sugar, a trace; ketones, a trace; the microscopic examination was negative. Later, a test showed no sugar. There were no parasites, but a trace of occult blood was present in the feces.

Fractional examination of the gastric contents after an Ewald test breakfast revealed:

Total acidity:	40	45	60	80	90	75	60
Free hydrochloric acid:	25	30	50	70	80	60	55

On roentgen-ray examination, the heart and lungs were normal; the stomach was 4 inches below the umbilicus; there were no filling defects, and barium in seventy-two hours occupied the transverse colon.

The pathologic diagnosis was chronic colitis, possibly chronic pancreatitis; the functional diagnosis, hyperinsulinism; potential diabetes; hyperchlorhydria.

The etiologic factor was improper eating. The colitis may have been the focus of infection for a chronic pancreatitis.

Treatment and Result.—Food was taken every three hours while the patient was awake. Tincture of belladonna was prescribed. The patient improved, but has to take food every three hours.

CASE 3.—*History.*—Mrs. E. E. G., aged 39, white, married, with no children, Jan. 23, 1924, complained of often waking during the night with a feeling of extreme weakness and nervousness, and that she had to take the juice of an orange for relief. She suffered from gas in stomach and constipation; poor appetite; nervousness, and glycosuria.

The family history was unimportant.

She had the usual diseases of childhood, with no complications. She had a lung abscess in 1889, with hemorrhages, and was in bed for six months, after which she was an invalid for two years. She had malarial fever in 1914; influenza in 1918, and two mild attacks since.

She had been in the habit of eating excessively of sweets and pastry. She drank one cup of coffee a day.

Sugar had been found in the urine one and one-half years before, but was controlled by diet. She had no other symptoms of diabetes. She wakened at between 12 and 2 in the night, quivering, with weakness and a disturbed feeling, and found it necessary to take the juice of an orange for relief. The extremities were cold. Gastric distress, following a tooth extraction, began one year before, with general debility, gas, fulness and stubborn constipation. She had a poor appetite. She was very nervous and under high tension.

Examination.—The teeth had been extracted; the tonsils removed. The eyes reacted to light and in accommodation. There was slight exophthalmos. There was no apparent enlargement of the thyroid. There was a slight tremor of the hands. The lungs and heart and the abdomen were normal. The pulse was 100. The blood pressure was: systolic, 120; diastolic, 80; pulse, 40. The weight was 160 pounds (72.6 kg.); the maximum weight, in September, 1922, 210 pounds (95.2); the height, 5 feet, 4 inches, the standard weight being 136 pounds (61.7 kg.).

The urinalysis revealed: specific gravity, 1.015; a faint trace of albumin; no sugar; the microscopic examination was negative.

The hemoglobin was 90. There were 4,264,000 red cells and 7,600 white cells; polymorphonuclears, 64 per cent.; small lymphocytes, 35; transitionals, 0.1; no malaria. The Wassermann reaction was negative. There was no occult blood in the feces; the microscopic examination was negative. The blood sugar when the patient was fasting was 0.047; one hour after eating, 0.130; during a nervous spell, 0.095. After taking 20 gm. of glucose, she became much better. At another time, when she was fasting, the blood sugar was 0.111.

Fractional examination of gastric contents after an Ewald breakfast was unsuccessful on account of severe vomiting.

Roentgen-ray examination showed the heart normal; slight fibrosis of the lungs: the gastro-intestinal tract and stomach level with the umbilicus; no filling defects, and at the end of twenty-four hours, the barium occupying the cecum to the hepatic flexure.

The pathologic diagnosis was: endocrine disturbance, chronic colitis, and mild diabetes; the functional, hyperinsulinism, hyperchlorhydria, and intestinal toxemia. She was 24 pounds (11 kg.) overweight.

The etiologic factors were overeating and a diet deficient in vitamins.

Treatment and Result.—The treatment prescribed was rest; a low fat, low carbohydrate diet and buttermilk or orange juice between meals and at night if she awakened. Her condition became much improved.

CASE 4.—*History.*—Miss O. S., aged 29, white, a teacher, seen March 15, 1924, complained of being very nervous and weak about noon and that she was worse if she had eaten a light breakfast. She was underweight. She suffered from urticaria, poor appetite, and weakness.

The family history was not important.

She was healthy and strong during childhood, having the usual infectious diseases without complications. She had a malarial attack in 1898; severe tonsillitis, with tonsillectomy, in 1922, and chronic appendicitis for several years without having an operation.

She had felt weak and nervous since the tonsillectomy in 1922. In October, 1923, while in school, she began having an eruption on the thighs and the knees and later on the arm, splotches of rash with raised red spots, itchy at first, lasting half an hour. About noon she usually felt weak and became more nervous until she ate something. This was worse if she had eaten a light breakfast.

Examination.—The patient was slender and undernourished. The teeth and gums were normal; the tonsils had been removed; the eyes were normal. There was a slight fulness in the region of the thyroid. The heart, lungs and abdomen were normal. No skin lesion was present at the time of the examination. The pulse was 84. The blood pressure was: systolic, 110; diastolic, 70; pulse, 40. Her weight was 96 pounds (43.5 kg.); height, 5 feet 5½ inches (153.6 cm.), the standard weight being 132 pounds (59.9 kg.).

Urinalysis revealed: specific gravity, 1.020; albumin, 0; sugar, 0; indican, 0; the microscopic examination was negative.

The hemoglobulin was 80; red cells, 3,754,000; white cells, 13,200; polymorphonuclears, 62 per cent.; small lymphocytes, 24 per cent.; large lymphocytes, 12 per cent.; eosinophils, 1 per cent.; basophils, 1 per cent.; no malaria. There was no occult blood in the feces, and microscopic examination was negative. The Wassermann reaction was negative. The blood sugar at noon, when the patient was fasting, was 0.056.

Gastric analysis, fractional, revealed:

Total acidity:	12	30	40	52	55
Free hydrochloric acid:	0	12	25	45	45

On roentgen-ray examination, the heart and lungs were seen to be normal. Gastro-intestinal examination showed the stomach 3 inches below the umbilicus; there were no filling defects; there was normal motility and no stasis in twenty-four hours.

No pathologic diagnosis was made. The functional diagnosis was hyperinsulinism, hyperchlorhydria, and visceroptosis.

The etiologic factors were heredity and overwork.

Treatment and Result.—The treatment consisted in hyperalimentation, including a pint of milk every three hours. There have been no symptoms since the increase in the diet.

CASE 5.—*History.*—R. M., a white man, aged 59, a manufacturer, married, with four children, three of whom were living, seen March 6, 1924, complained of an uncomfortable feeling in the stomach and a gnawing sensation, and said that at times it felt like a vacuum. Taking food relieved this sensation for about two hours, solid food giving a longer period of relief. Three or four hours after meals the distress came on again. He suffered from weakness and constipation. He was in the habit of eating fruits before retiring.

His mother, who was alive, aged 84, had apoplexy; his father died of erysipelas.

He had always been rather a large eater, eating rapidly; the diet consisted largely of meats, eggs, vegetables and carbohydrates. He had used tobacco excessively, but no alcohol.

The patient had had the usual diseases of childhood, with mild bronchitis nearly all his life. In 1887 he had malaria and a nervous breakdown, using morphin for eighteen months. In 1874 he had spinal meningitis, with a good recovery. In 1884 he had gallbladder trouble and gallstone colic five times each year until 1904. In 1907 he had a fall, with an injury to the lower part of the spine, which crippled him for three years.

Two years before, he had a distressed feeling in the stomach, associated with slight pain. The indigestion became worse, so that for nine months he lived on a strict diet, but he did not improve very much. For the past two months he had been eating liberally and had not felt any worse. He now complained of a distressed, empty feeling in the epigastrium in a circumscribed area of 5 inches, coming on from two to three hours after meals; he was nearly always relieved by eating or taking soda, which caused an expulsion of gas. He felt all right when lying down. He was nauseated occasionally. He had gas and fulness and constipation. He was weak and had lost 34 pounds (15.4 kg.) in two years.

Examination.—The patient had pterygium of both eyes; many bridges in the mouth and gum irritation; small cryptic embedded tonsils; the thyroid was normal. The heart and the lungs were normal, except for an accentuated aortic sound, with tenderness above and below the umbilicus. The pulse was 72; the blood pressure was: systolic, 220; diastolic, 115; pulse, 105. His weight was 151 pounds (68.5 kg.); height, 5 feet, 8 inches (172.7 cm.), the standard weight being 162 pounds (73.5 kg.).

Urinalysis revealed: specific gravity, 1.025; albumin, negative; sugar, negative; indican, a trace; bile, a trace; a few pus cells; no casts.

The hemoglobulin was 80; red cells, 4,056,000; white cells, 8,200; polymorphonuclears, 62 per cent.; small lymphocytes, 36 per cent.; large lymphocytes, 1 per cent.; eosinophils, 1 per cent.; transitionals, 0.1 per cent.; no malaria. There was a trace of occult blood, but no parasites, in the feces. The Wassermann reaction was negative; the blood sugar when the patient was fasting at 11 a. m. was 0.067; and 1 p. m., two hours after eating, 0.077.

Fractional examination of the gastric contents after an Ewald test breakfast revealed:

Total acidity:	25	40	60	50
Free hydrochloric acid:	20	25	30	20

A roentgen-ray examination of the heart and the lungs showed them apparently normal. A gastro-intestinal tract examination showed a slight filling defect in the duodenal bulb near the pyloric ring and a hypertonic stomach 2 inches below the umbilicus. There was no six-hour residue. After twenty-five hours the barium meal occupied the colon from the cecum to the splenic flexure. The appendix was not seen.

The pathologic diagnosis was arteriocapillary fibrosis; a suggestion of duodenal ulcer; chronic cholecystitis; probable chronic pancreatitis; chronic tonsillitis, and oral sepsis. The functional diagnosis was arterial hypertension; slight hyperchlorhydria; hyperinsulinism, and intestinal toxemia. The patient was underweight 11 pounds (5 kg.).

The etiologic factors were infection from the teeth and the tonsils; an excessive use of tobacco; rapid eating; an excessive diet of meat and starchy foods, and overwork.

Treatment and Result.—Rest was advised and bromids, belladonna and laxatives were prescribed. Removal of the tonsils was advised. The patient lived some distance from Birmingham, and we have had no report from him.

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"OPTIMAL" DIETS FOR DIABETIC PATIENTS *

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In 1910, Woodyatt [1] suggested, in explanation of the ketolytic action of glucose, that 1 molecule of acetoacetic acid might react with 1 molecule of alcohol or glucose and thus undergo oxidation at the expense of the simultaneous reduction of the glucose. This assumption was based on analogy with the observed behavior of ketones and alcohol when these were exposed to bright sunlight, as had been reported by Cimician and Silber, and is in harmony with what is known of the behavior of the acetone bodies in metabolism. Although Geelmuyden [2] can be credited with an earlier hypothesis of intermolecular chemical reaction between the acetone bodies and glucose, Woodyatt was responsible for stimulating much of the investigation of this subject. Geelmuyden proposed a conjugation of glucose and the acetone bodies, a view with which Ringer's [3] hypothesis of ten years later harmonized.

The demonstration by Shaffer,[4] in 1921, of an in vitro analogy to the ketolytic action of glucose accelerated the recent activity in this field of study. The oxidation of glucose in alkaline solution by hydrogen peroxid was found to remove acetoacetic acid if the latter was present in the solution. Fructose and glycerol exerted the same effect, but lactic acid did not. The ketolytic action increased with alkalinity and temperature, suggesting that dissociation of the glucose into some more reactive derivative was essential to the reaction.

In a communication that accompanied the publication of these purely chemical investigations, Shaffer reported the results of calculations of the balance of ketogenic (fatty acid) and ketolytic (glucose) molecules in various human subjects who, by reason of fasting, fat feeding or diabetes, were excreting acetone, and concluded that the molecular ratio of ketogenic to ketolytic substances must be 1:1 or less, in order to avoid ketonuria.

A few months later, Woodyatt [5] published his paper, "Objects and Method of Diet Adjustment in Diabetes," in which he proposed that diets for diabetic patients should be adjusted in carbohydrate, protein and fat, to make the ratio in grams of fatty acids to glucose 1.5:1

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* From the Division of Medicine, Mayo Clinic.

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